THE RESPIRATORY EPITHELIUM ACTIVELY CONTRIBUTES TO DIFFERENCES IN CLINICAL DISEASE CHARACTERISTICS BETWEEN MYCOPLASMA PNEUMONIAE AND STREPTOCOCCUS PNEUMONIAE

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Background: Mycoplasma pneumoniae (Mp) and Streptococcus pneumoniae (Sp) are the most common bacteria to cause pneumonia in children. The clinical characteristics of Mp pneumonia are markedly different from Sp pneumonia. Respiratory epithelium plays an important role in the host response. We hypothesized that the differences in clinical infection characteristics could be explained by differences in the epithelial cell response to the two bacteria.

Methods: Primary human bronchial epithelial cells (pHBECs), derived from lung resection material, were cultured in air-liquid-interface to obtain 3D bronchial tissue cultures. 3D tissue cultures or epithelial cell lines A549, Calu-3 and Detroit 562, were stimulated with Mp and Sp. Cytokine and chemokine expression were determined at 6h or 24h using qPCR or ELISA. TLR signaling after bacterial stimulation was assessed using a pHNifty2Luc reporter system.

Results: Sp induced a stronger pro-inflammatory response in pHBECs compared to Mp, with up to 10-fold higher levels of IL-6, IL-8, CCL2 and CCL20. This difference was present in epithelial cell lines derived from both upper and lower respiratory tract. In contrast to cytokine responses, Mp induced stronger TLR2-mediated signaling than Sp, indicating qualitatively different responses. Indeed Mp maintained expression of Th2-associated IL-33 and IL25R, whereas these markers were downregulated by Sp, both under homeostatic and Th2-promoting conditions.

Conclusions: The clinical disease characteristics induced by Mp and Sp already arise at the epithelial cell level and show quantitative and qualitative differences in the immune response to Mp and Sp. Additionally, Mp maintained Th2-associated cytokine production, which concurs with the known association of Mp infection with asthma. By directly comparing Mp and Sp we demonstrate that the respiratory epithelium is an active contributor to the different clinical disease characteristics of Mp and Sp pneumonia.

Clinical Trial Registration: No results from a controlled trial were used in this work.
Background: Determining the host molecular genetic characteristics of childhood pneumonia may inform the development of new clinical interventions for the treatment and prevention of the disease. We performed a genome-wide association study to identify the genes associated with all-cause pneumonia.

Methods: DNA collected from healthy Nepalese children and Nepalese children admitted to Patan Hospital, Kathmandu with clinician diagnosed pneumonia were genotyped using Illumina Global Screening Arrays. Array data underwent QC and filtering before undergoing imputation using the HRC R1.1 2016 reference panel. Association analysis, by conducting a logistic regression using multidimensional scaling values, was performed using PLINK 1.9.

Results: Following filtering, 773 children with pneumonia (cases) and 2121 healthy community based children (controls) were analysed. A single variant within an intergenic region on chromosome 13 was strongly associated with all-cause pneumonia \( (p=1.1 \times 10^{-10}, \text{MAF cases} = 0.09 \text{ vs MAF controls} = 0.04, \text{OR 2.3, 95% CI 1.8-2.9}) \). Two further variants, on chromosomes 2 \( (p=9.5 \times 10^{-7}, \text{MAF cases} = 0.005 \text{ vs MAF controls} 0.029, \text{OR 0.2, 95% CI 0.1-0.3}) \) and 17 \( (p=2.8 \times 10^{-7}, \text{MAF cases} = 0.229 \text{ vs MAF controls} = 0.3, \text{OR 0.7, 95% CI 0.6-0.8}) \) respectively, were associated with all-cause pneumonia.

Conclusions: We identified host genetic variants associated with all-cause pneumonia. Further studies confirming this association and its biological role in pneumonia are needed.

Clinical Trial Registration: ClinicalTrials.gov N/A
THE ROLE OF BREAST MILK BACTERIAL COMMUNITIES AND THE METABOLOME IN SHAPING THE COMPOSITION OF THE INFANT GUT MICROBIOTA

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Background: Breastfeeding contributes to shaping of the infant gut microbiome through a variety of mechanisms. Breast milk contains a diverse population of skin bacteria and intestinal organisms that directly seed the infant gut, but also contains compounds such as human milk oligosaccharides, which can selectively shape the growth and function of beneficial microbes.

Methods: We used 16S rRNA gene sequencing to assess the microbiota composition in breast milk samples and rectovaginal swabs from 90 Gambian women, and the rectal swab samples from their infants at birth and at day 60 of life. After DNA extraction, 16S amplicon libraries were generated and sequenced. Taxonomic and functional analyses were then performed. Source tracking analysis was used to estimate the contribution of the breast milk microbiome to the infant gut microbiome. The breast milk samples also underwent metabolomic profiling using a multiphase approach.

Results: Bacterial communities were distinct in breast milk, maternal rectovaginal swabs and infant rectal swabs, differing in both composition and diversity. Overall, a greater proportion of the infant gut microbiome was derived from the infant’s mother’s breast milk (39.9%) than the maternal rectovaginal (15.1%) microbiomes. Dynamic changes in breast milk composition were characterized over the first 60 days of lactation. Metabolites identified as altering in abundance over lactation included fucose, di- and triacylglycerols, and short chain fatty acids, known to be important for infant immunological, neurological, and gastrointestinal development, as well as being an important source of energy.

Conclusions: The results of this study indicate that bacteria in mother's breast milk seed the infant gut and that distinct metabolomic profiles in milk may contribute to the development of the infant microbiome, underscoring the importance of breastfeeding in the development of the infant gut microbiome.

Clinical Trial Registration: Not applicable
Group A Streptococcus Infection Associated with Kikuchi Disease

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Title of Case(s): Group A Streptococcus infection associated with Kikuchi disease

Background: Kikuchi disease, or idiopathic histiocytic necrotizing lymphadenitis, is an uncommon condition that presents with cervical lymphadenopathy and fever, frequently in young female patients of East Asian origin. The pathogenesis is thought to be an immune response of CD8 cytotoxic T-lymphocytes and histiocytes to infection, autoimmune disease, or malignancy. Several infectious triggers have been described. We describe patients with Kikuchi disease possibly triggered by recent streptococcal infection.

Case Presentation Summary: Between September 2018 and December 2019, during a period of increased streptococcal infection in the UK, three teenage female patients with European and South Asian ancestry were diagnosed with Kikuchi disease following cervical lymph node resection. Two of three patients had travelled to South Asia prior to onset of symptoms. All patients presented with prolonged fever and cervical lymphadenopathy. Two had associated sore throat and rash. All patients received antibiotics without resolution of symptoms. Bacterial studies (blood, urine and throat swab cultures) were negative. Viral serology (cytomegalovirus, Ebstein-Barr virus, hepatitis and HIV) were negative, and serology for brucella, bartonella, toxoplasma was negative. Tuberculosis screen was negative. All had normal immunoglobulin and complement levels. Autoimmune screen was negative. Bone marrow aspirate and trephine did not suggest malignancy. The only positive finding in all patients was raised antistreptolysin-O-titre suggestive of recent group A Streptococcus infection. Symptoms in all patients resolved following lymph node resection.

<table>
<thead>
<tr>
<th>Patient</th>
<th>1 (AW)</th>
<th>2 (RV)</th>
<th>3 (IN)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>13</td>
<td>11</td>
<td>16</td>
</tr>
<tr>
<td>Sex</td>
<td>F</td>
<td>F</td>
<td>M</td>
</tr>
<tr>
<td>Background</td>
<td>Indian descent</td>
<td>Kenyan-Indian descent</td>
<td>Italian-Pakistan descent</td>
</tr>
<tr>
<td>Presenting symptoms</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prolonged fever</td>
<td>+ 6 weeks</td>
<td>+ 12 weeks</td>
<td>+ 6 weeks</td>
</tr>
<tr>
<td>Cervical lymphadenopathy</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Rash</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Initial sore throat</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Headache</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Other</td>
<td>Hair loss, nail discolouration, intermittent hip pain</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Focal right sided seizure</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Travel</td>
<td>Kerala, India two months before presentation</td>
<td>Travel to Portugal, Barbados and France within the year prior to presentation</td>
<td>Pakistan nine months before presentation</td>
</tr>
<tr>
<td>Investigations</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak CRP</td>
<td>87</td>
<td>20</td>
<td>4</td>
</tr>
<tr>
<td>Peak ESR</td>
<td>61</td>
<td>76</td>
<td>17</td>
</tr>
<tr>
<td>ASOT</td>
<td>400-800</td>
<td>800-1600</td>
<td>800-1600</td>
</tr>
<tr>
<td>Bone marrow biopsy</td>
<td>No abnormal lymphoid population</td>
<td>Hypocellular marrow, no abnormal lymphoid populations, Necrotising histiocytic lymphadenitis (Kikuchi’s disease)</td>
<td>No abnormal lymphoid population</td>
</tr>
<tr>
<td>Lymph node</td>
<td>Necrotising histiocytic lymphadenitis (Kikuchi’s disease)</td>
<td>Necrotising histiocytic lymphadenitis (Kikuchi’s disease)</td>
<td>Necrotising histiocytic lymphadenitis (Kikuchi’s disease)</td>
</tr>
<tr>
<td>Treatment</td>
<td>3 weeks of oral amoxicillin, 1 week of IV ceftriaxone and oral azithromycin, 2 weeks of oral doxycycline</td>
<td>1 week of oral amoxicillin</td>
<td>1 week of oral co-amoxiclav, 2 days of IV ceftriaxone, 10 days of oral penicillin</td>
</tr>
</tbody>
</table>
Learning Points/Discussion: Group A streptococcus infection may be an infectious trigger for Kikuchi disease in susceptible patients. Kikuchi disease often resolves with conservative management. There is association of autoimmune disease (systemic lupus erythematosus) and Kikuchi disease, though autoimmune markers for our patients were negative and their symptoms did not recur. This is the first case series describing group A streptococcal infection associated with Kikuchi disease.
LOCAL IMMUNE RESPONSES DURING LOWER RESPIRATORY TRACT INFECTIONS ARE SHAPED INDEPENDENTLY OF THE INFECTION-CAUSING PATHOGEN

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Background: Lower respiratory tract infections (LRTIs) in children can be caused by several pathogens. However, LRTI clinical outcome is not only the result of microbial factors but environmental factors and the local host immune response as well. However, what determinants are most important in shaping the local host immune response during LRTI is unknown. We asked if the infection-causing pathogen is the major driver of the local immune response during LRTI.

Methods: Within a LRTI-cohort we included children with fever >38.5°C, respiratory tract symptoms, no alternative infectious diagnosis and available induced sputum samples. LRTIs were attributed to specific pathogens using a pre-specified clinical algorithm based on microbiological and clinical data. We measured immune system-related proteins in induced sputum using Olink's proteomics panel and used these proteomics measurements as input for unsupervised clustering analysis.

Results: Patients (n=37) who met inclusion criteria and had detectable protein levels of at least 20% of proteins in the panel were included. Hierarchical Clustering Analysis revealed three robust clusters of patients based on the proteomics data (Figure 1). A proteome signature consisting of 24 cytokines/chemokines was sufficient to separate LRTI patients into one of these three patient clusters (Figure 2). Patient clusters did not relate to specific pathogens as attributed by the clinical algorithm. Furthermore, patient age and levels of systemic inflammation (i.e. CRP) were not significantly different between patient clusters as well.
Conclusions: Our data suggest that the causative pathogen is not the major driver of the local immune response during LRTI. Other factors such as genetic predisposition and microbiome composition could play an important role. Further research should identify the mechanisms responsible for shaping immune responses during LRTI.

Clinical Trial Registration: Clinical trial registration: N/A
Background: Hand hygiene (HH) is the most effective safeguard against healthcare-associated infections (HAIs). It is particularly important in the pediatric intensive care unit (PICU), where young age and an immunocompromised status make patients particularly vulnerable to infections. Surveillance data on HH compliance within pediatric European hospitals are poor. Our aim was to measure the degree of compliance with HH practices in PICUs across Europe and identify targets for improvement.

Methods: RANIN-KIDS (Reducing Antimicrobial use and Nosocomial INfections in KIDS) is a European network with the aim of achieving optimal clinical outcomes among pediatric patients. This was an observational study carried out in 9 PICUs in 7 European countries in a 6 month-period, using WHO’s “Five moments of Hand Hygiene” definitions. Observations were conducted in every unit by trained observers, using a data collection tool developed based on WHO guidelines. Compliance and appropriateness rates were defined as [(performed actions/opportunities)x100] and [(appropriately performed actions/performed actions)x100] respectively.

Results: 1715 HH opportunities were observed. Across all PICUs, the median HH compliance rate was 82.3%(IQR:71.6%-94.5%). Compliance to moment 5 was the lowest across hospitals (Table 1). Stratified by type of professional, compliance was comparable among doctors and nurses, but lower for non-unit healthcare personnel (HCP) and non-HCP (Table 1). "Alcohol-based handrub" was substantially preferred to soap and water. Cleaning and drying technique was considered appropriate in a median of 93% of observations(IQR:86.4%-96.3%).
Conclusions: The overall level of HH compliance in European PICUs is high but surveillance allowed us to identify targets for improvement. Moment 5 is the most frequently missed opportunity and non-healthcare personnel show lower adherence to WHO guidelines than doctors and nurses. These results will be used to inform tailor-made interventions in participating units with the aim of reducing HAIs and MDR spreading.

<table>
<thead>
<tr>
<th>Compliance by moment:</th>
<th>Median</th>
<th>IQR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Before touching a patient</td>
<td>87.1%</td>
<td>83%–96.2%</td>
</tr>
<tr>
<td>2. Before Clean/Aseptic procedures</td>
<td>100.0%</td>
<td>66.7%–100%</td>
</tr>
<tr>
<td>3. After body fluid exposure/risk</td>
<td>93.3%</td>
<td>75%–100%</td>
</tr>
<tr>
<td>4. After touching a patient</td>
<td>82.1%</td>
<td>77.1%–96.3%</td>
</tr>
<tr>
<td>5. After touching patient surroundings</td>
<td>71.4%</td>
<td>52.6%–80.0%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Compliance by profession</th>
<th>Median</th>
<th>IQR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doctors</td>
<td>90.0%</td>
<td>83.3%–92.1%</td>
</tr>
<tr>
<td>Nurses</td>
<td>87.1%</td>
<td>79.5%–95.3%</td>
</tr>
<tr>
<td>Non-unit doctors / nurses</td>
<td>81.3%</td>
<td>66.7%–100%</td>
</tr>
<tr>
<td>Non-Doctors Non-Nurses</td>
<td>66.7%</td>
<td>47.8%–90.3%</td>
</tr>
</tbody>
</table>
THE IMPACT OF LOW-COST INTERVENTION BUNDLE ON INFECTION CONTROL PRACTICES DURING CHILDBIRTH IN RURAL HEALTH FACILITIES IN ZAMBIA

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Background: In low- and middle-income countries, postpartum maternal and neonatal infections continue to be important causes of morbidity and mortality. These risks are amplified in community healthcare sites, where a large disparity in resources exists compared to tertiary care hospitals. Interventions at the primary care level are crucial in bridging this gap.

Methods: A quasi-experimental study was conducted at five rural health facilities in Southern Province of Zambia from December 2018 to August 2019. Data collection occurred before and after 3 months of interventions, including infection prevention and control (IPC) education, alcohol hand rub provision, and SMS reminders. Infection Control Assessment Tool (ICAT), a survey completed by the in-charge nurse, was used to assess the health facility’s comprehensive IPC measures. Logbook was reviewed for pre- and post-intervention rates of maternal and newborn infections, complications, and hospital outcomes including mortality and transfers.

Results: Wilcoxon paired signed rank test showed the mean ICAT score was 69.4/140 and 77.2/140 at pre- and post-intervention (p=0.23). ICAT scores for the hand hygiene module (p=0.04) and labor and delivery practices (p=0.06) showed improvements. There were no significant changes on modules on facility, general IPC program or practices, or postpartum care. Logbook review of 654 mothers and 655 newborns showed one case of newborn fever. Logistic regression showed no significant change in newborn outcomes, while there was a post-intervention reduction in maternal transfers due to complications (p=0.04).

Conclusions: Low-cost intervention bundle can improve aspects of IPC at rural health facilities in Zambia, although systematic and behavioral improvements may require further interventions. Rates of newborn and maternal infection in community settings were low, but charting practices were inconsistent. Higher quality routine health center data would assist in studying newborn and maternal health.

Clinical Trial Registration: Clinical trial registration: ClinicalTrials.gov NCT03809741
Background: Pharyngeal carriage is the reservoir for Neisseria meningitidis in the population and the first step in disease transmission. Especially in young infants and adolescents, N. meningitidis can cause serious invasive infection with high fatality rates and high rates of long-term sequelae among survivors. Aim of this study was to determine N. meningitidis colonization rates and serogroup distribution of carried meningococcal isolates in asymptomatic health care professionals at a tertiary university paediatric hospital. Furthermore, we sought to identify risk factors for carriage.

Methods: This cross-sectional meningococcal carriage survey was conducted between April and October 2018 at the Department of Paediatrics and Adolescent Medicine at the Medical University of Vienna. Individuals working as nurses, paediatricians or medical students were enrolled. Oropharyngeal swabs were directly plated onto selective agar plates and conventional culture was used for bacterial identification. Meningococcal isolates were further characterized using whole genome sequencing.

Results: A total of 437 oropharyngeal specimens were collected. The median age of participants was 33 (IQR 17) and 85.6% (374/437) of the study population were female. Overall meningococcal prevalence was 1.14% (5/437), with 0.7% (3/437) for capsular genotype B, and 0.5% (2/437) for capsular genotype W. Mean age of carriers was significantly lower than of non-carriers (24.2 vs. 35.8; p = 0.004). The highest carriage rate of 4.4% (4/91) was found in the age group 18-25. Carriage was negatively associated with age and timespan working in paediatrics.

Conclusions: This is the first study evaluating the prevalence of Neisseria meningitidis carriage in health care professionals working in Paediatrics and Adolescent Medicine. Carriage was in general lower than expected for all age groups, implicating a low risk of horizontal meningococcal transmission via this population.

Clinical Trial Registration: not available
MOLECULAR EPIDEMIOLOGY OF METHICILLIN-SENSITIVE STAPHYLOCOCCUS AUREUS IN NEONATAL INTENSIVE CARE UNIT

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²Juntendo Graduate School of Medicine, Department Of Pediatrics And Adolescent Medicine, Tokyo, Japan,
³Tokyo Rinkai Hospital, Department Of Pediatrics, Tokyo, Japan, ⁴National Center for Global Health and Medicine Hospital, Amr Clinical Reference Center, Tokyo, Japan, ⁵San-Ikukai Hospital, Department Of Pediatrics, Tokyo, Japan

Background: Staphylococcus aureus is one of the major causes of neonatal infections. Methicillin-resistant Staphylococcus aureus (MRSA), a hospital environmental bacterium, has been declining in the neonatal intensive care unit (NICU) due to the spread of infection control. On the other hand, methicillin-sensitive Staphylococcus aureus (MSSA) is still detected in a certain number from blood culture. We evaluated the epidemiological factor of MSSA in NICU for controlling MSSA infection in NICU.

Methods: We collected nasal vestibule swabs and isolated S.aureus from patients, their parents, and healthcare workers in the NICU at our hospital from October 2018 to March 2019. Whole-genome sequencing (WGS) was performed on MSSA isolates from patients and their parents. Healthcare workers' isolates were identified by PCR-based ORF Typing (POT), along with WGS for some isolates. Multi-locus sequence typing, spa typing, and single-nucleotide polymorphism analysis were performed.

Results: Sixteen of 89 sampled neonates were MSSA positive. There were 52 families that could sample both neonates and parents, and the parental MSSA carriage rate was 24%. Of these, three families had MSSA in both patient and either parent. Only one out of these three groups were identified homology in WGS. Thirty-five of 97 sampled healthcare workers were MSSA carriers. Four neonate isolates showed homology with those from healthcare workers. In addition, three neonate groups had the same strain, one of which was twins.

Conclusions: The MSSA transmission pathway of neonates has the same horizontal transmission as MRSA, but it has been suggested that the colonization of healthcare workers may be one of the important acquisition pathways. Control of S. aureus in the NICU needs to consider not only infection control that suppresses horizontal transmission among patients, but also surveillance and carrier measures for healthcare workers.
EXPERIMENTAL EVIDENCE OF THE EFFECT OF SCHOOL GATHERING INTERVENTIONS ON THE DYNAMICS OF DENGUE EPIDEMICS

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Background: Dengue fever is an important vector-transmitted disease worldwide. By controlling mosquitoes’ breeding places, this study aims to analyze the effect of reducing transmission in elementary schools (grades 1–9) on the dynamics of the epidemic at a regional level. Dengue virus transmission occurs within the community or schools, and there is evidence that transmission in schools plays an important role in the progression of dengue epidemics. In Mexico, elementary schools are left unattended for almost two months during the summer break; many of them become a suitable environment for mosquitoes. After the break, students return to classes (25% of the population in Mexico). Thus, a great deal of the population suddenly increases their exposure to the vector.

Methods: We implemented a massive campaign in a region of México (Colima state, 5,191 km², population 568,000) focused on training janitors to locate and avoid mosquitoes’ breeding places, the objective being to maintain elementary schools free of mosquitoes. Colima is one of the states with a higher dengue incidence in Mexico. We implemented a special statewide campaign before the beginning of classes, in 482 schools with 75,000 students (average school size 120+-131). There were a total of 1,284 attendees at the meetings that included personnel from 91% of schools in the state of Colima, including public and private schools.

Results: We observed a 45% reduction in dengue incidence compared to the previous year. In contrast, the rest of Mexico observed an 81% increase in incidence on average.
Conclusions: We conclude that the described intervention gave empirical evidence to avoid dengue transmission in elementary schools. Costs associated with campaigns focusing on cleaning schools are meager, and results seem to be promising. Nevertheless, more controlled studies are needed worldwide.

Clinical Trial Registration: No Clinical trial registration needed.
THE KNOWN CHALLENGES AND HIDDEN COSTS OF VANCOMYCIN USE DURING THE TREATMENT OF METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS BACTEREMIA IN CHILDREN WITH ACUTE HEMATOGENOUS OSTEOMYELITIS

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Background: Slow bactericidal activity, limited bone penetration, and potential for nephrotoxicity raise concerns about continued use of vancomycin as first-line therapy for acute osteomyelitis with concurrent MRSA bacteremia. This audit explores the effort and resources devoted to the use of vancomycin in this setting and evaluates the utility of AUC/MIC calculation to modify future dosing strategies including loading with 30 mg/kg.

Methods: Children with osteomyelitis and concurrent MRSA bacteremia from 2009-2018, who were treated with a sufficient duration of vancomycin to evaluate serum trough and AUC/MIC were retrospectively studied. Data collected: antibiotic susceptibilities; duration of bacteremia; number of dose/interval changes; vancomycin trough and creatinine levels; rate of achieving therapeutic trough and AUC/MIC > 400; rate of acute kidney injury; length of stay.

Results: 85 children with MRSA osteomyelitis had bacteremia for 4.1 days on average. Target trough (15-20 µg/mL) was achieved in 59 (69.4%) children within 4.9 days. There were 231 dose/interval adjustments, 918 serum creatinine levels, and 648 vancomycin troughs obtained. Ten children (11.8%) experienced AKI with LOS 25.8 days compared to 14.9 days in children without AKI. AUC/MIC was > 400 for 62 (72.9%) children while trough was therapeutic in only 12 (14.1%) children. Loading with 30 mg/kg produced higher AUC/MIC (668.0 vs.520.8) and trough (11.1 vs. 9.1 µg/mL) without AKI.

Conclusions: This study illustrates the resources devoted to vancomycin use in children with osteomyelitis and concurrent bacteremia. The challenges and hidden costs raise consideration about alternative antibiotic therapy strategies in this setting. If vancomycin is utilized, a deliberate approach should be taken to mitigate risk of AKI, including AUC/MIC ratio calculation, commitment to 30 mg/kg loading dose, and limiting concurrent use of other nephrotoxic agents, including contrast, loop diuretics, aminoglycosides, and NSAIDs.
NO SYSTEMIC PROTECTION AFTER VACCINATION WITH MENB-4C IN PATIENTS TREATED WITH ECULIZUMAB FOR ATYPICAL HEMOLYTIC UREMIC SYNDROME.

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Background: Atypical hemolytic-uremic syndrome (aHUS) consists of microangiopathic hemolytic anemia, thrombocytopenia and renal failure. aHUS is induced by uncontrolled complement activation and limited treatment options were at hand until the introduction of Eculizumab. Eculizumab is a complement C5 inhibitor that prevents formation of the membrane attack complex, but increases the risk for Meningococcal infections. Therefore, vaccination with the tetravalent vaccine against Meningococcal serogroup A, C, W-135, Y and MenB-4C is mandatory. In this study we investigated whether pediatric aHUS patients treated with Eculizumab show increased protection in a serum and whole blood killing assay after MenB-4C vaccination.

Methods: Neisseria meningitidis serogroup B (MenB) was incubated for 30 min with pre- and post-vaccination serum from 5 aHUS patients and binding of IgG, complement C3 and C5b-9 were determined using flowcytometry. Serum killing experiments were performed by incubating MenB for 30 min with autologous pre- and post- vaccination serum. Whole blood killing experiments were performed similarly, except MenB was incubated with serum depleted whole blood from a healthy donors.

Results: Increased IgG and complement C3 binding to the Meningococcal surface was observed with serum post-MenB-4C vaccination. No complement C5b-9 binding to the Meningococcal surface was detected, which corresponded to a failure to kill the bacteria in a serum killing assay. In contrast to previous results in patients with complement deficiencies, no MenB-4C-vaccine induced increase in whole blood killing was observed in aHUS patients using Eculizumab.

Conclusions: Despite an MenB-4C-induced increase in IgG and complement C3 binding to the Meningococcal surface, there was no increase in complement or whole blood mediated killing. Suggesting that Eculizumab eliminates complement- as well as opsonophagocytosis-mediated killing of MenB in MenB-4C vaccinated aHUS patients.

Clinical Trial Registration: Not Applicable
Background: Novel treatments have revolutionized the care and outcome of patients with JIA. DMARDs manage to control this disease, however data regarding response and long-term immunological memory to specific vaccines are lacking. Patients with rheumatic diseases are susceptible to infections due to their defective immune system and the immunosuppressive treatment received. We aimed at a comprehensive assessment of how anti-IL6 therapy may interfere with vaccine-specific-IgG titers in children with polyarticular JIA, by evaluating the persistence of specific-IgG levels during anti-IL6 treatment.

Methods: Monocentric cross-sectional controlled study was held over a period of three years, comprising 23 patients and 35 matched controls. All participants had completed their vaccination scheme. There were specific exclusion criteria set. Seroprotection rates as well as measles, rubella, tetanus, hepatitis B (HBV) and Hemophilus (Hib) specific-IgG titers were measured by ELISA and were expressed as Geometric mean Concentrations (GMC’s).

Results: The two groups had similar demographic characteristics, vaccination history and immunization status. Seroprotection rates for HBV, measles and Hib were similar between the two groups. However, seroprotection rates were lower in the poly-JIA group for tetanus and rubella compared to the control group (p<0.05). Moreover, tetanus and measles GMCs were significantly lower in the poly-JIA compared to the control group (p<0.05). The same was also evident for rubella to a more pronounced degree (p<0.01).

Conclusions: Children with poly-JIA who received anti-IL6 (tocilizumab) treatment appeared to have lower tetanus, measles and rubella specific-IgG titers. Further studies are required to address the question of long-term immunity conveyed by immunizations given at an early stage in children with rheumatic diseases on biologics, while proposing perfunctory studies to evaluate the effect of JIA and its associated treatment on lymphocyte ‘behavior’ and function.
THE EFFECT OF VARYING REFERENCE VALUES ON THE PREVALENCE RATE OF IGA DEFICIENCY IN YOUNG CHILDREN WITH RECURRENT RESPIRATORY TRACT INFECTIONS COMPARED WITH CONTROLS

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Background: Recurrent respiratory tract infections (rRTIs) have considerable impact on health in young children and can lead to failure to thrive, developmental delays and pulmonary damage. IgA deficiency is the most common immunodeficiency in children with rRTIs, with prevalence rates in published cohorts between 1:4 and 1:65. However, the clinical relevance of prevalence studies is hampered by the lack of control groups and use of different reference values to define IgA deficiency.

Methods: In this case-control study we compare prevalence rates of IgA deficiency in Dutch children <7 years with rRTIs (n=426) and in controls (n=227) in whom IgA was determined for celiac disease screening. Children with confirmed celiac disease, underlying systemic diseases or immune disorders other than IgA deficiency were excluded. IgA deficiency was defined as an IgA concentration below the lower limit of the age-normalized reference interval based on several published reference values: Sanquin, Mayo clinic and CALIPER study.

Results: Both in children suffering from rRTIs and in controls prevalence rates of IgA deficiency differ greatly depending on which reference values are used (1.9%-9.2% and 2.2%-11.0%, respectively, see Figure). In multivariable analysis we observed trends towards higher OR for IgA deficiency in children suffering from rRTIs compared to controls for two of the reference values used (OR 1.69, p=0.07; OR 2.70, p=0.09; OR 1.50, p=0.28, see Figure).
Conclusions: Widely ranging published IgA reference values in literature, even when similar analysis methods are used, lead to large differences in prevalence rates. The lack of harmonization for IgA reference values in children complicates the proper comparison and interpretation of studies into the clinical relevance of IgA deficiency as well as the development of management guidelines for IgA deficient children suffering from recurrent infections.
IDENTIFICATION OF NEW MUTATIONS IN PAEDIATRIC PATIENTS WITH MYCOBACTERIAL INFECTION

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Background: Mycobacterial infections are important causes of morbidity and mortality among children. Rare monogenic inborn errors of immunity were found to predispose to mycobacterial disease. The aim of this study was to identify genetic variants that confer susceptibility to mycobacterial disease in Moldavian children.

Methods: Whole exome sequencing (trio-based and candidate-gene approaches) was conducted in nine patients with mycobacterioses (eight with severe BCG complications and one with generalized tuberculosis) suspected for Mendelian Susceptibility to Mycobacterial Disease (MSMD). cDNA analysis was applied to validate the effect of mutations on pre-mRNA splicing in two patients.

Results: 11 heterozygous variants in 7 MSMD-associated genes (STAT1, IFNGR1, IL23R, JAK1, TYK2, IL12B, and IL12RB1) were identified via candidate gene approach. Genes STAT1, IFNGR1 and IL12B were of particular interest, since STAT1 and IFNGR1 are responsible for autosomal dominant MSMD and IL12B comprises two novel mutations (c.877A>G (p.Lys293Glu) and c.89-14T>C) in a compound heterozygous state. The missense mutation c.40G>A (p.Val14Met) in IFNGR1 is a known variant with partial or complete IFNGR1 deficiency. The variant c.373-2A>C in STAT1 is a novel splice site mutation; cDNA analysis demonstrated that c.373-2A>C activates a cryptic splice site leading to skipping of the exon and partial intron retention in a patient with disseminated tuberculosis. In addition, 22 disease-associated variants in 14 presumed causative genes, including compound heterozygous variants in GBP2, TTN (two patients), GAL3ST2, HMCN1, ZCWPW1 and LRP1B, de novo variants in PPP1R9B and HEATR3, X-linked recessive variants in SRPX2, RBMXL3, H2BFM and KDM6A, and homozygous recessive variants in SIGLEC6 and IFNW were identified by trio-based analysis.

Conclusions: Our findings expand the spectrum of genetic variation possibly predisposing to mycobacterial infections in children. Funding Alexander von Humboldt Foundation and Hanover Unified Biobank.

Clinical Trial Registration: (Please input N/A if not registered)
LONGITUDINAL STUDY OF ANTIFUNGAL CONSUMPTION IN PEDIATRIC AND NEONATAL PATIENTS

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Background: Antifungal drug consumption has increased due to the recent increase of patients at risk for invasive fungal infections. Data on overuse of antifungal agents in children are limited both at national and European level. The aim of the study is to assess the pattern and time trends of antifungal consumption in pediatric and neonatal departments of a tertiary care level hospital.

Methods: A retrospective study was conducted in a pediatric intensive care unit (PICU), a neonatal intensive care unit (NICU), a pediatric hematology/oncology department (PONC), a pediatric surgery and two general pediatric departments, located in a single hospital. Data on antifungal consumption from 2010 to 2019 were obtained from the hospital pharmacy and expressed as defined daily doses per 100 bed-days (DDD/100BD) according to World Health Organization.

Results: Median total antifungal consumption exhibited a trend from 104.1 to 131DDD/100BD (p=0.1). Amphotericin B was the most commonly prescribed antifungal agent (45%) throughout study period and in all pediatric departments except PONC. The second most common antifungal used was voriconazole, whose consumption ranged from 21.8 to 40.8DDD/100BD and was mainly used in PONC. Consumption of both fluconazole and micafungin had a significant increase from 8.0 to 14.9DDD/100BD (p=0.004) and from 0.2 to 24.3DDD/100BD (p=0.02), respectively(fig.1). The highest antifungal use was found in PONC, followed by PICU and NICU.

![Figure 1: Consumption of antifungal agents in DDDs/1000BD](image-url)
Conclusions: Longitudinal analysis of antifungal consumption in pediatric and neonatal patients using the Daily Defined Dose methodology was feasible. Majority of antifungal agents were prescribed to pediatric oncology and critically ill neonates and children as expected. Recording the pattern and trends of antifungal use can contribute in identifying potential targets in order to improve their appropriate use in pediatric and neonatal population.
MATERNAL FACTORS PREDICT THE ASSOCIATION BETWEEN OBESITY AND ANTIBIOTICS IN YOUNG CHILDREN

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Background: Early antibiotic exposure is associated with childhood obesity. When untreated infections are accounted for, early infections predict subsequent obesity, and antibiotic exposure in later infancy (>6 months of age) is no longer associated. However, antibiotic exposure in early infancy (<6 months) remains associated with later childhood obesity. We surveyed a birth cohort in Southern California Kaiser Hospitals (SCAL) to assess this association.

Methods: Among SCAL children born between 2008 - 2012, term infants with 2 years of follow-up and a body-mass-index (BMI) measurement at 48 - 59 months were studied. Gender, method of delivery; maternal BMI; timing and number of antibiotic exposures by 2 years of life; and BMI at age 48-59 months were recorded. Maternal and infant predictors of later elevated BMI (>95%ile) were assessed by multi-variable analysis.

Results: In this cohort of 66 735 infants, most (64%) received antibiotics by age 2 years. In multi-variable analysis, maternal obesity was a strong predictor of childhood obesity (hazard ratio (HR) = 2.74; 95% confidence interval 2.47 - 3.04). Very early antibiotic exposure (ie, <6 months) predicted later obesity in children of non-obese mothers (HR = 1.15; 1.07-1.24), but among children of obese mothers, the opposite trend was seen, with very early use of antibiotics associated with a decrease in subsequent obesity (HR=0.90; 0.79-1.03).
Conclusions: As in previous studies, the risk of childhood obesity was higher after very early antibiotic exposure in our population, but this increased risk is mitigated by the mother's obesity status. While children of obese mothers are at high risk of obesity in general, this risk may be lower in those exposed to very early antibiotics. The reasons for this disparity should be the subject of further study.
STRONG DOWNWARD TREND OF OUTPATIENT ANTIBIOTIC PRESCRIPTIONS IN GERMAN CHILDREN AND ADOLESCENTS IN THE YEARS 2010 TO 2018

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Background: A former study reported higher prescribing of systemic antibiotics in German paediatric outpatients compared to their Dutch, Danish and British peers in the years 2005-2008. This population-based retrospective study aimed to assess recent trends of antibiotic prescribing in German children and adolescents.

Methods: This study was conducted as sequential annual cross-sectional analyses based on a full sample of outpatient prescription claims of the German Statutory Health Insurance. All statutory health insured German children and adolescents aged 0-14 years (n=9,389,183 in 2018) were included, covering 83% of the German paediatric population. Annual antibiotic prescription rates (2010–2018) were calculated per 1,000 persons for the age groups 0–1, 2–5, 6–9 and 10–14 years. Poisson regression was employed to estimate trends of prescription rates.

Results: Over the course of the study the age-standardized antibiotic prescription rate fell from 746 prescriptions per 1,000 persons in 2010 to 428 in 2018 (-43%, p<0.001). Decrease was most marked in the age groups 0–1 year (~50%) and 2–5 years (~44%). In 2018, use was highest in the age group 2-5 years, amounting to 683 prescriptions per 1,000 persons (0–1 year: 320, 6–9 years: 417, 10–14 years: 273). Prescription rates varied by a factor of 1.9 between federal states. Overall, 32% of prescribed antibiotics were cephalosporins (2nd and 3rd generation).

Conclusions: Considerable reductions of paediatric antibiotic use indicate a change towards more judicious prescribing habits. In contradiction to recommendations by German practice guidelines, high use of 2nd and 3rd generation cephalosporins suggests frequent first-line prescribing of these antibiotics for common childhood infections. Substantial spatial variations of paediatric antibiotic prescribing indicate the need for regionally targeted interventions.
CANDIDA AND VANCOMYCIN RESISTANT ENTEROCOCCUS COLONISATION IN SEPTIC NEONATES ON VANCOMYCIN TREATMENT

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Background: Antibiotic exposure interferes with normal flora leading to colonisation with resistant organisms. Data on vancomycin resistant enterococcus (VRE) and candida colonisation in neonates are sparse, often limited to single-centre studies. Colonisation is linked with invasive infection, with associated morbidity/mortality. Preliminary colonisation data are presented from septic infants recruited to the NeoVanc trial (www.neovanc.org) from 14 NICUs in Estonia, Greece, Italy, Spain and UK.

Methods: Stool/rectal, axilla and nasal swabs were collected at Day 0 (D0—initiation of vancomycin), end of vancomycin therapy (EVT), short-term follow-up (STFU). Samples were plated onto selective agar to screen for VRE/candida. Morphologically different colonies were purity-plated and species identified using MALDI–TOF. Vancomycin susceptibility testing was performed to confirm VRE.

Results: Data are available for 1667 samples from 215 infants. 115/215 (53.5%) were male; median PMA was 32 (IQR 29–37) weeks. 8/215 (3.7%) infants were colonised with VRE (all Enterococcus faecium) at ≥1 timepoint. Median PMA 36 (IQR 35–39) weeks. 4/8 (50%) infants acquired VRE colonisation during/after vancomycin treatment. 6/7 (85.7%) infants were colonised at STFU. VRE colonised infants were from 3 sites (2 Greek; 1 Italian); prevalence was 12.5–25% at these sites. 57/215 (26.5%) were colonised with Candida spp. at ≥1 timepoint. Median PMA 32 (IQR 29–36) weeks. 21/57 (33.3%) infants became colonised during/after vancomycin therapy. Colonisation with Candida albicans (30/57) was most common followed by Candida parapsilosis (22/57). 12/21 (57.1%) acquisitions were non–C. albicans species. 13/57 infants acquired candida between D0 and EVT; 18/57 colonised at D0 lost this by EVT. 32/57 (56.1%) were colonised at STFU.

Conclusions: VRE colonisation was infrequent in this neonatal population, occurring in older babies and then persisting. Candida colonisation was more prevalent and intermittent. Candida attained after D0 was more common with non–C. albicans species; likely acquired from the NICU environment. On behalf of NeoVanc Consortium

Clinical Trial Registration: ClinicalTrials.gov NCT02790996
Background: Surgical Antibiotic prophylaxis (SAP) decreases the incidence of surgery-associated infection, but inappropriate antibiotic use is frequently documented. The WHO’s 2018 Guidelines recommend for SAP prior to surgical incision and against SAP prolongation after completion of the operation. The aim of this study was to describe SAP practices in children across European hospitals and to identify possible targets for improvement.

Methods: A prospective observational study was conducted among 10 hospitals in 6 countries from the RANIN-KIDS Network (Reducing Antimicrobial use and Nosocomial INfections in KIDS). Data collected on 50 consecutive operations per hospital included the type of procedure, wound-class classification, choice of antibiotic, timing of administration related to surgical incision and its duration. Data on clean and clean-contaminated operations were analyzed.

Results: 582 operations were recorded; 482 were clean or clean-contaminated. Antibiotics were administered in 312(65%) cases. In 6/10 hospitals SAP was mostly given at the operating room (OR), right before the incision. In 1 hospital more than half of antibiotics were administrated at the OR after the incision. 5/10 hospitals reported cases of SAP given only after the end of the operation. Administration of antibiotics after the operation showed great variability among hospitals [median 69% (IQR:50-83.3%)] with high percentages even past 24 hours [median:31.3%(IQR: 27.9-61.0%)] and SAP as commonest reason given(Table1).
Table 1. Percent of antibiotic regimens continued after the end of clean and clean-contaminated operations, percent extending past 24 hours and reasons provided among 10 hospitals

<table>
<thead>
<tr>
<th>Hospital</th>
<th>After the operation</th>
<th>After the operation and over 24 hours</th>
<th>Unknown/Not documented</th>
<th>Prophylaxis</th>
<th>Infection</th>
<th>Fever</th>
<th>Positive culture</th>
<th>Surgical drain in place</th>
<th>Other reason not related to the surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>13</td>
<td>76.5</td>
<td>11</td>
<td>64.7</td>
<td>1</td>
<td>9.1</td>
<td>9</td>
<td>81.8</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>15</td>
<td>83.3</td>
<td>9</td>
<td>50.0</td>
<td>1</td>
<td>11.1</td>
<td>1</td>
<td>11.1</td>
<td>3</td>
</tr>
<tr>
<td>3</td>
<td>7</td>
<td>43.8</td>
<td>5</td>
<td>31.3</td>
<td>1</td>
<td>20.0</td>
<td>3</td>
<td>60.0</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>36</td>
<td>97.3</td>
<td>5</td>
<td>13.5</td>
<td>1</td>
<td>20.0</td>
<td>3</td>
<td>60.0</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>10</td>
<td>50.0</td>
<td>6</td>
<td>30.0</td>
<td>1</td>
<td>16.7</td>
<td>1</td>
<td>16.7</td>
<td>3</td>
</tr>
<tr>
<td>6</td>
<td>8</td>
<td>61.5</td>
<td>6</td>
<td>46.2</td>
<td>5</td>
<td>83.3</td>
<td>0</td>
<td>0 -</td>
<td>0 -</td>
</tr>
<tr>
<td>7</td>
<td>61</td>
<td>37.7</td>
<td>44</td>
<td>27.2</td>
<td>0</td>
<td>-</td>
<td>42</td>
<td>95.5</td>
<td>0 -</td>
</tr>
<tr>
<td>8</td>
<td>19</td>
<td>100</td>
<td>19</td>
<td>100</td>
<td>0</td>
<td>-</td>
<td>9</td>
<td>47.4</td>
<td>0 -</td>
</tr>
<tr>
<td>9</td>
<td>2</td>
<td>50.0</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
<td>-</td>
<td>0</td>
<td>0 -</td>
<td>0 -</td>
</tr>
<tr>
<td>10</td>
<td>5</td>
<td>83.3</td>
<td>5</td>
<td>83.3</td>
<td>5</td>
<td>100</td>
<td>0</td>
<td>0 -</td>
<td>0 -</td>
</tr>
</tbody>
</table>

**Conclusions:** We report significant variability in the practices of SAP in pediatric patients undergoing clean and clean-contaminated operations both in terms of the time of administration and duration. These preliminary data will be used as a guide for tailor-made interventions in each hospital.
DOSE-DEPENDENT INCREASE IN RISK OF OFFSPRING EAR NOSE AND THROAT PROCEDURES FOLLOWING IN UTERO ANTIBIOTIC EXPOSURE: A DATA LINKAGE STUDY OF THE NORWEGIAN POPULATION

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**Background:** Pregnancy antibiotic exposure increases the risk of offspring hospitalisation with upper and lower respiratory tract infections, but whether there are similar associations for commoner, less severe infections is unknown. We used linked population data from Norway to investigate the relationship between pregnancy antibiotic exposure and offspring risk of ear, nose and throat (ENT) procedures, which reflect previous recurrent mild infections.

**Methods:** All live-born, singleton births between 2008 and 2018 were identified from national registries. Antibiotic exposure during pregnancy was defined from the prescription database. ENT procedures in the child before age 10 years were identified by procedural codes. Exposure and risk of first ENT procedure were analysed in Cox proportional hazard models (covariates in Table). We evaluated the timing and number of prescribed antibiotics and performed a sensitivity analysis in a pre-specified sub-population; healthy mothers, no pregnancy complications, vaginal birth and normal birth parameters.

**Results:** Of 538,028 included children, 151,363 (28%) were exposed to antibiotics prenatally and 48,556 (9%) underwent a procedure. Exposure was associated with increased risk of ENT procedures (hazard ratio, HR 1.27, 95% CI 1.25-1.30) in a dose-dependent manner. Caesarean section was associated with increased risk of procedures compared to vaginal delivery (HR 1.17, 95% CI 1.14-1.20). Pregnancy antibiotics and mode of birth did not show an interaction effect. Estimates from the sub-population sensitivity analysis were comparable.
Table 1: Cox-proportional hazard model with time to first operation as outcome in relation to pregnancy antibiotic exposure.

<table>
<thead>
<tr>
<th>Exposure to antibiotics</th>
<th>Total number exposed</th>
<th>Number of cases</th>
<th>Hazard Ratio (95%CI)</th>
<th>Adjusted* Hazard Ratio (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No pregnancy antibiotic</td>
<td>386665</td>
<td>32026</td>
<td>ref</td>
<td>ref</td>
</tr>
<tr>
<td>Any pregnancy antibiotic</td>
<td>151363</td>
<td>48556</td>
<td>1.27 (1.25-1.30)</td>
<td>1.26 (1.23-1.29)</td>
</tr>
<tr>
<td>Specific ENT procedure</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Procedures involving the ear</td>
<td>151363</td>
<td>30811</td>
<td>1.26 (1.22-1.29)</td>
<td>1.24 (1.20-1.28)</td>
</tr>
<tr>
<td>(Adeno)tonsillectomy</td>
<td>151363</td>
<td>37242</td>
<td>1.31 (1.28-1.33)</td>
<td>1.29 (1.26-1.32)</td>
</tr>
<tr>
<td>Number of antibiotic courses prescribed</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 antibiotic course</td>
<td>100251</td>
<td>10170</td>
<td>1.20 (1.17-1.22)</td>
<td>1.16 (1.13-1.18)</td>
</tr>
<tr>
<td>2 antibiotics courses</td>
<td>31947</td>
<td>3788</td>
<td>1.37 (1.32-1.42)</td>
<td>1.32 (1.26-1.36)</td>
</tr>
<tr>
<td>3+ antibiotics courses</td>
<td>18797</td>
<td>2522</td>
<td>1.55 (1.49-1.61)</td>
<td>1.44 (1.38-1.51)</td>
</tr>
<tr>
<td>Timing of antibiotics in pregnancy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Last antibiotic in first trimester</td>
<td>65913</td>
<td>7436</td>
<td>1.31 (1.28-1.34)</td>
<td>1.26 (1.22-1.29)</td>
</tr>
<tr>
<td>Last antibiotic in second trimester</td>
<td>47145</td>
<td>4998</td>
<td>1.25 (1.21-1.29)</td>
<td>1.20 (1.17-1.24)</td>
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<tr>
<td>Last antibiotic in third trimester</td>
<td>38305</td>
<td>4096</td>
<td>1.25 (1.21-1.29)</td>
<td>1.21 (1.17-1.25)</td>
</tr>
</tbody>
</table>

*Adjusted for mother’s age at birth, parity, maternal asthma, maternal diabetes mellitus, maternal hypertension, maternal kidney disease, HELLP, pre-eclampsia, maternal smoking in pregnancy, offspring sex, mode of delivery, gestational age, birth weight, and birth length.

Conclusions: Antibiotic exposure during pregnancy is associated with increased risk of ENT operations in childhood, which may be indicative of heightened susceptibility to recurrent early life infections. These findings are relevant for antibiotic prescribing and stewardship in pregnancy. A possible contributory mechanism to this increased risk is disruption of the postnatal microbiome by antibiotics in pregnancy, with concomitant effects on early immune development.
AGE-DEPENDENT SENSORY IMPAIRMENT IN COVID-19 INFECTION AND ITS CORRELATION WITH ACE2 EXPRESSION

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Background: Rates of taste and smell dysfunction in COVID-19 positive children have not been reported. We analyzed sensory impairment in COVID-19 positive children and adults, and correlated our findings with data regarding nasal ACE2 expression.

Methods: Children (aged 5-10 and 11-17 years) and adults (aged 18-25 years, and 26 and older) residing in several households, were evaluated for impairment of olfactory and gustatory senses. Scores of sensory impairment in the four age groups were correlated with ACE2 expression in persons infected with COVID-19 of corresponding age groups. Statistical evaluation was performed using the T-test, chi square test and the Pearson correlation test.

Results: 73 respondents, including 31 children and 42 adults were evaluated. Any impairment of taste and smell was reported in 51% of individuals, including 25.8% of the children and 71.4% of the adults (p=0.00014). Sensory impairment scores were higher in older (>25 years) than in younger adults (18-25 years) (p=0.038). Stratifying the pediatric group by age revealed higher scores of altered taste and smell in older (11-17 years) than in younger (<10 years) children (p=0.005). Sensory impairment differences correlated with reported differences in ACE2 expression among corresponding age groups (Fig. 1).
Conclusions: Sensory sensation was significantly less impaired in COVID-19 positive children than in adults. A stepwise increase in taste and smell impairment with increased age was observed, correlating with ACE2 expression in similar age groups. This supports the possibility that the distribution and expression of ACE2 receptors, could contribute to these differences suggesting that ACE2 expression is a key factor for the different manifestations between COVID-19 infected children and adults.
CELL ADHESION PROTEINS IN THE CEREBROSPINAL FLUID OF NEONATES EXPOSED TO ZIKA VIRUS BEFORE BIRTH

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Background: In 2015 zika virus (ZIKV) quickly spread and caused an outbreak in Brazil. Several studies have shown that ZIKV has positive tropism for neuronal cells including direct effects on development, proliferation, differentiation and cell death of neural progenitor cells, culminating in tissue damage. Cerebrospinal fluid (CSF) proteins have the potential to help understand the disease development. To compare cell adhesion molecules concentrations in CSF between Zika virus (ZIKV)-exposed neonates with and without microcephaly (cases) and controls.

Methods: Sixteen neonates underwent lumbar puncture (LP) during the ZIKV epidemic (2015-2016), 8 (50%) with and 8 (50%) without microcephaly. All mothers reported ZIKV clinical symptoms during gestation, all neonates presented with congenital infection findings and other congenital infections were ruled out. Fourteen neonates fulfilled criteria to be controls and underwent LP in the same laboratory (2017-2018). Five cell adhesion proteins were measured in the CSF by mass spectrometry and compared in the studied subgroups.

Results: Three cell adhesion proteins were significantly lower in the CSF of the case group. When only microcephalic or non-microcephalic cases were compared to controls, all of these proteins were significantly lower among cases. When cases with or without microcephaly were compared, no protein was significantly lower in the microcephalic subgroup. Positive correlation was found between cephalic perimeter and concentration of 2 cell adhesion proteins.

Conclusions: Several cell adhesion proteins are significantly lower in the CSF of neonates exposed to ZIKV before birth, irrespective of being born with microcephaly. However, the lesser the cephalic perimeter is, the lower the CSF cell adhesion protein concentration. Some cell adhesion proteins levels in the CSF probably reflect the impact of ZIKV congenital infection in the brain.
VERY LOW BIRTH WEIGHT INFANTS HAVING BEEN FECAL CARRIERS OF ESBL PRODUCING ENTEROBACTERALES AT THE NICU - A SIX YEARS FOLLOW-UP ON THE RISK OF GASTROINTESTINAL INFECTIONS

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Background: We recently published data on ESBL-producing Enterobacterales (ESBL-E) in stool-surveillance cultures at the NICU being not a risk factor for necrotizing enterocolitis in very low birth weight infants over an 11-year time period (Eberhart et al., Infection 2020). A large part of this population was now followed until the age of 6 years to evaluate the risk of gastrointestinal infections or complications.

Methods: Retrospective single center case-control study of preterm infants below 1500 grams (VLBW) with positive surveillance cultures of ESBL-E during neonatal stay between 2005 and 2013 were followed until the age of 6 years. We looked for bacterial and viral diseases, febrile seizures, appendicitis, ileus, volvulus, gastritis/enteritis, diarrhea, gastroesophageal reflux disease, and neurodevelopmental impairments. Ethical approval was given by the local ethic committee of the Medical University of Graz (EK Nr 32-052 ex 19/20)

Results:

<table>
<thead>
<tr>
<th>Follow-up ESBL-E positive cases and controls until 6 years (2005-2013)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ESBL</strong></td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>Number</td>
</tr>
<tr>
<td>Death</td>
</tr>
<tr>
<td>Follow-up infants</td>
</tr>
<tr>
<td>Visits</td>
</tr>
<tr>
<td>Hospitalizations</td>
</tr>
<tr>
<td>Rehospitalization days</td>
</tr>
<tr>
<td>Diarrhea</td>
</tr>
<tr>
<td>Gastritis</td>
</tr>
<tr>
<td>Diarrhea-Vomiting</td>
</tr>
<tr>
<td>Appendicitis</td>
</tr>
<tr>
<td>Condition</td>
</tr>
<tr>
<td>----------------------------</td>
</tr>
<tr>
<td>Viral Infections</td>
</tr>
<tr>
<td>Bacterial Infections</td>
</tr>
<tr>
<td>Febrile convulsions</td>
</tr>
<tr>
<td>Asthma</td>
</tr>
<tr>
<td>Illeus</td>
</tr>
<tr>
<td>12</td>
</tr>
<tr>
<td>GERD</td>
</tr>
<tr>
<td>Developmental impairments</td>
</tr>
</tbody>
</table>

Conclusions: ESBL-E positive VLBW infants did not experience more health problems during the first six years of life than matched controls.

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Background: Despite a high coverage of 97–99% for at least three doses of acellular pertussis (aP) vaccination for the last 2 decades in Sweden, pertussis is the least controlled vaccine-preventable disease with a significant burden in infants too young to have received the full infant series. This study estimates vaccine effectiveness (VE) in preschool children after vaccination (2+1 schedule), 2007–2018.

Methods: Reported laboratory confirmed pertussis cases, aged 24–71 months, from 2007 to 2018 with complete information on vaccination status were included. Full vaccination was defined as ≥ three doses of aP vaccine ≥ 15 days before disease onset for cases. Data on pertussis vaccine three-dose coverage was systematically collected from healthcare centres. Only 2- or 3-component DTaP combination vaccines approved by the Swedish Medical Product Agency were used during this period. VE was calculated using the screening method, comparing the proportion of fully vaccinated laboratory confirmed cases (PCV) and vaccination coverage.

Results: For each age group under surveillance from 2007 to 2018, vaccination coverage varied between 98.1–98.3%, while the proportion of fully vaccinated laboratory confirmed cases varied between 57–72%, corresponding to VEs varying between 95–97% (Table).

Table. Total number of pertussis cases, proportion of fully vaccinated cases, vaccination coverage and VE estimates by age group, 2007–2018.

<table>
<thead>
<tr>
<th>Age group</th>
<th>Average annual population</th>
<th>Total cases* (missing data on vaccination status)</th>
<th>Fully vaccinated cases*</th>
<th>PCV**</th>
<th>Vaccination coverage</th>
<th>VE***</th>
</tr>
</thead>
<tbody>
<tr>
<td>months</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>% (95% CI)</td>
<td>% (range)</td>
<td>% (95% CI)</td>
</tr>
<tr>
<td>24–35</td>
<td>114,909</td>
<td>91 (0)</td>
<td>52</td>
<td>57 (47–67)</td>
<td>98.1</td>
<td>97 (93–100)</td>
</tr>
<tr>
<td>36–47</td>
<td>112,862</td>
<td>100 (2)</td>
<td>72</td>
<td>72 (63–81)</td>
<td>98.2</td>
<td>95 (91–100)</td>
</tr>
<tr>
<td>48–59</td>
<td>111,264</td>
<td>96 (1)</td>
<td>63</td>
<td>66 (56–75)</td>
<td>98.3</td>
<td>96 (93–100)</td>
</tr>
<tr>
<td>60–71</td>
<td>108,607</td>
<td>74 (0)</td>
<td>44</td>
<td>59 (48–71)</td>
<td>98.3</td>
<td>97 (93–100)</td>
</tr>
</tbody>
</table>

* Laboratory confirmed pertussis cases
** PCV, proportion of fully vaccinated laboratory confirmed cases
*** VE, vaccine effectiveness
Conclusions: This study indicates high effectiveness of routine aP vaccination in the Swedish national immunization program for the studied age groups. There is, however, still a risk of pertussis for young infants in Sweden before the first vaccination.
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**Background:** Following the introduction of a 2, 4 and 12 month schedule of a group B meningococcal vaccine (4CMenB) into the UK infant immunisation schedule in 2015, there has been a 57% reduction in group B meningococcal (MenB) disease in the immunised 2 year-old cohort. Here we report the serum bactericidal antibody titres (SBA) observed in this cohort following the UK ‘reduced-dose’ schedule.

**Methods:** Blood samples were taken at approximately 2 years of age from children previously enrolled into the Sched3 study, in which they were randomised 1:1 to receive a 2+1 or 1+1 schedule of 13-valent pneumococcal vaccine, and received 4CMenB at 2, 4 and 12 months. Human complement SBA (hSBA) titres against MenB reference strains 5/99 (NadA), NZ98/254 (PorA) and 44/76-SL (fHbp) were determined and compared to those measured post-booster (13 months).

**Results:** Seventy-six children had bloods taken between 21 and 33 months of age. No significant difference in hSBA titres was seen between the PCV schedules. The proportion of overall participants with hSBA titres ≥4 were 26% for NZ98/254, 43.8% for 44/76-SL and 85.9% for 5/99. hSBA Geometric mean titres for NZ98/254 fell from 26.6 post-booster (13 months) to 1.7, for 44/76-SL from 34 to 2.5, and for 5/99 from 1394.8 to 54.2.

**Conclusions:** Despite the observed fall in hSBA titres, the effectiveness of the 4MenC vaccine appears to be sustained with surveillance data suggesting a reduction in meningococcal B disease following the introduction of the schedule. Understanding the significance of these results will require ongoing surveillance for MenB disease, with particular consideration of which strains are causing vaccine failures. Funded by NIHR Policy Research Programme and Gates Foundation.

**Clinical Trial Registration:** Assessment of Post Booster Antibody Responses in UK Infants Given a Reduced Priming Schedule of Meningococcal Serogroup B and 13 Valent Pneumococcal Conjugate Vaccines ClinicalTrials.gov identifier (NCT number): NCT02482636
SEVERE CLINICAL SPECTRUM WITH HIGH MORTALITY COVID-19 IN PEDIATRIC PATIENTS WITH MULTISYSTEM INFLAMMATORY SYNDROME (MIS-C)

M.F. Badue Pereira¹, N. Litvinov¹, T. Fink¹, S. Farhat², A. Eisencraft², M.A. Gibelli³, W. De Carvalho⁴, V. Fernandes¹, K. Galleti⁵, A. Fante⁵, M.F. Fonseca⁶, A. Watanabi⁷, C. Sanson Yoshino De Paula¹, G. Palandi¹, C. Silva⁸, H.H. Sousa Marques¹
¹Instituto da Criança Hospital das Clínicas da Universidade de São Paulo, Department Of Infectious Diseases, São Paulo, Brazil, ²Instituto da Criança, Pediatric Emergency, SAO PAULO, Brazil, ³Instituto da Criança, Neonatology, SAO PAULO, Brazil, ⁴Instituto da Criança, Hospital das Clínicas da Universidade de São Paulo, Intensive Care/ Neonatology, SAO PAULO, Brazil, ⁵Instituto da Criança, Hospital das Clínicas da Universidade de São Paulo, Pediatric Intensive Care, SAO PAULO, Brazil, ⁶Instituto da Criança, Hospital das Clínicas da Universidade de São Paulo, Pediatric Oncology, SAO PAULO, Brazil, ⁷Instituto da Criança, Hospital das Clínicas da Universidade de São Paulo, Pediatric Nephrology, SAO PAULO, Brazil, ⁸Instituto da Criança, Hospital das Clínicas da Universidade de São Paulo, Adolescent And Pediatric Rheumatology, SAO PAULO, Brazil

Background: Until June/2020, more than 9 million subjects have been infected with the novel coronavirus disease 2019. This emerging infectious disease has been described mainly in adult patients, and laboratory-confirmed pediatric COVID-19 were rarely reported. A systematic review revealed that in contrast to adults, the vast majority of infected children and adolescents with SARS-CoV-2 had a milder disease, and deaths were rarely described. Recently, a severe spectrum of this disease, called multisystem inflammatory syndrome, was globally reported. However, an evaluation comparing patients with and without it, mostly including pediatric preexisting chronic and immunocompromising diseases, was not carried-out.

Methods: A cross-sectional study selected n=471 samples for SARS-CoV-2 suspicious, collected for n=371 patients(age<18 years). Study group was n=66/371(18%) laboratory-confirmed pediatric COVID-19 patients: positive real time RT-PCR for SARS-CoV-2 in n=64(97%) and serology in n=2(3%). MIS-C was diagnosed according to Center of Disease Control criteria.

Results: MIS-C was diagnosed in 6/66. The frequencies of gastrointestinal symptoms (67%vs.22%,p=0.034); SARS(67%vs.13%,p=0.008); hypoxemia(83%vs.23%,p=0.006) and hypotension(50%vs.3%,p=0.004) were higher in patients with MIS-C. The frequencies of CRP>50 mg/L(83%vs.25%,p=0.007) and D-dimer>1000 ng/mL(100%vs.40%,p=0.007) were higher in MIS-C, as well as median of D-dimer, troponin and ferritin levels(p<0.05). The frequencies of pediatric intensive care unit admission(100%vs.60%,p=0.003), mechanical ventilation(83%vs.7%,p<0.001), vasoactive agents(83%vs.3%,p<0.001), shock(83%vs.5%,p<0.001), cardiac abnormalities(100%vs.2%,p<0.001) and death(67%vs.3%,p<0.001) were also higher in MIS-C; likewise oxygen therapy(100%vs.33%,p=0.003), intravenous immunoglobulin(67%vs.2%,p<0.001), aspirin(50%vs.0%,p<0.001) and acute renal replacement therapy(50%vs.2%,p=0.002). Logistic regression analysis showed that MIS-C were significantly associated with gastrointestinal manifestations[OR=10.98;95%CI=1.20-100.86;p=0.034] and hypoxemia[OR=16.85;95%CI=1.34-211.80;p=0.029]. Univariate analysis showed an association between MIS-C and death[OR=58.00;95%CI=6.39-526.79;p<0.0001].
## Conclusions

Laboratory-confirmed pediatric COVID-19 patients with MIS-C had a severe clinical spectrum with high mortality rate. This emphasizes the importance of MIS-C investigating for pediatric COVID-19 patients presenting with gastrointestinal involvement and hypoxemia.
THE IMPACT OF COVID-19 INFECTIONS IN PREGNANCY: THE BELGIAN EXPERIENCE

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¹University of Antwerp, Centre For The Evaluation Of Vaccination, Vaccine & Infectious Diseases Institute, Wilrijk, Belgium, ²University of Antwerp, Pediatrics, Wilrijk, Belgium

Background: In view of infectious diseases, pregnant women are considered as immunologically different from the general population. Scientific evidence on the impact of COVID-19 infections in pregnant women is limited. Therefore, researchers and health care workers do have concerns on the possible enhanced risk for severe disease in this vulnerable population.

Methods: Pregnant women in the Belgian population were surveyed through an online questionnaire between April 3th - May 15th, 2020 to monitor possible clinical consequences of suspected and confirmed COVID-19 cases in pregnancy.

Results: In total, 4363 pregnant women were approached of which 3344 met the inclusion criteria and were included in this analysis. In this cohort, 816 (24.40%) women experienced possible COVID-19-related symptoms during their pregnancy of which 100 women recently had close contact with a clinically suspected or laboratory confirmed SARS-CoV-2 patient. In those 816 women who experienced COVID-19 related symptoms, following adverse events were reported during pregnancy: premature contractions (N=10; 1.22%), IUGR (N=1; 0.12%) and spontaneous abortion (N=1; 0.12%). These rates are comparable to those of pregnant women who did not experience COVID-19 related symptoms. From the clinically suspected COVID-19 cases (N=816), only 52 women were subjected to testing of whom 12 tested positive. In the entire study population (N=3344), 116 women were tested for COVID-19, 15 tested positive.

Conclusions: Prevalence of laboratory-confirmed SARS-Cov-2 infections in this study is low. However, during the study period only limited testing was available, which might have resulted in underreporting of laboratory-confirmed cases. In this study, pregnant women will be further followed during their entire pregnancy up till one year postpartum to monitor possible negative outcomes of COVID-19 on the pregnancy outcome and on the offspring.

Clinical Trial Registration: Clinicaltrials.gov registration in progress
CHARACTERISTICS OF FAMILY CLUSTERS OF COVID-19, INCLUDING CHILDREN: AN ITALIAN EXPERIENCE

P. Costenaro¹, C. Di Chiara¹, F. Bonfante², C. Cosma³, S. Cozzani⁴, A. Bortolami², R. Petrara⁵, M. Plebani³, A. De Rossi⁵, D. Donà¹, C. Giaquinto¹

¹Department for Women's and Children's Health, University of Padua, Division Of Pediatric Infectious Diseases, Padova, Italy, ²Istituto Zooprofilattico Sperimentale delle Venezie (IZSVe), Department Of Comparative Biomedical Sciences, Virology Laboratory Legnaro (pd), Italy, Legnaro (PD), Italy, ³University of Padua, Medicine Of Laboratory, Padova, Italy, ⁴ULSS3 Serenissima, Paediatric General Practition, Mestre (VE), Italy, ⁵Veneto Institute of Oncology IOV – IRCCS, Padova, Italy

Background: SARS-CoV-2 infection has been spreading, worldwide. This study analyze characteristics and impact of Coronavirus disease 2019 (COVID-19) in family clusters.

Methods: A prospective observational study started in Veneto Region (Italy), in April 2020. Families including children (0-14 years) were enrolled if one or more members had COVID-19, confirmed by positive SARS-CoV-2 molecular assay at nasopharyngeal (NP) swab, for clinical follow-up and detection of serum SARS-CoV-2 IgG/IgM and plaque reduction neutralization test (PRNT). Chi-square and one-way ANOVA were used for either categorical or quantitative variables; simple linear regression assessed relationship between PRNT and age. P-value <0.01 was considered statistically significant.

Results: Forty-two family clusters analyzed included 69 children (M 40, F 29) with mean age 7.38 years (SD 5.79) and 83 parents (42 F, 41 M) aged 41.16 years (SD 8.33). 31(45%) children and 55(66%) parents had confirmed COVID-19. Among 28 symptomatic children with COVID-19, the majority had fever (n=21), diarrhea (6), cough (5), asthenia (5); 6 (20%) were admitted to Hospital and all recovered. Table 1 reports characteristics of children. Positive SARS-CoV-2 serology (IgG>1.100 kAU/L) was detected in 91.3% of paediatric COVID-19, 61.5 days (IQR 44-71) after 1st NP swab. In addition, 46.2% of children with negative swab had positive serology, 59.5 days (IQR 35-70.5) after 1st swab. Median IgG was 5.427 (IQR 1.702-11.790) in children with COVID-19 and 0.3665 (IQR 0.027-5.288) in those with negative swab; parent’s median IgG was 1.108 (IQR 0.14-5.62). Median PRNT log of children (n=31) and adults (n=34) were 5 (IQR 4-6) and 4 (IQR 3-4), respectively. At linear regression, younger age was correlated with higher PRNT log (R²=0.288, p-value<0.0001).

Conclusions: Children of COVID-19 family clusters have mild disease, however they may develop high levels of SARS-CoV-2 antibodies.

Clinical Trial Registration: Our study is not a controlled clinical trial, therefore it was not registered at ClinicalTrials.gov.
Background: Community-acquired pneumonia (CAP) is a common cause of pediatric hospitalization. Despite some studies performed during the last years, knowledge about etiology is still scarce. This study aimed to describe the etiology of a cohort of hospitalized children and adolescents with CAP in Spain, including patients with associated PPE. We also aimed to find clinical, analytical, and radiographic predictors of the etiology.

Methods: Observational, multi-center, prospective study from April 2012 to May 2019 performed in 15 centers in three regions of Spain. Etiology of CAP was studied through an extensive microbiological workup. Baseline, socio-demographic, clinical, radiographic and analytical variables were described and analyzed to determine factors associated with the different etiologies.

Results: 495 patients were enrolled. 480/495 (97%) patients received antibiotics. At least one pathogen was identified in 262/495 (52.9%) [viruses 155/262 (59.2%), atypical bacteria (AB) 84/262 (32.1%), typical bacteria (TyB) 40/262 (15.3%)]. 391/495 (79%) had radiograph with consolidation [viruses 89/138 (65.4%), AB 74/84 (88.1%), TyB 40/40 (100%)]. Paraneumonic pleural effusion was found in 112/495
(22.6%) patients; 61/112 (54.5%) with a likely causative pathogen [viruses 12/61 (19.7%), AB 23/61 (37.7%), TyB 26/61 (42.6%)]. Several significant distinctive data were found according the different etiologies (Figure).

**Conclusions:** Viruses and AB are the main cause of pediatric CAP in Spain. Viruses and AB can cause PPE. Children and adolescents hospitalized with CAP do not always need antibiotics. The need for antibiotic treatment in children admitted with CAP has to be individualized.
UNRAVELING THE EFFECT OF MATERNAL PERTUSSIS IMMUNIZATION ON HUMORAL IMMUNE RESPONSES IN PRETERM BORN INFANTS

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¹University of Antwerp, Centre For The Evaluation Of Vaccination, Vaccine & Infectious Diseases Institute, Wilrijk, Belgium, ²University of Antwerp, Centre For Health Economic Research And Modelling Infectious Diseases, Vaccine & Infectious Diseases Institute, Wilrijk, Belgium, ³University Hospital Antwerp, Neonatology, Edegem, Belgium

Background: Few data are available on the effect of maternal immunization on immune responses in preterm infants. We report on maternal antibody transfer and, for the first time, on pertussis-specific humoral immune responses to a DTaP-IPV-HB-PRP~T vaccine in term and preterm infants following this strategy.

Methods: In a prospective cohort study, women delivering at term or prematurely were either vaccinated with a Tdap vaccine (Boostrix) during pregnancy or not vaccinated for at least 5 years. Cord and maternal blood were collected at delivery. Infants were vaccinated with a hexavalent vaccine (Hexyon) and bled before and one month after primary (8-12-16 weeks) and before and one month after booster vaccination (13 or 15 months). Immunoglobulin G antibodies against Pertussis Toxin (PT) and Filamentous Hemagglutinin (FHA) were measured using a multiplexed assay developed by Sanofi Pasteur.

Results: At delivery, higher titers of maternal antibodies were measured in term versus preterm infants (PT/FHA: p<0.001), yet preterms from Tdap-vaccinated women had higher GMCs compared to preterms from unvaccinated women (PT/FHA: p<0.001). In infants from Tdap-vaccinated women, comparable GMCs were noted between term and preterm infants after priming. After boosting, higher GMCs were observed in term versus preterm infants (PT p<0.003; FHA p<0.002). In the absence of maternal immunization, higher GMCs for FHA were seen after priming in term versus preterm infants (p=0.038), yet not for PT. After boosting, no differences between term and preterm infants were detected. No blunting was observed in the preterm cohorts probably due to reduced maternal antibody titers at birth.
Conclusions: Preterm infants benefited from maternal immunization. Prematurity did not influence the pertussis-specific primary immune response in the presence of maternal antibodies, but was associated with lower booster immune responses.

Clinical Trial Registration: NCT02511327
ROLE OF PNEUMOCOCCAL PROTEINS SP1500 AND SP0785 IN COLONIZATION, VIRULENCE AND IMMUNITY

L. Moujaes, F. Zhang, R. Malley, Y. Lu
Boston Children's Hospital, Infectious Diseases, Boston, United States of America

Background: There is a need for a serotype-independent pneumococcal vaccine to circumvent coverage limitations of conjugate vaccines. We had previously identified several proteins that conferred protection against pneumococcal colonization. We wished to further examine the protective capacity of two of these proteins, SP1500 and SP0785, in different models of pneumococcal disease and colonization.

Methods: Double knockout mutants were generated in a type 3 pneumococcal background, and the virulence of these mutants was compared to their re-integration counterparts in two invasive disease models (sepsis and pneumonia). We genetically fused the two proteins SP1500 and SP0785, then purified the fusion from E. coli. Mice were immunized intranasally with the fusion protein and cholera toxin and then challenged intranasally with serotype 6B of pneumococcus in a colonization model. Rabbit sera obtained after immunization with the fusion of SP1500-SP0785 was tested in a modified opsonophagocytic killing assay.

Results: The deletion of the two genes encoding for SP1500 and SP0785 in WU-2 (a type 3 pneumococcus) resulted in significant reduction in virulence in the two mouse disease models. Intranasal immunization with the fusion of SP1500-SP0785 adjuvanted with cholera toxin protected mice against colonization by type 6B pneumococcus. Rabbit antibody directed against the fusion protein had in vitro killing activity against 3 different serotypes of pneumococcus (6B, 23F and 35B).

Conclusions: The deletion of sp1500 and sp0785 results in a significant reduction in virulence of a type 3 pneumococcus. The fusion of the two proteins confers protection against colonization in a mouse model and generates opsonic antibodies that assist in the killing of pneumococcal strains. This fusion protein should be further evaluated as a serotype-independent pneumococcal vaccine candidate.

Clinical Trial Registration: Clinical trial: N/A
MULTI-INFLAMMATORY SYNDROME IN CHILDREN RELATED TO SARS-COV-2 IN SPAIN


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Background: Clusters of children with multisystem inflammatory syndrome (MIS-C) linked to SARS-CoV-2 infection have been described in Europe. The syndrome shares features of Kawasaki disease, toxic shock syndrome and macrophage activation syndrome. The specific link with SARS-CoV-2 remains unclear. We aim to describe the epidemiological and clinical features of children with MIS-C in Spain.

Methods: Case series of children (0-18 years old) with MIS-C associated with SARS-CoV-2 enrolled from March 1st to June 1st 2020 in the Epidemiological Study of COVID-19 in Children (EPICO-AEP), a multicentre (49 hospitals) prospective registry cohort of children with SARS-CoV-2 infection in Spain.

Results: 31/252 (12%) hospitalized children were diagnosed with MIS-C and/or Kawasaki disease. All but one patient (97%) had microbiological or serological evidence of SARS-CoV-2 infection: 17/31 (55%) positive RT-PCR, 10/17 (59%) positive IgM and 19/21 (90%) positive IgG. 13/31 children (45%) fulfilled complete or incomplete Kawasaki disease criteria. Table 1 summarizes the clinical, microbiological and laboratory features of the children included. One patient (3%) did not fulfilled MIS-C WHO criteria: a 12-month old girl with cardiogenic shock, chronic oral corticosteroid therapy, positive RT-PCR and human metapneumovirus coinfection but no inflammatory markers.
Conclusions: Our series support the impression that not only a temporal association exists between MIS-C and SARS-CoV-2, but also a microbiological association. SARS-CoV-2 could be a trigger for a delayed cytokine storm and inflammatory disease, with potential severe consequences. Paediatricians should be aware of this condition in children during COVID-19 epidemics. More studies are necessary to clarify the physiopathology of this syndrome.
BACKGROUND: Objectives: Characterisation of the clinical features of patients under 19 years admitted to hospital with laboratory-confirmed SARS-CoV-2 infection in the UK and factors associated with admission to critical care and development of multisystem inflammatory syndrome in children and adolescents temporarily related to covid-19 (MIS-C).

METHODS: Prospective multicentre observational cohort study across 260 acute care hospitals in England, Wales, and Scotland between 17th January and 5th June 2020, with a minimum follow-up time of two weeks (to 19th June 2020). 451 children and young people <19 years old admitted to 116 hospitals and enrolled into the International Severe Acute Respiratory and emergency Infections Consortium (ISARIC) WHO Clinical Characterisation Protocol UK study with laboratory-confirmed SARS-CoV-2. Complete data were not available for all variables, hence denominators differ between analyses. Fisher's exact test, Kruskal-Wallis and Jaccard similarity coefficient.
Results: A muco-enteric symptom cluster closely mirrored the WHO MIS-C criteria (Figure). 12% of children (36/303) met the WHO MIS-C criteria. They were older, (median 10.8 years vs 2.0, p<0.001) and more likely to be of non-White ethnicity (70%(23/33) vs 43%(101/237), p=0.005). Children with MIS-C were more likely to be admitted to critical care (61%(22/36) vs 15%(40/267, p<0.001), present with headache (45%(13/29) vs 11%(19/171), p<0.001), myalgia (39%(11/28) vs 7%(12/170), p<0.001) and sore throat (37%(10/27) vs (13%(24/183), p = 0.004) and have a platelet count <150 x10^9/L (30%(10/33) vs 10%(24/232), p=0.004).

Conclusions: Our data confirms less severe covid-19 in children and young people than in adults and we provide evidence for refining the WHO MIS-C case definition. The muco-enteric symptom cluster suggests MIS-C may be the severe end of a spectrum of disease.
LATE BREAKING ORAL
LIVE - LATE BREAKING ORAL PRESENTATION 3: COVID-19 LATE BREAKERS
10-28-2020 9:30 AM - 10:30 AM

THE SPANISH COHORT OF COVID-19 HOSPITALIZED CHILDREN


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**Background:** Spain is one of the most affected countries during COVID-19 pandemic. The spectrum and severity of the disease in children is still unclear.

**Methods:** The Epidemiological study of COVID-19 in Children (EPICO) is a multicenter prospective national study involving 50 hospitals aiming to shape the COVID-19 disease in Spanish children.

**Results:** By July 1st, 351 children under 18 years were diagnosed of COVID-19 and 291 (83%) of them were admitted: 213 (73%) due to relevant COVID-19 disease, and others due to other reasons (13%) or isolation (15%). PCR was positive in 93% and serology for SARS-CoV-2 IgM+ 9% and IgG+ 23%; 160/291 (55%) were male, 52% had contact with a known COVID-19 adult patient, and 44% had comorbidities. Four (1%) patients died, all with serious comorbidities. Coinfections were detected in 54/291 (19%) patients. Diagnosis in patients admitted with COVID-19 were: pneumonia 100/291 (34%); upper respiratory tract infection 41/291 (14%); inflammatory multisystemic syndrome related with SARS-CoV-2 (PIMS-TS) 36/291 (12%); fever without a source 30/291 (10%); gastrointestinal symptoms 25/291 (9%); bronchiolitis, bronchitis or asthma flare, 10/291 (3%). 32% (93/291) of patients needed O2, 19% (54/291) of patients were admitted in the PICU, and 7% (20/291) were mechanically ventilated. Complications (93/291, 32%) were cardiologic (10%, only 1% coronary abnormalities), pleural effusion (5%), sepsis (5%), renal failure (4%), and pneumothorax (1%). In the X-ray at admission of 252 patients, 22% had consolidation and 33% had infiltrates. Risk factor for severe outcome (PICU or high flow) included pneumonia, PIMS-TS features, higher age, comorbidities, lower Hb, lymphopenia, inflammatory markers, and high urea. Time to PCR negativization in 108 patients with follow up was 13.5 days.

**Conclusions:** COVID-19 in children has a wide range of features and severity. The Spanish cohort shows a significant proportion of seriously ill patients.

**Clinical Trial Registration:** Not apply.
Background: School closures have been important in Covid-19 containment strategies in most countries worldwide, despite a lack of knowledge on outbreak characteristics. A school SARS-CoV-2 outbreak affecting 52 people from a large school community in Santiago, Chile was identified (March 12), ten days after the first country case. We assessed the magnitude of the outbreak and the role students and staff played using a self-administered antibody detection test and survey.

Methods: The school was closed on March 13, and the entire community was placed under quarantine. After school and ethical approval, we implemented a home delivery-self-administered IgG/IgM antibody test and survey to a classroom stratified sample of students and all staff from May 4-19. We aimed to determine overall seroprevalence rates by age group, reported symptoms, contact exposure and to explore the dynamics of transmission.

Results: Antibody positivity rates were 9.9% (95%CI: 8.2-11.8) for 1,009 students and 16.6% (95%CI: 12.1-21.9) for 235 staff. Among students, positivity was associated with younger age (P=0.010), lower grade level (P=0.045), prior RT-PCR positivity (P=0.031), and history of contact with a confirmed case (P<0.001). Among staff, positivity was higher in teachers (p=0.012) and in those previously RT-PCR positive (P<0.001). Excluding RT-PCR positive individuals, antibody positivity was associated with fever in adults and children (P=0.022; P=0.002), abdominal pain in children (P=0.001), and chest pain in adults (P=0.016). Within antibody positive individuals, 40% of students and 18% of staff reported no symptoms (P<0.014).

Conclusions: Teachers were more affected during the outbreak and younger children were at higher infection risk, most likely due to transmission from teachers and/or adult household members. Self-administered antibody testing, supervised remotely, proved to be a suitable and rapid tool. Our study provides useful information for school re-openings.

Clinical Trial Registration: This is a Clinical Study, with no direct intervention
FEVER WITHOUT SOURCE (FWS) AS THE FIRST MANIFESTATION OF SARS-COV-2 INFECTION IN INFANTS UNDER 90 DAYS OF LIFE.

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Background: This study aims to know the clinical characteristics of infants under 90 days of age with fever without source (FWS) as the first manifestation of SARS-CoV-2 infection.

Methods: This is a case series of infants with fever without source (FWS) associated with SARS-CoV-2 infection registered in the EPICO-AEP database, a multicenter (49 hospitals) prospective cohort of children with SARS-CoV-2 infection in Spain. Results: By June 26th, 336 children with COVID-19 had been included. A total of 67/336(20%) were under 3 months of age and 27/67(40%) presented with FWS as the first manifestation. Twenty-four (89%) were admitted to the hospital. Blood cultures were performed in 24/27(89%) children and were negative in all but one child with Swachmann-Diamond Syndrome, severe neutropenia, S.mitis bacteremia and E.cloacae in urine culture. Otherwise, urine culture was performed in 26/27(97%) and was negative in all, except in 2 patients. Cerebrospinal fluid cultures were negative when performed (0/6). Two children showed bacterial coinfection (2/27;7.4%). Median values of C-reactive protein (CRP) and procalcitonin at admission were 1.9mg/L(0.6-5) and 0.12ng/mL(0.1-0.15), respectively (figure). Six of 27(22%) children required oxygen therapy by nasal cannula. One child was admitted to the PICU because of apnea episodes. No patient required mechanical ventilation and all survived.
Conclusions: FWS is a common manifestation of SARS-CoV-2 infection in infants under 3 months of age. Children with SARS-CoV-2 and no bacterial coinfection showed low CRP and PCT values, so standardized markers to rule out bacterial infection seem to remain useful in this population.
THE IMPACT OF THE COVID-19 PANDEMIC ON CHILDREN'S HEALTH

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Background: The Covid-19 pandemic poses unprecedented challenges for healthcare and has led to alterations in the medical care utilization patterns by the pediatric population. Concerns have been raised regarding the consequences for non-Covid patients due to decreased access to medical care. We aimed to describe the impact of the pandemic on children’s health, wellbeing, and access to medical care.

Methods: We conducted a retrospective cross-sectional study through an anonymous online survey via social networks. We accepted responses from parents with children and adolescents living in Portugal. The survey was organized into four sections - sociodemographic characterization; pandemic-related information, including children belonging to a risk group for Covid-19 and parental degree of concern; information regarding the utilization of healthcare services during the pandemic; and assessment of the consequences of Covid-19 on the child’s health and wellbeing.

Results: We obtained responses to the survey regarding 19,745 children. Children belonging to a risk group for Covid-19 (28.1%) did not attend an emergency department in significantly higher rates than other children but showed significantly higher rates of invasive interventions and hospitalization. 54.2% of the scheduled medical appointments were postponed by health institutions and 21.6% of planned vaccinations were missed. Parents expressed concerns regarding psychological, social, and physical consequences for their children.

Conclusions: In summary, the impact of the Covid-19 pandemic on children’s health includes decreased access to care as well as relevant psychological, social and physical consequences that should not be overlooked. In view of the uncertain future course of the pandemic, further studies are necessary to fully comprehend the outcomes of the current health emergency. Defining strategies regarding the urge to vaccinate children and not postpone urgent evaluations should be a public health priority to minimize negative outcomes in the short and long-term.
HOSPITALIZATIONS FOR VACCINE-PREVENTABLE INFECTIONS AMONG ALLOGENEIC AND AUTOLOGOUS PEDIATRIC HEMATOPOIETIC CELL TRANSPLANT RECIPIENTS

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Background: Hematopoietic cell transplant (HCT) recipients are at risk for vaccine preventable infections (VPIs) with poor outcomes compared with the general population. Given the paucity of contemporary pediatric-specific data, we performed this study to evaluate the epidemiology of VPIs in children and young adults in the first 5 years post-HCT and to determine risk factors for VPI hospitalizations comparing HCT recipients with and without VPIs.

Methods: We used the Pediatric Health Information System (PHIS) database to identify pediatric HCT recipients with a first hospitalization for VPI (defined by ICD-9/ICD-10) within 5 yrs post-HCT, between 1/1/10 -12/31/18, at 45 US PHIS hospitals. Prevalence of overall VPI and per infection were determined at initial HCT admission, HCT discharge-D100, D101-D180, 6-12 months, 1-2 years, and 2-5 years. Risk factors for VPI hospitalizations were analyzed using multivariate logistic regression.

Results: Among the 9,591 unique HCT recipients identified (6,602, 69% allogeneic and 2,989, 31% autologous), 684 were hospitalized with VPI within 5 years post-HCT, for an overall prevalence of 7.1%. VPI hospitalizations occurred most frequently in the first 6-12 months post-HCT (Figure 1). Influenza (4.05%), varicella (1.21%) and pneumococcal disease (1.08%) were the most common infections. Younger age, primary immune deficiency (PID), and GVHD were independent risk factors for VPIs during the initial HCT admission; on subsequent admissions, allogeneic graft source was an independent predictor associated with VPIs.
Conclusions: VPI hospitalizations occurred in 7.1% of children in the first 5 years after HCT, most frequently in the first 6-12 months. Young age, PID and GVHD were predictors for VPIs during the initial HCT hospitalization, whereas receipt of an allogeneic-HCT was a risk factor for subsequent VPI hospitalizations. Continued efforts to improve vaccination early post-HCT in these children are warranted.
Background: The Gram-negative opportunistic bacterium *Stenotrophomonas maltophilia* has emerged as an important nosocomial pathogen exhibiting intrinsic resistance to many currently available broad-spectrum antibiotics. Limited data exist on its clinical relevance in pediatric cancer patients. In a retrospective cohort study, we analyzed the epidemiology and clinical features of 33 patients with *S. maltophilia* colonization and/or infection at our center of Pediatric Hematology and Oncology over a 10-year period.

Methods: 23 patients had oncological (70% acute leukemias), and 10 patients hematological and immune disorders. 17 patients had received an allogeneic hematopoietic stem cell transplantation (HSCT). *S. maltophilia* primarily colonized the gastrointestinal and respiratory tract in 17 patients each. Nine patients (6 post HSCT) developed *S. maltophilia* infection including bacteremia, central venous catheter associated infection, and/or tissue infection, with previous colonization in 6 patients.

Results: Patients commonly presented with fever, respiratory symptoms, and a defective skin barrier, increased levels of C-reactive protein (17mg/dL) and procalcitonin (101ng/mL), but regular white blood cell and absolute neutrophil counts (6x10³/µL and 5.8x10³/µL, respectively). Microbial co-colonizations and co-infections were found in 85% with abundance of *Staphylococci, Pseudomonas aeruginosa,* and *Candida spp.,* leading to bacteremia and candidemia in 9 and 2 cases, respectively.

Conclusions: *S. maltophilia* isolates showed highest susceptibility to tigecycline (90%), levofloxacin (88%), and trimethoprim/sulfamethoxazole (84%), but enhanced phenotypic resistances to colistin (63%) and ciprofloxacin (61%). Whole-genome sequencing-based typing of selected blood culture isolates did not result in genetic relationship among the detected genotypes. After a median follow-up time of 500 days, 21 patients were alive while 12 were deceased. In patients with *S. maltophilia* infection, infection-related mortality was 55% (n=5; 3 of 6 patients post allogeneic HSCT). *S. maltophilia* infection demands early identification and appropriate antimicrobial therapy to prevent infection-related mortality.
INCREASED INCIDENCE OF CLOSTRIDIODES DIFFICILE INFECTION AMONG PEDIATRIC ONCOLOGY PATIENTS: EVALUATING RISK FACTORS FOR INFECTION AND OUTCOMES

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Background: Clostridioides difficile infection (CDI) incidence in children has been increasing, ranging from 2-12 per 1,000 patients. Pediatric oncology patients, frequently immunosuppressed, exposed to medications known to increase risk for CDI, and hospitalized, are expected to be at substantial risk for infection and complications. Certain C. difficile ribotypes have been associated with more severe infection in adults; such an association has not been described in children.

Methods: To study CDI epidemiology among pediatric oncology patients, we conducted a retrospective chart review of patients aged 1-18 years treated at The University of Texas M. D. Anderson Children’s Cancer Center in Houston, Texas, USA during 2000 to 2017. We sought to identify risk factors for CDI and complications. We used fluorescent based PCR ribotyping to identify C. difficile ribotypes causing disease at our institution.

Results: Two hundred and seven CDI cases were identified during the study period. CDI incidence in our pediatric oncology population was 37 per 1,000 patients. Incidence was highest in patients with acute myeloid leukemia, neuroblastoma and desmoplastic small round cell tumor, (105, 66, and 111 per 1,000 patients, respectively, p< 0.001). Fever, leukocytosis, neutropenia, elevated creatinine, abdominal radiation, and exposure to fluoroquinolones during CDI treatment were associated with complications. Patients with severe CDI experienced increased mortality (p=0.02). Ribotypes associated with severe infection were few and did not correlate with mortality.

Conclusions: This is the largest study of CDI on pediatric oncology done to date. The study identifies increased rates of CDI and oncologic specific risk factors that predict increased risk of infection and poor outcomes. As CDI treatment guidelines are developed for this population, this data will be of use for risk stratification of patients in need of early, aggressive treatment.
Background: Almost 3 million neonatal deaths occurred yearly, mostly in low-income countries, and around a quarter of which are due to severe infections. In these settings, data on the burden of neonatal infection is scarce and there is a lack of data regarding infections occurring in the community, which may differ from cases admitted to the hospital. Also, the role of the different factors involved in the transmission of bacteria remains unclear, particularly mother-to-child. Data are needed for these countries to prioritize interventions to decrease neonatal infections.

Methods: We conducted a prospective cohort of 2500 newborns in Madagascar, Cambodia and Senegal, both in rural and urban areas. Newborns were enrolled at birth at the community level and were actively followed-up. Data on clinical symptoms and all results of biological and bacteriological samples taken were collected. Survival analysis were performed to identify risk factors associated with neonatal infections.

Results: The global incidence of community-acquired neonatal infections was 35.8 cases per 1,000 live births [95% CI, 25.4-50.8], with 75% during the first week of life. The most common bacteria isolated were gram-negative (70%). Almost two-thirds of the pathogens isolated were resistant to current WHO-recommended treatment for neonatal sepsis. Prevalence of extended-spectrum beta-lactamase producing Enterobacteriaceae and *agalactiae streptococcus* carriage among pregnant women were heterogeneous between the different countries and ranged from 19% to 78% and from 5% to 14%, respectively. Risk factors for neonatal infections were identified for each country.

Conclusions: We showed a high incidence of neonatal infections in the community and highlighted that current recommended treatment for neonatal sepsis is no longer adapted. These results should help the implementation of interventions to improve the prevention, early diagnosis, and case management of neonatal infections in low-income countries.

Clinical Trial Registration: NCT02074865
IDENTIFYING EOS CASES USING THE EOS CALCULATOR; PRELIMINARY RESULTS OF AN IPD META-ANALYSIS

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Background: The early onset sepsis calculator (EOS calculator) is a new strategy to allocate empiric antibiotics in newborns. Implementation of the EOS calculator is associated with remarkable reduction in unnecessary antibiotics. Uncertainty remains about its sensitivity to identify EOS cases. The aim of this individual patient data meta-analysis is to provide potential users of the EOS calculator with a representative analysis of this sensitivity.

Methods: A systematic search of EOS calculator literature in the Cochrane, Embase, and PubMed/MEDLINE databases and major pediatric conferences was performed. From studies evaluating the EOS calculator that include one or more culture-confirmed EOS cases, we collected individual patient data and recalculated EOS risk and recommendations using the EOS calculator in a consistent way.

Results: After removing duplicates, we screened 498 search results. We selected eligible studies evaluating EOS cases prospectively or retrospectively with the EOS calculator. For preliminary analysis of 18 studies resembling representative birth cohorts, we obtained individual patient data from 125 culture-proven EOS cases, from a total of >285,000 births. The EOS calculator assigned immediate treatment to 59 cases (47%). Enhanced monitoring for 24 hours (± blood culture) without immediate treatment was recommended for 19 (15%) cases. Routine vital signs were recommended for 47 (38%) cases; all well-appearing infants with low risk estimates. Most cases (58/66, 88%) not treated immediately after birth were recognised because of development of signs of illness within 24 hours.

Conclusions: The EOS calculator algorithm allocates immediate empiric antibiotics or enhanced observation to around 2/3 of confirmed EOS cases, but a significant proportion may be classified as low risk. Clinical vigilance for at least 24 hours remains crucial, even for low-risk infants.

Systematic Review Registration: Update and extension of registered systematic review, registered in PROSPERO (CRD42018116188).
COMPARING PRESCHOOL DTAP-IPV BOOSTER RESPONSES IN CHILDREN WHOSE MOTHERS WERE RANDOMISED TO ONE OF TWO PERTUSSIS-CONTAINING VACCINES OR NO PERTUSSIS-CONTAINING VACCINE IN PREGNANCY

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Background: An antenatal pertussis vaccination programme was introduced in 2012 in the UK following a national outbreak of pertussis. Two DTaP-IPV vaccines were recommended; REPEVAX® (2012-2014) and BOOSTRIX® (2014 onwards). Following antenatal vaccination, a lower antibody response to primary immunisation was shown in infants, known as blunting, but the longer-term effects of this have not been documented in the UK where the first DTAP-IPV booster is given pre-school at the age of 40 months. The study aims to compare antigen-specific IgG geometric mean concentrations (GMCs) before and after the preschool booster in children whose mothers did or did not receive a pertussis-containing antenatal vaccine.

Methods: This was a phase IV extension study, funded by the NIHR policy research programme, comparing vaccine responses in children receiving the preschool booster (REPEVAX®), whose mothers were randomised to one of two pertussis-containing antenatal vaccines (BOOSTRIX® or REPEVAX®), or no pertussis-containing antenatal vaccine (control). Blood samples were obtained prior to and 1 month after the preschool booster. Pre- and post-vaccination IgG GMCs of anti-pertussis toxin (PT), anti-filamentous haemagglutinin (FHA), anti-fimbriae 2 & 3 (FIM), anti-diphtheria and anti-tetanus toxoid were compared.

Results: 64 children were recruited; 26, 22 and 16 in the BOOSTRIX, REPEVAX and control groups respectively. The difference in IgG GMCs pre- and post-vaccination between the vaccinated groups was not statistically significant. The difference in IgG GMCs between the vaccinated and control groups was only statistically significant for anti-PT in the BOOSTRIX group pre-vaccination (Table 1).
Conclusions: To our knowledge, this is the first study to explore the influence of antenatal pertussis vaccination on children’s antibody response beyond 2 years of age. The impact of blunting post-primary immunisation can persist until preschool age, although the clinical significance remains unclear.

Clinical Trial Registration: Clinical trial registration: ClinicalTrials.gov Identifier NCT03578120
A MESSENGER RNA (mRNA) VACCINE AGAINST CYTOMEGALOVIRUS (CMV) INFECTION: PHASE 1 INTERIM DATA

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Background: A safe and effective vaccine against cytomegalovirus (CMV) infection is a high priority in the effort to prevent congenital CMV. We present interim safety and immunogenicity data from a Phase 1 trial of mRNA-1647, a mRNA-based vaccine encoding CMV pentamer complex (PC) and glycoprotein B (gB) antigens.

Methods: This Phase 1, first-in-human, randomized, placebo-controlled, dose-ranging study is assessing the safety and immunogenicity of mRNA-1647 administered on a 0, 2, 6-month schedule in 154 CMV-seronegative and CMV-seropositive healthy adults aged 18-49. Safety and immunogenicity through 1 month post-third vaccination in 30, 90, and 180µg treatment groups and through 1 month post-second vaccination in the 300µg treatment group is presented. Immunogenicity is reported as PC- and gB-specific neutralizing antibody (nAb) titers.

Results: The most common solicited local adverse reaction (AR) was injection site pain. The most common solicited systemic ARs were headache, fatigue, myalgia and chills. Neutralizing antibody titers increased in a dose-dependent manner in both CMV-seronegative and CMV-seropositive participants. In CMV-seronegative participants post-third vaccination, PC-specific nAb titers were up to 10-fold higher and gB-specific nAb titers up to 1.4-fold higher than that of natural CMV infection. In CMV-seropositive participants post-third vaccination, PC-specific nAb titers were up to 40-fold over baseline and gB-specific nAb titers were up to 6-fold over baseline. The 300µg mRNA-1647 treatment group continued to demonstrate a dose-dependent increases in nAb titers post-second vaccination.

Conclusions: These phase 1 interim data indicate that mRNA-1647 was generally well-tolerated, induced nAb responses exceeding that of natural CMV infection in CMV-seronegative participants, and substantially boosted nAb titers in CMV-seropositive participants. This first-in-human trial demonstrates the potential of mRNA-1647 to prevent CMV infection.

Clinical Trial Registration: ClinicalTrials.gov NCT03382405
Are the Differences in Infant and Toddler Pertussis Immune Responses After Maternal Pertussis Vaccination Observed with a 2-Dose and 3-Dose Primary Vaccination Schedule?

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**Background:** Maternal vaccination helps protect infants from infections in their first months of life but can interfere with infant and toddler immune responses to some pediatric vaccines. A descriptive analysis (on data from two follow-up studies of a randomized pertussis maternal immunization study) was performed to assess the impact of different primary series dosing schedules on interference with pertussis responses in infants and toddlers.

**Methods:** Infants born to mothers who had received reduced-antigen-content diphtheria-tetanus-3-component-acellular-pertussis vaccine (dTpa group) or placebo (control group) during pregnancy (27⁰7 – 36⁰7 weeks’ gestation) in a phase IV, randomized, observer-blind study were enrolled in primary/booster vaccination follow-up studies. Infants received a 2-dose or 3-dose primary series plus booster with DTPa-HBV-IPV/Hib and 13-valent pneumococcal conjugate vaccine according to local/national immunization schedules. Post-primary and post-booster immune responses to pertussis antigens were evaluated descriptively by primary vaccination schedule (2-dose vs 3-dose).

**Results:** Of 601 enrolled infants, 528 received 3-dose priming (dTpa group: 264, control: 264; mostly 2-4-6 months) and 73 received 2-dose priming (dTpa group: 32, control: 41; mostly 3-5 months). Trends for lower post-primary vaccine response rates and geometric mean concentrations (GMCs) for pertussis antigens were observed in the dTpa vs control group, both after the 2-dose and 3-dose DTPa-HBV-IPV/Hib primary schedule (Figure-A/B). For both primary vaccination dosing schedules, booster response rates for pertussis antigens were similar between the dTpa and control group (Figure-C), while post-booster GMCs trended lower in the dTpa group for anti-pertussis-toxin and anti-filamentous-hemagglutinin (Figure-D).
Conclusions: These descriptive analyses suggest that interference of maternal pertussis antibodies with infant and toddler immune responses to pertussis antigens occurred both after 2-dose and 3-dose priming. Further studies specifically designed to investigate this are required to confirm these observations. Funding: GlaxoSmithKline Biologicals SA
Clinical Trial Registration: ClinicalTrials.gov; NCT02377349; NCT02422264; NCT02853929
Background: Isavuconazole is a new triazole antifungal with a favourable safety profile approved for the treatment of invasive aspergillosis and mucormycosis in patients >18 years. Compassionate use may be considered in paediatric patients in certain situations. Since optimal dose is not yet established for paediatric patients TDM may be useful in this population.

Methods: Descriptive, retrospective, single-center study including all paediatric (<18 years) patients that received isavuconazole (intravenous and/or oral) from January 2018 to December 2019. Isavuconazole was chosen for patients with invasive fungal disease (IFI) when conventional treatments were suboptimal, contraindicated or produced unbearable toxicity. TDM was performed weekly; target range was 2,5-5 mcg/ml.

Results: Six patients, median age 11 years (IQR 6,7-13,7), 4 male. Underlying diseases: 3 stem cell transplant, 1 acute lymphoblastic leukaemia, 1 lung transplant, 1 severe influenza infection (this last two with ECMO). IFI EORTC diagnosis: 3 proven, 1 probable, 2 possible. Reason to initiate isavuconazole: beneficial PK/PD (2), failure/toxicity of previous antifungals (4). Outcome: complete response (2), partial response (1), progression (1) and death (1 attributed/1 non-attributed to IFI). Toxicity led to withdrawal in 1 case. TDM was performed in 5/6 patients with 73% (22) determinations above/below the target range.

Conclusions: Paediatric use of isavuconazole was appropriated in selected cases when other antifungal drugs were suboptimal or contraindicated, with an acceptable safety and rate of response. Only one patient presented significant liver toxicity that had been preceded by significant liver disease (grade IV GvHD). TDM of isavuconazole is recommendable in the paediatric setting until more PK/PD data is available.
THE USE OF VORICONAZOLE IN CHILDREN: HIGHER DOSES IN YOUNGER CHILDREN AND CONTROL OF INFLAMMATION ARE KEY POINTS FOR AN OPTIMAL TREATMENT

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Background: It is known that voriconazole (VCZ) plasma levels (PL) are highly variable. Dose recommendation changed in 2012 for paediatric patients between 2 and 12 years old (yo). Little data on therapeutic drug monitoring (TDM) after these new recommendations is available. We aim to evaluate TDM of VCZ in paediatric patients with invasive fungal infection (IFI) and its relationship with safety and effectiveness.

Methods: Prospective observational single-centre study from Jan 2014 to August 2018. All consecutive patients aged 2-12 yo receiving VCZ were included. TDM was performed weekly and doses were changed according to local protocol. IFI were categorized as possible/probable/proven, response to treatment was evaluated according to EORTC/MSG group criteria and adverse events were recorded following the Common Terminology Criteria for Adverse Events v5.0. Factors potentially influencing PL were analysed.

Results: We obtained 229 PL from 28 IFI episodes (18 probable/proven). More than one-third of PL were not within therapeutic range (1-5.5mg/L): 27.5% below; 8.3% above. After dose modification according with our protocol, 75% therapeutic PL were achieved. Dose to achieve therapeutic PL in patients below 8 yo (21mg/kg/day) was higher than recommended and higher than in older patients. Severe hypoalbuminemia and marked elevation of C-reactive protein (CRP) were associated with worse PL adequacy. Non-infratherapeutic PL were associated with better treatment response at late evaluation, and supratherapeutic PL were associated with liver and renal dysfunction.

Conclusions: VCZ PL variability remains high despite current updated recommendations and it’s influenced by severe hypoalbuminemia and increased CRP. Therefore, additional efforts to control inflammation in children with IFI should be encouraged. Higher doses should be considered in patients below 8 yo. Therapeutic VCZ PL are related to treatment effectiveness and safety; thus, TDM of VCZ is mandatory.

Clinical Trial Registration: Not available
USE OF CANDIDA SPP. REAL TIME PCR IN A PAEDIATRIC TERTIARY CARE HOSPITAL

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Background: Diagnosis of invasive candidiasis is a complex task due to its unspecific clinical presentation and to the low performance of standard diagnostic methods. Candida spp. detection with real time – polymerase chain reaction (RT-PCR) is a complementary technique that increases sensitivity and reduces response time. Our aim was to describe the use of Candida spp. RT-PCR and its implications in clinical practice in a paediatric tertiary care hospital.

Methods: We performed a descriptive, retrospective and single centre study (June 2018-November 2019), including all the paediatric patients (<18 years) with Candida spp. determination by RT-PCR in sterile samples (blood, cerebrospinal fluid (CSF) and/or biopsy), using the kit Fungiplex Candida (Bruker), that informs qualitatively the presence of C. glabrata / C. krusei / Candida sp. (C. albicans, C. parapsilosis, C. tropicalis).

Results: Ninety-seven PCR-RT were performed in 57 patients (median age 2y [IQR 0.2-6y], 80% carrying a central venous catheter); mainly for the Intensive Care Unit (61%) and Oncohematology Department (25%). Samples were blood (86), CSF (9), liver biopsy (1), cardiac valve (1); 9 were positive for Candida spp (8 blood, 1 CSF); 7/9 patients were under antifungal prophylaxis and conventional cultures were negative. Negative PCR fit with negative cultures. In 35 cases, antifungal treatment was changed after the result: suspension (25), maintenance (6), start (4); without subsequent episodes of invasive candidiasis.

Conclusions: The addition of Candida spp. RT-PCR to conventional methods allowed confirming and/or ruling out invasive candidiasis, increasing sensitivity without false negative results. Agreement with conventional cultures was low, probably due to previous antifungal treatment or prophylaxis. Although more studies are needed, this approach seems useful, especially in patients receiving antifungal prophylaxis and may be considered as a part of Antifungal Stewardship Programs.
ACUTE FLACCID MYELITIS AND GUILAN BARRÉ SYNDROME, A COMPARATIVE STUDY WITH EVALUATION OF DIAGNOSTIC CRITERIA

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Background: Acute flaccid myelitis (AFM) is a condition characterized by acute flaccid weakness and MRI abnormalities in the spinal cord, which, has been associated with enterovirus D68. At onset of disease it may be difficult to differentiate AFM from Guillain Barré syndrome (GBS). In this study we searched for differentiating features by comparison of two previously described cohorts. Furthermore we evaluated current diagnostic criteria for GBS and AFM.

Methods: A retrospective cohort of 26 children with AFM associated with enterovirus D68 was compared to a cohort of 156 children with GBS from the Netherlands. A comparison was made for preceding prodromal syndrome, clinical features and results of diagnostic studies. Furthermore Brighton criteria, used for GBS diagnosis, were applied on the AFM group and CDC AFM criteria were applied on the GBS group.

Results: Several differences were found between the AFM and GBS cohorts. These include time between prodromal syndrome and weakness (7 vs. 11 days, p=0.002), time until maximal severity of weakness (3 vs 8 days, p=<0.001), presence of bilateral weakness (38% vs. 90%, p=<0.001), sensory symptoms (0 vs. 40%, p=<0.001) and pain (33 vs. 71%, p=<0.001), CSF leukocyte number (79 vs. 4, p=<0.001) and CSF protein concentrations. (0.44 vs 0.76, p=0.004). Brighton criteria and CDC AFM criteria were not always adequate in differentiating GBS and AFM.

Conclusions: Important differences between the AFM and GBS cohort were found in clinical features and diagnostic studies. These features may help in differentiating both disorders at onset of disease. Diagnostic criteria for GBS and AFM were not always adequate for making the right diagnosis, possibly urging partial revision of these criteria.
Background: Vertical transmission of Zika virus can dramatically affect the development of the fetus, causing anatomical abnormalities and even fetal loss. The molecular mechanisms involved in congenital Zika infection are still unknown but the placenta could play a key role.

We developed an in vitro model to simulate the placental Zika infection in order to study 1) local immune response involved in the virus-host interaction, 2) differential host transcriptomic response between two different Zika strains, 3) how culture conditions modulate gene expression and 4) evolution of the immune response over time.

Methods: We have cultivated and infected placental cotyledon explants from two patients and infected them in vitro with two different Zika strains. We have measured the gene expression in the placental tissue before and after infection (24-72 hours) with a panel of 576 genes related to the immune response using nCounter technology.

Results: The differential immune response produced by the infection is represented by 17 genes, many of them related to an overexpression of routes such as interferon, cellular immunity and inflammatory response. The pathways analysis pointed to routes related to differentiation of Th17, Th1 and Th2 cells, cytokine-cytokine interaction and JAK / STAT.

In addition, we have observed that culture conditions affect the immune response and that this response is progressive over time. We have not seen significant differences in the transcription patterns generated by different virus strains.
Conclusions: Th17 cells could have an impact in the cortical development of the fetus after maternal Zika infection, conditioned by the maternal inflammatory response via Th17-IL17a during pregnancy. We have found a transcriptomic signature of 17 genes that specifically identifies acute transplacental Zika infection.

Clinical Trial Registration: Clinical trial registration: N/A
Background: Enteroviruses (EV), in the genus *Enterovirus* in the family of *Picornaviridae*, are highly prevalent in humans worldwide, causing outbreaks of neurological and other infections. Echoviruses, within species *Enterovirus B*, are especially notorious for causing neurological infections. Knowledge on yearly circulation patterns of these viruses is essential for detecting, responding to and preparing for outbreaks. Additionally, changes in circulation patterns can provide clues for changes in viral pathogenicity and immunogenicity. However, due to the large number of asymptomatic infections, data on the prevalence of EVs is highly incomplete. Since immunity against EVs is thought to be type-specific and lifelong, seroprevalence studies could contribute to our knowledge on EV circulation.

Methods: We performed a serological study for 7 echoviruses (Echovirus 6 (E6), E9, E11, E16, E18, E25 and E30) using 492 serum samples from healthy Dutch individuals, collected in 2006/2007 and 2016/2017. For each sample, neutralization assays were performed for all viruses to determine antibody titers. Samples with a titer ≥ 1:8 were considered positive.

Results: Overall, seroprevalence for all viruses by timepoint ranged between 45% and 98%. GMTs for all viruses by timepoint ranged between 1:27 and 1:95. Participants in older age groups were seropositive for more viruses than participants in younger age groups. In general, a trend of increasing seroprevalence until the age of 20 was visible, as well as a trend of declining GMT by age.

Conclusions: The high seroprevalence illustrates the extensive circulation of all seven echoviruses in the Netherlands. The steep increases in seroprevalence in the youngest age groups and the stabilization of seroprevalence in the older age groups, show that the viruses circulate mainly among children, while circulation among adults is limited. The decline in GMTs by age implies waning immunity.

Clinical Trial Registration: Not Applicable
INFECTION OF B-LYMPHOCYTES BY MEASLES VIRUS CHANGES B-CELL DIVERSITY AND DIMINISHES PRE-EXISTING ANTIBODIES: IMMUNE AMNESIA LESSONS FROM ANIMAL MODELS AND CLINICAL STUDIES

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Background: Measles, caused by the highly-infectious measles virus (MeV), is responsible for over 100,000 deaths yearly. Epidemiological studies have associated measles with increased morbidity and mortality for several years after infection. Non-human primate and in vitro studies proposed various mechanisms underlying this prolonged immune impairment, but the precise mechanisms are unknown. A measles outbreak in the Dutch Orthodox Protestant community provided a unique opportunity to study this in unvaccinated children.

Methods: Paired blood samples were collected before and after measles. Viral tropism and measles-associated changes in lymphocyte subsets in PBMC were studied by flow cytometry. VirScan, an assay that tracks antibodies to thousands of pathogen epitopes in blood, was used to study paired sera obtained from 77 children. B cell receptor sequencing was performed on naive and memory B-lymphocytes isolated from paired PBMC samples.

Results: Measles caused significant changes in subset composition of PBMC. Two mechanisms underlying immune suppression were identified: (i) incomplete reconstitution of naive B cells and (ii) depletion of previously expanded B memory clones. This caused an elimination of up to 73% of the antibody repertoire to other pathogens. Recovery of antibodies was detected after natural re-exposures. Notably, these immune suppressive effects were not observed in infants vaccinated against MMR (measles, mumps, and rubella).

Conclusions: Measles causes changes in B lymphocyte diversity that persist after resolution of clinical disease. The elimination of pre-existing antibodies generates potential vulnerability to future infections, highlighting the importance of MeV vaccination for the control of measles and maintenance of herd immunity to other pathogens. These data support our immune amnesia hypothesis and offer an explanation for the long-term effects of measles on host resistance.

Clinical Trial Registration: The study protocol was approved by the medical ethical committee of Erasmus MC, the Netherlands (MEC-2013-302, CCMO register NL45323.078.13/2.)
EVIDENCE FOR BCG-INDUCED PROTECTION AGAINST HETEROLOGOUS INFECTIONOUS DISEASE IN UGANDAN NEONATES: AN INVESTIGATOR-BLIND RANDOMISED CONTROLLED TRIAL.

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Background: A growing number of studies suggest that BCG produces non-specific protection against diseases other than tuberculosis. The hypothesis remains contentious because many of the trials reporting beneficial non-specific effects of BCG have been conducted in low birth-weight neonates in one setting in West Africa. Uncertainty exists as to the generalizability of these findings, and thus their broader public health implications.

Methods: We conducted an investigator-blind randomised controlled trial comparing BCG vaccination on the day of birth, with BCG vaccination at 6 weeks of age in 560 healthy Ugandan neonates. All-cause illness rates during the first 10 weeks of life were measured by active participant follow-up, comprising cost-free access to review and treatment, regular routine physician reviews and weekly telephone interviews. Incidence rates of non-tuberculous infections were compared between BCG groups, using Poisson regression with robust standard errors to allow for within-child clustering.

Results: Infants receiving BCG at birth had a 29% reduction in physician-diagnosed non-tuberculous infectious disease in the first 6 weeks of life compared to BCG unvaccinated infants (Hazard Ratio (HR) 0.71, 95% CI (0.53-0.95)). This reduction was more pronounced in low birth-weight infants ≤2500g (HR 0.10 (0.01-0.75)) compared to normal birth-weight infants (HR 0.79 (0.59-1.07) interaction p-value 0.04), and in boys (HR 0.57 (0.36-0.89)) compared to girls (HR 0.87 (0.59-1.27) interaction p-value 0.16). After the delayed group received BCG at 6 weeks of age, there was no significant difference in non-tuberculous infectious disease incidence between the two groups.

Conclusions: BCG has non-specific beneficial effects in neonates in diverse high-mortality settings, and in normal birth-weight as well low birth-weight neonates. Prioritisation of BCG vaccination on the first day of life may have significant public health benefits through reductions in all-cause infectious disease morbidity and mortality.

Clinical Trial Registration: ISRCTN 59683017.
Background: RSV is the leading cause of severe-LRTI hospitalisation in infants, with the highest burden in low-middle income settings. We undertook post-hoc country-specific (South Africa) vaccine-efficacy analysis of RSV F-protein vaccine immunization of pregnant women against RSV-LRTI in their infants.

Methods: Healthy, pregnant, HIV-negative women between 28-36 weeks gestation were randomized to a single intramuscular dose of RSV F-nanoparticle vaccine, or placebo in a global multi-centre study. Active and passive surveillance for symptomatic RSV infections to ascertain medically-significant RSV-LRTI (MS RSV-LRTI; primary endpoint), RSV-LRTI with severe hypoxemia and/or RSV-LRTI hospitalization was undertaken through 180 days age.

Results: Fifty-two percent (2422/4636; 1604 vaccine and 818 placebo-recipients) of all maternal participants were enrolled in South Africa, who delivered 2383 live-births. This, with a higher-than-anticipated attack rate of MS RSV-LRTI in South African infants (5.5% vs. 4.0% projected) allowed for country-specific vaccine-efficacy estimates. Table 1: Efficacy analysis against RSV-LRTI in infants born to pregnant women vaccinated with RSV F-vaccine or placebo in South Africa. Vaccine-efficacy estimates in the per-protocol analysis were similar to expanded-ITT analyses.
<table>
<thead>
<tr>
<th>Observation-period; days</th>
<th>Expanded Intent-to-Treat analysis (site and hospital data)</th>
<th></th>
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<tbody>
<tr>
<td></td>
<td>Placebo N=799; n(%)</td>
<td>Vaccine N=1572; (%)</td>
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<tr>
<td>Medically-significant RSV-LRTI (LRTI-signs, SpO₂&lt;95% or tachypnea, RSV+):</td>
<td></td>
<td></td>
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<tr>
<td>0-90days</td>
<td>44 (5.51)</td>
<td>38 (2.42)</td>
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<tr>
<td>0-180days</td>
<td>49 (6.13)</td>
<td>53 (3.37)</td>
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<tr>
<td>RSV-LRTI with hospitalization (LRTI-signs, hospitalization, RSV+)</td>
<td></td>
<td></td>
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<tr>
<td>0-90days</td>
<td>45 (5.63)</td>
<td>34 (2.16)</td>
</tr>
<tr>
<td>0-180days</td>
<td>48 (6.01)</td>
<td>43 (2.74)</td>
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<tr>
<td>RSV-LRTI with severe hypoxemia (LRTI-signs, SpO₂&lt;92%, RSV+)</td>
<td></td>
<td></td>
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<tr>
<td>0-90days</td>
<td>27 (3.38)</td>
<td>14 (0.89)</td>
</tr>
<tr>
<td>0-180days</td>
<td>29 (3.63)</td>
<td>17 (1.08)</td>
</tr>
</tbody>
</table>

**Conclusions:** RSV F-protein vaccination of pregnant women was most efficacious in preventing RSV-LRTI, including 70.2% reduction in RSV-LRTI with severe hypoxemia, in South African infants from predominantly low income settings.

**Clinical Trial Registration:** ClinicalTrials.Gov: NCT02624947
The accuracy of Xpert MTB/RIF Ultra in pediatric pulmonary tuberculosis in a low-burden region: A prospective study from the Spanish pediatric tuberculosis research network (PTBRED)


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Background: Childhood pulmonary tuberculosis (PTB) remains a diagnostic challenge, as clinical and radiologic features lack specificity, and respiratory samples typically contain few bacilli. The Xpert®MTB/RIF PCR assay (Xpert) allows the detection of M. tuberculosis complex and rifampicin resistance, but has suboptimal sensitivity in children. A newer version, Xpert®MTB/RIF Ultra (Ultra), has a lower detection limit, with previous studies reporting increased sensitivity in adults. This study aimed to estimate and compare Xpert and Ultra diagnostic accuracy in children.

Methods: Prospective, multicenter, diagnostic accuracy study, January-2018 to December-2019. Children with suspected PTB were recruited at 10 paediatric units in Spain. Up to 3 gastric or sputum samples were taken on 3 consecutive days and simultaneously analysed with both assays. Test sensitivity and specificity were compared using McNemar-test. Fifty-nine children were included (median age 5 years, IQR:2.8-9.4, 47.5% female). The final diagnosis was PTB in 84.7% children (44% of them culture positive), and not-TB in 15.2%. Overall, 154 samples were analyzed by PCR, including gastric aspirates (83.8%) and sputum samples (16.2%).

Results: Using culture as reference standard and comparing individual samples, sensitivity was 39.1% (9/23) for Xpert and 73.9% (17/23) for Ultra (p=0.008), specificity was 99.2% (130/131) and 94.7% (124/131) respectively (p=0.06) (Table 1). The area under the curve (AUC) was 0.69 (IC95%:0.59-0.79) for Xpert and 0.85 for Ultra (IC95%:0.75-0.94). When clustering for individual participants and comparing positive results on any sample, the sensitivity was 42.8% (6/14) for Xpert and 71.4% for Ultra (10/14,p=0.125), specificity was 97.7% (44/45) and 86.7% (39/45,p=0.06).

Conclusions: Our data indicate the Ultra assay has a significant higher sensitivity than the previous generation assay in children with PTB. Further studies are needed to confirm these findings in other
patient populations.
PERFORMANCE OF QUANTIFERON-TB PLUS ASSAYS IN CHILDREN WITH ACTIVE TB COMPARED WITH OTHER INTERFERON-GAMMA RELEASE ASSAYS AND THE TUBERCULIN SKIN TEST – A MULTICENTER PTBNET STUDY (PTBNET QFT PLUS STUDY)


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Background: In 2017 a new interferon-gamma release assay (IGRA) was introduced, the QuantiFERON-TB Gold Plus assay (QFT-Plus), which incorporates two antigen-stimulated tubes (TB1 and TB2) and is claimed to have improved sensitivity in active tuberculosis (TB). We aimed to determine the performance of the QFT-Plus, compared with QFT Gold-in-Tube (QFT-GIT), T-SPOT.TB and tuberculin skin tests (TST), in children with TB disease in Europe.

Methods: Ambispective cohort study within the Paediatric Tuberculosis Network European Trials Group (ptbnet), a research network comprising >300 physicians and researchers, capturing TB cases <18 years-of-age diagnosed between January 2009 and December 2019.

Results: 831 TB cases from 14 countries were included (male 54.1%; mean age: 7.3 years). In culture-confirmed cases (n=411) the sensitivity of QFT-Plus, QFT-GIT, T-SPOT.TB and TST was 87.1% (95%CI:80.8-91.6%), 84.3% (79.1-88.4%), 75.0% (57.7-87.0%) and 87.1% (83.1-90.3%), respectively; there was no statistically significant difference between test sensitivities (chi-square p=0.24). Similar sensitivities were observed in probable cases (n=420): 81.7%, 86.2%, 91.3% and 90.1%, respectively. All tests had lower sensitivity in immunocompromised children than in non-immunocompromised children: QFT-Plus 76.0% vs. 84.9% (p=0.25), QFT-GIT 59.1% vs. 88.0% (p<0.001), T-SPOT.TB 45.4% vs. 90.9% (p=0.002), TST 64.3% vs. 90.7% (p<0.001). QFT-Plus TB1 and TB2 tubes showed 93% agreement regarding categorical assay results, and there was a strong linear correlation between background-corrected interferon-gamma concentrations detected in both tubes (r²=0.80;p<0.0001).

Conclusions: Our data show that the latest generation IGRA, the QFT-Plus assay, does not perform better than previous generation IGRAs or the TST in children with active TB. All tests showed worse performance in children with immunocompromise. None of the immunological tests evaluated in this study had sufficiently high sensitivity to be used as rule-out tests in children with suspected TB.

Clinical Trial Registration: not applicable
MACHINE LEARNING ALGORITHMS EVALUATE IMMUNE RESPONSE TO NOVEL MYCOBACTERIUM TUBERCULOSIS ANTIGENS FOR DIAGNOSIS OF TUBERCULOSIS

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Background: Tuberculosis diagnosis in children remains challenging. Microbiological confirmation of tuberculosis disease is often lacking, and standard immunodiagnostics including the tuberculin skin test and interferon-γ release assay for tuberculosis infection have limited sensitivity. Recent research suggests that the inclusion of novel Mycobacterium tuberculosis antigens have the potential to improve standard immunodiagnostics for tuberculosis. Objective: To identify optimal antigen-cytokine combinations using novel Mycobacterium tuberculosis antigens and cytokine read-outs by machine learning algorithms to improve immunodiagnostic assays for tuberculosis.

Methods: A total of 80 children undergoing investigation of tuberculosis were included (15 confirmed tuberculosis disease, 5 unconfirmed tuberculosis disease, 28 tuberculosis infection and 32 unlikely tuberculosis). Whole blood was stimulated with 10 novel Mycobacterium tuberculosis antigens and a fusion protein of early secretory antigenic target (ESAT)-6 and culture filtrate protein (CFP) 10. Cytokines were measured using xMAP multiplex assays. Machine learning algorithms defined a discriminative classifier with performance measured using area under the receiver operating characteristics.

Results: We found the following four antigen-cytokine pairs had a higher weight in the discriminative classifier compared to the standard ESAT-6/CFP-10-induced interferon-γ: Rv2346/47c- and Rv3614/15c-induced interferon-gamma inducible protein-10; Rv2031c-induced granulocyte-macrophage colony-stimulating factor and ESAT-6/CFP-10-induced tumor necrosis factor-α. A combination of the 10 best antigen-cytokine pairs resulted in area under the curve of 0.92 ± 0.04.

Conclusions: Conclusion: We exploited the use of machine learning algorithms as a key tool to evaluate large immunological datasets. This identified several antigen-cytokine pairs with the potential to improve immunodiagnostic tests for tuberculosis in children.

Clinical Trial Registration: registered at ClinicalTrials.gov NCT03044509
TREATMENT RESPONSE IN SOUTH AFRICAN CHILDREN TREATED FOR MULTIDRUG-RESISTANT TUBERCULOSIS: A PROSPECTIVE COHORT STUDY

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Background: Multidrug-resistant (MDR) tuberculosis (TB) affects ~30,000 children each year. The aim of this study was to describe the clinical characteristics, safety and treatment response in children treated for MDR or rifampicin mono-resistant (RMR) TB in Cape Town, South Africa prior to global recommendations regarding injectable sparing regimen.

Methods: Prospective observational study of the pharmacokinetics and safety of second-line TB drugs in children on routine MDR/RMR TB treatment from October 2012 to May 2013 in Cape Town. Children were followed prospectively to assess safety and tolerability and treatment outcomes.

Results: 136 cases were included (median age 3.3 years; 19.9% HIV co-infected). Severe disease was present in 48 (37.8%) and 61 (44.8%) were bacteriologically confirmed. Median TB treatment duration was 15.5months (IQR:13.5-18.3) and 91.5% had a favorable treatment outcome. 107 (78.7%) were treated with an injectable drug and 8 (7.5%) developed hearing loss. The median time to culture conversion from respiratory samples in confirmed cases (n=44) was 28.5days (IQR:14.5-45). Older age and the presence of cavities predicted delayed culture conversion in multivariate Cox regression analysis but neither remained significant in multivariate analysis(Table1).
Conclusions: In this large prospective cohort of children treated for MDR/RMR-TB, clinical outcomes were excellent despite the use of regimens excluding clofazimine, bedaquiline, delamanid and linezolid, and with high prevalence of HIV infection and severe TB. Monitoring response to treatment in children with TB, especially MDR-TB, is challenging and new tools are required.
NOVEL CYTOKINE BIOMARKERS IN QUANTIFERON SUPERNATANTS IMPROVE DISTINCTION OF CHILDREN WITH ACTIVE TUBERCULOSIS FROM THOSE WITH PNEUMONIA AND LATENT TUBERCULOSIS INFECTION.

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Background: Although much research has been done related to biomarker discovery for Tuberculosis (TB), a set of biomarkers that can discriminate between active TB, other respiratory diseases and latent TB infection (LTBI) remains elusive. With the use of Luminex assay, we aimed at identifying differences in cytokine biomarkers detected in Quantiferon (QFT) supernatants from children with active TB or LTBI, pneumonia and healthy controls.

Methods: The study population comprised of children who underwent evaluation for suspected TB in our Outpatient TB Clinic. Participants were assigned to groups according to whether the diagnosis was culture-confirmed TB (18), LTBI (20), pneumonia (20) or healthy subjects (20). Luminex assay for a panel of 23 cytokines was performed in QFT supernatants in order to identify single or sets of differentially expressed cytokines between the groups.

Results: Fourteen cytokines were significantly differentially abundant between active TB and pneumonia, while two of the cytokines (Perforin and EGF) were significantly differentially abundant between TB and LTBI. Using random forest, a unique ‘biosignature’ of 14 cytokines achieved an overall area under the curve (AUC) of 85%.

Conclusions: We managed to determine a cytokine ‘biosignature’ in QFT supernatants that helped distinguish TB from other phenotypically similar diseases. Further evaluation of the performance of the identified signatures in a larger sample size will be required to confirm the robustness of the biomarkers and the reproducibility of our findings.

Clinical Trial Registration: (02/02/2018, Protocol No: 1463).
Background: Infection with Mycobacterium ulcerans leads to Buruli ulcer, a chronic infection causing permanent disfigurement and long-term disability. Bacillus Calmette–Guérin (BCG) immunisation may be the only available preventive measure against Buruli ulcer. Studies on its clinical efficacy have conflicting results and immunological data are lacking.

Methods: Immune responses to M. ulcerans were measured in vitro using intracellular cytokine analysis 10 weeks after BCG vaccination in 130 Australian infants randomised to one of three BCG vaccine strains given at birth (BCG-Denmark, n=31; BCG-Japan, n=38; BCG-Russia, n=35) or at 2 months of age (BCG-Denmark, n=26).

Results: Proportions of single, double, and triple cytokine-producing CD4 T-cells (IFN-γ, IL-2 and/or TNF-α combinations) were all significantly higher following M. ulcerans-stimulation (Figure). These proportions were not different between BCG vaccine strains or with different timing of vaccination. The M. ulcerans-specific responses showed a similar trend but were lower compared with those observed following M. tuberculosis stimulation.

Figure: Immune responses to in vitro stimulation 10 weeks after neonatal BCG immunisation.
Proportions of single, double and triple cytokine-producing CD4 and CD8 T-cells after in vitro stimulation with heat-killed *M. ulcerans*, heat-killed *M. tuberculosis*, or purified protein derivative. The box plots show the lower, median, and upper quartiles, with 5th and 95th percentiles. Proportions in the stimulated wells are compared with the negative control (proportions in non-stimulated wells) using paired non-parametric tests. *: \( p<0.05 \); **: \( p<0.01 \); ***: \( p<0.001 \); BCG: bacilli Calmette-Guerin; nil: negative control (media alone); PPD: purified protein derivative.

**Conclusions:** Infant immunisation with BCG-Denmark, BCG-Japan, or BCG-Russia induces a significant *M. ulcerans*-specific immune response. These findings add to the evidence from clinical studies supporting the cross-protective effect of BCG immunisation against *M. ulcerans* infections.

**Clinical Trial Registration:** Australian New Zealand Clinical Trials Registry: no. ACTRN12608000227392
BCG VACCINATION OF INFANTS CONFERS PROTECTION AGAINST MYCOBACTERIUM TUBERCULOSIS (MTB) DISEASE THAT IS CLINICAL MTB STRAIN-SPECIFIC

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Background: Tuberculosis (TB), caused by Mycobacterium tuberculosis (Mt) infection, was responsible for 233,000 deaths and a million new cases among children in 2017. The only WHO-approved vaccine BCG, given to infants at birth, is partially protective against TB disease although it has significant protective efficacy against severe disseminated disease. To date, the exact mechanism of the protective effect of BCG remains unknown. We examined the leukocyte cytokine/chemokine response, elicited by BCG vaccination, in the presence or absence of in vitro Mt exposure, to better understand the nature of the protective response and the diversity in protective efficacy.

Methods: PBMCs from 10-week old infants, either unvaccinated (n=25) or BCG-vaccinated at birth (n=25) were cultured in vitro with or without clinical Mt isolate HN878 (a hyper-virulent strain) or CDC1551 (an immunogenic strain), and the culture supernatants were used to determine the cytokines/chemokines released by the Luminex assay.

Results: Non-infected PBMCs from BCG vaccinated infants released significantly higher levels of pro-inflammatory markers, including TNF-α and IFN-γ and lower levels of the anti-inflammatory markers IFNA2 and IL-1RA, compared to cells from unvaccinated infants. In vitro infection of PBMC from BCG-vaccinated infants with Mt HN878 resulted in elevated levels of host-inflammatory molecules such as IP-10 and MCP-1, while Mt CDC1551 infection led to increased anti-inflammatory markers, including IL-1RA. In contrast, the non-vaccinated PBMCs produced increased IL-4 (anti-inflammatory) in response to HN878 exposure and increased TNF-α (pro-inflammatory), following CDC1551 infection.

Conclusions: Our results suggest that BCG-vaccination skews the PBMCs towards a host-protective, Th1 phenotype. However, the ability of BCG vaccination to protect against TB disease may be determined by the exact nature of the leukocyte cytokine/chemokine response following exposure to Mt and appears to be Mt strain-dependent.

Clinical Trial Registration: Not applicable
GETTING THE DIAGNOSIS RIGHT: “RAPAED-TB” – A DIAGNOSTIC VALIDATION STUDY FOR CHILDREN WITH TB


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Background: The diagnosis of tuberculosis(TB) in children remains challenging: current detection methods neither perform reliably nor are sampling methods child-friendly.

Methods: RaPaed-TB aims to enrol 1000 children with presumptive TB in five endemic countries: South Africa, Mozambique, Malawi, Tanzania, and India. Enrolment of children ≤14years was initiated in January 2019. Clinical and laboratory workup is standardized across sites, and diagnostic classification follows the current NIH-consensus statement. Comprehensive new testing encompasses pathogen detection, host-immune response, biomarker assays, with biobanking. Recruitment, data entry and analysis are underway; presented data are preliminary and totals differ dependent on data entry status.

Results: As of mid-January 2020, 360 participants were enrolled at four African sites, the Indian site started enrolment in December 2019. The median age was 4.5years (IQR 6.02years), with 25% of children being <1-year-olds (90/344), and 61% <5years (211/344). Overall, 18% (66/362) are HIV-infected, while 15% (55/362) were HIV-exposed uninfected. The overall microbiological confirmation rate (PCR/culture) was 24% (89/360). GeneXpertUltra® results for 412 samples were positive in 18% (43/243) of induced sputum and in 21% (9/43) spontaneous sputa samples. Other sample types included nasopharyngeal aspirate (positivity 8%; 7/90), cerebrospinal fluid (positivity 38%; 3/8), biopsy (positivity 100%; 2/2), and others (positivity 40%; 4/10).

Conclusions: RaPaed-TB is one of the largest paediatric TB-diagnostic trials with the evaluation of several new tests in children in Africa and India. After approximately one year of recruitment, a third of participants have been enrolled with high rates of confirmed TB. The inclusion of a large proportion of infants make this an especially important cohort with the potential to generate highly relevant data on novel test performance. More in-depth analyses on new test performances, against a reference standard of microbiological data, are planned.

Clinical Trial Registration: NCT03734172
SENSITIVE AND FEASIBLE SPECIMEN COLLECTION AND TESTING STRATEGIES FOR DIAGNOSING TUBERCULOSIS IN YOUNG CHILDREN IN KENYA

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Background: Tuberculosis is a leading cause of death among children globally. Reference standard specimens for children, gastric aspirate (GA) and induced sputum (IS), are invasive and rarely collected in practice. A sensitive, minimally invasive approach is needed to improve tuberculosis diagnosis in children.

Methods: Up to eight specimens, including two GA and two IS, were collected from children aged <5 years with tuberculosis symptoms in Kenya (October 2013–August 2015). Samples were tested for Mycobacterium tuberculosis complex by fluorescence microscopy, Xpert MTB/RIF, and mycobacteria growth indicator tube culture (MGIT). We used resampling to compare the cumulative and incremental diagnostic yield of combinations of specimen types and tests.

Results: Of the 300 children enrolled, 32 (11%) had confirmed tuberculosis. Of the 31 children with confirmed tuberculosis and ≥4 specimen types collected, 24 (77%) had positive results for up to two GA samples and 20 (64%) for up to two IS samples. The yield of two nasopharyngeal aspirate (NPA; 23/31 [74%]), of one NPA and one stool sample (22/31 [71%]), or of one NPA and one urine sample (21.5/31 [69%]) was similar to reference standard specimens. Combining up to two each of GA and NPA had an average yield of 28/31 (90%).

Conclusions: NPA, either in duplicate or in combination with stool or urine specimens, was readily obtainable with a diagnostic yield comparable to reference standard specimens. This combination could be used to improve tuberculosis diagnosis among children in resource-limited settings. Combining GA and NPA had greater yield than that of the current standards and may be useful in certain clinical and research settings.

Clinical Trial Registration: No clinical trial registration
DETECTION OF A 2-HOST RESPONSE GENE EXPRESSION SIGNATURES DISCRIMINATING BACTERIAL FROM VIRAL INFECTION ON A MICROCHIP TECHNOLOGY AT THE POINT-OF-CARE

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Background: The World Health Organization (WHO) estimates that 14.9 million of 57 million annual deaths worldwide are related directly to diseases caused by bacterial and/or viral infections. The first crucial step in order to build a successful surveillance system is to accurately identify and diagnose patient health conditions. We describe how to detect RNA biomarkers on our microchip technology allowing rapid diagnosis of bacterial and viral infections in febrile children.

Methods: We selected 22 clinical samples from a cohort of 455 febrile children, 11 samples from patients with bacterial infection and 11 with a viral infection. We detected the 2-gene signature through the Reverse Transcription Isothermal Amplification (RT-LAMP) and validated it using standard fluorescent-based qPCR instruments. We then combined the RT-LAMP assays with our semiconductor-based Lab-on-Chip platform that uses an array of chemical sensors to monitor the pH changes during nucleic-acid amplification in real-time referred to as electronic LAMP (eLAMP). In order to define a decision boundary between bacterial and viral patients on our platform, we used the multivariate Logistic regression.

Results: Successful and rapid amplification on-chip to detect a 2-gene signature discriminating bacterial and viral infections in pediatrics clinical samples has been demonstrated and compared with the gold standard techniques (RT-PCR) showing good sensitivity (limit of detection down to 10 copies/reaction), specificity and appropriate speed for point-of-care applications (time-to-positive reaction <20min). Observed sensitivity and specificity were 100% and AUC was 1.0 for all methods. RT-LAMP and eLAMP showed a lower limit of detection of 10 copies per reaction within 25 minutes (time-to-positive).

Conclusions: The 2-gene signature combined with eLAMP technology provides an affordable and ultrafast diagnostic solution for discriminating bacterial from viral infection in febrile children at the Point-Of-Care.

Clinical Trial Registration: No clinical trial
A HOST-PROTEIN SIGNATURE THAT DIFFERENTIATES BETWEEN BACTERIAL AND VIRAL INFECTIONS CAN CONTRIBUTE TO REDUCTION OF ANTIBIOTIC MISUSE IN CHILDREN: A PROSPECTIVE, DOUBLE-BLIND, MULTICENTRE, VALIDATION STUDY

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Background: Identifying infectious disease etiology is essential for the appropriate use of antibiotics. Previous studies showed that a host-protein signature comprising TNF-related apoptosis induced ligand (TRAIL), interferon gamma induced protein-10 (IP-10) and C-reactive protein (CRP) accurately differentiates between bacterial and viral infections.

Methods: In this prospective, double-blind, multinational study “AutoPilot-Dx” (NCT03052088) we aimed to validate the diagnostic accuracy of the signature and evaluate its potential impact on antibiotic use. We recruited children aged > 90 days with respiratory tract infections or fever without a source at hospitals in Germany and Italy. Infection etiology was assigned by unanimous adjudication of three experts based on clinical and laboratory investigations.

Results: A total of 1140 patients were recruited between February 2017 and December 2018; the primary study cohort comprised 732 children (mean age 3.5 years, 41.9% female). A viral infection was adjudicated for 628 children (85.8%) and a bacterial infection for 104 children (14.2%). The signature discriminated bacterial from viral infections with sensitivity of 93.7% (95% CI 86.6-97.3), specificity of 94.2% (91.9-95.8), positive predictive value of 72.7% (65.5-78.8), negative predictive value of 98.9% (97.7-99.5), with 9.8% equivocal test results, outperforming procalcitonin, CRP, white blood count and absolute neutrophil count. This performance has the potential to reduce unwarranted antibiotics in children with viral infections from 29.6% to 9.1% (factor 3.3).

Conclusions: This is the largest prospective study of the three host-protein signature in children to date, validating high diagnostic performance and supporting its potential to reduce antibiotic overuse in children with viral infections.

Clinical Trial Registration: ClinicalTrials.gov NCT03052088
APPLYING STANDARDISED MOLECULAR DIAGNOSTICS TO 2000 EUROPEAN PAEDIATRIC PATIENTS WITH FEVER

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Background: Identification of the causative pathogen in febrile children presenting to emergency departments remains difficult, despite advances in detection using molecular methods. A high proportion of febrile children are treated with antibiotics without microbiological confirmation of bacterial infection. The PERFORM study aimed to establish the cause of fever in children presenting to hospitals in the EU using state-of-the-art molecular methods in addition to standard hospital diagnostics.

Methods: 1957 febrile children and 307 non-febrile control children presenting to 5 hospitals in 3 EU countries were investigated using molecular methods to identify 21 different pathogens in respiratory samples, and 9 viral, 23 bacterial and 3 fungal pathogen targets in blood. A clinical phenotype (bacterial, viral or uncertain infection) was assigned by the local clinical team, based on the results of microbiological methods available at each hospital. We investigated whether the molecular diagnostic findings were consistent with the clinical phenotype.

Results: Molecular diagnostics identified pathogens in 59% of patients, doubling the rate of detection of viruses, and increased detection of bacteria by 29%. More than one pathogen was identified in 34% of patients. When the frequency of detection of pathogens was compared between patients assigned as having bacterial or viral infections, significant increased detection of pathogens in the corresponding phenotype was observed for influenza (OR 5.4), RSV (OR 4.7), enterovirus (OR 2.79), N.meningitidis (OR 16), S.pneumoniae (OR 5.4) and S.pyogenes (OR 9.9). For the 47 remaining viral and bacterial assays, differences in detection were non-significant.

Conclusions: Broad ranging molecular pathogen diagnostics increased pathogen detection in febrile patients. For many targets, detection did not correlate with their bacterial or viral phenotype. Future work to compare pathogen results with host biomarkers may help establish causative aetiologies.

Clinical Trial Registration: Not a clinical trial
IDENTIFICATION OF NOVEL PROTEIN BLOOD BIOMARKERS USING A MULTI-PLATFORM APPROACH TO DISTINGUISH BETWEEN BACTERIAL AND VIRAL INFECTIONS IN FEBRILE CHILDREN

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Background: Differentiating between self-resolving viral infections and severe bacterial infections in febrile children is challenging for clinical teams. Current routinely used hospital-based diagnostic methods often fail to assist in clinical decision making. Studying the host’s response with novel molecular approaches can lead to the identification of biomarkers of infection which can ultimately be developed into accurate, rapid point-of-care tests.

Methods: The SomaScan platform was used to perform targeted proteomic analysis for a cohort of 79 serum samples. Tandem mass spectrometry was used for untargeted proteomic profiling of two cohorts of 149 and 150 plasma samples. All samples had confirmed bacterial and viral infections. The proteomes of samples with bacterial and viral infections were explored through differential abundance analysis, and an in-house feature selection method, FS-PLS, was used to select a small signature of non-correlated proteins. In parallel, the levels of 25 proteins were measured in a discovery and validation cohort using Luminex.

Results: Table 1 shows the number significantly differentially abundant (SDA) proteins for each proteomic cohort and Luminex assay, including the number of proteins with increased abundance in bacterial or viral infections. A total of 15 proteins were identified as SDA in all three proteomic cohorts. FS-PLS identified signatures composed of 4, 5 and 5 proteins for the SomaScan, MS discovery and MS validation cohorts, respectively, achieving AUC values between 94.4% to 99.0%. 15 of the 25 Luminex candidates were also identified as SDA in a proteomic cohort.

Table 1: Summary of the differential abundance analysis per cohort

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Total significantly differentially abundant</th>
<th>Up in bacterial</th>
<th>Up in viral</th>
</tr>
</thead>
<tbody>
<tr>
<td>SomaScan</td>
<td>431</td>
<td>198</td>
<td>233</td>
</tr>
<tr>
<td>MS Discovery</td>
<td>54</td>
<td>20</td>
<td>34</td>
</tr>
<tr>
<td>MS Validation</td>
<td>97</td>
<td>28</td>
<td>69</td>
</tr>
<tr>
<td>Luminex Discovery</td>
<td>14</td>
<td>14</td>
<td>0</td>
</tr>
<tr>
<td>Luminex Validation</td>
<td>11</td>
<td>11</td>
<td>0</td>
</tr>
</tbody>
</table>
Conclusions: This work represents a multi-platform, multi-cohort attempt to search for novel, promising protein biomarkers for diagnosing bacterial and viral infections. These results highlight the benefit of using multiple platforms for proteomic profiling through the identification of shared and additional markers across the multiple datasets.

Clinical Trial Registration: Not applicable
MINIMAL OPTIMISED HOST BLOOD GENE EXPRESSION SIGNATURE OF BACTERIAL INFECTION

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Background: A rapid diagnostic test for the detection of bacterial infection in children using host gene expression from whole blood would provide significant benefit to health systems globally. We hypothesised that a minimal gene expression signature could distinguish bacterial infection from other febrile illnesses. By including diverse conditions in the non-bacterial group we aim to ensure that the resulting signature will be applicable across multiple healthcare settings globally.

Methods: 2844 paediatric patients with acute febrile illness were prospectively recruited from 98 hospitals across Europe as part of the EUCLIDS study. RNA-sequencing was performed on a subset of these samples consisting of 348 patients with definite bacterial infection, 262 with viral infections, 24 with malaria, 65 with tuberculosis and 536 with inflammatory disease. Whole blood gene expression profiling was performed using RNA sequencing during the PERFORM study. Samples were randomly assigned to two batches which were used for discovery and validation.

Results: Using feature selection methods, a minimal gene expression signature was identified in the discovery cohort (n=631) and its performance was evaluated in the validation cohort (n=604). The signature was able to reliably detect the presence of bacterial infection across many clinical syndromes independently of co-detection or co-infection with viruses. A cost factor was implemented to ensure high sensitivity in detecting bacterial infection.

Conclusions: Novel rapid host-based diagnostics for bacterial infection are urgently needed. Here we show that a small host-RNA signature can be used to detect, with high accuracy, the presence of bacterial infection, independent of viral co-infection. Rapid quantification of these genes in the patients’ blood in a cost-effective manner at the point of care may offer unprecedented insights to the clinical teams and assist decision making.

Clinical Trial Registration: no controlled trial
DIAGNOSTIC PERFORMANCE OF BIOMARKERS IN CHILDREN WITH SERIOUS BACTERIAL INFECTIONS: POSITIONING OF AN IMPROVED CLASSIFICATION ALGORITHM

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Background: The limited diagnostic accuracy of biomarkers in children at risk of a serious bacterial infection (SBI) might be due to the imperfect reference standard of SBI. We aimed to evaluate the diagnostic performance of a new classification algorithm for biomarker discovery in children at risk of SBI using four previously published, prospective observational cohorts.

Methods: The Alder Hey ED (n=1,120), Alder Hey PICU (n=355), Erasmus ED (n=1,993) and Maasstad ED (n=714) cohorts were used and included children aged 0-16 years. Biomarkers of interest were NGAL (2 cohorts), Resistin (2 cohorts), and PCT (4 cohorts). The new classification algorithm included 8 categories: definite bacterial, probable bacterial, bacterial syndrome, unknown (bacterial and/or viral), viral syndrome, probable viral, definite viral and other, accounting for the uncertainty of the final diagnosis in a large proportion of febrile children. The diagnostic performance of this algorithm was compared to the traditional dichotomous SBI vs nonSBI classification.

Results: Definite bacterial infections had significantly higher levels of NGAL, resistin, and PCT compared with definite viral infections (table 1). The degree of uncertainty of the remaining six clinical phenotypes of the new algorithm corresponded accurately with the concentrations of biomarkers. Area under the Receiver Operating Curves (AUCs) of the new algorithm for definite bacterial vs definite viral diagnoses (range 0.65-0.81) were comparable with ROCs of the SBI vs nonSBI classification (range 0.64-0.75).
Conclusions: The four case studies illustrate a high correlation of biomarkers with our new classification algorithm, thus supporting its validity in biomarker discovery studies. The new algorithm clearly demonstrates the level of uncertainty of the final diagnoses in most febrile children. Our proposed algorithm provides a novel framework for phenotyping children with suspected or confirmed infection for future biomarker studies.

Clinical Trial Registration: Not applicable

Table 1. Biomarker concentrations in children with acute infections.

<table>
<thead>
<tr>
<th></th>
<th>All patients</th>
<th>Definitive bacterial</th>
<th>Definitive viral</th>
<th>ROC: definitive bacterial vs definitive viral (95% CI)</th>
<th>ROC: SBI vs non-SBI (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alder Hey ED cohort SBI: 337 (29%)</td>
<td>174 (15%)</td>
<td>113 (10%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NGAL (ng/L)^</td>
<td>78.1 (52.5–121.4)</td>
<td>113.5 (64.0–179.7)^</td>
<td>76.4 (53.6–114.9)</td>
<td>0.64 (0.58–0.71)</td>
<td>0.65 (0.62–0.69)</td>
</tr>
<tr>
<td>Resistin (ng/L)^</td>
<td>40.3 (21.4–73.8)</td>
<td>65.2 (31.3–119.3)^</td>
<td>37.2 (19.6–77.8)</td>
<td>0.65 (0.58–0.71)</td>
<td>0.65 (0.61–0.68)</td>
</tr>
<tr>
<td>PCT (µg/L)^</td>
<td>0.23 (0.1–0.8)</td>
<td>0.69 (0.15–4.17)^</td>
<td>0.23 (0.10–0.75)</td>
<td>0.65 (0.58–0.71)</td>
<td>0.64 (0.57–0.70)</td>
</tr>
<tr>
<td>Alder Hey PICU cohort SBI: 208 (59%)</td>
<td>49 (14%)</td>
<td>49 (14%)</td>
<td></td>
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<td></td>
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<tr>
<td>NGAL (ng/L)^</td>
<td>123.1 (72.1–233.0)</td>
<td>181.2 (102.7–327.6)^</td>
<td>88.8 (38.5–151.9)</td>
<td>0.76 (0.64–0.88)</td>
<td>0.64 (0.56–0.72)</td>
</tr>
<tr>
<td>Resistin (ng/L)^</td>
<td>57.17 (29.8–102.8)</td>
<td>80.0 (41.5–147.6)^</td>
<td>42.0 (14.1–65.8)</td>
<td>0.76 (0.64–0.68)</td>
<td>0.63 (0.55–0.71)</td>
</tr>
<tr>
<td>PCT (µg/L)^</td>
<td>0.64 (0.10–5.70)</td>
<td>10.25 (1.61–114.0)^</td>
<td>0.41 (0.09–1.80)</td>
<td>0.82 (0.72–0.91)</td>
<td>0.65 (0.61–0.69)</td>
</tr>
<tr>
<td>Erasmus cohort SBI: 230 (12%)</td>
<td>71 (4%)</td>
<td>109 (6%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCT (µg/L)^</td>
<td>0.18 (0.10–0.54)</td>
<td>0.64 (0.23–3.55)^</td>
<td>0.15 (0.09–0.40)</td>
<td>0.76 (0.64–0.88)</td>
<td>0.75 (0.69–0.80)</td>
</tr>
<tr>
<td>Maasstad cohort SBI: 103 (14%)</td>
<td>46 (4%)</td>
<td>52 (7%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCT (µg/L)^</td>
<td>0.21 (0.10–0.68)</td>
<td>1.36 (0.31–3.27)^</td>
<td>0.21 (0.16–1.29)</td>
<td>0.76 (0.64–0.86)</td>
<td>0.74 (0.67–0.81)</td>
</tr>
</tbody>
</table>

^median, interquartile range; *p<0.05
THE IMPACT OF RAPID VIRAL AND STREPTOCOCCAL TESTING ON ANTIBIOTIC PRESCRIPTION RATE IN FEBRILE CHILDREN WITH RESPIRATORY SYMPTOMS VISITING EMERGENCY DEPARTMENTS (EDs) IN EUROPE

Background: Most children attending the ED suffer from self-limiting viral respiratory tract infections. However, many of them receive unnecessary antibiotics, which might contribute to antimicrobial resistance. We aimed to assess the impact of rapid testing for respiratory viruses and group A streptococcus bacteria on antibiotic prescription.

Methods: This study is part of the MOFICHE study (Management and Outcome of Fever in children in Europe), which is embedded in the PERFORM project. The MOFICHE study is an observational multicentre study, which includes routine data of febrile children aged 0-18 years attending 12 European EDs. Febrile children with respiratory symptoms attending EDs equipped with rapid viral tests or rapid streptococcal tests were included.

Results: We included 15,823 children (median age 2.6 years, IQR 1.2-5.0) from 7 EDs equipped with rapid viral tests. A rapid viral test was performed in 1595 (10%) children. Overall antibiotic prescription was 38.7% (618/1595) in patients with viral tests performed and 30.2% (4261/14,089) in patients without viral tests performed. Antibiotic prescription rate was 36% (300/834) in those testing positive and 41.8% (318/761) in those testing negative. In addition, we included 9341 children (median age 3.2 years, IQR 1.7-6.1) from 3 EDs equipped with rapid streptococcal tests. A rapid streptococcal test was performed in 1459 (16.3%) children. Overall antibiotic prescription was 66.7% (973/1459) in patients with streptococcal tests performed and 28.7% (2191/7629) in patients without streptococcal tests performed. Antibiotic prescription rate was 99.3% (693/698) in those testing positive and 36.8% (280/761) in those testing negative.

Conclusions: Rapid viral testing did not reduce antibiotic prescription, even in patients testing positive for a virus. Rapid group A streptococcal testing increased antibiotic prescription in positively tested patients and reduced antibiotic prescription in negatively tested patients.
Clinical Trial Registration: Not applicable
PILOT 2-WAY STUDY IDENTIFIES HOST GENOMIC FACTORS RELATED TO ZIKA INFECTION USING WHOLE EXOME SEQUENCING

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Background: Zika virus (ZIKV) is an emerging flavivirus responsible for one of the most important severe pandemic emergencies of the last decade. This pathogen has been associated to neonatal brain severe disabilities. The understanding of genomic background which could explain the different symptomatology of Congenital Zika Syndrome (CZS) is essential for the better comprehension of this disease.

Methods: An initial assessment of statistical association of whole exome sequencing was carried out taking into account a double way analysis. Eighty paired samples were collected (mainly from American continent): 40 mothers that had been infected by ZIKV during their pregnancy and their 40 babies; 20 asymptomatic and 20 showing outcomes probably related to ZIKV infection (mainly microcephaly and CZS).

Results: Population stratification results did not show any relation with the phenotype. Allelic test and gene collapsing method tested point to three genes (PANO1, PIDD1 and SLC25A22) as plausible explanation for the different phenotypes of the children. These are linked with early infantile epileptic encephalopathy, symptoms strongly related with CZS. KEGG and reactome analysis showed that one of these genes is deeply related with apoptosis and P53 route, which is associated with microcephaly. We did not found a genomic association in mothers which could also explains the different phenotype in children.

Conclusions: We found three genes which could predict susceptibility to congenital ZIKV infection. Two of these genes are related with early infantile epileptic encephalopathy and another one is associated with microcephaly, which could likely explain the most severe complications seen in CZS (i.e seizures, brain damage, microcephaly and detrimental neuromedical growth). This project has received funding from the European Union’s Horizon 2020 research and innovation program under grant agreement No. 734584.

Clinical Trial Registration: Clinical trial registration: N/A
Background: Rapid and accurate diagnosis of HSV-1 and -2 (HSV1/2) in cerebrospinal fluid (CSF) is important. We performed a systematic review and meta-analysis of the diagnostic accuracy of commercialized rapid sample-to-answer PCR assays (results in <90 minutes, without a separate nucleic acid extraction step) for HSV1/2 detection in CSF.

Methods: We searched four databases and three conference abstract datasets (Jan. 2012 – July 2019). We included diagnostic accuracy studies of FilmArray Meningitis-Encephalitis Panel™ (Biomérieux) and Simplexa™ HSV 1&2 Direct Kit (Focus Diagnostics), compared to PCR reference standard, for HSV1/2 detection in CSF clinical samples. Quality was assessed using QUADAS-2 criteria. Accuracy estimates were pooled using random effects models. Protocol registered in PROSPERO (CRD42019145336).

Results: Thirteen studies met inclusion criteria (9 FilmArray; 4 Simplexa), comprising 3,138 samples, with 49 HSV-1 and 150 HSV-2 infections. Pooled sensitivities were 99.6% (95% confidence interval, 91.3%-100%) for detecting HSV-1 and 100% (97.7%-100%) for HSV-2. Pooled specificities were 99.8% (99.3%-100%) for HSV-1 and 99.8% (98.7%-100%) for HSV-2. For FilmArray, sensitivities were 89.6% (54.1%-100%) and 99.9% (89.8%-100%) for HSV-1 and HSV-2, respectively; specificities were 100% (99.7%-100%) and 100% (100%-100%). For Simplexa, sensitivities were 100% (92.7%-100%) and 100% (96.6%-100%) for HSV-1 and HSV-2, respectively; specificities were 99.3% (98.2%-99.9%) and 97.4% (94.0%-99.6%). Full text articles (n=7) and conference abstracts (n=6) showed similar pooled sensitivities and specificities. Underreporting frequently led to unclear risk of bias. Several FilmArray studies did not report the number of true negatives for HSV1/2, which led to their exclusion.

Conclusions: Our results suggest that commercialized sample-to-answer PCR assays have high sensitivities and specificities for HSV1/2 detection in CSF. However, definitive conclusions cannot be made, due to the limited number of studies and the low prevalence of infections.

Systematic Review Registration: Systematic review protocol registration: PROSPERO (CRD42019145336)
MATERNAL AND CHILD CHARACTERISTICS AND THE RISK OF HOSPITALISATIONS FOR SEPSIS AND MENINGITIS IN EARLY CHILDHOOD: A POPULATION-BASED COHORT STUDY

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Umeå University, Department Of Clinical Sciences, Umeå, Sweden

Background: Sepsis and meningitis are major causes of morbidity and mortality in early childhood. However, there is a scarcity of national population-based studies with maternal and child characteristics. Therefore, the aim of this study was to examine the association between child and maternal characteristics, and hospitalisations for sepsis and meningitis in early childhood (from 28 days to 2 years of age), in Swedish children born between 1997 and 2013.

Methods: We created a database by combining the Swedish Medical Birth Register, the National Inpatient Register, the Cause of Death Register and the Total Population Register and the Longitudinal integration database for health insurance and labour market studies. Exposures were child (sex, gestational age, small for gestational age, large for gestational age and congenital malformation) and maternal (age, education level, smoking, BMI and parity) factors. Outcomes were hospitalisations in sepsis and bacterial meningitis. Associations between variables and hospitalisations were estimated using logistic regression models and presented as adjusted odds ratios (aOR).

Results: Analyses included 1,406,671 children who were followed from 28 days until 2 years of age or censoring. Of these children, 1,011 were hospitalised for sepsis and 382 for meningitis. Extreme prematurity was strongly associated with sepsis (aOR 12.16; 95% CI 7.97–18.56) and meningitis (aOR 6.43; 95% CI 2.36–17.51). Moreover, children born small for gestational age, large for gestational age or with congenital malformation were more likely to be hospitalised for sepsis and/or meningitis (table). Finally, low maternal education level was associated with an increased risk of sepsis and meningitis.
**Conclusions:** In our study, prematurity and several other child and maternal characteristics were associated with an increased risk of hospitalisations for sepsis and meningitis in early childhood.  

**Clinical Trial Registration:** Not a controlled trial.
WHERE DO HOT CHILDREN SEEK CARE? HEALTH INEQUALITIES IN PRESENTATIONS TO ENGLISH PAEDIATRIC EMERGENCY DEPARTMENT

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2Great North Children's Hospital, Paediatric Infectious Diseases And Immunology, Newcastle upon Tyne, United Kingdom, 3Imperial College, Paediatric Infectious Disease, London, United Kingdom, 4University of Liverpool, Institute Of Psychology, Health And Society, Liverpool, United Kingdom, 5Newcastle University, Translational And Clinical Research Institute, Newcastle upon Tyne, United Kingdom, 6The University of Liverpool, Institute Of Infection And Global Health, Liverpool, United Kingdom

Background: Fever is one of the commonest reasons (<30%) to attend paediatric emergency departments (PED). We explored the relationship between deprivation, presentation, diagnosis and outcome of febrile children and young people attending three tertiary PED in England.

Methods: This prospective multi-centre observational study was part of PERFORM study assessing the management and outcome of febrile children in Europe. 10,033 children and young people aged 0-16 years presenting with fever (temperature >=38.0 °C) or history of fever were included. Data was collected from January 2017 until April 2018. Main outcome measures included attendance in PED, use of diagnostics and antibiotics, admission for >24 hours or to PICU and death. Data was analysed using multivariate regression.

Results: Median age 2.35 years, 45% female, 22% with co-morbidity and 49% triaged as high urgency categories. 58% of attenders were self-referrals. For 66% it was their first healthcare visit. 54% presented with viral infections, 15% with bacterial infections, 2% with inflammatory conditions and the remaining 29% with unknown or trivial diagnoses. 74% were discharged immediately, only 13% were admitted >24 hours. 47% of all patients came from quintile 1 (most deprived) and only 6% from quintile 5 (least deprived.) Using logistic regression there was no relationship between Index of Multiple Deprivation and severity of outcome (admission over 24 hours, to PICU or death) or use of antibiotics. However use of diagnostic tests was less frequent in the most deprived children, compared to the least deprived. (p=0.001 se 0.001coefficient -0.004)

Conclusions: There is a clear relationship between increasing deprivation and attendance to Emergency Departments. Across all quintiles there was no difference in life saving interventions, antibiotics prescribed or severity of outcome which suggests there is no difference in underlying causative disease. Reasons for disparity in attendance need to be explored and may help to inform future interventions.

Clinical Trial Registration: not applicable
RESPIRATORY Syncytial Virus-ASSOCIATED HOSPITALIZATIONS IN CHILDREN: A 10-YEAR POPULATION-BASED ANALYSIS, 2008-2018

E. Uusitupa¹, V. Koski¹, M. Waris², T. Vuorinen², T. Heikkinen³
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Background: Respiratory syncytial virus (RSV) is the leading cause of hospitalization in infants and young children. Several studies with different designs have assessed annual RSV hospitalization rates among children, yielding largely varying results. Knowledge about detailed RSV hospitalization rates especially in the youngest infants is important for the development of preventive and treatment strategies, but few population-based studies with laboratory-confirmed cases of RSV hospitalization are available.

Methods: The study population consisted of all children ≤16 years of age who were hospitalized with laboratory-confirmed RSV infection at Turku University Hospital, Finland, during the 10-year period of September 1, 2008, to August 31, 2018. Viral sampling for identification of respiratory viruses was routine for children hospitalized with respiratory symptoms. Age-stratified data on the population were derived from Statistics Finland. Overall, the study comprised 838,174 person-years of follow-up.

Results: In total, 1043 children were hospitalized with RSV; 765 (73.3%) of them were <1 year of age. The average annual rate of hospitalization peaked among infants 1 month of age (53.3/1000), followed by infants aged <1 month (35.6/1000) and 2 months (34.1/1000). In all children <1 year of age, the rate of RSV hospitalization was 16.3 per 1000 children. A total of 127 (12.2%) of all 1043 children were treated at the pediatric intensive care unit.

Conclusions: This 10-year study with a clearly defined population and active search for viruses in hospitalized children demonstrated that the annual rates of RSV hospitalization among the youngest infants were substantially (>2-fold) higher than reported previously in corresponding studies in the United States. These data may help inform the development of strategies for the prevention and management of RSV illnesses in young children.
Background: A large number of refugees have arrived in Europe in recent years. Interrupted vaccination programmes or incomplete vaccinations in many countries of origin may have resulted in low vaccination coverage among asylum seekers. Recent serological surveys among adult asylum seekers in Europe have reported relatively high but still potentially insufficient immunity for herd protection. Limited data exists on immunity to vaccine-preventable diseases (VPD) among children. We analyzed immunity to seven VPDs among asylum seekers in Finland.

Methods: Asylum seekers of all ages from Iraq, Russian Federation, Somalia and Afghanistan were invited to participate in the study between May 2018 and August 2019. A blood sample was collected before any vaccination in Finland. IgG antibodies against measles, mumps, rubella (enzyme immunoassay), and diphtheria, tetanus and Haemophilus influenza type b (Hib)(multiplex immunoassay) and neutralizing antibody titers against polio types 1 and 3 (neutralization test, NT) were determined. Participants were considered seropositive when IgG concentrations/titers were above or equal to the disease-specific cut-offs: 150 mIU/ml for measles, titer 230 for mumps, 4 IU/ml for rubella, 0.01 IU/ml for diphtheria and tetanus, and 0.15 µg/ml for Hib. Polio NT titers ≥8 were considered seropositive.

Results: Overall, the proportions of seropositive adults were relatively high against all VPDs. In contrast, the proportions of individuals who have antibodies were lower against all VPDs among Russian children, especially among children <6 years of age coming from the Russian Federation the proportion of seropositive individuals was very low confirming the need for checking and updating vaccinations as soon as possible.

Conclusions: Seropositivity against most studied VPDs was relatively high among adult asylum seekers. Among children <6 years of age coming from the Russian Federation the proportion of seropositive individuals was very low confirming the need for checking and updating vaccinations as soon as possible.
Clinical Trial Registration: Not a clinical trial
IMMUNIZATION IN MIGRANT UNACCOMPANIED MINORS. DO WE NEED TO DO SEROLOGY FIRST?

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Background: As a consequence of political instability in Africa and Middle East, there has been a dramatic increase in the number of unaccompanied minors (UMs) arriving to Europe in recent years. This population frequently has an incomplete immunization status due to obstacles in access to health care in their countries and during their journey. Our aim is to describe the immunization rates of UMs attended in a Spanish tertiary hospital.

Methods: Descriptive retrospective study. We included all of the UMs referred from reception centers in Madrid and attended in a reference Unit for Pediatric Tropical Diseases from January 2018 to October 2019. We reviewed the information involving immunization status and serology tests (HBV, HAV, measles, varicella, rubella and mumps). We compared minors born in Morocco and those born in any other country.

Results: 140 UMs were included. Mean age: 16.7 ± 0.8 years. 94.3% male and 60% Moroccans. 61 minors (45.1%) were seronegative for HBV, 27 (23.9%) for measles, 24 (21.4%) for HAV, 14 (12%) for varicella, and 6 (5.5%) for rubella and mumps. Measles IgG seroprevalence was significantly lower ($\chi^2_{p<0.001}$) in Moroccan minors. 22 UMs (16.3%) had had a previous HBV infection, and 12 (8.9%) had an active infection. HBV infection prevalence was significantly higher ($\chi^2_{p<0.001}$) in minors who were not born in Morocco.

Conclusions: UMs are a highly unprotected and vulnerable population with variable vaccination rates, but definitively lower than native European minors. Routine serology tests are undoubtedly recommendable in UMs to detect active infections and to update the immunization schedule. Nonetheless, prompt vaccination according to the local recommended schedule is a priority even if immunization status is unknown and serology tests are not available.
SOIL-TRANSMITTED HELMINTHS INFECTION IN BANGLADESH: ASSESSMENT OF THE PREVALENCE, ASSOCIATED FACTORS AND PERFORMANCE EVALUATION OF LABORATORY DIAGNOSTIC METHODS.

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Background: Soil-transmitted helminth (STH) infections continue to be a major global cause of morbidity, have been recognized as endemic in Bangladesh for over a century. The study aimed to assess the prevalence of intestinal parasitosis with associated risk factors and to compare different diagnosis methods.

Methods: A mixed-method study, was conducted between July 2017 to June 2018 in Dhaka and Sylhet districts of Bangladesh. Stool samples from 400 school-aged children were collected and examined using direct smear, Kato-Katz, and Harada-Mori technique. Eight focus group discussions (FGDs) and eight in-depth interviews (IDIs) were also conducted among guardians of children, school teachers, and health officers.

Results: The prevalence of \textit{Ascaris lumbricoides} was the highest (29.33\% and 25.00\%) followed by \textit{Trichuris trichiura} (11.33\% and 10.00\%), \textit{Ancylostoma duodenale} (02.67\% and 05.00\%) and \textit{Necator americanus} (02.33\% and 03.00\%) were recorded in Sylhet and Dhaka respectively. The prevalence of \textit{Strongyloides stercoralis} was found 12.67\% in Sylhet. Significant association (p<0.05) was found with the educational status of the household heads, having domestic animals in the house, walk-in barefoot and household latrine type. Kato-Katz method was found to be more effective in diagnosing \textit{A. lumbricoides} and \textit{T. trichiura} while Harada-Mori culture was found more effective for \textit{S. stercoralis} detection. Some of the major barriers associated with the national parasites control program found in this study were lack of information about population dynamics, inadequate community engagement, MDA drug distribution policies, and information dissemination gap.

Conclusions: Despite the bi-annual mass drug administration program since 2008, the prevalence of intestinal parasitic infections is very high among the school children. Multiple intervention strategies (such as the provision of clean water, health education, and maintenance of functioning sanitation systems) are essential to reduce the disease burden.

Clinical Trial Registration: ClinicalTrials.UGM2059
IMPACT OF ROTAVIRUS VACCINATION ON INCIDENCE OF INTUSSUSCEPTION IN ENGLAND: A TEN-YEAR ECOLOGICAL ANALYSIS.

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Background: Rotavirus vaccination (RV) has been linked to a small early increase in the risk of intussusception, which has substantially influenced immunisation policies. It is unclear whether RV is causative or precipitates inevitable events. We sought to determine whether introduction of RV was associated with a change in the overall and age group-specific incidence of childhood intussusception in England.

Methods: Using Hospital Episode Statistics data, we employed Poisson regression to compute incidence rate ratios (IRR) for intussusception, comparing the post-vaccine period (2014-2017) to the pre-vaccine period (2008-2012) in 0-12 months and 0-36 months age groups and in subgroups 8-16 weeks, 17-24 weeks, 25-32 weeks, and 33-40 weeks. We conducted interrupted time series analysis to compute IRRs in the 0-12 months and 0-36 months age groups accounting for baseline temporal trends.

Results: An increase in incidence in the 8-16 weeks age group (IRR 1.46, 95% CI 1.12-1.91), those receiving vaccination, was compensated for by decreases in the 17-24 weeks (0.77, 0.63-0.94) and 25-32 weeks (0.71, 0.59-0.86) age groups (Figure 1). We observed no significant change in incidence in the 0-12 months (0.88, 0.74-1.05) or 0-36 months (0.90, 0.78-1.03) age groups. The proportion of patients receiving surgical or radiological interventions was not significantly different (p = 0.76) between the pre-vaccine (44.3%) and post-vaccine (43.7%) periods.
Conclusions: This is the first study to demonstrate the absence of an increase in overall incidence of intussusception in a country exclusively using the monovalent vaccine. A transitory increase in incidence in the peri-vaccination age group is compensated for by a reduction in older infants, suggesting that RV may reveal individuals already predisposed to intussusception. These findings will reassure policymakers and the public regarding the safety of the rotavirus immunisation programme.

Clinical Trial Registration: Not applicable.
Background: There are no spatio-temporal studies of the impact of rotavirus vaccination on rotavirus (RV) and acute gastroenteritis (AGE) hospitalizations. The geographic mapping of vaccination impact is an important tool to understand changes in RV epidemiology.

Objective: RotApp presentation, the first app allowing to explore RV vaccination impact on RV and AGE hospitalizations in a space-time framework in children <3 years of Valencia Region of Spain.

Methods: Interactive shiny app mapping the avoided hospitalizations by RV vaccination, vaccine coverage and RV and AGE-hospitalization risk. Dynamic maps are available by health care district and department, age groups and sex. Temporal trends are also included. Electronically recorded population data (socio-demographic, vaccination status and hospitalizations) of children <3 years between 2005-2016 were used. Statistics: Besag-York-Mollie model was used to smooth risks estimations in maps sectored by health care district. RV vaccination impact (avoided hospitalizations) was estimated by a Bayesian spatio-temporal model.

Results: Information of 721,741 children was collected. Of them, 189,247 were vaccinated, 17,482 hospitalizations for GEA and 4,871 for RV were registered. Overall, ~1866 hospital admissions for RV were averted in vaccinees during 2007-2016 (the number of hospitalisations averted by vaccination was coverage-dependent). Important spatio-temporal patterns in RV and AGE hospitalisations, RV vaccination coverage and in their associated adverted hospitalisations were shown.

Conclusions: RotApp is an easy tool that allows users to access and interact with real spatio-temporal data on RV epidemiology. Impact of different vaccine coverage rates in terms of avoided hospitalisations in a geographical-time framework is provided. Designing interactive Apps improves the visualization and interpretation of the results. Therefore, it results an easy way to reach a wider audience. Website link: (https://rotapp.shinyapps.io/app_-_-vt3/)
LESSONS LEARNED FROM THE TREATMENT OF CHILDREN WITH STAPHYLOCOCCUS AUREUS BACTEREMIA ASSOCIATED WITH ACUTE HEMATOGENOUS OSTEOMYELITIS: IMPLICATIONS OF SEVERITY OF ILLNESS STRATIFICATION ON ANTIBIOTIC AND SURGICAL TREATMENT

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Background: Children with acute hematogenous osteomyelitis (AHO) and associated *Staphylococcus aureus* bacteremia (SAB) create antibiotic and surgical treatment challenges with limited evidence-based guidance. Children with severe illness are frequently treated with a variety of antibiotics in combination or succession, including vancomycin, with potential for nephrotoxicity. This audit investigates whether antibiotic and/or surgical decisions might be tailored according to severity of illness of the affected child.

Methods: Children with AHO and SAB who were treated from 2009-2018 were retrospectively studied. Severity of Illness was determined using a previously validated scoring system ranging from 0 (mild) to 10 (severe). Cohort comparison was accomplished by severity of illness groups: mild (0-3); moderate (4-7); and severe (8-10). Cohorts were compared according to antibiotic selections and duration, surgical treatment, and treatment outcomes.

Results: 246 children with AHO and SAB were stratified: mild (80), moderate (99), severe (67). Mild illness had fewer antibiotic selections (1.9 vs. 2.3 vs. 3.6), less vancomycin usage (24.7% vs. 56.0% vs. 92.3%) and fewer surgeries (0.4 vs. 1.0 vs 3.1). Severity impacted bacteremia duration (1.6 vs. 2.4 vs. 4.7 days), IV treatment (4.6 vs 9.8 vs 23.3 days), acute kidney injury occurrence (0 vs 1 vs 13 cases), length of stay (5.5 vs. 8.9 vs. 21.3 days), readmissions (7.8% vs. 1.1% vs 26.2%), and CRP normalization (7.9 vs. 14.3 vs. 31.1 days).

Conclusions: Treatment of AHO and SAB should be tailored to the severity of illness of the child. A “one size fits all” approach has pitfalls which may subject children with mild illness severity to suboptimal antibiotic combinations, potentially including nephrotoxic agents, and unnecessary invasive procedures. For children with severe illness, aggressive surgical source control and a more simplified, sustained bactericidal antibiotic strategy should be pursued.
THE CORRELATION BETWEEN ANTIBIOTIC SUSCEPTIBILITY, GENOTYPE, AND CLINICAL OUTCOME IN EUROPEAN INFANTS LESS THAN 90 DAYS AFFECTED BY BLOODSTREAM INFECTIONS CAUSED BY ENTEROBACTERALES

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Background: Mortality in neonates with Gram-negative bloodstream infections (GN-BSIs) has remained unacceptably high over the last decade (10-15%), despite improvements in neonatal care. This analysis was part of a retrospective study including European infants <90 days affected by Enterobacterales sepsis, aiming to evaluate any potential association between the patient, pathogen, treatment determinants and neonatal mortality. Patients were retrieved from the NeoMero, CLAHRC, and NeonIN studies.

Methods: A survival analysis to investigate 28-day mortality probability and predictors was performed including (I) infants <90 days (II) with an available Enterobacterales blood isolate with (III) clinical, treatment and 28-day outcome data. Isolates were identified by MALDI-TOF and characterised by Whole-Genome Sequencing (Illumina MiSeq platform). Antibiotic susceptibility profiles were obtained with disk diffusion test (EUCAST 2019). Virulome and resistome were categorised as number of virulence and resistance mechanisms carried by each isolate.

Results: Seventy-seven infants from six European countries between 2010-2015 were included, with a median age at onset of 11 days (Q1-Q3 6.4-26). By survival analysis, the 28-day death probability was 19.5%. In the descriptive analysis, early age at onset, culture positive for Escherichia coli and number of virulence mechanisms per isolate were significantly associated with mortality. By Cox multivariate regression, none of the investigated variables was significant. Among the different organisms, E. coli had significantly more virulence mechanisms involved compared with other species (p<0.0001).
Conclusions: Previous studies failed to demonstrate a significant correlation between underlying conditions, pathogen, resistance phenotype, treatment and neonatal outcome. This pilot study has demonstrated the feasibility of investigating the association between neonatal sepsis mortality and the causative Enterobacterales isolates virulome. This relationship needs further exploration in larger studies, ideally including host immunopathological response, in order to develop a tailor-made therapeutic strategy.
PREDICTION OF SEVERITY AND FINAL DIAGNOSIS IN CHILDREN WITH ACUTE INFECTIONS: A MULTICENTRE OBSERVATIONAL STUDY FROM THE PERFORM CONSORTIUM

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Background: Fever is a common acute paediatric presentation, however, only a small number of cases progress to life threatening disease. We used published scores to predict disease severity and phenotype.

Methods: The PERFORM cohort comprises children with fever who presented to emergency departments and inpatient units across Europe. Detailed clinical data was captured, and phenotyping performed using robust protocols. PEWS, qSOFA, risk group using the NICE guidelines’ warning signs of sepsis and the physiological scores described in the recent re-analysis of the FEAST trial were calculated using triage observations and used to predict PICU admission with a critical care intervention or death within 2 days. Statistical testing was performed with non-parametric tests.

Results: Complete case data were available for 1283 children (total cohort 4885). 98 children (7.7%) were admitted to PICU with an intervention or died within 2 days. 801 (62%) were identified as high-risk by the NICE guidelines, of these 92 were in the PICU group or died with 2 days. For our outcome, PEWS had an AUC of 0.87 (95%CI 0.83-0.90), qSOFA 0.68 (95%CI 0.63-0.73) and the physiological scores 0.88 (95%CI 0.84-0.91). The median physiological score in the PICU group was 164 (IQR 127-225) compared to 84 (IQR 64-112) in those who were not in this group (p<0.001). Although the scores identified critical illness well, they did not distinguish between bacterial and viral infections (physiological scores p=0.1, PEWS p=0.4, qSOFA p=0.2).

Conclusions: PEWS and the physiological scores effectively differentiate disease severity in a large cohort of febrile children. However, they do not distinguish bacterial from viral illness. Clinical recognition of disease severity can be achieved using physiological parameters but other approaches, such as biomarkers, will be needed to identify patients with bacterial infection.

Clinical Trial Registration: not applicable
Background: The identification of life-threatening infection in febrile children presenting to the Emergency Department (ED) remains difficult. We aimed to evaluate a modified, age-adjusted qSOFA score (LqSOFA) for the identification of life-threatening infection in febrile children presenting to the ED. This rapid bedside score ranges from 0-4 and is based on age-adjusted heart rate and respiratory rate, capillary refill time, and conscious level on the Alert, Responds to Voice, Responds to Pain and Unresponsive scale.

Methods: Children presenting to the ED with fever ≥38°C, history of fever or a suspected infection in whom blood tests were performed (with complete observation and outcome data) were included from the prospective multi-centre observational PERFORM study. The LqSOFA, age-adjusted qSOFA, and PEWS were calculated. The primary outcome was PICU admission within 48 hours and the secondary outcome was 28-day mortality.

Results: 2885 children were included with a median age of 4.4 years (IQR 1.6-9.5 years). There were 25 deaths (0.9%) and 277 admissions to PICU (9.6%) within 48 hours. LqSOFA predicted PICU admission within 48 hours with an area under the curve (AUC) of 0.77 (95%CI 0.73-0.80), versus qSOFA 0.60 (95%CI 0.57-0.64), and PEWS 0.82 (95%CI 0.79-0.84). LqSOFA predicted 28-day mortality with an AUC of 0.78 (95% CI, 0.62-0.94), versus qSOFA 0.82 (95% CI, 0.66-0.97), and PEWS 0.80 (95% CI, 0.65-0.95).

Conclusions: In this independent data set the LqSOFA outperforms the qSOFA in predicting PICU admission in children presenting to the ED with fever or a suspected infection. PEWS performs well for both outcomes, although is far more extensive and time-consuming to calculate than the LqSOFA. The simple and rapid calculation of the LqSOFA score makes it an attractive bedside tool despite the modest performance characteristics.
DECREASING MACROLIDE RESISTANCE AMONG GROUP A STREPTOCOCCI CAUSING PHARYNGITIS IN PORTUGAL

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Background: Current guidelines recommending rapid antigen detection tests for diagnosing Group A Streptococci (GAS) tonsillo-pharyngitis result in infrequent isolation of GAS, leading to scarce epidemiological information. This prospective study aimed to evaluate macrolide resistance and determine the diversity of resistant GAS lineages causing tonsillo-pharyngitis in Portugal.

Methods: During 2014-2016, suspected cases of pediatric streptococcal tonsillo-pharyngitis in Centro Hospitalar de Leiria, Portugal, were confirmed by pharyngeal swab culture. A total of 1090 non-duplicate GAS isolates were recovered and tested for erythromycin and clindamycin susceptibility by disk diffusion, according to CLSI guidelines. The presence of resistance genes, the emm type and the multilocus sequence type (ST) were determined for all erythromycin resistant isolates.

Results: The overall macrolide resistance rate was 2.8% (n=31), presenting a decreasing trend during the study (p=0.009). Twenty isolates showed inducible clindamycin resistance (iMLSb) and carried the erm(TR) gene, three presented constitutive clindamycin resistance (cMLSb) carrying erm(B), and eight were susceptible to clindamycin (M) harboring mef(A). Three emm types were identified: emm77 (n=20 iMLSb, ST63), emm75 (n=8 M, ST49; n=2 cMLSb, ST150), and emm11 (n=1 cMLSb, ST403).

Conclusions: The decrease in macrolide resistance is in line with that reported in a multicenter study in previous years, indicating that macrolide resistance among GAS causing pharyngitis remains low, despite stable and significant macrolide consumption in Portugal (2.75-3.05 DDD/100,000 persons/day). The dominant lineage was emm77/ST63/erm(TR)/iMLSb, similarly to that found in 2013 in the multicenter study. The emm75 isolates comprised two distinct lineages: emm75/ST150/erm(B)/cMLSb and emm75/ST49/mef(A)/M. In Portugal, mef(A) had been previously identified among emm75 isolates presenting ST657 or ST150. The emm11/ST403/erm(B)/cMLSb lineage persists but at low frequency. The disappearance of the large diversity of macrolide-resistant lineages found prior to 2013 remains unexplained.

Clinical Trial Registration: Clinical trial registration: N/A
Background: Care bundles aim to standardize sepsis recognition and treatment and have been shown to improve outcomes for children. In view of the difficulty identifying sepsis in children, there is concern that such campaigns may adversely impact antimicrobial stewardship. The Queensland State-wide Sepsis Collaborative introduced sepsis pathways into Emergency Departments in 2018. We sought to describe the quantity and appropriateness of antimicrobial use in children evaluated on the sepsis pathway.

Methods: A prospective study of antibiotic use in children evaluated using the sepsis pathway in three Emergency Departments (EDs) in South-East Queensland, Australia. Data relating to clinical presentations occurring in 2019 were entered into a REDCap database. Antibiotic use was evaluated in terms of consumption, and appropriateness. Baseline data from 2017 were analysed in a comparator group, matched by ED discharge code.

Results: 1042 children were evaluated on the pathway, of whom sepsis was considered likely in 28%. Median time to antibiotics was 172 minutes overall, and 124 minutes in children considered likely to have sepsis. 51% of children received empirical antibiotics, and 42% (223/527) of these received more than one agent. 35% considered unlikely to have sepsis received antibiotics, including 62/210 who received more than agent. Empirical antibiotic prescriptions were more often appropriate in 2019 than in 2017 (87% v 80%, p=0.003), and antibiotic duration shorter (median 1 v 2 days, p<0.001).

Conclusions: Many children evaluated on the sepsis pathway received antimicrobials, even if sepsis was unlikely. Appropriateness of empirical prescribing improved following the introduction of the pathway. Incomplete matching of the comparator group limits interpretation of the observed differences. Further analysis of the baseline dataset, alongside department-wide analysis of antimicrobial consumption will allow more robust inferences about the impact of the pathway.
COMPARING WATCHFUL WAITING APPROACH VS. ANTIBIOTIC THERAPY IN CHILDREN WITH NON-SEVERE ACUTE OTITIS MEDIA: A RANDOMISED CLINICAL TRIAL

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Background: Acute otitis media (AOM) is a common childhood disease. Currently, American Academy of Pediatrics (AAP) guideline suggests two treatment options for AOM including the use of antibiotics and watchful waiting approach. The aim of this study was comparing both approaches for treatment of non-severe AOM in Iran.

Methods: This randomized clinical trial was undertaken in pediatric infectious diseases clinic in Buali tertiary hospital in Sari, north of Iran from March 2016 to 2018. All previously healthy children with AOM diagnosis, between 6 months to 6 years old, included the study. The patients were randomly assigned into intervention (80 mg/kg/day Amoxicillin for 7-10 days) and control (watchful waiting approach) group. Recovery from AOM and adverse reactions were evaluated after the first 72 hours. The patients were followed for frequency of AOM and middle ear effusion (MEE) one and 3 months after the intervention.

Results: A total of 396 children (188 cases in intervention group, mean age: 29.05±16.6 months, and 208 cases in control group, mean age: 28.88±15.9 months) were participated. AOM recovery was significantly different (73% and 44% in intervention and control group, respectively, p<0.01). Recurrence of AOM and persistence of MEE, one month following the intervention was not different between two groups, but AOM recurrence between 1 and 3 months was more frequent in control group, p<0.05. Frequency of diarrhea was higher in intervention group (p<0.01) but there was no significant difference between two groups regarding vomiting and skin rash.

Conclusions: The faster recovery from AOM is achieved when antibiotic treatment regimen is applied, although the risk of potential side effects should be considered.

Clinical Trial Registration: IRCT20111224008507N2
THE ADOLESCENT PARADOX AT THE ED: YOUNG PEOPLE VISITING THE ED – NOT TO BE UNDERESTIMATED.

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Background: Most studies regarding febrile children have focused on identifying infants and young children with serious or invasive bacterial infections. Although case series of invasive bacterial infections in adolescents have been described, little is known on the population of adolescents visiting the ED with fever. We aimed to describe the patient characteristics, diagnosis and management of febrile adolescents visiting the ED.

Methods: The MOFICHE / PERFORM study prospectively collected data on febrile children (0–18 years) presenting to 12 European Emergency Departments (ED’s).

We performed descriptive and univariate analysis regarding patient characteristics, markers of disease severity (e.g. vital signs, Paediatric Early Warning Score, (PEWS)), management (diagnostic tests, therapy, admission) and diagnosis (focus, viral/bacterial disease), comparing adolescents (12-18 years) to younger children (< 12 years).

Results: 38,480 children were included, of which 2,577 were adolescents. Adolescents were more often triaged as high-urgent (OR 1.2, 95%CI 1.1-1.2) and described as ill-appearing (OR 1.6, 1.6-1.6) than younger children. Non-classical symptoms (e.g. dehydration) were more common in adolescents with sepsis/meningitis (OR 1.6, 1.6-1.7). CRP was performed more frequently in adolescents and more often reached levels >60 mg/l (OR 1.9, 1.9-2.0). Adolescents were more often diagnosed with bacterial disease (OR 1.6, 1.6-1.7), in particular sepsis/meningitis (OR 1.9, 1.7-2.0) and more often required admission, intravenous antibiotics or life-saving interventions (OR 1.4, 1.4-1.4).

Conclusions: Febrile adolescents have significantly different presenting signs and symptoms and different diagnosis and management compared to younger children. Although younger children presented to the ED more frequently, adolescents were more often diagnosed with invasive bacterial infections such as sepsis/meningitis and more often were treated with intravenous antibiotics.

Our data should raise awareness about the higher risk for more serious infections in this group with not always typical presentation.
Background: Children exposed to Zika virus (ZIKV) while in uterus may develop acquired defects, among others, neurodevelopmental delays. Recent evidence shows language and cognitive delays in ZIKV-infected normocephalic children, and in ZIKV-uninfected children born to women with confirmed ZIKV infection.

Methods: A hospital-based prospective observational study was conducted at Hospital Clinic Barcelona and Hospital Sant Joan de Déu, Spain, from 2016 to 2019. Children born to women with ZIKV infection were followed up to assess psychomotor development at months 1, 2, 6, 12 and 24. Last follow up visit included a tool to assess cognitive, sub-receptive language, expressive language, gross and fine motor skills, the Bayley Scales of Infant and Toddler Development®, Third Edition. Data on socioeconomic status was obtained from families of children assessed.

Results: A total of 20 children were followed up. A neurodevelopmental delay in the language function was found in 35% of them. One child (5%) scored below average in the cognitive function, and seven (35%) in the language function (-1 to -2SD). Motor function for all the children was within average score (±1 SD). One child presented a delay in the domain-specific score for the gross motor function. One third of parents had low levels of education (only completed elementary education), and 41% of mothers and 17% of fathers were unemployed.

Conclusions: This is the first observational study conducted in a non-endemic area reporting neurodevelopmental outcomes in ZIKV exposed uninfected children. In line with recent evidence, our study shows that there might be an association between prenatal ZIKV infection and language delay in early childhood. These findings are important even considering the educational and social factors, more studies are needed to clarify these findings.
Background: Prognostic markers associated with fetal involvement in cytomegalovirus (CMV) infection during pregnancy are not well understood. Furthermore, it is unclear whether the cell-mediated immune response in pregnant women influences CMV intrauterine transmission.

Methods: Multicenter prospective study started at 10 hospitals in Spain in January 2017. Blood samples were collected from pregnant women at the time of diagnosis of CMV infection. Primary CMV infection was defined as the presence of CMV seroconversion during pregnancy or a positive IgM and IgG with low avidity index. T-Cell mediated immune response to CMV was assessed by the evaluation of the number of specific interferon-γ CD4 and CD8 producer cells against CMV. Quantitative analysis of CMV-CD8+/CD4+IFN-γ was performed by intracellular cytokine flow cytometry. Intrauterine CMV transmission was diagnosed by detection of viral DNA by real-time PCR, either in amniotic fluid or newborn’s urine.

Results: 133 pregnant women with a suspected CMV infection were evaluated. 22 cases were excluded because fetal/newborn infection was still unknown or blood samples were not available. Among the remaining 111 women, 64 were primary infections. Forty-three mothers (68.3%) had other children under 3 years of age. One half (48.4%) showed symptoms during pregnancy. Eighteen mothers (29.5%) received treatment with cytomegalovirus hyperimmune globulin and 14.3% with valacyclovir. There were 25 transmitters and 39 non-transmitters women. There were no differences between transmitters and non-transmitters in blood and urine viral load, total lymphocyte count, CMV-CD8+IFN-γ or CMV-CD4+IFN-γ count.
Conclusions: In this cohort of pregnant women with primary CMV infection, the total lymphocyte count, CMV-CD8+IFN-γ and CMV-CD4+IFN-γ count were not associated with CMV transmission to the fetus. 
Clinical Trial Registration: IRB: 17/007
Background: Prognostic markers of symptomatic congenital cytomegalovirus (cCMV) infection are uncertain. Furthermore, whether the specific cell-mediated immune response in infants with cCMV is associated or not with sequelae remains unknown.

Methods: Multicenter prospective study at 8 hospitals in Spain from January 2017 until December 2019 within REDICCMV. Blood samples were collected during the first 28 days of life from newborns diagnosed with cCMV. Total lymphocyte count, lymphocyte subpopulations and specific CMV T-cell responses were evaluated. CMV-CD8/CD4+IFN-γ counts were performed by intracellular cytokine flow cytometry. Sequelae were evaluated at 6 and 12 months of age. Sensorineural hearing loss was defined as a hearing threshold >25dB by BSER in either ear. Neurologic abnormalities at 12 months were defined as the presence of epilepsy, inability to remain seated without assistance, motor impairment, chorioretinitis, microcephaly, or neurodevelopmental delay.

Results: Sixty-six newborns with cCMV infection were evaluated. Seven were excluded because CMV-CD8/CD4+T-cell count were not available. Among the remaining 59 infants, 46 had available data regarding sequelae. Twelve (12/46, 26.1%) presented sequelae, including sensorineural hearing loss (10/12, 83.3%), neurologic abnormalities (4/12, 40%) and visual impairment (1/12, 8.3%). Infants with sequelae showed a lower CD4+ T-cell percentage and count during the first month of life than those without sequelae (18.0% vs 39.3%, p=0.028; 1154 cells vs 1722,p=0.042 ). Total lymphocyte count, CMV-CD8+IFN-γ and CMV-CD4+IFN-γ counts were not associated with a higher risk of sequelae.

Conclusions: In this cohort, a lower CD4+T-cell count was associated with sequelae during the 1st year of life. Since sample size was small, larger studies are needed to better understand the real role of cell-mediated immune response in cCMV infection.

Clinical Trial Registration: IRB: 17/007
MOLECULAR EPIDEMIOLOGY, INCIDENCE AND MORTALITY OF NEONATAL GROUP B STREPTOCOCCAL SEPSIS AND MENINGITIS IN THE NETHERLANDS

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Background: *Streptococcus agalactiae* (Group B streptococcus, GBS) is the most common cause of invasive disease in neonates. It causes substantial mortality and morbidity. We assessed the molecular epidemiology, incidence and mortality of GBS invasive disease in the Netherlands over the past 30 years. We compared incidence, serotype, and sequence type (ST) distribution of meningitis with sepsis cases aged 0 to 3 months.

Methods: We performed a nationwide surveillance study with data from the Netherlands Reference Laboratory for Bacterial Meningitis from 1987 to 2016. All culture positive GBS cases in patients 0-3 months old were selected. Serotyping was performed by latex agglutination. Capsule-, multi locus sequence typing, and clade profiles were extracted from whole genome sequences. Outcome data was obtained through the Municipal Personal Records Database.

Results: 521 meningitis and 875 sepsis cases were identified. For meningitis, mean annual incidence was 0.09 (95%CI:0.08-0.10) per 1000 live births and remained stable (b<0.001;p=0.646). The annual incidence of sepsis cases increased (b=0.009;p<0.001), mainly due to a rise in ST17 (b=0.003;p<0.001). In meningitis, ST17 increased with a concurrent decline of ST19 cases (b=-0.001;p<0.001). Serotype III (62%) and ST17 (34%) predominated in both sepsis and meningitis. 54% of serotype III isolates were ST17 and 24% ST19. Overall mortality was 6.7%. Serotype Ib was associated with mortality in meningitis (OR 8.78 95%CI:1.92-40.05).
Conclusions: Hypervirulent strain ST17 that express the serotype III polysaccharide capsule, causes most cases of meningitis as well as sepsis in neonates. The incidence of this GBS type is rising, resulting in increasing rates of neonatal sepsis. It is also becoming more common in meningitis, but overall meningitis incidence did not increase due to a concurrent decline in other sequence types.
SEROLOGICAL CORRELATE OF PROTECTION AGAINST INVASIVE GROUP B STREPTOCOCCUS IN SOUTH AFRICAN INFANTS: AN OBSERVATIONAL BIRTH-COHORT STUDY.

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Background: Licensure of a Group B streptococcus (GBS) vaccine for protecting infants against invasive GBS disease (IGbsD) will likely need to be based on demonstrating vaccine safety in pregnant women and benchmarking immunogenicity against a serological correlate of protection (CoP). We investigated the association between naturally-derived maternal GBS serotype-Ia and III anti-capsular IgG and risk reduction of IGbsD in infants ≤90 days age.

Methods: In a matched case-control study, IGbsD cases were identified from a cohort of 38,233 mother-newborn dyads, supplemented by cross-sectional enrolment of additional IGbsD cases. Mothers colonized vaginally with serotype Ia or III at birth, and their healthy infants were eligible as matched-controls. Serotype-specific anti-capsular IgG was measured on maternal and cord blood/infant sera by multiplex Luminex assay; and the IgG threshold associated with 90% risk reduction of IGbsD derived by estimating absolute disease risk.

Results: In infants born ≥34 weeks gestation age, IgG geometric mean concentrations were lower in cases than controls for serotype Ia (0.04 vs. 0.47 µg/ml; p<0.001) and III (0.12 vs. 0.36 µg/ml; p<0.001). Serotype-specific infant IgG threshold of ≥1.22 and ≥1.25 µg/ml were associated with 90% risk reduction of serotype-Ia and III IGbsD, respectively. For serotype III, the maternal serological CoP threshold associated with 90% risk reduction was ≥2.91 µg/ml (2.33-fold higher than the corresponding infant threshold).

Conclusions: The CoP identified on infant sera against serotype-Ia and III IGbsD supports the case for licensure of a GBS polysaccharide-protein conjugate vaccine based safety evaluation in pregnant women, and immunogenicity evaluation benchmarked against the defined thresholds.

Clinical Trial Registration: ClinicalTrials.gov NCT02215226.
Background: Neonates, who develop septic shock, have a high incidence of adrenal insufficiency. Early hydrocortisone may result in early reversal shock by upregulation of catecholamine receptors and may improve outcomes. We compared early hydrocortisone versus placebo for 14-day mortality in neonates with fluid-refractory shock.

Methods: We enrolled consecutive neonates with fluid-refractory shock in two gestational age strata - ≤30 weeks, >30 weeks. At the time of starting inotropes, we randomly assigned them to receive either early hydrocortisone (1.0 mg/kg every 6 hourly for 48 hours followed by 1.0 mg/kg 12 hourly for three days) or placebo (normal saline). All study investigators were blinded except the bedside nurse. If any neonate developed catecholamine resistant shock [shock persisted despite >10 µg/kg/min dopamine and a directly acting vasoactive agent (either epinephrine >0.3 µg/kg/min or dobutamine >10 µg/kg/min)], we discontinued study drug, and started open-labelled hydrocortisone. We followed neonates for mortality within 14 days of shock onset, and other outcomes.

Results: Eighty-four neonates were randomised to early hydrocortisone (n=43) and placebo groups (n=41). Both groups had comparable demographic characteristics, maternal risk factors, clinical variables, acid-base and echocardiographic characteristics at baseline. Twenty-seven neonates had positive blood culture and 55 had positive sepsis screen. All-cause mortality within 14 days was comparable between ‘Early hydrocortisone’ group and ‘Placebo’ group [37 (72.1%) vs 34 (82.9%) neonates, [RR 0.70 (95%CI 0.37, 1.33), p=0.30). The two groups had comparable duration of inotropes, mean & total inotrope scores, incidence of gastro-intestinal hemorrhage, perforation, hyperglycemia, necrotising enterocolitis, bronchopulmonary dysplasia and retinopathy of prematurity. Serum cortisol was comparable between survivors and non-survivors although markedly depressed at baseline..

Conclusions: There was no difference in 14-days mortality between early hydrocortisone and placebo groups in neonatal septic shock.

Clinical Trial Registration: CTRI/2016/09/007276
LONG-TERM OUTCOME OF NEONATES WITH LATE ONSET NEONATAL SEPSIS (LOS) WITH AND WITHOUT MENINGITIS IN NEOMERO STUDIES

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Background: Up to 25% of neonates with culture proven LOS also have meningitis. Due to reluctance to undertake lumbar puncture (LP), especially in very preterm infants, cases of meningitis may go undiagnosed and undertreated, with possible impact on long-term outcomes. We aimed to compare long-term neurodevelopmental outcome (LTND) of participants of NeoMero1 (NM1; LOS) and NeoMero2 (NM2; meningitis) trials based on diagnosis of meningitis.

Methods: Surviving infants of the NM1 (n=252) and NM2 (n=51) trials were invited to LTND assessment at the age of 22mo 16d – 28mo 15d of corrected age. We grouped infants based on meningitis as follows: confirmed/probable by LP (Group 1); unknown, no LP performed (Group 2) and excluded by LP (Group 3). Neurodevelopmental impairment (NDI) was defined as BSID III composite cognitive (CC) and/or motor score <85 and/or cerebral palsy and/or hearing impairment requiring amplification (>40dB; one ear) and/or visual impairment and/or blindness (<20/60 or <20/200 visual acuity following refractive correction in one eye).

Results: In NM1 131 (52%) and in NM2 26 (51%) infants participated in LTND assessment. LP was performed in 78 (50%); 23 and 55 in groups 1 and 3, respectively. Demographic characteristics and LTND outcome are presented in Table. Multivariate linear regression analysis identified confirmed/probable meningitis, postnatal corticosteroids, surgery, vasoactive support, gender and weight Z-score as risk factors for lower BSID III composite cognitive score.

Table. Demographic characteristics and BSID III composite scores by meningitis diagnostic group.
Data are presented as mean (SD) if not stated otherwise.

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n=23)</th>
<th>Group 2 (n=69)</th>
<th>Group 3 (n=55)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GA, wk</td>
<td>32 (7)</td>
<td>31 (5)</td>
<td>32 (6)</td>
<td>0.42</td>
</tr>
<tr>
<td>Birth weight, g</td>
<td>1.9 (1.3)</td>
<td>1.5 (0.9)</td>
<td>1.9 (1.2)</td>
<td>0.58</td>
</tr>
<tr>
<td>Male, N= (%)</td>
<td>16 (70)</td>
<td>31 (45)</td>
<td>26 (47)</td>
<td>0.12</td>
</tr>
<tr>
<td>Age at main study inclusion, d</td>
<td>25 (25)</td>
<td>24 (18)</td>
<td>19 (17)</td>
<td>0.14</td>
</tr>
<tr>
<td>NDI</td>
<td>10/17* (59)</td>
<td>19/49* (39)</td>
<td>10/36* (28)</td>
<td>0.10</td>
</tr>
<tr>
<td>BSID III cognitive</td>
<td>85 (18)a</td>
<td>90 (16)b</td>
<td>99 (16)ab</td>
<td>0.002</td>
</tr>
<tr>
<td>BSID III motor</td>
<td>84 (22)</td>
<td>92 (16)</td>
<td>94 (17)</td>
<td>0.15</td>
</tr>
<tr>
<td>BSID III language</td>
<td>76 (20)</td>
<td>87 (17)</td>
<td>87 (17)</td>
<td>0.19</td>
</tr>
<tr>
<td>Seizures</td>
<td>3 (14)</td>
<td>1 (2)</td>
<td>2 (3)</td>
<td>0.11</td>
</tr>
</tbody>
</table>

ab - difference between groups statistically significant according to pairwise test multiple comparison of mean rank sums (Dunn’s-test) with Holm adjusted p-values

*- number of infants for whom at least one NDI component met pre-specified NDI criteria or all components were assessed
Conclusions: Higher BSID III CC score in infants with LOS and meningitis excluded by LP, compared to those with LOS and no LP performed or with meningitis confirmed by LP, suggests underdiagnosis of meningitis and potential for improved outcomes through timely diagnosis and adequate antibacterial therapy. LP should be undertaken in all neonates with LOS.

Clinical Trial Registration: IRAS ID 159011
REDUCTION IN CARRIAGE OF NEISSERIA MENINGITIDIS GROUP W FOLLOWING IMPLEMENTATION OF MENINGOCOCCAL B AND MENINGOCOCCAL ACWY VACCINES IN SOUTH AUSTRALIAN ADOLESCENTS

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Background: Carriage prevalence of Neisseria meningitidis is highest in adolescents. In South Australia (SA) in 2017, 34,489 senior school students were vaccinated during a cluster randomised controlled trial. In February 2019 a state funded 4CMenB program was introduced for 15-20 year olds. Additionally, a nationally funded MenACWY vaccine program was introduced in April 2019 for 14-19 year olds. This study aimed to assess the impact of 4CMenB vaccine on carriage prevalence in school leavers (aged 18-19 years) in SA.

Methods: Repeat cross-sectional study assessing carriage prevalence in 2018, 2019 and 2020. An oropharyngeal swab was obtained from each school leaver and a risk factor questionnaire completed. Vaccination history was confirmed for all participants.

Results: 4062 swabs were collected in 2018 (February-July) and 2859 in 2019 (February-November) with collection of swabs ongoing in 2020 (from February). Carriage of Neisseria meningitidis was 9.6% in 2018 compared to 8.3% in 2019 (Odds Ratio (OR)=0.85 (95%CI 0.71, 1.01)). Carriage of disease-associated meningococci was 5.5% in 2018 compared to 4.1% in 2019 (OR=0.73 (95%CI 0.57, 0.93)). Carriage of genogroup W and Y was lower in 2019 compared to 2018 (OR=0.16 (95%CI 0.04, 0.70), OR=0.70 (95%CI 0.48, 1.00)) respectively. Carriage prevalence of all Neisseria meningitidis in 2019, was lower in 4CMenB vaccinated (7.6%) compared to unvaccinated (10.4%) adolescents (OR=0.71 (0.52, 0.98); p=0.035). There was no reduction in carriage of group B. Drinking ≥3 alcoholic drinks in one session and kissing ≥1 person were independent risk factors for carriage of disease-causing strains (adjusted OR=3.0 (95%CI 1.86, 4.87), adjusted OR=2.1 (95%CI 1.42, 3.03)).

Conclusions: Reduction in carriage of group W was observed following introduction of meningococcal B and MenACWY vaccine programs in adolescents. Funding: Supported by GlaxoSmithKline Biologicals SA.

Clinical Trial Registration: ClinicalTrials.gov: NCT03419533
Background: This is a phase III B, long-term follow-up of an observer-blinded, multi-country, randomised, controlled trial (NCT00226499) evaluating protection of GSK’s live attenuated varicella-virus containing vaccines (one- or two-dose schedule) against varicella, in European children. We present vaccine efficacy (VE) and immune response persistence at year 10 post-vaccination in Czech, Lithuanian, Polish, Slovakian and Romanian children (in perspective, relative to the overall study).

Methods: In phase A of the overall study, 5803 children from Italy/Czechia/Greece/Lithuania/Norway/Poland/Russia/Slovakia/Sweden/Romania, 12–22 months of age (at first vaccination) were randomised (3:3:1) and received two doses of measles-mumps-rubella-varicella (MMRV) vaccine (MMRV-2Dose group), one dose of monovalent varicella vaccine after one dose of measles-mumps-rubella (MMR) trivalent vaccine (OKAH-1Dose group), or two doses of MMR vaccine (active Control group), 42 days apart. We assessed VE from 6 weeks until year 10 post-vaccination and anti-varicella zoster virus (VZV) antibody persistence (using ELISA, in children without varicella disease) until year 10. Safety was also evaluated (in phase A: solicited/unsolicited symptoms within 43 days post-vaccination, in a subset of children; throughout the study: serious adverse events, in all children).

Results: VE was similar among countries (except Romania where too few cases occurred for a relevant analysis) and with the overall study, reaching >95% post-dose 2 of MMRV vaccine (MMRV-2Dose group), Table. Anti-VZV antibodies persisted until year 10 post-vaccination and geometric mean concentrations were similar among countries post-dose 2 of MMRV vaccine (Table). No new safety concerns emerged from the study.
Conclusions: Similar to the overall study, two doses of MMRV vaccine administered during the second year of life provided long-term protection against varicella (of any severity) in children from these European countries and induced anti-VZV antibody responses that persisted until 10 years post-vaccination. Funding: GlaxoSmithKline Biologicals SA
Clinical Trial Registration: Not Applicable

| Table. Number of children, vaccine efficacy and persistence of antibodies against varicella in the overall study and for each country, 10 years post-vaccination with monovalent or combined live attenuated varicella-virus containing vaccines (GSK) |
|---|---|---|---|---|---|---|
| **Number of children** |  |  |  |  |  |
| **Cohort** | Overall | Czechia | Lithuania | Poland | Slovakia | Romania |
| TVC | 5803 | 1286 | 647 | 946 | 491 | 335 |
| ATP-E | 5289 | 1212 | 597 | 869 | 462 | 289 |
| ATP-P | 5235 | 1239 | 607 | 868 | 472 | 269 |

<table>
<thead>
<tr>
<th><strong>Efficacy against varicella (of any severity)</strong></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group</strong></td>
<td>Overall</td>
<td>Czechia</td>
<td>Lithuania</td>
<td>Poland</td>
<td>Slovakia</td>
</tr>
<tr>
<td>MMRV-2Dose</td>
<td>N (n)</td>
<td>VE % (95% CI)</td>
<td>N (n)</td>
<td>VE % (95% CI)</td>
<td>N (n)</td>
</tr>
<tr>
<td>2279 (76)</td>
<td>95.4 (94.0; 96.4)</td>
<td>525 (28)</td>
<td>97.2 (95.7; 98.1)</td>
<td>256 (5)</td>
<td>95.4 (88.0; 98.2)</td>
</tr>
<tr>
<td>OKAH-1Dose</td>
<td>N (n)</td>
<td>VE % (95% CI)</td>
<td>N (n)</td>
<td>VE % (95% CI)</td>
<td>N (n)</td>
</tr>
<tr>
<td>2266 (469)</td>
<td>67.2 (62.3; 71.5)</td>
<td>516 (196)</td>
<td>73.5 (67.0; 78.7)</td>
<td>255 (40)</td>
<td>59.3 (34.7; 74.7)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><em><em>Anti-varicella zoster virus antibody persistence</em> (at year 10)</em>*</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group</strong></td>
<td>Overall</td>
<td>Czechia</td>
<td>Lithuania</td>
<td>Poland</td>
<td>Slovakia</td>
</tr>
<tr>
<td>MMRV-2Dose</td>
<td>N</td>
<td>GMC, mIU/mL (95% CI)</td>
<td>N</td>
<td>GMC, mIU/mL (95% CI)</td>
<td>N</td>
</tr>
<tr>
<td>1169</td>
<td>471.3 (443.2; 501.2)</td>
<td>469</td>
<td>494.4 (448.6; 544.8)</td>
<td>173</td>
<td>483.5 (414.7; 563.8)</td>
</tr>
<tr>
<td>OKAH-1Dose</td>
<td>N</td>
<td>GMC, mIU/mL (95% CI)</td>
<td>N</td>
<td>GMC, mIU/mL (95% CI)</td>
<td>N</td>
</tr>
<tr>
<td>831</td>
<td>404.6 (373.0; 438.8)</td>
<td>289</td>
<td>419.9 (369.6; 477.2)</td>
<td>148</td>
<td>428 (350.1; 523.2)</td>
</tr>
</tbody>
</table>

*In children without varicella disease; TVC, total vaccinated cohort; ATP-E, according-to-protocol cohort for efficacy (for phase A and B); ATP-P, according-to-protocol cohort for persistence (adapted); MMRV-2Dose, children who received 2 doses of MMRV vaccine (GSK) in phase A of the study (from day 0 until 2 years post-vaccination); OKAH-1Dose, children who received 1 dose of monovalent varicella vaccine after an initial dose of measles-mumps-rubella (MMR) trivalent vaccine (GSK), in phase A; N(n), total number of children with available results (number of children for whom ≥1 event was reported); VE, vaccine efficacy; CI, confidence interval (lower limit; upper limit); NC, not computed because there were no varicella cases in the control group, to calculate VE; GMC, geometric mean concentration; mIU/mL, milli-international units/milliliter.
GENDERNEUTRAL HPV-VACCINATION IN FLANDERS 2019 – PRELIMINARY RESULTS OF VACCINATION UPTAKE IN BOYS COMPARED TO GIRLS

G. Top, A. Paeps, H. Huyck, D. Wildemeersch, I. De Schutter
Flemish Agency for Care and Health, Prevention, Brussels, Belgium

Background: In Flanders, in September 2010, HPV-vaccination was introduced for girls in the first year of secondary school. In 2016 vaccination coverage was 91%. Since September 2019, the programme became genderneutral. The 9-valent HPV-vaccines are available free of charge, but all vaccinations must be registered in the vaccination registry. For the schoolyear-based programme, the first dose is administered in the first and the second dose in the third trimester. We report the preliminary results of the uptake for the first dose in boys compared to girls.

Methods: We compared the number of vaccines ordered for the target group of girls and boys in the first trimester of schoolyear 2019-2020 to the number of vaccines ordered in the same period of previous schoolyears for girls only. We also extracted all registered vaccination data of the target group from the vaccination registry in order to evaluate a possible difference in vaccination uptake in girls and boys.

Results: The number of HPV-vaccines ordered from August to December 2019 for the target group of girls and boys was about double of the number ordered in previous years for vaccination of girls only. The number of registered vaccinations from September to December 2019 was comparable for girls and boys, with a boys/girls ratio of 1.04, which suggests a comparable vaccination uptake.

Conclusions: As the number of ordered vaccines doubled compared to the time only girls were vaccinated, it indicates that a comparable number of boys intended to get vaccinated. Data analysis of registered vaccinations showed a comparable coverage for first HPV-dose in girls and boys, at a high coverage rate, which suggests a good acceptancy of this vaccination as well in girls as in boys in Flanders.
Background and Objective: Success of National immunization program (NIP) in preventing vaccine-preventable diseases depends on several factors one of which includes vaccine coverage rates (VCR). Globally, the approach to measuring, reporting and monitoring VCR is heterogenous across different countries. The objective of the study was to describe the publicly available VCR data for HPV vaccination (HPVv) NIP in WHO Europe (WHO/ER) geographical region.

Methods: A targeted literature review of WHO database and country specific websites (e.g. ministry of health, public health authorities) was conducted between August 2018-September 2019 across WHO/ER countries (n=53). Data was retrieved on VCR (monitored and targeted) as reported including the target timeframe, population of interest and dosing schedule, when available. When monitored and targeted VCR were available for a country, the difference (monitored – targeted VCR) was calculated.

Learning Points/Discussion: Of the 53 countries in WHO/ER, 38 (72%) had an HPVv NIP. Of those 38, 29 (76%) had a monitored HPVv VCR reported for girls’ primary cohort and 28 (74%) did not have a defined VCR target. VCR targets ranged from 60%-95%. Only one country reported VCR that exceeded its target (Portugal, VCR >85%). Of the 9 countries with VCR less than their target, the difference between the target and the monitored VCR ranged from 6%-71%. The lowest monitored VCR was reported in Bulgaria (4%), while the highest VCR was reported in Portugal (90%-94%). Lack of common definition of VCR limits the ability to directly compare VCRs across countries. In WHO/ER, most countries with NIPs did not establish a VCR target, and a substantial number of countries do not have published national VCR. Establishing a target and monitoring progress towards achieving it may help countries improve protection of populations against HPV diseases.
HIGH BURDEN OF VACCINE PREVENTABLE DISEASES AS CAUSE OF DEATH: USING INNOVATIVE POST-MORTEM SAMPLING, THE ETHIOPIAN CASE

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¹Haramaya University, Harar, Ethiopia, College Of Health And Medical Sciences, harar, Ethiopia, ²London School of Hygiene and Tropical Medicine, Infectious Diseases Epidemiology, London, United Kingdom

Background: In 2019, 43% of children in Ethiopia received all basic vaccinations and ~20% did not received any. Pneumonia is a leading cause of death (CoD) in this country where also outbreaks of measles is commonly reported. Minimally invasive tissue sampling (MITS) is an innovative diagnostic tool, especially accurate to determine infectious diseases as CoD in children and it has been implemented in Ethiopia for a better understanding of CoD.

Methods: A mortality surveillance of stillbirths and under five children (U5) started in Haramaya University demographic surveillance (DSS) area, Ethiopia, in February 2019. Death notification system was implemented to detect MITS eligible cases. Conventional microbiology, multiplex PCR (TAQman-Array) and histopathology including, immunohistochemistry and molecular pathology were done. CoD was given through discussions among experts in different medical fields by reviewing all information and results available for each case.

Results: From February 2019 to January 2020, 1119 deaths were notified, 270 (24%) from the DSS. Fifty-eight (21.5%) were stillbirth, 97 (36%) neonates, 115 (42.5%) >28 days children. 58/168 approached, consented (34.5%). Thirty-six CoD were given and 10 (27.8%) were infant/children U5. Half of them (50%) a vaccine-preventable disease was identified as underlying/immediate CoD or in the casual pathway. The pathogens were a) Streptococcus pneumoniae: four cases, one of them with Neisseria meningitides and other with measles as co-infection; b): Neisseria meningitides: one case with underlying/immediate CoD.

Conclusions: Although representativeness still is a major challenge, MITS provides high quality data on CoD, accurately detecting infectious diseases. Vaccine-preventable diseases cause child deaths in a country where universal immunisation of children is offered for free in all regions. A better understanding of this low vaccine coverage is needed as well as wider use of immunizations to reduce child mortality in Ethiopia.
Conclusions:

D60/baseline ratios were 3.0, 6.9 and 3.5, respectively. D30/baseline ratios of total anti-RSV titers were reported. At D30, RSV AEs were reported through D60. No hospitalization for RSV-related serious AEs or grade 3 unsolicited serious AEs were reported through D60. No safety concerns with any ChAd155-RSV dose level. RSV-A

Background: Safe and effective RSV vaccines remain elusive. Here, we report results from our phase I/II trial of ChAd155-RSV, an investigational chimpanzee adenovirus-vectored vaccine encoding RSV proteins F (fusion), N (nucleocapsid) and M2-1 (transcription antitermination).

Methods: Healthy 12-23-month old RSV-seropositive subjects were randomized to receive intramuscular doses of ChAd155-RSV or placebo (1:1) on day (D)0 and D30. Dose escalation from low (LD=5x10^9 viral particles [vp]) to mid [MD=1.5x10^10 vp] and to high [HD=5x10^11 vp] level was permitted following favorable assessments of safety data on 22/82 and 25/82 subjects, respectively. Solicited, unsolicited and serious adverse events (AEs) including RSV-associated respiratory tract infection (RSV-RTI) were evaluated. Immunogenicity assessments included RSV-A neutralizing antibody ([NAb] geometric mean titers [GMTs]) and total anti-RSV-F Ab.

Results: 82 subjects were enrolled; 11 received ChAd155-RSV-LD, 14 ChAd155-RSV-MD, 18 ChAd155-RSV-HD and 39 placebo. Solicited AEs were similar across groups, except fever, which was more frequent among those receiving ChAd155-RSV-HD. Most fevers were grade 1 (<38.5°C axillary). No related serious AEs or grade 3 unsolicited AEs were reported through D60. No hospitalization for RSV-related lower RTI were reported. At D30, RSV-A NAb GMTs were 712 (95%CI: 230-2205), 1646 (95%CI: 816-3321) and 2204 (95%CI: 1384-3510) for ChAd155-RSV-LD, -MD and -HD (D30/baseline ratios: 5.6, 8.1 and 4.2, respectively. At D60, RSV-A NAb GMTs were 1081 (95%CI: 648-1803), 1747 (95%CI: 1034-2954), and 1908 (95%CI: 1331-2733) for ChAd155-RSV-LD, -MD and -HD (D60/baseline ratios: 8.5, 9.7 and 3.8, respectively. D30/baseline ratios of total anti-RSV-F Ab concentrations were 1.9, 4.8 and 4.7; D60/baseline ratios were 3.0, 6.9 and 3.5.

Conclusions: Through D60, there were no safety concerns with any ChAd155-RSV dose level. RSV-A
NAb GMTs increased following the first doses of ChAd155-RSV-MD and -HD but did not increase further post-second dose. **Funding:** GlaxoSmithKline Biologicals SA

**Clinical Trial Registration:** Clinical trial registration: clinicaltrials.gov NCT02927873
Background: Severe pertussis is reported to be more common among infants with select comorbidities, including congenital cardiac, pulmonary, gastrointestinal, neurological, metabolic and immunocompromising conditions and in premature infants. Among these conditions, acellular pertussis (aP) vaccine effectiveness (VE) has only been reported for preterm infants (<37 weeks gestation) which found VE to be similar to non-preterm infants. We examined pertussis burden and aP VE among infants with a broader range of medical conditions potentially associated with increased pertussis risk using a large population-based cohort.

Methods: Pertussis notifications, hospitalisations, Immunisation, birth and perinatal records in Western Australia and New South Wales for July 2001-December 2012 were linked. Prematurity (defined as <32 weeks gestation) and medical conditions were identified from perinatal and hospitalisation records. Medical conditions were categorised into risk groups according to published criteria (only available for invasive pneumococcal disease). Pertussis notification and hospitalisation rates and VE were calculated using Cox regression.

Results: Overall, 3.6% (47,721) of the cohort had ≥1 specified medical condition (including prematurity), most commonly respiratory (1.3%), cardiac (1.0%), kidney disease (0.7%) and birth <32 weeks gestation (0.6%). Hospitalised and non-hospitalised pertussis incidence was higher among children with medical conditions (Table). Point VEs were lower among children with medical conditions and only dose 3 VE against pertussis hospitalisation (69.5%; 95%CI 28.9-87.0) reached statistical significance (Table).
Conclusions: aP vaccine may be less effective for preventing pertussis disease in children with a range of medical conditions, including more extreme prematurity (<32 weeks gestation). These children may benefit from additional aP doses in infancy, particularly in settings using a 2+1 infant pertussis schedule. Larger studies identifying specific medical conditions associated with higher risk and lower VE may inform a risk- tailored pertussis immunisation schedule.

<table>
<thead>
<tr>
<th>Medical condition status</th>
<th>Dose number</th>
<th>Rate per 100,000 person-years (95% CI)</th>
<th>Incidence rate ratio (with medical risk vs without) (95% CI)</th>
<th>Adjusted VE (95% CI)</th>
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<tr>
<td><strong>Hospitalised cases of notified pertussis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>With medical conditions</td>
<td>0</td>
<td>289.5 (197.1-425.2)</td>
<td>1.40 (0.91-2.09)</td>
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<td>1</td>
<td>410.5 (272.8-617.8)</td>
<td>3.30 (2.05-5.07)</td>
<td>-46.4 (-220.0 to 33.0)</td>
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<tr>
<td>2</td>
<td>154.3 (80.3-296.6)</td>
<td>7.49 (3.20-15.98)</td>
<td>29.9 (9.8-74.5)</td>
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<tr>
<td>3</td>
<td>48.5 (29.7-79.2)</td>
<td>6.05 (3.31-10.40)</td>
<td>69.5 (29.9-87.0)</td>
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<td>0</td>
<td>206.1 (190.5-223.1)</td>
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<td>80.9 (71.5-87.1)</td>
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<td>1.51 (0.95-2.30)</td>
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<td>1.56 (0.90-2.53)</td>
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<td>1.40 (0.66-2.62)</td>
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<td>3</td>
<td>188.1 (146.6-241.2)</td>
<td>1.74 (1.32-2.25)</td>
<td>23.6 (48.6 to 60.7)</td>
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<tr>
<td>Without medical conditions</td>
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<td>169.1 (155.0-184.6)</td>
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<td>70.9 (66.5-74.8)</td>
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</tbody>
</table>

*Children with medical risks compared to children without medical risks with the same number of pertussis doses.

1 Adjusted for state of origin, season, birthweight adjusted for gestational age, mothers age group, mother's ever breastfed, SEIFA, ARMS, number of mother's previous pregnancies, smoking in pregnancy, Indigenous status, delivery method, father's age group and Apgar at 5 minutes.

2 Adjusted for state of origin, season, birthweight adjusted for gestational age, mothers age group, mother's ever breastfed, SEIFA, ARMS, number of mother's previous pregnancies, smoking in pregnancy, Indigenous status.
Background: Immune responses after HPV exposure in vaccinated individuals might enhance ('boost') vaccine-induced immunity. We aimed to evaluate whether natural boosting occurs and associated factors up to 10 years post-vaccination in young women vaccinated with two or three doses of the Quadrivalent HPV (QHPV) vaccine.

Methods: Girls aged 9-13 years were randomized to receive two or three doses of QHPV. Blood samples were collected before and at 7, 24, 60 and 120 months post-first dose and surveys were taken at baseline and each year between 60 and 120 months. Antibodies were measured by the competitive Luminex (cLIA). A boosting event was defined as an increase in antibodies at any time point after the 7 month sample collection above the assay variability threshold without interval immunization. A generalized estimating equations (GEE) model was used to examine an association between antibody titres, socio-demographics, sexual behavior over time.

Results: Of 73 participants who completed blood sampling at all time points, 17 (23.3%) showed at least one boosting event for HPV6, 11, 16 or 18 during follow-up by cLIA. Those with higher antibody titres at any time point during follow-up had significantly lower odds for an increase in antibodies in the period thereafter. Geometric mean titres between two and three dose recipients were not significantly different, but two-dose recipients were more likely to show a boosting event during follow-up OR 3.44 (95%CI 1.07-11.11).

Conclusions: This study showed increasing antibody titres in 23% of adolescents vaccinated with QHPV during 10 years post-vaccination follow-up. An association with boosting was found for those with lower initial antibody titres and for participants receiving a two-dose schedule. The increase in antibody titres could reflect a response to natural exposure or maturation of the immune response.

Clinical Trial Registration: This study describes prolonged follow-up of the trial registered as clinicaltrials.gov NCT00501137.
PHASE 1 TRIAL OF AN MRNA-BASED COMBINATION VACCINE AGAINST HMPV AND PIV3

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Background: Background: Human metapneumovirus (hMPV) and parainfluenza virus type 3 (PIV3) are important causes of upper and lower respiratory tract infections, particularly in young children. Despite their public health impact, no effective therapeutic or preventive options are available. mRNA-1653 is a mRNA-based investigational combination vaccine against hMPV and PIV3, and consists of two distinct mRNA sequences encoding the fusion proteins of hMPV and PIV3 co-formulated in a lipid nanoparticle delivery system.

Methods: Methods: This phase 1, first-in-human, randomized, placebo-controlled, dose-ranging study assessed the safety and immunogenicity of mRNA-1653 in healthy adults aged 18-49. The 124-subject study evaluated four vaccine dose levels (25, 75, 150 and 300 µg) administered intramuscularly in either single-dose or two-dose (Day 1, Month 1) schedules, with a one year follow up. Objectives include safety and immunogenicity measured by hMPV- and PIV3-specific neutralizing antibody titers.

Results: Results: The mRNA-1653 vaccine was generally well-tolerated at all dose levels. Neutralizing antibodies against hMPV and PIV3 were present at baseline, consistent with prior exposure to both viruses. A single dose of mRNA-1653 boosted serum neutralization titers against both hMPV and PIV3, and the magnitude of boosting was similar at all dose levels. The geometric mean ratio of Month 1 to baseline titers was 6.04 for hMPV-A, 6.33 for hMPV-B and 3.24 for PIV3. A second dose of mRNA-1653 at Month 1 was not associated with further increase of hMPV or PIV3 neutralization titers. Neutralizing antibody titers remained above baseline through Month 13 for hMPV and through Month 7 for PIV3.

Conclusions: Conclusion: mRNA-1653 is well-tolerated and induces a functional immune response and is therefore a promising vaccine candidate for the prevention of pediatric respiratory tract diseases caused by hMPV and PIV3.

Clinical Trial Registration: NCT03392389
TEMPORAL ASSOCIATION BETWEEN NASOPHARYNGEAL CARRIAGE OF PNEUMOCOCCAL SEROTYPE 24F AND RELATED MENINGITIS IN CHILDREN: A 16-YEAR POPULATION-BASED SURVEILLANCE.

N. Ouldali¹,², C. Levy¹, F. Angoulvant³, S. Bonacorsi⁴, S. Béchet⁵, A. Wollner¹, F. Vie Le Sage⁶, E. Varon⁷, R. Cohen¹

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Background: An important increase of pediatric pneumococcal meningitis (PM) has been reported in France since 2015, mainly due to the emergence of serotype 24F. We aimed to assess whether this increase could be driven by nasopharyngeal carriage dynamics of this serotype.

Methods: We conducted two French nationwide continuous prospective surveillances from 2001 to 2016, assessing pneumococcal carriage during acute otitis media (AOM) in children under 2 years, and PM in children under 15 years. The temporal association between carriage and PM was assessed by spearman coefficient.

Results: We included 10,204 children with AOM and a nasopharyngeal swab, and 1,778 children with PM. Among them, serotype 24F was isolated in 94 children with PM, and found in carriage in 138 children. The incidence of PM due to serotype 24F increased from 0.01 per 100,000 children in 2001 to 0.24 in 2016, while serotype 24F carriage rate increased from 0.6% to 2.8%. The correlation between PM and carriage dynamics of serotype 24F was very high (rho=0.78, p=0.0003, Figure).
Conclusions: A substantial part of the increase in PM due to serotype 24F was driven by its concomitant dynamics in nasopharyngeal carriage in young children. This suggest that continuous carriage surveillance could help understanding unexpected evolution of invasive pneumococcal diseases.
CONTINUING INCREASE OF PNEUMOCOCCAL SEROTYPES 19A AND 6C CARRIAGE IN BELGIAN CHILDREN ATTENDING DAY-CARE CENTRES (DCC) FOUR YEARS AFTER PCV-13-TO-10 VACCINE SWITCH

E. Ekinci¹, S. Desmet², L. Van Heirstraeten³, I. Wouters¹, C. Lammens³, J. Verhaegen², H. Goosens³, P. Van Damme¹, P. Beutels⁴, S. Malhotra-Kumar³, H. Theeten¹
¹University of Antwerp, Centre For The Evaluation Of Vaccination, Wilrijk, Belgium, ²University Hospitals leuven, Medical Microbiology, Leuven, Belgium, ³University of Antwerp, Laboratory Of Medical Microbiology, Wilrijk, Belgium, ⁴University of Antwerp, Centre For Health Economics Research And Modelling Infectious Diseases, Wilrijk, Belgium

Background: The Belgian pneumococcal conjugate vaccine (PCV) programme for children changed from PCV13 to PCV10 in 2015-2016. A nationwide nasopharyngeal (NP) carriage study in healthy children (6-30 months) attending day-care centres (DCC) was initiated in January 2016. Carriage of S. pneumoniae (SP) was analysed over four collection periods.

Methods: During 4 seasonal collection periods, 760-1100 children/period were recruited to take a single NP-swab. Demographics, clinical characteristics and vaccination status were collected via a questionnaire. SP was cultured, screened for antibiotic resistance, and serotyped (Quellung reaction). Carriage proportions among culture positives and carriage increases between period 3 (P3) and period 4 are presented (significant at a level < 0.05 (Chi² Test)).

Results: Samples from 995 children were collected in period 4 (November 2018-March 2019). The proportion of children that were age-appropriately vaccinated exclusively with PCV10 increased from 75.9% (P3) to 93.0%. Among 669 samples (random selection) analysed by culture, 469 carried SP. Carriage of PCV13-serotypes increased from 10.3% (P3) to 16.8%. Carriage of 19A, the most frequent among PCV-13 vaccine serotypes from period 2 onward, increased from 8.10% (P3) to 13.6% (Figure 1A). Serotype 6C increased from 5.8% (P3) to 16.8% and became the most frequent non-vaccine serotype, whereas 23B (predominant in all periods) remained stable at 16.2%. Since 2016, antimicrobial non-susceptibility of cultured strains varied for penicillin (13.4%-19.9%), tetracycline (11.4%-25.8%), erythromycin (16.1%-26.0%) and cotrimoxazole (20.7%-39.6%) without a clear trend. Non-susceptibility against at least one antibiotic remained stable over the four periods (44.6%-49.0%).
Conclusions: In Belgian children attending DCC, the carriage increase of PCV13-vaccine serotype 19A continues four years after the PCV13-10-programme switch and the rate of its increase over the last two years is matched by non-vaccine serotype 6C only.

Clinical Trial Registration: 00000000000
REAL LIFE EFFECTIVENESS OF PCV7 AND PCV13 AGAINST VACCINE-SEROTYPE OTITIS MEDIA (OM)

R. Dagan¹, B.A. Van Der Beek¹, S. Ben-Shimol¹², N. Givon-Lavi¹²
¹Ben Gurion Univ of the Negev, Faculty Of Health Sciences, Beer-Sheva, Israel, ²Soroka University Medical Center, Pediatric Infectious Disease Unit, Beer Sheva, Israel

Background: In the pre-PCV era, pneumococcal OM was caused mainly by vaccine-serotype (VT). Previous studies assessing PCV effect on VT-OM included immunogenicity, efficacy and impact with variable results. However, no real life serotype-specific effectiveness studies were ever conducted due to the paucity of culture-positive outcomes.

Methods: A nested case-control study, conducted between October 2009 and July 2013. PCV7 was implemented in Israel (Jul-2009) with catch-up in children <2y; PCV13 was introduced (Nov-2010) without catch-up. VT-OM episodes (mainly complex OM) were confirmed by middle ear fluid culture. Controls were rotavirus-negative gastroenteritis cases (from a prospective surveillance). Vaccine effectiveness (VE) of 1 and ≥2 PCV7/PCV13 doses was estimated using logistic regression, adjusted for age, ethnicity and time from vaccine introduction. PCV7 effectiveness against PCV7 serotypes (VT7), and PCV13 effectiveness against the six added serotypes (added-VT6), and all PCV13 serotypes (VT13) were assessed.

Results: 210 VT-OM episodes and 1,312 controls were included. Age distribution and age at vaccination was similar for cases and controls. Throughout the study, serotypes 19A and 19F were the most common serotypes causing VT-OM (together 55% of pneumococcal isolates). Generally, administration of ≥2 PCV7/PCV13 doses was effective, while 1 dose was largely ineffective (Figure). PCV7 VE against serotype 19F, (constituting 49% of all PCV7 serotypes), did not reach statistical significance. In contrast, PCV 13 showed a higher and significant VE against 19F despite a smaller sample size tested. PCV13 was highly effective against added-VT6, grouped and all VT13, grouped.
Conclusions: In this unique effectiveness study, ≥2 doses of PCV7 and PCV13 were effective against OM caused by VT7 and VT13, respectively. PCV13 showed also high VE against serotype 19F and added-VT6.

Clinical Trial Registration: Not applicable
Background: In 2015, PCV10 was introduced in the NIP in Slovenia on a 2+1 schedule with no catch-up. Vaccination rate increased from 48.8% in 2015 to 59.6% in 2018. We aimed to assess pneumococcal carriage in children 3 years after the introduction of the vaccine and to compare it to invasive disease (IPD).

Methods: A prospective study in children <6 years of age was performed in 10 primary pediatric practices from October 2018 to July 2019. NP swabs were obtained and a questionnaire was completed. Serotyping was performed using the Neufeld-Quellung method. Risk factors for carriage were assessed using logistic regression. Carriage serotypes were compared to IPD serotypes in children in Slovenia during the study period.

Results: Of 451 included children, 101(22.4%) were positive for S. pneumoniae. In univariate analysis, increasing age (highest OR 14.26 in 12-23 month-olds), day-care attendance (OR 2.41) and presence of URTI (OR 3.08) were significant risk factors for carriage, while in the multivariate analysis, only URTI presence remained significant (OR 2.54, p=.0008). 261(58%) of 451 included children were vaccinated, 235(90%) of them with PCV10. Serotype distribution vs. vaccination status is shown in Figure 1. The most prevalent serotypes were 23A, 10A and 15B. In PCV10-vaccinated children vaccine serotype carriage was significantly reduced (OR 0.26, p=.007). During the study period, 45 IPD cases were observed in children in Slovenia with the most prevalent serotype being 19A, followed by 7F, 9V and 14.
Conclusions: After 3 years of PCV10 use in the NIP in Slovenia with moderate vaccine coverage a prevalence of non-vaccine serotype carriage was observed while in IPD vaccine serotypes predominate with 19A being the most frequent among them.

Clinical Trial Registration: National Medical Ethics Committee of Slovenia: 0120-641/2017/9
POTENTIAL SEROTYPE COVERAGE OF THIRD-GENERATION PCVS IN ISRAEL AND FRANCE IN CHILDREN 6-23 MONTHS OLD

R. Cohen¹,2, S. Ben-Shimol³,4, C. Levy¹,2, N. Ouldali¹,5, D. Danino³,4, B.A. Van Der Beek⁴, N. Givon-Lavi³,4, E. Varon²,6, R. Dagan⁴

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Background: Third-generation pneumococcal conjugate vaccines (PCVs), expanding PCV13 serotype coverage, including PCV15 (adding serotypes 22F and 33F) and PCV20 (adding serotypes 8, 10A, 11A, 12F, 15B/C, 22F, 33F), are currently in clinical development. We compared the prevalence of these additional serotypes in Israel and France in invasive pneumococcal disease (IPD) and in carriage, in children 6-23 months old during mucosal diseases, in the late-PCV13 period (2015-2018).

Methods: Multiple population-based, surveillance systems in both countries were used. Clinical syndromes included: IPD; carriage in healthy children (both countries); carriage during acute otitis media (AOM, France) vs. carriage during lower respiratory tract infection (LRI, Israel). PCV13 was implemented in Israel and France in 2010, with >90% uptake in children 6-23 months. Proportions (%) of all pneumococcal isolates of PCV13, additional-PCV15 and additional PCV20 serotypes in Israel and France were compared.

Results: 3,653 cases (1,975-France; 1,678-Israel) were recorded. In both countries, PCV13 serotypes have not completely disappeared (Table). In carriage, the potential coverage of serotypes included in PCV15 and in PCV20 was similar in both countries. In IPD, the proportions of PCV15 and PCV20 serotypes were higher in Israel than in France. These differences were driven by higher proportions of serotypes 12F and 33F in Israel (30.7% and 14.4%, respectively) vs. France (2.2% and 4.5%, respectively), where emergence of serotype 24F (non-PCV20 serotype) was observed.
Conclusions: During the late-PCV13 period (2015-2018) in Israel and France, PCV20 serotypes play a major role in both IPD and carriage during mucosal diseases. Implementation of third-generation PCVs has the potential to prevent a large proportion of invasive and mucosal pneumococcal diseases in both countries. Notably, PCV13 serotypes are still detected in the late PCV13 period in carriage and disease in both countries.
SMALL DIFFERENCES IN AGE AT FIRST DOSE OF PCV7 RESULT IN SIGNIFICANT DIFFERENCES IN IMMUNE RESPONSE

R. Dagan¹, B.A. Van Der Beek¹, S. Ben-Shimol¹², N. Givon-Lavi¹²
¹Ben Gurion Univ of the Negev, Faculty Of Health Sciences, Beer Sheva, Israel, ²Soroka University Medical Center, Pediatric Infectious Disease Unit, Beer Sheva, Israel

**Background:** The factors influencing infant response to pneumococcal conjugate vaccines (PCVs) are not fully elucidated. We studied response to infant vaccination with 7-valent PCV (PCV7) in relationship to anti-capsular maternally-derived IgG (ACMIgG) at 2 months, and age at first dose administration.

**Methods:** A prospective study in which PCV7 was administered to children at 2, 4, 6, 12 months (3+1 schedule; Dagan, Vaccine, 2018,36:2774). ACMIgG was measured at 2 months (pre-PCV7; maternally-derived); post-primary (7m) and post-booster (13m), by ELISA. The children received the 1st dose at age 2 months (pre-determined range 55 to 82 days, median = 65d; 90.7% aged 55-75d). We compared children receiving PCV7 before the median age (<65d) and at or after median age (≥65d). Estimates of antibody response were calculated using linear regression adjusting for maternal antibody concentration and ethnicity (Jewish vs. Bedouin children).

**Results:** Serotype specific ACMIgG geometric mean titers (GMC, µg/ml) did not differ in children receiving the vaccine at age <65d or ≥65d (Figure 1A). In contrast, post-primary IgG GMCs were significantly higher among those receiving the vaccine at ≥65d (Figure 1B). Post-booster, differences between the groups were no longer found (Figure 1C). Similar patterns were found when each ethnic group was analyzed separately. Each additional day of age at the administration of the first dose showed an increased immune response ranging from 1% (serotype 14) to 6% (serotype 6B).
Conclusions: Even extremely small increase in age at administration of first PCV7 dose, led to a significant difference in immune response to infant series. In contrast, ACMIgG at day of first dose did not influence response. This suggests a rapid maturation of immune response to PCV at around 2 months of age.

Clinical Trial Registration: Current Controlled Trials, Ltd. ISRCTN28445844
PUBLIC HEALTH IMPACT IN CHILDREN UNDER 5 AFTER 10 YEARS OF THE 13 VALENT PNEUMOCOCCAL VACCINE USE IN EUROPE

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Background: 2020 marks 20 years of global pneumococcal conjugate vaccine (PCV) use. The 7-valent vaccine was licensed in Europe in 2001, however country vaccine technical committees individually and gradually included a PCV7 in their national immunization programs (NIPs). When higher-valent PCVs (PCV10 and PCV13) were licensed in Europe in 2009, countries rapidly adopted higher serotype formulations into their NIPs. This analysis evaluates the public health benefits seen from PCV13 use in Europe.

Methods: An Excel-based model was developed to estimate cases, deaths, and costs avoided in children <5 in European countries with PCV13 NIPs. Infants vaccinated was derived using country population and WHO vaccine uptake statistics. Disease and death rates were taken from published literature on pneumococcal disease and mortality rates in <5 year olds. Vaccination impact was determined by applying post vaccination incidence rates or vaccine efficacy. Vaccine and healthcare costs were derived from literature.

Results: Thirty-three countries with PCV13 NIPs were included in the analysis. In these countries, 76.8 million infants were born since 2010, of which 53.7 million were vaccinated with PCV13. Over this period, PCV13 was estimated to have averted 21.2 million cases of pneumococcal cases and over 23,800 associated deaths (Table).
**Conclusions:** PCV13 use has had considerable public health and economic benefit to Europe over the past 10 years, reducing mortality and morbidity associated with pneumococcal disease. As this analysis focused on children <5, excluding the well documented herd effects of PCV13 vaccination, results likely underestimate full public health benefits. Substantial pneumococcal disease burden remains; opportunities exist to increase uptake and protect against serotypes not covered in currently available vaccines. Continued prioritization of pneumococcal vaccination is important to healthcare in Europe.

**Clinical Trial Registration:** Not Applicable

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**Table. Impact of 10 years of PCV13 use in Europe**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of births (in PCV13 NIP Countries)</td>
<td>76,828,716</td>
</tr>
<tr>
<td>Number of children vaccinated with PCV13</td>
<td>53,761,837</td>
</tr>
<tr>
<td>Disease cases averted</td>
<td>21,217,306</td>
</tr>
<tr>
<td>Invasive pneumococcal disease</td>
<td>118,663</td>
</tr>
<tr>
<td>Pneumococcal Pneumonia</td>
<td>402,225</td>
</tr>
<tr>
<td>Otitis media</td>
<td>20,696,418</td>
</tr>
<tr>
<td>Under 5 Deaths averted</td>
<td>23,847</td>
</tr>
<tr>
<td>IPD deaths averted</td>
<td>9,899</td>
</tr>
<tr>
<td>Pneumococcal Pneumonia deaths averted</td>
<td>13,948</td>
</tr>
</tbody>
</table>
Background: Vaccine hesitancy is defined as a delay in acceptance, or refusal, of vaccines, despite availability. It is a complex and context specific phenomenon, and identified as a global health priority. Given this complexity, it has been difficult to measure. Our aim was to administer the ‘Parent Attitudes about Childhood Vaccines’ (PACV) questionnaire, a validated screen for vaccine hesitancy, to parents/caregivers of children attending outpatients.

Methods: Each item in the 17-question survey was scored individually, an overall score was then calculated from 0 to 34, with higher scores indicating increased hesitancy. A receiving operator characteristic (ROC) curve was used to assess accuracy. The optimal cut-point for classifying vaccine hesitancy was identified (maximising the product of the sensitivity and specificity for non-vaccination). Univariate analysis was conducted to identify factors associated with higher PACV score and non-vaccination.

Results: 436 participants completed the PACV. The mean score was 9. Overall, 22 (5.3%) were non-vaccinators. The area under the ROC curve for PACV in relation to non-vaccination was 0.81. The optimal cut-point was 14.5, which classified 24.5% of participants as vaccine hesitant. The positive and negative predictive values were 16.8%(95%CI 10.1-26.5%) and 98.4%(96.3-99.5%) respectively. The PACV score was higher in the non-vaccinated (median=20[15-25]) compared to the vaccinated (median=9[5-14]) (p<0.0001). 95(22.9%) participants had concerns about vaccines, most frequently HPV and MMR, 76(17.4%) had side-effect concerns, most frequently autism.

Conclusions: This study is the first use of the PACV in an Irish population. The optimal cut-score identified was lower than used in previous research (17, 50% of maximal score). PACV score was a good predictor of non-vaccination. In the time constraints of clinical practice, the PACV can be used to target vaccine education to those most likely to not vaccinate.
ESTIMATING PNEUMOCOCCAL DISEASE BURDEN IN EIGHT EUROPEAN COUNTRIES DUE TO SEROTYPES CONTAINED IN CURRENT AND INVESTIGATIONAL PNEUMOCOCCAL CONJUGATE VACCINES

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Background: The two pneumococcal conjugate vaccines currently available in Europe (PCV10 and PCV13) have had a substantial public health impact since their introduction in 2009-2010. Two investigational PCVs (PCV15 and PCV20) cover more serotypes and therefore offer the opportunity to further reduce disease. We sought to estimate and compare the clinical and economic burden due to serotypes included in the four aforementioned PCVs in eight European countries in children <5 years of age.

Methods: The burden of disease caused by serotypes contained in the four PCVs was calculated in the United Kingdom (UK), France, Germany, Italy, Spain, Austria, Netherlands, and Finland. Clinical, population, and cost data were derived or estimated from country-specific published sources where available. Up to the three most recent years of data were included for invasive pneumococcal disease (IPD) serotype distributions. The distributions were extrapolated to calculate the number of cases of disease (IPD, pneumonia, and otitis media (OM)) based on country specific incidence in children <5. Case fatality rates and associated costs were then applied to relevant outcomes.

Results: are summarized Table 1. Country-specific IPD serotype coverage ranges by PCV formulation: PCV10=5%-46%, PCV13=15%-74%, PCV15=19%-74%, and PCV20=54-77%. Across the eight countries, approximately 153 deaths and 1.17 million total pneumococcal disease cases are attributed to serotypes contained in the PCV20 formulation. Total combined economic burden for PCV20 serotypes was €134 million.
Conclusions: Investigational PCVs offer broader serotype coverage and will continue to protect infants against serotypes contained in current vaccines. Higher-valency vaccines have the potential to deliver additional public health impact and economic value in European countries.

Clinical Trial Registration: N/A - This is a modelling study and not a clinical trial.
MONITORING AND EVALUATION OF THE SEROLOGICAL PROFILE OF CHAGAS DISEASE INFECTED CHILDREN WITH MULTIPLEX IMMUNOASSAY

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Background: Chagas disease (CD) caused by Trypanosoma cruzi affects approx. 6-7 million people in Latin America and is currently widely dispersed worldwide. Evaluation of therapeutic response in chronic CD is a challenge due to prolonged persistence of parasite-specific antibodies measured by conventional serological test. New early markers of cure are needed. The aim of this study was to evaluate a newly developed antibody profiling Multiplex assay as a predictive tool for treatment response.

Methods: Eighty-two children with acute or chronic CD were enrolled in a long term prospective longitudinal study with clinical, serological and parasitological follow-ups (Parasitology Service, Hospital de Niños Ricardo Gutierrez, Buenos Aires, Argentina). At baseline and during follow-up, conventional serology tests (CS) (ELISA, Indirect Hemagglutination) were carried out, and parasitemia was evaluated (Microhematocrit test and/or qPCR). A Multiplex platform was used to print fifteen T. cruzi antigens selected for their proven immunogenic properties.

Results: Antibodies response in serum samples from treated patients with a multiplex immunoassay for CD (MultiCruzi) were evaluated. At baseline (before treatment) CS were reactive in 100% of patients, and 53% showed detectable parasitemia. A decrease of T. cruzi antibodies by standard ELISA was observed until seroreversion in 39%. A predictive model based on an algorithm, considering seroreduction of antibodies to different antigens in the multiplex assay, was evaluated as a predictive tool for treatment response.

Conclusions: The interpretation algorithm predicted efficiently the full seroreversion that was confirmed at a later stage by CS. The antigens were identified antibodies that correlates with the parasite persistence. The results validate the use of the MultiCruzi assay as a monitoring tool and highlight its predictive properties to assess and identify children that responded to anti-parasitic therapy. The study was supported by DNDi
Background: Visceral leishmaniasis (VL) is endemic in parts of Southern Europe and presents with unspecific but important symptoms such as fever, organomegaly and pancytopenia. Haemophagocytic lymphohistiocytosis (HLH) is one of the most severe clinical presentations. In this study we describe the epidemiologic and clinical characteristics of paediatric VL.

Methods: The medical records of all children (<14y) admitted (2004-2018) with VL to any of the participating paediatric centers in Andalusia (Southern Spain) were retrospectively reviewed. For inclusion, the diagnosis of VL had to be based on clinical features, unequivocal serology, PCR or bone marrow findings. HLH-diagnosis was established according to the HLH-2004 criteria.

Results: 127 patients were identified. Median age was 14.5 months and the main clinical presentation were fever (95.3%), splenomegaly (95.3%) and hepatomegaly (71.1%). The main laboratory abnormality was anemia (79.5%) followed by thrombocytopenia(67.7%) and neutropenia (63%) and 29.1% fullfilled the HLH criteria.

Treatment: 124 patients (97.6%) received liposomal amphotericin b (L-Amb) with 4 treatment relapses, all responsive to a 2nd L-Amb cycle. Thirteen of the 37 HLH patients received adyuvant corticosteroid treatment. One patient deceased in the context of the leishmania infection.

Conclusions: We present here data from the biggest paediatric VL cohort in Europe. Similar to previous studies 30% of childhood cases fulfill HLH criteria. L-Amb was the treatment of choice and successful in most cases. In our region VL is a frequent cause of fever and cytopenia and should be suspected also in those patients fulfilling HLH criteria as management of these two entities is highly different. Interestingly 80% of the HLH cases had underlying diseases. Prospective recruitment as well as subgroup analysis is ongoing in order to better understand the VL etiology, pathophysiology and treatment responses.
Background: We have previously shown that among neonates exposed to Zika virus (ZIKV) during foetal life born with microcephaly cerebrospinal fluid (CSF) protein is significantly increased. In this study, we aimed to compare inflammatory markers in the CSF of ZIKV-exposed neonates with and without microcephaly (cases) and neonates not exposed to ZIKV during pregnancy, without other congenital infection, microcephaly nor central nervous system illness.

Methods: We identified 14 neonates who underwent lumbar puncture (LP) in the CSF Laboratory in Salvador, Brazil, during the ZIKV epidemic. All mothers reported ZIKV clinical symptoms during gestation. Then, we identified neonates who underwent LP in the same Lab and fulfilled criteria to be controls: age ≤4 days, CSF White Blood Cell count ≤8/mm³, CSF protein ≤132mg/dL, CSF Red Blood Cell count ≤1,000/mm³, no Central Nervous System illness, no congenital infection, nor microcephaly. 29 cytokines were measured and compared as median (p25th-p75th).

Results: Fourteen controls were included and tapped due to sepsis (n=6), maternal syphilis (n=5), seizure, fever without source, and maternal acute cytomegalovirus infection (n=1 each). Congenital syphilis and cytomegalovirus infection were ruled out. GCSF (16.0[12.9-19.6] vs. 13.0[11.0-14.3]; p=0.047), IL1A (31.0[20.6-39.3] vs. 18.2[13.8-22.5]; p=0.008), IL7 (13.3[11.9-14.4] vs. 11.5[9.8-13.5]; p=0.048), IP10 (1425.5[657.8-2274.6] vs. 447.8[182.5-1358.0]; p=0.031) were significantly higher among controls. Conversely, IL4 (10.0[9.5-10.7] vs. 11.5[10.2-13.0]; p=0.01) was significantly higher among cases with microcephaly in regard to controls.

Conclusions: Our results suggest that neonates exposed to ZIKV during foetal life find it difficult to mount an immune response, along with exacerbated activity of antibody-producing cells.

Clinical Trial Registration: ClinicalTrials.gov Identifier NCT01200706
Background: Malnutrition underpins 45% of deaths in children under-five globally. Severe acute malnutrition (SAM) is a life-threatening form of malnutrition characterised by wasting with or without oedema, and impaired immune function. Mortality among those requiring hospitalisation remains high (10-40%) and is predominantly driven by infections. Identifying the factors associated with mortality would help identify children at highest risk.

Methods: We searched EMBASE, Ovid MEDLINE, the Cochrane Library, and clinicaltrials.gov for studies published between 2000-2020, among children <59 months hospitalised with SAM. Studies had to employ multivariable analysis to control for confounding factors. Where 20% or more studies investigated the same predictive factor, we conducted a random-effects meta-analysis, stratified by the stated measure of effect.

Results: 28 out of 1423 articles fulfilled inclusion criteria: 19 studies included all children with SAM; 9 studies only reported on a sub-population with SAM. All 19 main studies were from Africa, across 8 countries, with media n 365 children per study. Mean inpatient mortality was 15.7% [95% CI 10.4-21.0%] and HIV prevalence ranged from 2.1-51%. Nine predictive factors were included in meta-analysis [See Figure], of which four were infectious: HIV infection (n=8; HR 4.31 [2.30-8.06]; OR 2.04 [0.87-4.70]), diarrhoea (n=6; HR 2.84 [1.40-5.75]; OR 2.90 [1.96-4.28]), pneumonia (n=4; HR 1.90 [1.19-3.02]; OR 2.21 [1.08-4.62]), and presence of shock (n=4; HR 3.67 [2.24-6.01]). Of the five non-infectious factors only lack of appetite (n=5; HR 2.16 [1.48-3.16]) and a higher weight-for-height Z-score (n=4; HR 0.89 [0.69-1.14]; OR 0.44 [0.24-0.79]) showed significant associations with mortality; age, sex, oedema were not significant.

Conclusions: Infectious are independently associated with mortality in children hospitalised with SAM, giving an insight into how pathogens can decompensate the underlying pathological processes occurring in this complex multi-system disorder.

Systematic Review Registration: The systematic review/meta-analysis protocol was registered with PROSPERO [CRD42019152267]. PRISMA guidelines followed throughout the review.
LONG TERM FOLLOW UP OF MICROCEPHALIC CHILDREN IN UTERO EXPOSED TO ZIKA VIRUS IN BRAZIL

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Background: In Brazil, a set of congenital abnormalities was linked to in utero Zika virus (ZIKV) infection. It may include microcephaly, craniofacial disproportion, irritability, spasticity, seizures, feeding difficulties, ocular abnormalities, and hearing loss, as well as abnormalities on neuroimaging studies. We aim to describe the long term follow up of a cohort of microcephalic children exposed to ZIKAV in utero.

Methods: Descriptive study of a cohort of ZIKAV in utero exposed children. Continuous variables will be described in median and interquartile range (IQR), and categorical variables in frequencies and percentiles.

Results: We followed 28 microcephalic children, for a median of 24 months (IQR=12-28), 15 were female and 13 male. The median cephalic perimeter at birth was 29 cm (IQR=27-31). Seventeen children were born with severe microcephaly (z-score<-3, Intergrowth 21sr1). The most common abnormalities on neuroimaging were: 22 (79%) cortical abnormalities; 13 (46%) abnormalities on the corpus callosum; 25 (89%) ventriculomegaly; and 24 (86%) calcifications. The EEG was abnormal in 17 (61%) of the patients. A total of 9 (32%) presented abnormalities on ophthalmoscopy exam, 4 (14%) on Brainstem Evoked Response Audiometry exam, and 7 (25%) other malformations. During follow up 13 (46%) presented sleep disorders, 11 (39%) irritability, and 23 (85%) epilepsy. The median onset age for epilepsy was 4 months (IQR=2-10), the median number of drugs used to control the epilepsy was 2 (IQR=2-3). A total of 19 (68%) presented with dysphagia, and during their follow up 10 children required gastrostomy.

Conclusions: Children with microcephaly due to ZIKAV presented with several complications during their follow up, and the health care system must be prepared to deal with them and their impact on the system.

Clinical Trial Registration: not a clinical trial
LONG-TERM PROGNOSIS OF 7 DAYS VERSUS 28 DAYS ALBENDAZOLE MONOTHERAPY IN THE TREATMENT OF SINGLE LESION NEUROCYSTICERCOSIS IN CHILDREN- AN OBSERVATIONAL STUDY

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¹Postgraduate Institute of Medical Education and Research, Allergy And Immunology Unit, Advanced Pediatrics Centre, Chandigarh, India, ²Postgraduate Institute of Medical Education and Research, Pediatric Neurology Unit, Advanced Pediatrics Centre, Chandigarh, India, ³Postgraduate Institute of Medical Education and Research, Child Psychology Unit, Advanced Pediatrics Centre, Chandigarh, India, ⁴Postgraduate Institute of Medical Education and Research, Department Of Radiology, Chandigarh, India

Background: Neurocysticercosis (NCC) is a major cause of epilepsy in the tropics and the most common cause of focal seizures in North Indian children. Both one-week and four-week albendazole regimens have been found to be equally efficacious for the treatment of single lesion NCC in children in the short-term. However, the benefit of these regimens in long-term seizure control and radiological resolution remains unclear.

Methods: A cross-sectional observational study was conducted over a period of 1 year. One hundred and three consecutive children aged 5-14 years diagnosed with single lesion NCC and who received either 7 days or 28 days of albendazole monotherapy and subsequently had completed at least 5 years of follow up in Neurocysticercosis Clinic, Advanced Paediatrics Centre, Postgraduate Institute of Medical Education and Research, Chandigarh, India were included.

Results: Fifty-five children received 7 days albendazole and 48 received 28 days albendazole therapy. Partial seizures were the most common initial presentation (58.3%). Most (92.3%) of the single lesions were ring-shaped, equally distributed bilaterally, mostly in parietal lobe (57.3%). At follow-up, complete resolution was found in 52.7% receiving 7 days and 54.2% receiving 28 days albendazole (p=0.17). Seizures recurred in 20% receiving 7 days and 20.8% receiving 28 days albendazole (p=0.80). Cognitive outcome was also comparable between the two groups.

Conclusions: Albendazole cysticidal therapy for 7 days is equally effective as 28 days in single lesion neurocysticercosis in the long-term for seizure control and radiological resolution of lesion. Neurocysticercosis impacts cognition, behavior and scholastic performance in children in the long-term, highlighting the need for early intervention, although the outcomes are comparable in both treatment regimens. A regular follow-up and case-to-case consideration for anti-epileptic withdrawal should be kept.
Background: Children with cancer and infection may develop augmented renal clearance (ARC) possibly resulting in sub-therapeutic concentrations of antibiotics and therapeutic failure. Adjustment in dosing requires correct assessment of renal function. Most widely used creatinine-based estimated glomerular filtration rate (eGFR) is known to be imprecise in this population due to rapid changes in muscle mass.

We aimed to describe renal function by measured GFR (mGFR) using iohexol clearance and correlate it with eGFR and cystatin C in children and young adults with cancer and infection.

Methods: Hospitalised patients aged 0.5-25 years (children <19 years, adults ≥19 years) with suspected/confirmed infection receiving piperacillin-tazobactam or cefepime were included if their eGFR was ≥80 mL/min/1.73 m² according to Schwartz (children) or MDRD or CKD-EPI equation (adults). Iohexol concentrations measured prior to, 5 min, 0.5, 3-3.5, 5.5-8 h after administration were described by population pharmacokinetic model in NONMEM. mGFR using individual estimates of iohexol clearance (CL) from final model was calculated as mGFR=CL/60*1000/(body surface area)*1.73.

Results: Median (range) eGFR measurements from 23 children (mean (SD) age 10.7 (5.5) years, weight 42.1 (28.9) kg) and 9 adults (mean (SD) age 23.6 (2.1) years, weight 42.1 (28.9) kg) were 148 (74-914) and 134 (119-158) (by CKD-EPI) mL/min/1.73 m², respectively. Three-compartment model with allometric scaling of central, one peripheral compartment and clearance (with power 0.75) to weight fitted the best. Median (range) mGFR was 98 (68-138) in children and 112 (70-140) mL/min/1.73 m² in adults. Correlations of mGFR were the best with cystatin C but weak with eGFR (Figure).
Conclusions: High values of eGFR as compared with mGFR using iohexol CL may overestimate renal function and thus adjustment of doses may need more reliable renal function measurements than creatinine-based equations.

Clinical Trial Registration: EudraCT numbers 2015-000631-32 and 2016-003374-40
Background: Visceral leishmaniasis (VL) is a neglected parasitic disease affecting spleen, liver and bone marrow. Pharmacokinetics (PK) of miltefosine, the only available oral drug for VL, is characterized by slow clearance. Miltefosine has shown notably lower efficacy in children in East Africa with a conventional linear weight-based regimen derived from adult doses. Adopting an allometric dosing regimen, our study aimed to increase systemic exposure to miltefosine and efficacy in paediatric patients, and to characterize nonlinearities in miltefosine PK, using population PK modelling.

Methods: 30 paediatric patients (4-12 years of age) in a phase II clinical trial in Kenya and Uganda were treated with miltefosine for 28 days. Daily dosing was based on an allometric fat-free-mass-based regimen (median 3.2, range 2.7-3.9 mg/kg/day). PK samples were collected during both treatment and follow-up.

Results: Exposure in the first treatment week was more than two-fold higher than those observed in the linear weight-based dosing regimen. Median plasma concentrations on D7 were 5.88 µg/mL with allometric dose compared to 2.67 µg/mL with conventional dose, and there was 33% less variability in PK profiles among patients treated with the allometric dose. However, total treatment exposure did not increase proportionally with the dose, since a halt in miltefosine accumulation was observed in the third week of treatment. Population PK modelling showed miltefosine bioavailability was affected by the cumulative dose, possibly due to saturation of absorption.

Conclusions: Miltefosine PK is characterized by dose-dependent nonlinearities that obstructed initially expected exposure levels in children. Nevertheless, with improved exposure in the first treatment week and less variability in exposure, the allometric miltefosine dose regimen resulted in improved efficacy and is therefore recommended for the treatment of paediatric VL patients.

Clinical Trial Registration: Clinical trial registration: ClinicalTrials.gov Identifier: NCT00696969
Background: Real-time therapeutic drug monitoring (TDM) of beta-lactam antibiotics is increasingly recommended to improve efficacy, reduce the risk of the emergence of drug resistance and limit toxicity. M4S device for bedside application is a method based on the specific and quantitative recognition of beta-lactams by a biosensor. Objective: to demonstrate the capability of the M4S device for bedside TDM of beta-lactams in newborns and children receiving meropenem (MEM) or piperacillin-tazobactam (PIP-TAZ).

Methods: Venous blood samples (0.3-1mL) were taken at the steady state (≥3 days of treatment) for peak and trough concentrations. Ultrafiltrates were prepared by centrifugation through membrane and analyzed immediately with the M4S device. The same samples were thereafter stored at -80°C and sent for analysis with a validated assay method (LC-MS-MS).

Results: Altogether 21 neonates and 14 children were included (Estonia and France); 15 received MEM, 20 PIP-TAZ. 27 plasma ultrafiltrates were assayed for MEM and 38 for PIP-TAZ concentrations with M4S device. The median (IQR) trough and peak concentrations for MEM in neonates were 4.7 (1.3-11.8)mg/L and 41.04 (24.1-113.0)mg/L, respectively. For PIP-TAZ respective values for neonates were 7.7 (5.0-37.0)mg/L and 27.0 (15.3-117.0)mg/L, for older children 5.0 (5.0-99.0)mg/L and 108.0 (37.8-208.0)mg/L. There was good correlation between concentration measured with M4S device and LC-MS-MS ($R^2=0.9780$) for PIP-TAZ but not for MEM (probably due its larger instability compared to PIP during the long storage times imposed by logistical reasons [median 7 months; range 1.5-11 months]).

Conclusions: The bedside TDM of beta-lactam concentrations in children is feasible with the M4S device with measured MEM and PIP-TAZ concentrations in expected ranges. It is important for MEM to run the control assays (LC-MS-MS) as soon as possible after sampling to avoid undue degradation resulting in poor correlation.

Clinical Trial Registration: NA, considered as a device study by the local authorities.
IMPACT OF SOCIO-ECONOMIC FACTORS ON VACCINE UPTAKE IN A GIS BASED CLUSTER RANDOMIZED CHOLERA VACCINE TRIAL IN BANGLADESH

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Background: Cholera is a severe diarrhoeal disease causing 1.3 to 4.0 million cases and 21,000 to 143,000 deaths annually. Oral cholera vaccines (OCVs) have been playing an important role in prevention and control efforts. However, the vaccine uptake rates vary in different geographic regions which could impact on vaccine effectiveness. This study describes the effect of socioeconomic predictors on vaccine uptake in a geographically defined cluster randomized cholera vaccine clinical trial.

Methods: A three-arm (vaccine, vaccine plus behavioral change, and non-intervention) cluster randomized trial was conducted in Dhaka, Bangladesh among 268,896 participants. A geographical information system (GIS) was used for design and implements the vaccination program. A logistic regression model was used for analysis.

Results: Among 188,206 study participants in vaccine and vaccine plus behavioural change arms, 123,686 (66%) received two complete doses and 64,520 participants (34%) received incomplete or no doses of vaccine. Vaccine uptake rate was significantly higher in females than males (aOR: 1.80; CI =1.75-1.84) and in adults than the younger participants (aOR: 2.19; CI=2.13-3.26). Individuals living in their house or having higher monthly family expenditure were more likely to receive two doses of the vaccine in comparison to those resided in rental housing with lower monthly family expenditure (aOR:1.60; CI =1.50-1.70 ; aOR: 1.14; 95% CI=1.10-1.18 respectively). Vaccine uptake was also significantly higher in participants Individuals who treated water for drinking and used own tap as source of water were more likely to receive the vaccine than their counterpart (aOR:1.23; CI 1.17-1.29 ; aOR: 1.14; CI =1.02-1.25 respectively).

Conclusions: The GIS tools greatly enhanced our ability to conduct vaccine trial. Socioeconomic predictors identified in this study will help in the decision making and organizing an effective vaccination program in future.

Clinical Trial Registration: ClinicalTrials.gov number,NCT01762930
MENACWY VACCINATION CAMPAIGN FOR ADOLESCENTS IN THE NETHERLANDS: UPTAKE AND ITS DETERMINANTS.

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**Background:** Between 2015 and 2018 the incidence of meningococcal disease serogroup W cases increased tenfold in the Netherlands with the highest case fatality among adolescents and young adults. In 2018/2019 a national mass vaccination campaign, with reminder after no-show, was implemented targeting 14- to 18-years old. This study evaluated the vaccination campaign by estimating the MenACWY-vaccine uptake and investigating its determinants.

**Methods:** The uptake *before* the start of the vaccination campaign was estimated from the number of vaccines administered by Municipal Health Services and dispensed by public pharmacies, and *within* the campaign from the national vaccination register. Possible determinants of uptake *within* the campaign were investigated among the first group invited for vaccination (born in May-December 2004) using random forest classification analysis.

**Results:** The uptake was 86% (of which 1.9% *before* campaign) among all eligible adolescents and 88% among the first group invited, including 5% achieved after the reminder. The most important predictors of vaccination after the first invitation were parents’ country of birth (lower uptake when parents were born abroad) and after reminder, distance to vaccination location (lower uptake with larger distance), percentage of votes for the reformed political party per municipality (lower uptake with higher percentage) and parents’ country of birth (higher uptake when parents were born abroad, opposing the first invitation).

**Conclusions:** This adolescent vaccination campaign achieved a high uptake, with minor MenACWY-vaccine use before the campaign started. Ethical background, religious objection (i.e. votes for the reformed political party) and accessibility to the vaccination location were the most important predictors of vaccination. The reminder enhanced the uptake and was valuable to diminish immunization disparities. Future vaccination campaigns should put more effort into reaching non-Dutch ethnical groups.
COMBINATION TESTING OF CEFTAZIDIME-AVIBACTAM WITH AZTREONAM IN BACTERIAL ISOLATES OF PEDIATRIC PATIENTS FROM CRITICAL CARE UNIT.

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²Sanjay Gandhi Post Graduate Institute of Medical Sciences Lucknow, Critical Care Medicine, Lucknow, India

Background: Ceftazidime-avibactam, has excellent in-vitro activity against extensively drug resistant (XDR) Gram-negative bacteria. It is approved in pediatric patients of age more than three years with major hospital acquired infections. However it is ineffective against metallo-beta-lactamase (MBL) producers. Combination of aztreonam with this antibiotic can restore its action. Routine testing by E-test strip combination can be great help to clinicians regarding management MBL producing bacteria.

Methods: 112 isolates of Gram negative organisms were collected from various samples (urine, sputum, pus, blood) from pediatric patients of critical care medicine. They were identified by matrix assisted laser desorption/ionization-time of flight mass spectrometry (MALDI-TOF MS) method. Sensitivity testing were done by of E-Strips of Ceftazidime (0.01-256 µg/ml)-avibactam (4 µg/ml). Combination sensitivity testing was done by E-strips of ceftazidime-avibactam on Müller Hinton Agar containing aztreonam (4 µg/ml). The resistance genes in these organisms were detected by Polymerase Chain Reaction (PCR) and sanger sequencing.

Results: 48 XDR Klebsiella pneumoniae were isolated that were also resistant to carbapenems. Among these isolates, 16 (35%) were sensitive to ceftazidime-avibactam and 28(58%) to ceftazidime-avibactam and aztreonam combination. For 27 Escherichia coli isolates, 15 (55%) were sensitive to ceftazidime-avibactam and 24 (88%) were sensitive to triple drug combination. Among the 37 P. aeruginosa isolates the results were 43% and 58% respectively. Among the isolates that were sensitive to triple combination, 88% had new delhi beta lactamase gene (NDM).

Conclusions: With increased prevalence of MBL especially in K. pneumoniae, ceftazidime-avibactam with aztreonam can be used as colistin sparing option. Phenotypic synergy testing by E test strip method can be helpful in guiding therapy in day to day basis.

Clinical Trial Registration: Not controlled trial
CLASSIFICATION OF ECHOCARDIOGRAPHY IMAGES USING CONVOLUTIONAL NEURAL NETWORK TO ASSIST KAWASAKI DISEASE DIAGNOSIS

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Background: Kawasaki disease is the most common heart condition affecting young children under five years old in developed countries and especially in Asia [1]. It damages blood vessels all over the body and results in vasculitis, myocarditis and coronary dilation causing long term heart complications. Based on the success of Convolutional Neural Networks to solve computer vision problems such as images classification, this study aims to develop a system to ease the diagnosis of Kawasaki disease using echocardiographies focusing more specifically on coronary arteries.

Methods: We applied deep convolutional neural networks techniques to detect if a coronary artery was present in a 2D echocardiography image of a video extracted previously from a DICOM file. Two experienced cardiologists manually divided 3500 images from 30 DICOM files into four categories: right coronary, left coronary, both coronaries, and no coronary.

Results: Experiments comparing some well-known neural network architectures such as ResNet and VGG ones and the proposed solution which is a simpler neural network composed by 5 convolutional layers were made. Two different experiments were made, a binary one to distinguish between images that have some coronary and those in which there is no coronary present, and a four class problem to distinguish among four kind of images: images with both coronaries, images with the right coronary, images with the left coronary, and images with no coronary.
Conclusions: This research shows that machine learning can solve classification problems using medical images and great results can be expected with a more elaborated and more extensive data set. In clinical practice this will be useful to eliminate observer variability or even provide a tool where no experienced cardiologist is available but images can be obtained.
PROTEOMIC ANALYSIS DIFFERENTIATING THE ANTIBODY RESPONSE IN KAWASAKI DISEASE FROM HEALTHY AND FEBRILE CONTROLS

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¹Imperial College London, Section Of Paediatric Infectious Disease, London, United Kingdom, ²University of California San Diego, Health Sciences, San Diego, United States of America

Background: The aetiology of Kawasaki Disease (KD) remains unclear, though there is considerable clinical and epidemiological evidence to support microbial causes. As part of a study seeking direct evidence of microbial agents, we are directly investigating the antibody response through proteomics of precipitated immune complexes.

Methods: Samples (plasma or serum) were collected from children with confirmed subacute KD (>illness day 10; n=46) and contemporaneous febrile controls (n=35, >illness day 6) cared for at Rady Children’s Hospital (California, USA), and healthy controls (n=31) recruited at St Mary’s Hospital (London, UK). Immune complexes were precipitated using polyethylene glycol (PEG) precipitation. Samples underwent trypsin-digestion and mass spectrometry on an Orbitrap Fusion Lumos instrument. The analytic pipeline comprises peptide identification using MaxQuant search (false-discovery-rate 1%) against the UniProt human proteome and antibody sequences (abysis). Peptides are aligned with modified-Martin numbering and variable region peptides assigned corresponding V and J loci by BLAST against the IMGT database. Variable region peptide intensities undergo quantile normalisation. Differential abundance analyses of V/J loci and k-mers are undertaken with the limma package in R with scaling to unit sample intensity. Statistical tests are Benjamini-Hochberg corrected.

Results: Of 16,498 distinct peptide identifications, 10,594 correspond to the immunoglobulin variable region. 148 peptides were significantly over-represented in KD; 24 were unique (Fisher’s exact, p≤0.05). Significantly over-represented and unique peptides were also found in febrile and healthy patients. Limma analysis found IGKV4, IGHV7 and IGHJ4 to be overabundant in KD vs. healthy samples. An example plot of significant heavy chain k-mers is shown below. Group permutation reduced significant findings over 100-fold.

Conclusions: Mass spectrometry provides a means to investigate antibody responses. Functional correlation of findings may help to explore aetiopathogenesis, coupled with improvements in structural and functional modelling.

Clinical Trial Registration: Not applicable
Background: The number of children diagnosed with tuberculosis (TB) is estimated to be one million annually, with half of those occurring in children less than 5 years of age. However, this is thought to be underestimated due to the symptoms of TB having overlapping clinical features of other common childhood diseases, such as pneumonia and malnutrition, and the difficulty in obtaining microbiological confirmation. The risk of developing TB is 5-fold higher in children with HIV. TB detection and control requires improved diagnostic tests that are rapid, accurate and can be used at point-of-care.

Methods: To identify a diagnostic signature of TB from other diseases (OD) we analysed serum from children recruited for suspected TB in South Africa (n=157) and Malawi (n=189) and Kenya (n=127) with and without HIV infection. Sera were analysed on cationic, anionic and IMAC arrays using SELDI-TOF mass spectrometry. LC-MS/MS and immunoprecipitation were used for protein identification and antibody-based methods for validation.

Results: We identified 311 proteins with significantly different levels (p< 0.01) between TB and OD, irrespective of HIV status, in South African and Malawian children (discovery cohort). To identify the smallest number of proteins to distinguish TB from OD, patients were randomly assigned to training (80%) and test (20%) sets and logistic regression variable selection performed. A four protein signature comprised of peaks identified at 4.1, 11.8, 13.7 and 14.7kDa showed a combined AUC of 0.836 (HIV-) and 0.810 (HIV+). In Kenyan children (validation cohort), the combined AUC was 0.805 (HIV-) and 0.896 (HIV+).

Conclusions: Proteomic analysis of serum can derive host signatures of TB infection useful for diagnostic development. Our findings demonstrate that proteins identified by mass spectroscopy are translatable to antibody based methods for POC test development.

Clinical Trial Registration: There is no clinical trial number, not applicable
Background: Children account for a significant proportion of Ebola virus disease cases during outbreaks. A heterologous 2-dose vaccine regimen consisting of Ad26.ZEBOV (Ad26) followed by MVA-BN®-Filo (MVA) is being investigated for Ebola prophylaxis in children.

Methods: Three age cohorts [adolescents (12–17 years), children (4–11 years) and toddlers (1–3 years)], were randomized to receive Ad26 (dose 1) and MVA (dose 2) vaccination or meningococcal conjugate vaccine (ACWY) and placebo in a 56-day interval. Solicited and unsolicited AEs were assessed until 7 and 28 days post-dose, respectively. Serious adverse events (SAEs) were assessed until one year post-dose 1. Immune responses were measured by EBOV GP FANG ELISA and pseudovirion neutralization assay at Day 78, 240 and 360.

Results: 576 participants (192 adolescents, 192 children and 192 toddlers) were enrolled. The Ad26,MVA regimen was well tolerated with no safety concerns. The frequency of solicited and unsolicited AEs was similar between the Ad26,MVA and control regimens. Most AEs were mild to moderate. No SAEs were considered related to Ad26 or MVA vaccines. Robust humoral immune responses were observed in all age cohorts. At 21 days post-dose 2, geometric mean binding antibody concentrations of 9,929, 10,212 and 22,568, EU/mL were observed in adolescents, children and toddlers, respectively. These responses persisted at least up to 12 months post-dose 1 in most participants. Binding antibody responses correlated strongly with the neutralizing antibody responses. At 21 days post-dose 2, geometric mean neutralizing antibody titres were 2120, 2483 and 8142 IC50 in adolescents, children and toddlers, respectively.

Conclusions: The Ad26, MVA vaccine regimen was well tolerated, induced robust antibody responses and may be suitable for Ebola prophylaxis in paediatric populations. Antibody concentrations were highest in younger children.

Clinical Trial Registration: ClinicalTrials.gov NCT02509494
Background: Injudicious use of antibiotics in children has emerged as a major public health concern for developing countries including Bangladesh. However, comprehensive evidence from this region is limited. This study systematically investigated 15-year trends of antibiotic misuse in acute rotaviral diarrhea among 6-23 months old children as well as the factors associated, source, and types of antibiotics used in urban and rural Bangladesh.

Methods: This study included all the 6-23 months old children with culture-confirmed acute Rotavirus diarrhea enrolled in the Diarrheal Disease Surveillance System (DDSS) of Dhaka (urban) and Matlab (rural) hospitals of icddr, b during 2004-2018. Relevant clinical, epidemiological and socio-demographic data were extracted from the DDSS database. The chi-square test for trend was carried out to check for a linear trend in antibiotic use. Site-specific separate logistic regression models were built to identify the factors associated with antibiotic use in rotaviral diarrhea.

Results: In both the settings, the proportions of children with rotaviral diarrhea who received antibiotics have risen significantly (43% to 75.5% in urban, 35% to 69% in rural) from 2004 to 2018 (p<0.001). The majority of the children visited physicians' chambers (57.5% in urban, 65% in rural) before coming to icddr, b. Macrolides were the most used antibiotics (46.6% in urban, 38% in rural). Notable risk factors identified in both multivariable models were monthly family income >100US$ (OR=1.5; 95% CI 1.2, 1.9), and paternal literacy (OR=1.8; 95% CI 1.4, 2.3).

Conclusions: The rising trend of antibiotic use in Bangladeshi children with Rotavirus diarrhea, the tendency of physicians to prescribe antibiotics injudiciously, higher prevalence of antibiotic misuse among well-off, literate parents are alarming and warrant the necessity of public awareness campaigns.
A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL TO ASSESS THE SAFETY, TOLERABILITY, AND PHARMACOKINETICS OF A RESPIRATORY SYNCYTIAL VIRUS (RSV) NEUTRALIZING MONOCLONAL ANTIBODY (MK-1654) IN HEALTHY PARTICIPANTS

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¹Merck & Co., Inc., Research, Kenilworth, United States of America, ²Celerion, Research, Lincoln, United States of America, ³Celerion, Research, West Conshohocken, United States of America

Background: MK-1654 is a fully human, extended half-life, RSV neutralizing monoclonal antibody targeting site IV of the RSV fusion protein in clinical development to protect infants against RSV disease. This is a first-in-human study of MK-1654 in adults.

Methods: In this 2-part, placebo-controlled, double-blind study, healthy adults were randomized 3:1 to receive a single dose of MK-1654 or placebo. Part 1 followed a single ascending-dose design, including dose levels of 100-mg intramuscular (IM), 300-mg IM, 300-mg intravenous (IV), 1000-mg IV and 3000-mg IV. Part 2 consisted of 300-mg IM and 1000-mg IV expansion panels. Safety, pharmacokinetics, anti-drug antibodies (ADA), and RSV serum-neutralizing antibody (SNA) titers were evaluated through one year.

Results: 152 participants were enrolled and completed the trial. No deaths, discontinuations due to adverse events (AEs), dose-limiting tolerability issues, dose-dependent patterns of treatment-related AEs, or treatment-related serious AEs were observed. MK-1654 serum concentrations increased proportionally with dose and the antibody displayed a half-life of 73 to 88 days (Figure). The estimated bioavailability, as calculated using the 300-mg IV and 300-mg IM dosing arms, was approximately 69%. Three out of 114 (2.6%) participants receiving MK-1654 developed treatment-emergent ADA with no associated adverse events. Lastly, administration of MK-1654 resulted in a dose-dependent increase in RSV SNA titers. Figure. Mean Serum Concentrations Versus Nominal Time Following Single Dose IV or IM Administration of MK-1654 to Healthy Adults.
**Conclusions:** MK-1654 was generally well-tolerated in healthy adults, displayed an extended half-life compared to typical monoclonal antibodies and resulted in a dose-dependent increase in SNA titers and a very low incidence of ADA. These data support the continued development of MK-1654 for the prevention of RSV disease in infants.

**Clinical Trial Registration:** clinical trial registration - not applicable
EFFICACY OF CELL-DERIVED QUADRIVALENT INFLUENZA VACCINE IN PREVENTION OF CLINICAL INFLUENZA IN CHILDREN 2 TO < 18 YEARS OF AGE: RESULTS OF A RANDOMISED CONTROLLED TRIAL

A. Fortanier¹, A. Poder², L. Bravo³, H. Szymański⁴, M. Heeringa¹, W. Vermeulen¹, V. Matassa⁵, J. Edelman⁶, I. Smolenov⁶, B. Leav⁶, T. Nolan⁷

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Background: The manufacture of influenza vaccines using Madin Darby Canine Kidney (MDCK) cells offers the possibility of closer antigenic match to circulating strains of influenza virus by avoiding egg-adapted changes. We evaluated the efficacy of a quadrivalent cell-derived inactivated influenza vaccine (QIVc, Flucelvax Quadrivalent, Seqirus) in children 2 to <18 years-old.

Methods: Over three influenza seasons, 4,514 children 2 to <18 years of age from 8 countries were enrolled into a Phase III/IV, observer-blinded, randomised controlled trial to 0.5 ml of QIVc or a non-influenza comparator (MenACWY vaccine) in a 1:1 ratio. Based on influenza vaccination history, participants received one or two doses (28 days apart) of the study vaccine and were followed for at least 180 days for safety. A Cox proportional hazards model was used to evaluate the vaccine efficacy of QIVc on first occurrence of laboratory confirmed Type A or B influenza (primary objective). The presence of influenza virus in nasopharyngeal swabs from participants with influenza like illness (body temperature ≥37.8°C plus a respiratory symptom) was confirmed by real-time polymerase chain reaction and viral culture.

Results: Of the 4,514 subjects enrolled (mean follow-up: 225 days, SD: 27.6), 539 (12%) experienced at least one influenza episode. Compared with the control vaccinees, significantly fewer influenza episodes were observed in participants receiving QIVc (VE: 54.6% [95% CI: 45.7; 62.1]). The VE against laboratory-confirmed A/H1N1 was 80.7% [95% CI: 69.2; 87.9], for B-Yamagata/B-Victoria 47.6% [95% CI: 31.4; 60.0] and for A/H3N2 42.1% [95% CI: 20.3; 57.9]. The rates of adverse events were comparable between study vaccines.

Conclusions: This cell-derived QIV was efficacious in preventing influenza in children and adolescents (Funded by Seqirus Ltd. UK.)

Clinical Trial Registration: Clinical trial registration:ClinicalTrials.gov 01218308
E-POSTER VIEWING
E-POSTER DISCUSSION SESSION 01: RESPIRATORY INFECTIONS
10-28-2020 8:00 AM - 7:00 PM

ETIOLOGY, MANAGEMENT AND OUTCOME OF COMMUNITY-ACQUIRED PNEUMONIA (CAP) AMONG HOSPITALIZED CHILDREN (PERFORM PROJECT)

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1Children’s Hospital «P. and A. Kyriakou», 2nd Department Of Pediatrics, National And Kapodistrian University Of Athens, Athens, Greece, 2Instituto de Investigación Sanitaria, Genetics, Vaccines, Infectious Diseases And Pediatrics Research Group (genvip), Santiago de Compostela, Spain, 3Translational Pediatrics and Infectious Diseases., Department Of Pediatrics, Hospital Clínico Universitario De Santiago De Compostela, Santiago de Compostela, Spain, 4Imperial College London, Section Of Paediatric Infectious Disease, London, United Kingdom, 5Alder Hey Children’s Hospital, Department Of Infectious Diseases, Liverpool, United Kingdom, 6Erasmus MC-Sophia children's hospital, General Paediatrics, Rotterdam, Netherlands, 7Children Clinical University Hospital, Infectious Diseases, Riga, Latvia, 8Medical Research Council Unit The Gambia, At Lshtm, Fajara, Gambia, 9Emma Children Hospital, Amsterdam, UMC, University Of Amsterdam, Department Of Pediatric Immunology, Rheumatology And Infectious Diseases, Amsterdam, Netherlands, 10Radboud University, Medical Center, Nijmegen, Netherlands, 11Inselspital, BernUniversity Hospital, Pediatrics, Bern, Switzerland, 12University Medical Centre Ljubljana, Department Of Infectious Diseases, Ljubljana, Slovenia, 13Medical University Graz Austria, Department Of General Paediatric, Graz, Austria, 14Great North Children's Hospital, Paediatric Immunology, Infectious Diseases And Allergy, Newcastle upon Tyne, United Kingdom, 15Newcastle University, Translational And Clinical Research Institute, Newcastle upon the Tyne, United Kingdom, 16Newcastle University, Newcastle upon Tyne Hospitals NHS Trust, Newr Newcastle Biomedical Research Centre, Newcastle upon Tyne, United Kingdom, 17London School of Hygiene and Tropical Medicine, Faculty Of Infectious and Tropical Diseases, Department Of Clinical Research, London, United Kingdom, 18London School of Hygiene and Tropical Medicine, Department Of Global Health And Development, Faculty Of Public Health And Policy, London, United Kingdom, 19Hauner Children's Hospital, University Hospital, Ludwig Maximilians University (LMU), Div Paediatric Infectious Diseases, Munich, Germany, 20partner sit Munich, German Centre For Infectious Research (dzif), Munich, Germany, 21University Liverpool, Institute Of Infection And Global Health, Liverpool, United Kingdom, 22NIHR, Oxford Biomedical Research Centre, Oxford, United Kingdom

Background: Pediatric community-acquired pneumonia (CAP) remains one of the most common causes of hospitalization and morbidity worldwide. Pathogen patterns change due to factors such as vaccination coverage and antimicrobial resistance. In total, viruses account for the most pneumonia cases but their detection is still limited. We aimed to describe the etiology, management and outcome of children hospitalized with pneumonia in the context of PERFORM project.

Methods: Children<18 years with suspected infection or fever attending ED and who had blood samples taken in the context of PERFORM project (www.perform2020.org), were recruited prospectively between 2016 and 2019. Of 5,739 children, 574 (10%) were diagnosed with CAP. Of the latter, 401/574 (69.8%) were managed as inpatients for a median of 3.4 days (IQR 1.9-6.5). Median age was 4.2 years (IQR 1.9-8) and 59.6% were boys. Prematurity or an underlying illness were recorded in 133/401 (33.2%) of them.

Results: A causative pathogen was identified in 58/401 (14.5%) patients (Table): 42/401 (10.5%) were classified as Definite Bacterial and 16/401 (4%) as Definite Viral based on the classification algorithm previously published by Herberg et al.
374/401 (93.2%) were treated with antimicrobials. Of those considered to have CAP of viral or unknown etiology, 86.8% were treated with antimicrobials. In 33/401 (8.2%) chest drainage was performed. 2 underwent VATS. Of 109/401 (27.2%) patients admitted to PICU, 68/401 (16.9%) required mechanical ventilation. Of 397 children with known outcome, 97.5% fully recovered, 3 experienced severe complications, 3 died.

**Conclusions:** Pediatric community-acquired pneumonia still remains one of the leading causes of hospitalization and morbidity among children with fever in Europe. Current limitations in etiological diagnosis of pneumonia lead to antibiotic overuse and consequently development of antimicrobial resistance. New diagnostic tests able to differentiate between bacterial and viral community-acquired pneumonia are required to improve the management of children hospitalized with pneumonia.

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**Table 1** Causative pathogens in hospitalized children with CAP

<table>
<thead>
<tr>
<th>Causative pathogens</th>
<th>Number of patients</th>
<th>Sample and method of identification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definite Bacterial (DB)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td>18</td>
<td>Blood culture 7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pleural fluid culture 2, PCR 8, RAG 1</td>
</tr>
<tr>
<td><em>Group A Streptococcus</em></td>
<td>8</td>
<td>Blood culture 4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pleural fluid culture 2, PCR 2</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>4</td>
<td>Blood culture 3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pleural fluid culture 1</td>
</tr>
<tr>
<td><em>Mycoplasma pneumoniae</em></td>
<td>9</td>
<td>Serology 5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pleural fluid PCR 1</td>
</tr>
<tr>
<td><em>Mycobacterium tuberculosis</em></td>
<td>3</td>
<td>Pleural fluid culture 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sputum PCR 1, BAL PCR 1</td>
</tr>
<tr>
<td>Definite Viral (DV)*</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Adenovirus</td>
<td>1</td>
<td>URT PCR 1</td>
</tr>
<tr>
<td>Bocavirus*</td>
<td>1</td>
<td>URT PCR 1</td>
</tr>
<tr>
<td>Influenza A*</td>
<td>5</td>
<td>URT PCR 3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>URT RAG 2</td>
</tr>
<tr>
<td>Influenza B</td>
<td>2</td>
<td>URT PCR 2</td>
</tr>
<tr>
<td>PIV 4</td>
<td>1</td>
<td>URT PCR 2</td>
</tr>
<tr>
<td>RSV</td>
<td>6</td>
<td>URT PCR 3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>URT RAG 3</td>
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<tr>
<td>Rhinovirus*</td>
<td>2</td>
<td>URT PCR 2</td>
</tr>
<tr>
<td>Metapneumovirus</td>
<td>2</td>
<td>URT PCR 2</td>
</tr>
<tr>
<td>More than one virus</td>
<td>3</td>
<td>URT PCR 3</td>
</tr>
</tbody>
</table>

Total 58

URT, Upper Respiratory; RAG, Rapid AntiGen

*some patients had more than one virus identified

*pathogens identified in 2 of the 3 children who died
THE METHODOLOGY AND CLINICAL SIGNIFICANCE OF FILMARRAY RESPIRATORY PANEL 2 PLUS IN DIAGNOSING BORDETELLA PERTUSSIS IN NPS SPECIMENS

C. Li, J. Deng, C. Huang
Shenzhen Children’s Hospital, Division Of Infectious Diseases, Shenzhen, China

Background: To compare the performance of FilmArray Respiratory Panel 2 plus (FilmArray RP2+), quantitative real-time PCR (q-PCR), and culture for detection of *Bordetella pertussis* in nasopharyngeal swabs (NPS) specimens. Meanwhile, to describe pathogen spectrum in pediatric patients with and without *B. pertussis*.

Methods: Collect the NPS specimens from patients according to our criteria from March 1 to June 31, 2018 in Shenzhen children hospital. All the specimens were tested by FilmArray RP2+, q-PCR, and culture.

Results: 236 children with pertussis and 235 with pertussis-like syndrome were included. Culture as the gold standard, the sensitivity, specificity, PPV and NPV of FilmArray RP2+ were 85%, 77.4%, 50.3%, and 95%, respectively. FilmArray RP2+ and q-PCR had the similar detection effect. The positive rate of FilmArray RP2+ was much higher than culture in patients with age <6 months, cough course >7 days, and pertussis vaccine records <3. The most prevalent co-infectious pathogen was rhinovirus/enterovirus, parainfluenza virus and RSV in children with pertussis, which were the top pathogens in pertussis-like syndrome.
Table 3 Comparison of positive and negative results in qPCR and Filmarray using culture as gold standard

<table>
<thead>
<tr>
<th></th>
<th>Culture</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+</td>
<td>85</td>
<td>84</td>
<td>85.0</td>
<td>77.4</td>
<td>50.3</td>
</tr>
<tr>
<td></td>
<td>−</td>
<td>15</td>
<td>287</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Filmarray</td>
<td>+</td>
<td>82</td>
<td>98</td>
<td>82.0</td>
<td>73.6</td>
<td>45.6</td>
</tr>
<tr>
<td></td>
<td>−</td>
<td>18</td>
<td>273</td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

PPV, positive predictive value; NPV, negative predictive value.

Table 4 Comparison of positive and negative results in qPCR and Filmarray using qPCR as reference standard

<table>
<thead>
<tr>
<th></th>
<th>qPCR</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+</td>
<td>144</td>
<td>25</td>
<td>80.0</td>
<td>91.4</td>
<td>85.2</td>
</tr>
<tr>
<td></td>
<td>−</td>
<td>36</td>
<td>266</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

PPV, positive predictive value; NPV, negative predictive value.

Pathogens in patients with pertussis and pertussis-like. R/E, rhinovirus/enterovirus; BP, Bordetella pertussis; Para, parainfluenza virus; RSV, respiratory syncytial virus; Cov, coronavirus; hMPV, human metapneumovirus; ADV, adenovirus; FluA, Influenza A virus, MP, mycoplasma pneumoniae.
**Conclusions:** This study demonstrated the capability of FilmArray RP2+ for detection of *Bordetella pertussis* and co-infectious respiratory pathogens.
SERIOUS VIRAL INFECTIONS IN HOSPITALIZED CHILDREN ACROSS EUROPE (PERFORM PROJECT)

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Background: Serious viral infections(SVIs) are associated with an increasing burden of disease and significant morbidity and mortality worldwide, especially in children<5 years of age. However, they haven’t been studied as well as serious bacterial infections. We aimed to describe the etiology, clinical syndromes and impact of serious viral infections in children hospitalized with fever in the context of the PERFORM project.

Methods: Children<18 years with suspected infection or fever attending ED and who had blood samples taken in the context of PERFORM project (www.perform2020.org), were recruited prospectively between 2016 and 2019. Patients were included if they were classified as Definite Viral(DV) cases according to the classification algorithm previously published by Herberg J et al. Among patients with DV infections those admitted to PICU were considered to have an SVI.

Results: 735/5,379 (12.8%) were classified as DV, 376/735 (51.2%) were managed as inpatients.
Another 67/735 (9.1%) were admitted to PICU and classified as SVI(Table).

**Table 1.** Clinical syndromes and causative pathogens among patients with SVIs

<table>
<thead>
<tr>
<th>A. Clinical syndromes*</th>
<th>B. Pathogens identified</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lower Respiratory Tract</strong></td>
<td></td>
</tr>
<tr>
<td>Asthma exacerbation/viral induced wheeze (n=6)</td>
<td>Bocavirus (n=3)</td>
</tr>
<tr>
<td>Bronchiolitis (n=26)</td>
<td>Enterovirus (n=8)</td>
</tr>
<tr>
<td>Pneumonia (n=5)</td>
<td>Hantaan virus (n=1)</td>
</tr>
<tr>
<td>Undefined LRTI (n=10)</td>
<td>HSV 1** (n=3)</td>
</tr>
<tr>
<td></td>
<td>HSV 2 (n=1)</td>
</tr>
<tr>
<td><strong>Upper Respiratory Tract</strong></td>
<td></td>
</tr>
<tr>
<td>Acute tracheitis (n=1)</td>
<td>Human Metapneumovirus (n=1)</td>
</tr>
<tr>
<td>Croup (n=1)</td>
<td>Influenza A** (n=8)</td>
</tr>
<tr>
<td></td>
<td>Influenza B *** (n=4)</td>
</tr>
<tr>
<td><strong>CNS</strong></td>
<td>Norovirus (n=1)</td>
</tr>
<tr>
<td>Meningitis – Encephalitis **(n=9)</td>
<td>Parechovirus (n=2)</td>
</tr>
<tr>
<td>Febrile convulsions (n=5)</td>
<td>PIV 1-4 (n=6)</td>
</tr>
<tr>
<td>Seizures (n=3)</td>
<td>RSV (n=25)</td>
</tr>
<tr>
<td></td>
<td>Rhinovirus (n=14)</td>
</tr>
<tr>
<td><strong>Moderate/severe Diarrhea (n=2)</strong></td>
<td>VZV (n=1)</td>
</tr>
<tr>
<td><strong>Flu like illness (n=3)</strong></td>
<td>Patients with more than one virus identified (n=15)</td>
</tr>
</tbody>
</table>

*Some patients had more than one clinical syndrome recorded

**Some patients had more than one virus identified

**Clinical syndrome and ***Causative pathogens of the two children who died

Patients with SVI(61.2% boys) compared to DV hospitalized without PICU admission patients(52.9% boys, p=0.21), had a median age of 0.8 years (IQR 2.2 years) vs 3.03 (IQR 6.84 years)(p<0.001) and had an underlying illness or prematurity recorded in 30/67 (44.8%) and 19/67(28.4%) vs 104/376 (27.6%)(p=0.005) and 22/376 (5.8%)(p<0.001), respectively. Of the SVIs patients with known outcome, 90% fully recovered, 2 (3%) experienced severe complications and 2 (3%) died.

**Conclusions:** SVIs account for a large part of the morbidity and mortality burden in children with fever. However, they are often underestimated due to the generally self-limiting course of most viral infections and diagnostic limitations. Among patients with SVIs, the most common viruses identified included RSV, adenovirus, rhinovirus and influenza virus, while young age, underlying illness and prematurity were identified as risk factors.
EARLY LIFE EXPOSURE TO RESPIRATORY VIRUSES: A LONGITUDINAL BIRTH COHORT STUDY

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Background: Respiratory tract infections (RTI) in children (<5y) are mainly caused by viruses. Respiratory syncytial virus (RSV) and human metapneumovirus (hMPV) are considered to be the most pathogenic viruses. Rhinovirus (RV), in contrast, is the most commonly detected virus, although often found in asymptomatic children as well. Little is known about the health consequences of (a)symptomatic presence of respiratory viruses early in life. The objective is to examine exposure to respiratory viruses in the first year of life and relate exposure and timing thereof to development of symptomatic infections in a longitudinal birth cohort.

Methods: In a prospective birth cohort of 115 infants, we characterized a panel of 17 respiratory viruses longitudinally from birth to 12 months of age (11 consecutive sample moments and up to three ARTI moments [which included fever and respiratory complaints]; in total, n = 1,287 samples) by quantitative RT-PCR. Associations between viral presence and symptoms of an ARTI were tested by generalized estimating equation (GEE) models.

Results: RV was the most commonly detected virus, and often found in multiple consecutive sample moments, suggesting prolonged periods of infection. RV was negatively associated with ARTI symptoms (GEE: OR 0.40 [0.17-0.98]). In contrast, hMPV, RSV, parainfluenza (PIV) 2 and 4, and HKU corona were highly associated (OR > 10; p<0.05) with ARTI symptoms. Despite the asymptomatic behavior of RV, early life detection was associated with increased susceptibility to respiratory complaints in the first year of life (Kaplan-Meier survival analysis: p=0.021).

Conclusions: Early life rhinovirus presence is negatively associated with ARTI symptoms but is associated with future susceptibility for respiratory complaints. Further studies on potential ecological or immunological mechanisms explaining these findings are needed.

Clinical Trial Registration: Netherlands Trial register: NTR3986
DISSEMINATION OF CLINICAL-BASED RECOMBINANT HUMAN RESPIRATORY SYNCYTIAL VIRUSES IN PRIMARY DIFFERENTIATED AIRWAY CULTURES

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Background: Human respiratory syncytial virus (HRSV) is the leading cause of acute respiratory infections in infants. Prophylactic vaccines or antivirals are not yet available and their development is hampered by our limited understanding of the pathogenesis of severe HRSV disease. For a substantial part, this knowledge gap results from a lack of studies in relevant models systems. Furthermore, in most studies cell-culture adapted viruses are used. We developed an in vitro model that builds on primary cells grown at air-liquid interphase and clinical-based viruses expressing fluorescent reporter proteins to study HRSV infection and dissemination. In the future, we will use this model to test our hypothesis that severe lower airway disease only develops if HRSV rapidly advances and disseminates to the lower airways.

Methods: Nasal, bronchial and small airway respiratory epithelial cells cultured at air-liquid interphase (Epithelix®) were infected with two clinical-based recombinant viruses (HRSV²¹¹EGFP(5) and HRSV²⁰⁵EGFP(5)) and one laboratory-adapted virus (HRSV²³²EGFP(5)). Infection kinetics were studied and cytokine production was measured.

Results: HRSV predominantly infected the superficial ciliated epithelial cells in all cultures, and replicated faster in nasal and bronchial cells compared to small airway cells. The two clinical-based viruses resulted in more infected cells than the laboratory-adapted virus. Replication was followed by a cytokine response, which was dominated by type III interferons. Viral titers and cytokine responses correlated in magnitude and timing.

Conclusions: By combining clinical-based recombinant HRSV strains with primary airway cultures we developed a relevant model to study HRSV immunopathogenesis in vitro. This fluorescence-based model can be used to study early dissemination of HRSV and the interactions between HRSV, co-infections and the innate immune system to better understand the pathogenesis of severe HRSV disease.

Clinical Trial Registration: Clinical trial registration: N/A
Background: Human adenoviruses (HADVs) play a significant role in pediatric respiratory tract infections (RTI). However, there is little information regarding the burden and epidemiology of HADVs respiratory infections among children in developing countries. We initiated surveillance to determine the prevalence and identify the types of HADVs causing respiratory illness among children in the city of Accra, Ghana.

Methods: A total of 552 nasopharyngeal swabs were collected from children below 5 years of age, with acute lower respiratory tract infection treated at two pediatric hospitals, in 2006, and 2013 to 2014. Real-time PCR was used to screen for HADVs. All positive samples were sequenced. Demographics and clinical presentations were also analyzed.

Results: During the study period, 64 (12%) specimens were positive for HADVs. Among positive cases, the most prevalent species were HADV C (n= 28, 43.8%) and HADV B (n = 21, 32.8). Phylogenetic analysis of the hexon and fiber genes of 34 samples revealed 13 different HADV type: HADV1 (11) was detected most frequently, followed by HADV3 (8), HADV7 (4), and HADV6 (3). Recombinant strains carrying hexon and fiber genes of HADV3 and HADV7, respectively, were identified in three samples. HADVs circulated throughout the year with no marked seasonality. The incidence of HADV infection peaked in children aged below 2 years. The most common clinical diagnosis was respiratory tract infection, and the most common symptoms were cough, nasal discharge, fever, difficulty in breathing and gastrointestinal syndromes.

Conclusions: This study showed that HADVs are an important viral agent in children with RTIs in Ghana. The intraspecies recombinant HADV3 and HADV7 types could be relics from the past or newly emerging precursor strains of future HADV outbreaks in Ghana. This novel HADV types might be worthy of further study.

Clinical Trial Registration: This study is not a clinical trial.
A COMPUTER-ASSISTED TOOL CAN CATEGORIZE RADIOGRAPHS WITH PNEUMONIA IN CHILDHOOD

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Background: The variability in the interpretation of radiographs of pneumonia between different clinicians poses a long-standing problem. Artificial intelligence may help to solve this problem. Computer Vision Analysis can be used to build and validate an image classification algorithm in children using for the classification of radiographs with pneumonia according to the WHO categories (“consolidation” versus “other infiltrates” or “no consolidation/infiltrate”).

Methods: Three experts categorized 950 radiographs with pneumonia. The images were split into a training (80%) and a validation (20%) dataset. Three Convolutional Neural Network algorithms (vgg16, resnet50 and densenet120) were selected. The algorithms were re-trained with the training dataset to specialize them for classifying radiographs into the WHO categories. A software instrument using an explainable artificial intelligence tool was used to highlight in a heatmap the areas used by the algorithm. The best performing model was selected according to 5-fold cross-validation selecting the one that maximized the sensitivity for “consolidation”.

Results: The dataset had 403 (42%) radiographs with “consolidation” and 547 (58%) with “other infiltrates” or “no consolidation/infiltrate”. For every radiograph, the algorithm provides the WHO category and confidence. Compared to the experts’ categorization, the best algorithm (modified vgg16) yielded the following results: an area under the curve of 0.80 (+/- 0.03), a specificity of 81% and sensitivity of 69%. In the image heatmap, highlighted areas corresponded to consolidation (Figure 1).
Conclusions: We have created an image-recognition algorithm that could help physicians to classify pneumonia in children. Further development using larger datasets will improve its current accuracy. In the future, the incorporation of an improved decision support tool for classifying pediatric pneumonia in computerized health apps could significantly help attending physicians to accurately classify pneumonia and decreased the improper use of antibiotics.

*Areas highlighted in green are selected as consolidation sign by the model.*
HEMOLYTIC UREMIC SYNDROME ASSOCIATED WITH INVASIVE STREPTOCOCCUS PNEUMONIAE INFECTION: A SYSTEMATIC REVIEW OF THE LITERATURE

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Background: Streptococcus pneumoniae is a leading cause of haemolytic uraemic syndrome (HUS) and is associated with significant morbidity and mortality. The pneumococcal conjugate vaccines (PCV7 and PCV13) are highly effective in preventing invasive pneumococcal disease (IPD) across all age-groups through direct and indirect (herd) protection. The risk of HUS secondary to pneumococcus infection (pHUS) has not been systematically assessed.

Methods: We undertook a systematic review of the English literature published from January 2000 to December 2019 to evaluate the risk of HUS following invasive pneumococcal disease, serotype distribution, clinical presentation and outcomes. Data sources included MEDLINE, EMBASE, Cochrane library, and references within identified articles.

Results: We identified 603 potential studies and included 6 publications involving 10,477 participants in children less than 18 years old. The rate of pHUS was 3% (n=319) with a mean age of 17.6 months. Four studies (66.7%, 272 cases of pHUS) were during the PCV era while two studies (33.3%, 47 cases of pHUS) were before the introduction of PCV. The commonest clinical presentation was pneumonia (73%, n=89/122), followed by meningitis (19.7%, n=24) and septicaemia (6.6%, n=8). The majority of cases presenting with pneumonia were complicated by empyema (75%, n=67/89). The main responsible serotypes were 19A (n = 28/88), 3 (n = 12), 7F (n = 8), and non PCV13 serotypes (n=36/88). Comorbidity was reported in 17% (n=20/118) of cases and 12 (10%) died, including 9 with meningitis.

Conclusions: HUS associated with streptococcus pneumoniae persist as a significant cause of morbidity and mortality especially in children less than 2 years-old in the era of conjugate vaccines. Empyema remains the commonest clinical presentation with most fatality following meningitis. Almost half of the serotypes isolated are not included in the current PCV13.

Systematic Review Registration: N/A
GROUP B STREPTOCOCCAL COLONIZATION AND SEROTYPE-SPECIFIC IMMUNITY IN
JAPANESE MOTHER-INFANT PAIRS

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Background: In Japan, universal screening for group B streptococcal (GBS) colonization in pregnant women and intrapartum antibiotic prophylaxis (IAP) have been recommended to prevent neonatal GBS infection. However, severe GBS infection remains a leading cause of neonatal infection, especially late-onset disease. We aimed to determine the rates of colonization and serotype-specific immunity in Japanese mother-infant pairs under universal screening and IAP.

Methods: Rectovaginal swabs were collected from pregnant women between 33 and 37 gestation weeks. Nasopharyngeal and rectal swabs were collected from infants at birth, 1 week of life and 1 month of life. All specimens were subjected to GBS identification using our in-house real-time polymerase chain reaction method. GBS-positive isolates subsequently underwent capsular typing. In addition, maternal sera collected from GBS colonized pregnant women were tested in an opsono-phagocytic bacterial killing assay.

Results: The overall maternal and infant GBS colonization rates were 22.7% (57/251) and 8.8% (22/251) respectively. 55 colonized mothers were given IAP. In single analysis, maternal GBS colonization were found to be significantly associated with infant GBS colonization. Capsular types Ib (22.8%), III (19.3%), V (17.5%) were predominant among the isolates from pregnant women, whilst V (27.3%), Ib (22.7%) and III (18.2%) were predominant among the isolates from infants. The opsono-phagocytic killing assay geometric mean titer against serotypes Ia, Ib, III and V were 2413, 3066, 2723 and 2769 respectively.

Conclusions: Even if GBS colonized pregnant women received IAP, the risk of GBS carriage among their neonates is likely to be high. The ability of IAP to prevent GBS infection may be limited. Therefore, vaccine development should be considered. Antibody-mediated GBS phagocytic killing in maternal sera was high, which might contribute to the low incidence of invasive GBS disease in Japan.
HIGH PREVALENCE OF MULTIDRUG-RESISTANT GRAM-NEGATIVE BACTERIAL INFECTION FOLLOWING PAEDIATRIC LIVER TRANSPLANTATION

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Background: Bacterial infection is one of the most significant complications following liver transplantation (LT). Multidrug-resistant (MDR) gram-negative bacteria (GNB) infection remains problematic following LT in the adults. Moreover, an increased prevalence of Carbapenem-resistant Enterobacteriaceae (CRE) infection in adult LT has also been observed. However, data in children are scarce. We aimed to evaluate the prevalence and associated factors of MDR-GNB infection among paediatric LT recipients.

Methods: We performed a retrospective study of 118 children undergoing LT between January 2010 and December 2018 at a single transplant centre in Bangkok. Prevalence, clinical characteristics, types and sites of MDR-GNB infection within 3 months after LT, and the interested outcomes were collected. MDR organisms were those being non-susceptibility to at least one agent in three or more antibiotic classes.

Results: We noted 64 patients with a total of 119 episodes of bacterial infections. Fifty-eight episodes (48.7%) were caused by MDR-GNB, with a predominance of *Klebsiella pneumoniae* (32.7%) and *Escherichia coli* (31%). Interestingly, 10 (17.2%) of these isolates were CRE. The median time to MDR-GNB infection was 9 days (IQR5,33). Intraabdominal infection was the most common site (46.4%). In univariate analysis, exposure to antibiotics before LT, PELD-score >21, bile-leak, and re-operation were associated with MDR-GNB infection (p<0.05). Re-operation remained the only significant predictor of MDR-GNB infection (OR1.51[95%CI:1.01,2.25], p=0.04). The overall mortality was 6.7%.

Conclusions: We highlighted the high rate of MDR-GNB infection following paediatric LT. Re-operation was associated with a higher risk of MDR-GNB infection after LT. Therefore, caution on the emergence of MDR-GNB infection should be paid in children who underwent re-operation. The knowledge of the prevalence and resistant pattern are essential for guideline development to prevent and minimise the risk of MDR-GNB infection.
CARRIAGE RATES OF STREPTOCOCCUS PNEUMONIAE IN HEALTH CARE PROFESSIONALS AT A TERTIARY UNIVERSITY PAEDIATRIC HOSPITAL

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Background: Streptococcus pneumoniae is a commensal of the human upper respiratory tract. In certain cases, it can lead to serious invasive infections peaking in very young children and the elderly. Especially young children are frequent carriers and are thus regarded as the reservoir for horizontal transmission of pneumococci. Aim of this study was to determine S. pneumoniae colonization rates in asymptomatic health care professionals working in Paediatrics and Adolescent Medicine and to identify risk factors for carriage.

Methods: This cross-sectional pneumococcal carriage survey was conducted between April and October 2018 at the Medical University of Vienna. Individuals working as nurses, paediatricians or medical students at the Department of Paediatrics and Adolescent Medicine were enrolled. One oropharyngeal and one nasal swab per individual were directly plated onto appropriate agar plates and conventional culture was used for bacterial identification. Pneumococcal isolates underwent serotyping using Neufeld’s Quellung reaction with type-specific antisera.

Results: In total, 437 individuals participated in the study. S. pneumoniae was isolated in 4.8% (21/437) of the study cohort. Carriage was highest in individuals working in the outpatient department (8.2%; 8/98) and in those living in the same household with children under eight years of age (11.6%; 11/95). The most common serotypes found were 6C and 3. A total of 71.4% (15/21) of the carried serotypes are not included in any currently available pneumococcal vaccine. Nasal swabs were significantly less sensitive than oropharyngeal swabs in detecting S. pneumoniae carriage (2/437 vs. 21/437). The overall pneumococcal vaccination rate of participants was 14.4% (60/416).

Conclusions: This is the first study evaluating colonization with S. pneumoniae in health care professionals working in Paediatrics. We found a relevant amount of pneumococcal carriage bearing the risk of horizontal in-hospital transmission.

Clinical Trial Registration: not available
EMPIRIC THERAPY FOR DROWNING-ASSOCIATED PNEUMONIA

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²Erasmus MC-Sophia Children’s Hospital, Pediatric Infectious Diseases & Immunology, Rotterdam, Netherlands, ³Erasmus MC-Sophia Children’s Hospital, Intensive Care And Department Of Pediatric Surgery, Rotterdam, Netherlands, ⁴Amalia Children’s Hospital, Radboudumc, Pediatric Infectious Diseases, Nijmegen, Netherlands

Background and Objective: According to Dutch guidelines, empiric therapy for children with drowning-associated pneumonia consists of amoxicillin/clavulanic acid or piperacillin/tazobactam intravenously, dependent on clinical symptoms and aspect of water in which drowning occurred. However, recently respiratory cultures from drowned victims with pneumonia in our hospital revealed microorganisms resistant to this empiric therapy. Objective of this review is to give an overview of cultured microorganisms from drowned patients with pneumonia in relation to the type of water involved, in order to formulate adequate empiric therapy.

Methods: The MEDLINE database was reviewed for unique English full text publications from 1964 till December 2019, describing data concerning microorganisms from respiratory cultures in drowned patients with pneumonia and microorganisms from different water samples. Data from our own PICU were added. Optimal empiric therapy is proposed based on the cultured microorganisms, their sensitivity spectrum and the source of drowning water.

Learning Points/Discussion: - Most cultured microorganisms, both endogenous and aquatic pathogens, were sensitive to extended spectrum penicillin with beta-lactamase inhibitor; However, multi-drug resistant Enterobacteriaceae, Aeromonas and Pseudomonas species, mostly present in open fresh water, were also described (table 1). Scedosporium apiospermum, not sensitive to amphotericin B in contrast to most frequent cultured fungi Aspergillus species, appears to be present in strongly polluted fresh water. These data are based on scarce literature of 7 publications. - For drowning-associated pneumonia, empiric piperacilline/tazobactam will cover most common cultured microorganisms, including most Aeromonas and Pseudomonas species. However, for patients drowned in open fresh water, addition of an aminoglycoside is recommended to cover multi-resistant gram-negative microorganisms. When drowning took place in strongly polluted fresh water, we recommend to add voriconazol to cover possible infection with Scedosporium apiospermum.
Table 1
Selection of pathogenic microorganisms from respiratory cultures in patients with drowning-associated pneumonia (left column) and relation with type of water exposure.

<table>
<thead>
<tr>
<th>Organism</th>
<th>Fresh water</th>
<th>Salt water</th>
<th>Contaminated, stagnant water</th>
</tr>
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<tbody>
<tr>
<td><strong>Aerobic gram-negative bacteria</strong></td>
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<tr>
<td><em>Aeromonas</em> spp.</td>
<td>+++</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><em>Enterobacteriaceae</em></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>- <em>Klebsiella pneumoniae</em></td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>- <em>Enterobacter cloacae</em></td>
<td>+</td>
<td></td>
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<tr>
<td>- <em>Escherichia coli</em></td>
<td>+</td>
<td></td>
<td></td>
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<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>+</td>
<td></td>
<td>++</td>
</tr>
<tr>
<td><strong>Aerobic gram-positive bacteria</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><em>Staphylococcus aureus</em></td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td>++</td>
<td>+</td>
<td></td>
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<tr>
<td><strong>Fungi</strong></td>
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<tr>
<td><em>Aspergillus</em> spp.</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><em>Pseudallescheria boydii/ Scedosporium apiospermum</em></td>
<td></td>
<td></td>
<td>+++</td>
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</tbody>
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DANGER AND PROBLEMATIC TREATABILITY OF CHRONIC PSEUDOMONAS AERUGINOSA INFECTION IN CYSTIC FIBROSIS POPULATION.

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Background: Multidrug resistant (MDR) P. aeruginosa is the second one in the critical pathogens group from Priority Pathogens List published by WHO. Chronic P. aeruginosa respiratory infection is prevalent in CF population according to ECFS Register. Characteristic of P. aeruginosa isolates from lower airways of Russian CF patients with chronic infection before phase II clinical trial for innovative new medicine Fluorothiazinon was the goal of our investigation.

Methods: Cohort of 751 CF patients (several months - 68 years of age) was checked for P. aeruginosa infection by microbiological and molecular-genetic methods. Bacterial isolates were characterized by cytotoxic, biofilm formation, and Fluorothiazinon (inhibitor of type 3 secretion system, T3SS) sensitivity tests, and by whole genome sequencing (WGS).

Results: 45% of patients were infected by P. aeruginosa. 55 MDR isolates from chronically infected patients of different age groups belonged to 25 sequence types (ST). Infrequent ExoU lineage isolates (ST235, 313) were the most dangerous for CF patients’ respiratory function, and demonstrated 90-98% of cytotoxicity on the epithelial cells. These strains could be acquired form nosocomial environment. Common ExoS lineage isolates had various ST and lower or zero cytotoxicity. Comparison of two ST274 isolates revealed ExoS-conditioned cytotoxicity of one of them at 4 h.p.i., but forming matured biofilms on epithelial cell surface by non-cytotoxic isolate. According to WGS data isolates had equal alleles of exoS gene (T3SS), but different alleles of fha, hsp and vgrG genes, important for formation and function of T6SS. Fluorothiazinon suppressed both cytotoxicity, and biofilm formation.

Conclusions: Treatment efficiency of Fluorothiazinon in experiments in vitro suggests not only direct action of the medicine on T3SS effectors, but on all homologous bacterial cell structures, such as T6SS and flagella.

Clinical Trial Registration: ClinicalTrials.gov NCT03638830
RISK FACTORS FOR LONG-TERM CARRIAGE OF CARBAPENEM-RESISTANT GRAM-NEGATIVE BACTERIA IN SPECIAL CARE NEONATES AND CHILDREN

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Background: Carbapenem-resistance is a public health threat associated with increased mortality and prolonged hospitalization. Persistent carriage of such strains has therefore significant clinical and public health implications. There is a paucity of relevant data for pediatric patients at special care. We herein investigated risk factors for long-term colonization with carbapenem-resistant Gram-negative bacteria (CRGNB) in neonates and children.

Methods: We included patients (1d-16y), hospitalized in a tertiary level hospital during 2018-2019 and found to be colonized with CRGNB in routine surveillance cultures. Upon colonization detection, monthly rectal-swab cultures were collected for 12m. Decolonization was defined as 3 consecutive negative rectal-swab cultures, ≥1 week apart. Prolonged carriage was defined as duration of colonization >6m. Demographics, clinical characteristics, treatment administered and use of medical devices were recorded. Multivariate logistic regression analysis for prolonged carriage and sub-analysis for neonates were performed.

Results: 128 CRGNB carriers (median age 0.09y ,IQR: 0.55) were recorded, of which 78 (median age 15d, IQR: 19.75) were neonates (89.1% Enterobacteriales, 8.6% Pseudomonas spp, 2.3% Acinetobacter spp). 46 (35.9%) had prolonged carriage. In multivariate analysis, risk factors for prolonged carriage were: use of proton-pump inhibitors (PPIs) (OR: 7.45, 95%CI: 1.30-51.51), any antibiotic administration (OR: 31.40, 95%CI: 4.01-760.82), immunodeficiency (OR: 19.37, 95%CI: 3.07-212.24), and urinary catheter placement (OR: 10.58, 95%CI: 1.83-89.79). The multivariate analysis in neonates revealed that carbapenem administration (OR: 20.98, 95%CI: 2.48-219.55), and nasogastric tube placement (OR: 9.91, 95%CI: 1.06-96.96) were risk factors for prolonged carriage.

Conclusions: Broad-spectrum antibiotics and especially carbapenems, PPIs, immunodeficiency, urinary catheter, and nasogastric tube insertion, are differentially associated with persistent colonization among pediatric and neonatal CRGNB carriers. Efforts should be made to eliminate these factors in such patients in order to accelerate decolonization and limit the spread of CRGNB.

Clinical Trial Registration: Clinical trial registration:N/A
A LONGITUDINAL STUDY OF CARBAPENEM-RESISTANT GRAM-NEGATIVE BACTERIAL DECOLONIZATION AND CORRELATION WITH INFECTION IN PEDIATRIC AND NEONATAL PATIENTS

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Background: Antibiotic exposure may convert the intestinal tract to a reservoir of resistant bacteria. Colonizing strains may subsequently cause infections in susceptible hosts. 6-44.4% of colonized adults may develop infection involving the same isolate. The natural history of spontaneous decolonization of neonates and children colonized with carbapenem-resistant Gram-negative bacteria (CRGNB) and the risk of colonizing strain-related infection in this population is unknown.

Methods: Patients hospitalized in a tertiary care hospital, aged 1 day to 16 years, found to be colonized with CRGNB in routine surveillance cultures, were prospectively followed from January 2018 to December 2019 with monthly rectal-swab cultures until decolonization. Decolonization was defined as three consecutive negative rectal-swab cultures, at least 1 week apart. Patient demographics and development of infection of any system were recorded.

Results: 128 pediatric patients were included. 78 of them were neonates (median age 15d, IQR: 19.7). The median duration of colonization was 3 months (min 21d / max 736d). After recognition of colonization, patients showed a slow tendency to be decolonized. Colonization persisted >12 months in 5.5%. Specifically, neonates showed a faster decolonization trend. 1.3% remained colonized after 12 months. The rate of decolonization is illustrated in detail in Figure 1, for all patients (solid line) and for neonates (dashed line). 42 (32.8%) patients developed an infection due to CRGNB, mainly sepsis (26.2%) and urinary tract infections (26.2%).

Conclusion: Spontaneous decolonization occurs in almost all pediatric carriers of CRGNB within 12 months. A sizable percent of colonized patients may develop infections caused by CRGNB bacteria. Monitoring of carriers and contact precaution measures must be meticulously followed to restrict the spread of CRGNB.

Clinical Trial Registration: Clinical trial registration:N/A
E-POSTER VIEWING
E-POSTER DISCUSSION SESSION 03: VACCINES
10-28-2020 8:00 AM - 7:00 PM

RNA EXPRESSION RELIABLY DISTINGUISHES BACTERIAL INFECTION FROM TRANSIENT VACCINE REACTIONS IN YOUNG CHILDREN

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Background: Current diagnostics do not reliably differentiate serious bacterial infections from transient vaccine reactions in febrile young infants. We hypothesised that analysis of host RNA-expression could provide novel diagnostics for this specific common clinical setting.

Methods: RNA-sequencing was used to compare whole-blood RNA expression in healthy post-vaccination infants at 4-months of age with gene expression in young children under 5 years with definite bacterial infection from two distinct cohorts. Vaccinated infants received routine vaccinations according to the UK vaccination schedule, with half also receiving the 4CMenB vaccine. Batch correction was performed using the COCONUT R-package. Cases were split into training and test sets. To distinguish bacterial infection from vaccine reaction three minimal transcript signatures were selected using differential expression analysis and three separate machine learning tools on the training set. The performance of these signatures was evaluated on the test set.

Results: On the training set of 86 children (42 infections, 44 post-vaccination) we identified three signatures with 3-, 6- and 11-transcripts. In the test set (52 children) all three signatures performed similarly, with AUCs all above 0.99 (Figure 1). The best performing signature (11-transcripts) distinguished bacterial infection from vaccine reaction with 97% sensitivity and 93% specificity in the test set, outperforming both CRP and WCC in the whole cohort (CRP: sensitivity 83%, specificity 90%).

Conclusions: This preliminary work has identified novel transcript-sets that discriminate bacterial infection from vaccine reaction. Further testing is required to validate these findings. Our aim is to develop a quantitative PCR assay for clinical use, to help minimise admissions and antibiotic administrations in children suffering from a transient vaccine response.

Clinical Trial Registration: Not applicable
Background: Pertussis vaccination during pregnancy helps protect newborns from pertussis disease but can interfere with the infant immune response to primary pertussis vaccination. The current trial addressed whether this interference persists after pertussis booster vaccination.

Methods: This follow-up study enrolled 9-month-old infants who were born to mothers who had been randomized to receive reduced-antigen-content diphtheria-tetanus-3-component-acellular-pertussis vaccine (dTpa group) or placebo (control group) during pregnancy (27–36 weeks’ gestation, NCT02377349), and who had completed primary vaccination with DTPa-HBV-IPV/Hib (NCT02422264). Toddlers in both groups received a DTPa-HBV-IPV/Hib booster, co-administered with 13-valent pneumococcal conjugate vaccine (PCV13) at 11–18 months of age, according to local schedules. Immune responses to DTPa-HBV-IPV/Hib and PCV13 antigens and reactogenicity/safety were evaluated descriptively.

Results: 540 toddlers (dTpa group: 263; control group: 277) received a DTPa-HBV-IPV/Hib booster (mean age: 15 months). One month post-vaccination, booster response rates for pertussis antigens were ≥92.1% and seroprotection rates for all other DTPa-HBV-IPV/Hib antigens were ≥99.2% in both groups (Figure). Observed pre- and post-booster geometric mean antibody concentrations were lower in the dTpa group versus controls for anti-diphtheria, anti-pertussis-toxin, anti-filamentous-hemagglutinin (and anti-pertactin, pre-booster only), and similar in both groups for the other DTPa-HBV-IPV/Hib (Figure) and PCV13 antigens. Proportions of toddlers with post-booster serotype-specific pneumococcal antibody
concentrations ≥0.35 µg/mL were similar in both groups (≥98.1% except for serotype 3). Adverse event rates were comparable between groups. Serious adverse events were reported for three toddlers (all in the control group, none considered vaccination-related). One death occurred pre-booster (dTpa group, not considered vaccination-related).

**Conclusions:** Interference of maternally transferred pertussis antibodies with infant immune responses to pertussis primary vaccination is apparent (but reduced) post-booster vaccination in the second year of life; the clinical significance requires evaluation. **Funding:** GlaxoSmithKline Biologicals SA  
**Clinical Trial Registration:** ClinicalTrials.gov: NCT02853929
EFFECTIVENESS OF A SEROGRUP B MENINGOCOCCAL VACCINE (4CMENB) IN ENGLAND: A RE-ASSESSMENT APPLYING COMPUTATIONAL MODELLING TO REAL-WORLD EVIDENCE

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Background: In 2015, the serogroup B meningococcal (MenB) vaccine 4CMenB was introduced into the UK’s National Immunization Programme (NIP), with a reduced three-dose schedule for infants at 2, 4 and 12 months of age. Vaccine impact (VI) and effectiveness (VE) were recently reported for the first three years of the programme. Significant results were reported for VI (75% [95% confidence interval (CI): 64%; 81%]), estimated with a modelling approach, whereas VE, calculated using the screening method, was not statistically significant. Applying a modelling approach, we re-estimated the VE aiming at improving on limitations of the screening method.

Methods: We applied a previously validated Monte Carlo maximum likelihood (MCML) inferential method based on a computational model of MenB carriage transmission, disease and vaccination. The model accounted for age-and-time disease trends and vaccine uptake. It was parametrised using observed disease cases in the whole population and other real-world evidence, before and after 4CMenB introduction into the NIP in England.

Results: Applying MCML on the MenB model, we found that the VE was 33.9% (95%CI: 14.8%; 49.7%) after one dose, 79.1% (95%CI: 72.4%; 84.6%) after two doses (complete priming), and 79.9% (95%CI: 70.9%; 87.0%) after the booster (third dose). We estimated that 4CMenB introduction in the NIP has averted 328 cases of MenB disease (95%CI: 293; 364) in England between September 2015 and August 2018.

Conclusions: We confirm the effectiveness of 4CMenB in the UK NIP by showing results consistent with independent assessments of effectiveness and impact. When the traditional screening method – based on eligible cohorts only – does not reach statistical significance, VE estimation can be enhanced with validated computational models, which also account for available and relevant epidemiological evidence.

Funding: GlaxoSmithKline Biologicals SA

Clinical Trial Registration: Not applicable
PERTUSSIS VACCINATION DURING PREGNANCY IN WALLONIA (BELGIUM): FIRST ASSESSMENT, TWO YEARS AFTER FREE-OF-CHARGE DTPA VACCINE INTRODUCTION.

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Background: Superior Health Council of Belgium recommended for pertussis prevention a “Cocoon strategy” in 2009 and maternal vaccination between 24 and 32 weeks in 2013. Diphteria, tetanus, acellular pertussis vaccine was partially reimbursed for parents since 2009 and free of charge for pregnant women in Wallonia since June 2015. Pertussis vaccine coverage for mothers was assessed through Epi-Survey.

Methods: In 2015 and in 2019, two surveys based on WHO EPI Immunization Coverage Cluster Survey were performed. Children 18-24 months of age were randomly selected in around 50 municipalities of Wallonia. Trained investigators interviewed the parents at homes and assessed their pertussis vaccination by anamneses. Mothers of 2015 survey (group1), delivered in 2013 and of 2019 survey (group2), in 2017.

Results: In Group1 (n=562), pertussis coverage was 37,2% for mothers: 30,7% at post-partum time and 6,5% during pregnancy. In group2 (n=506), coverage was 53,9%: 11,6% for “cocoon strategy” and 42,6% during pregnancy. In group2, the only predictor factors for been vaccinated during pregnancy were Belgian nationality (46,6% vs 30,6% for non-Belgian) and primiparity (49,4% vs 37,2% for multiparity). During pregnancy, gynecologist vaccinated 41,7% of the mothers, GP, 37,2% and mid-wife 9,6%. All of them vaccinated equally at post-partum time.

Conclusions: Two years after the introduction of free-of-charge dTpa vaccine in Wallonia, strategy to protect newborns through vaccination during pregnancy was more effective. Coverage of pregnant women has increased and dramatically exceeded 2015 results of “cocoon” strategy. Additional strategies should focus of non-Belgian and multiparous women.
SAFETY AND IMMUNOGENICITY OF AN INVESTIGATIONAL TETANUS TOXOID CONJUGATED QUADRIVALENT MENINGOCOCCAL VACCINE (MENACYW-TT) IN HEALTHY MENINGOCOCCAL VACCINE NAÏVE ADOLESCENTS (10-17 YEARS OF AGE)

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Background: MenACYW-TT is an investigational quadrivalent meningococcal conjugate vaccine, intended for use in individuals 6 weeks of age and older. We evaluated the safety and immunogenicity of MenACYW-TT compared to licensed quadrivalent conjugate meningococcal vaccines [(Menveo®; MCV4-CRM) and Menactra®; MenACWY-D].

Methods: Herein we report the results pooled from two randomized studies from USA. In a pivotal Phase II study, 927 study participants randomly received single dose of either MenACYW-TT or MCV4-CRM vaccines. A Phase III study in individuals 10-55 years of age evaluated 1504 adolescents who randomly received either a single dose of one of the three lots of MenACYW-TT or single dose of MenACWY-D vaccines. Serum bactericidal assay with human complement (hSBA) and baby rabbit complement (rSBA) was used to measure antibodies against serogroups A, C, W and Y at baseline (Day 0) and 30 days post-vaccination (D30). Safety data were collected up to six months post-vaccination.

Results: At D30, majority of adolescents (≥ 95.2%) in the MenACYW-TT group had hSBA titers ≥ 1:8 (seroprotection). Higher vaccine seroprotection rates and seroresponse rates for all four serogroups were observed in adolescents who received MenACYW-TT compared to those who received MenACWY-D or MCV4-CRM. Meningococcal hSBA GMTs in the MenACYW-TT group were higher for all serogroups (62.0 A; 438 C; 93.5 W; 135 Y) than those in the MenACWY-D (44.2 A; 44.1 C; 59.2 W; 80.3 Y) and MCV4-CRM (35.2 A; 51.4 C; 36.0 W; 27.6 Y) groups at D30. The safety profiles of MenACYW-TT, MenACWY-D and MCV4-CRM were comparable.

Conclusions: MenACYW-TT vaccine was well tolerated and demonstrated a higher immune response compared to the licensed MenACWY-D and MCV4-CRM vaccines when administered as a single dose to meningococcal vaccine naïve adolescents.

Clinical Trial Registration: ClinicalTrials.gov NCT# 02199691 ClinicalTrials.gov NCT# 02842853
COMPREHENSIVE EVALUATION OF THE BROAD BURDEN OF SEROGROUP B INVASIVE MENINGOCOCCAL DISEASE CHANGES COST-EFFECTIVENESS ANALYSIS RESULTS OF 4CMENB INFANT VACCINATION

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Background: Serogroup B invasive meningococcal disease (MenB IMD) is uncommon but potentially severe with substantial impact beyond the acute phase and beyond the patients. Previously-published cost-effectiveness analyses (CEAs) of MenB vaccination didn’t, or only in part, consider this broad impact. The present CEA of serogroup B meningococcal vaccine (4CMenB) infant vaccination in England, retrospective before its introduction in 2015, aims to comprehensively consider the MenB IMD burden and assess the impact on the incremental cost-effectiveness ratio (ICER).

Methods: Aspects from costs and health outcomes perspective to be considered for evaluation of the broad MenB IMD burden were determined based on a review of previous MenB vaccination CEAs and grouped into five categories added to a conventional CEA framework: comprehensive sequelae impact on patients, humanistic burden beyond patients, economic burden beyond direct medical costs, societal preference to prevent severe IMD and, discounting methods to reflect the long-term nature of disease consequences. Stepwise assessment of these categories shows their impact on the ICER.

Results: Modelling results show that within 5 years of introducing a 4CMenB infant national immunization program (NIP), MenB IMD incidence decreased by 46.1% in 0-4-year-olds. Adding the five burden categories stepwise (Figure 1) reduced the ICER of 4CMenB infant vaccination from £359,969 to £18,592/quality-adjusted life year (QALY), thus being cost-effective at the UK £20,000/QALY threshold, when comprehensively considering the broad disease burden.

Figure 1: Stepwise impact on the cost-effectiveness of 4CMenB infant vaccination of including 5 disease burden categories

Conclusions: This stepwise approach provides policy-makers with important insights regarding the potential impact of broader consideration of disease burden on the cost-effectiveness of 4CMenB vaccination, thus highlighting the need for comprehensive assessment of MenB IMD. Considering the latest evidence and the broad MenB IMD burden, 4CMenB infant NIP can be cost-effective, contrary to most of the previous CEAs reporting high ICERs.

Clinical Trial Registration: Non applicable
Background: Varicella continues to be a public health concern with high infection rates, related complications and associated economic burden. Introducing universal varicella vaccination (UVV) based on monovalent vaccines (quadrivalents are currently not marketed in the UK), could help reduce this burden. A two-dose strategy was assessed in the United Kingdom (UK) which has an existing herpes zoster (HZ) vaccination programme for adults [since 2013].

Methods: Previously published dynamic and cost-utility models were adapted for the UK to estimate varicella / HZ incidence and cost-effectiveness of UVV versus no vaccination, assuming a 12- and 13-month schedule with a respective coverage of 90.8% and 87.2%. Vaccine efficacy after the first and the second doses was 67% and 95%, respectively.

Results: Adding UVV to the HZ vaccination programme reduced varicella incidence by 91% and HZ incidence by 96% at equilibrium (100 years post UVV start). Although a shift in the average age at infection was predicted, varicella incidence across all age groups was drastically reduced at equilibrium compared to the period before UVV introduction. There was no increase in HZ incidence following UVV implementation. At equilibrium, the distribution of the average age at HZ infection before and after UVV were broadly similar. The base-case incremental cost-utility ratio was £4,837 per quality-adjusted life year (QALY) gained from the payer perspective.

Conclusions: A two-dose monovalent UVV reduced considerably the incidence of varicella. There was no increase in HZ incidence to levels higher than the pre-vaccination era after UVV implementation. A UVV programme is likely a cost-effective alternative to no vaccination for reducing the burden of varicella in the UK.

Clinical Trial Registration: GlaxoSmithKline Biologicals SA funded this study (HO-15-15990) and supported all costs of the related publications.
SAFETY AND IMMUNOGENICITY OF ESCALATING DOSE FORMULATIONS OF HIGH-DOSE QUADRIVALENT INFLUENZA VACCINE IN CHILDREN AGED 6 MONTHS THROUGH

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**Background:** Children do not respond immunologically as well as adults to standard-dose (SD) influenza vaccination and remain at increased risk of influenza and its complications. One approach to improve efficacy in children may be to increase antigen concentration per dose, a strategy successfully used in adults ≥65 years old with a high-dose influenza vaccine (IIV4-HD).

**Methods:** Safety and immunogenicity of IIV4-HD in US and Canadian children were evaluated in a Phase 2, modified double-blind study (NCT03698279). Children (n=661, 6 months—<18 years) were randomly assigned to receive 1 of 3 formulations of IIV4-HD intramuscularly (30, 45, or 60 µg HA/strain/dose), a licensed quadrivalent SD influenza vaccine (IIV4-SD), or a licensed adjuvanted trivalent influenza vaccine (aIIV3). Depending on the child’s previous influenza vaccination status and age, they received 1 or 2 doses of study vaccine 28 days apart. Reactogenicity data were collected through 1-week post-vaccination; safety data were collected through 6 months. Geometric mean titers (GMTs) against the 4 vaccine strains were measured using hemagglutination inhibition (HAI) and seroneutralization assays 28 days after each vaccination.

**Results:** IIV4-HD was more reactogenic compared to IIV4-SD, but unsolicited related AEs were similar. No related severe AEs occurred. Compared with IIV4-SD, the 60 µg HA/strain/dose formulation of IIV4-HD generated the highest HAI GMT ratios, high seroconversion rates, and high seroneutralization GMT fold rises for all 4 strains in US children, particularly in those 6 months through <3 years of age. Canadian children receiving IIV4-HD generated incongruent HAI titers compared to US children receiving IIV4-HD, limiting direct comparison against aIIV3.
Conclusions: The favorable safety profile and immunogenicity results of IIV4-HD support pediatric dose selection of 60µg HA/strain/dose as most appropriate to evaluate in Phase 3.

Clinical Trial Registration: Clinical trial registration: ClinicalTrials.gov NCT03698279, EudraCT Number: 2018-005026-39
ROTAVIRUS ACUTE GASTROENTERITIS (RVAG) MORBILITY AND CHANGES IN SEASONALITY IN THE CONTEXT OF LOW VACCINE COVERAGE

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Background: In Portugal, RV remains an important cause of AG. Two RV vaccines have been used on the private market since 2006, with estimated coverage ~45% between 2010-2018. A high effectiveness to prevent admissions and observation in the emergency service (ES) was shown in a case-control study. Our aim is to describe the annual epidemics and characterize RVAG admissions over the last 8Y.

Methods: 4200 children aged ≤36M observed in the ES from Jan/2012 to Jun/2019 with AG (defined as ≥3 watery or looser than normal stools within a 24-hour period with or without vomiting) and a stool sample tested for RV using a rapid test based on immunochromatography, were analysed. A more detailed analysis was done for children who were hospitalised.

Results: Following several years with slight variations in size of the annual epidemic, there was an increase in 2016, followed by an important decrease in 2017 (fig.1). We observed varying seasonality, with the peak in first semester but an unexpected large number of cases occurred between Oct/2016–Jan/2017. Admissions decreased in after 2017. Median age was 1.3Y; the main reasons for admission were dehydration (severe in 7%, 3% with acute kidney injury) and vomiting; 85% needed IV/NGT hydration and one intraosseous access. 4% were vaccinated of whom all had mild infection.

Conclusions: Despite the high effectiveness of the vaccines, there isn’t an overall downward trend in observations in the ES probably due to low vaccine use. However, there was a reduction of admissions in the last two years. Some children had a very severe infection. The unusual seasonality in 2016-17 could be explained by the accumulation of a pool of non-vaccinated susceptible children or introduction of a novel RV strain into this community.
ROUTINE CHILDHOOD VACCINATION COVERAGE RATES AMONG LOW BIRTH WEIGHT AND
PRETERM INFANTS IN ISRAEL

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**Background:** Vaccinating premature and low birth weight (LBW) infants according to chronological age has been found safe and effective. Although these infants are more susceptible to infections, routine vaccinations are often delayed. The Israel National Immunization Registry (INR) has created an opportunity to study immunization coverage in a large national cohort, instead of surveys, health care provider reports or random sampling.

**Methods:** A retrospective national cohort study. INR data were linked to the “birth file” of all Israeli newborns in 2016 (n=181,543 children). The main variables were birth weight and gestational age (GA). The vaccine doses and dates were retrieved. Vaccinations included: Hepatitis B, Diphtheria – Tetanus - Acellular Pertussis, IPV, Haemophilus influenzae b, Polio Oral Bivalent, Rotavirus, Pneumococcal Conjugate, Measles-Mumps-Rubella, Varicella and Hepatitis A.

**Results:** Preterm infants, born before 37 weeks comprised 7.0% (n = 12,264); LBW infants, below 2500 grams were 7.7% (n=13,950). LBW distribution: 6.8% were born at 1500-2500 grams, 0.6% 1000-1500 grams and 0.3% below 1000 grams. Compared to normal birthweight infants (2500 grams and above) NBW, the LBW infants showed delayed initiation of routine vaccination. Odds ratio (OR) for delayed DTaP1 was 1.51, 95%CI 1.41-1.62 and for delayed Rota1 the OR was 1.46, 95%CI 1.32-1.61. At the age of 2 years there was no significant difference between the groups’ vaccination coverage.

**Conclusions:** This is the first analysis of vaccination converge (VC) among preterm/LBW infants in Israel. Significant delay was found in vaccination initiation among LBW infants. By 24 months LBW infants VC showed catch-up to NBW infants. Vaccinating preterm and LBW infants according to the official recommendations provides protection from life-threatening infectious diseases. Our data provide basis to develop a public health targeted intervention plan within this risk group.
E-POSTER VIEWING
E-POSTER DISCUSSION SESSION 04: VACCINES 2
10-28-2020 8:00 AM - 7:00 PM

THE RISK OF AUTOIMMUNE, NEUROLOGICAL AND OTHER CONDITIONS FOLLOWING THE IMMUNIZATION OF ADOLESCENT GIRLS WITH BIVALENT HUMAN PAPILLOMA VIRUS VACCINE IN FINLAND: A NATIONWIDE REGISTER-BASED COHORT STUDY

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Background: A bivalent human papillomavirus vaccine (2vHPV) was introduced into the Finnish national vaccination programme in November 2013 for girls aged 11-13 years, with a catch-up for girls 14-15 years. In 2018, we assessed the possible 2vHPV associated adverse events (AEFIs) for the first time. We now re-assessed the risks for possible AEFIs with additional two years of data and analyses.

Methods: We performed a nationwide register-based cohort study with an individual-level linkage between five Finnish registers. We included girls aged 11–18 years between Nov-2013 and Dec-2018 with first life-time occurrences of ICD-10 codes for autoimmune, neurological diseases and other conditions. Risks of 59 individual outcomes and 19 pooled groups of outcomes following the first 2vHPV dose were studied using the Cox regression [hazard ratios (HR); 95\%CIs]. Results were adjusted for comorbidities, geographic area, previous health care visits and other immunizations.

Results: Of the 294,771 girls in the cohort, 169,861 (57.6\%) received at least one 2vHPV dose. For 58 of 59 individual outcomes and for 17 of 19 outcomes groups, no increased risk among the vaccinated was observed. An increased risk was observed for myositis (aHR 4.70; 1.22–18.11), however, only 5 cases were diagnosed within 12 months after the first dose; and for the gastrointestinal group (aHR 1.16; 1.01–1.35); and a subgroup of this group, the inflammatory bowel disease (IBD) (aHR 1.24; 1.00–1.54).

Conclusions: Of the nearly 80 outcomes/outcome groups evaluated, we observed an association of the 2vHPV vaccination with myositis, gastrointestinal and IBD outcome group, but these findings were relatively weak, especially for the latter two. Our results provide reassurance that 2vHPV is unlikely to be associated with an elevated risk of significant AEFIs.
Background: Tick borne Encephalitis (TBE) is one of the most common cause of viral meningoencephalitis in many endemic regions. Recently case reports in Europe, claimed that in TBE-vaccine failures suffer from more severe disease courses than non-vaccinated cases. As these studies are subject to referral and selection biases, here we analyze hospitalized TBE vaccine failures on a population level-basis, were all serologically confirmed TBE infections were included, also those without CNS manifestations.

Methods: TBE cases of any age were identified as reported to the Centre of Disease Prevention and Control of Latvia from year 2007 through to 2018 and combined with additional data derived from the patient’s medical records in Latvian hospitals. These cases were categorized by TBE vaccination history (i.e. vaccinated vs non-vaccinated) and compared with Fisher’s exact test and Wilcoxon rank test.

Results: A total of 3,106 TBEV-infections were identified in Latvia during the 12 study years. A total of 58 cases (1.8%) had received at least one prior TBE vaccine dose. Analyzing TBE cases according to European Centre for Disease Prevention and Control (ECDC) case definition (non-CNS forms excluded) a total of 7/35 (20%) TBE-vaccinated and 214/2245 (9.5%) of non-TBE-vaccinated cases were suffering from severe TBE. However, when all TBEV-infections were included, mild cases (non-CNS TBE) were relatively more frequent among TBE vaccinated cases (23/58; 39%) than non-TBE-vaccinated cases (782/3027; 25%).

Conclusions: The population-based analysis and data presented here indicate that the percentage of “severe cases” depends on the denominator used and that TBE vaccination is highly effective. Future studies will need to consider “true infection rates” as well as vaccine uptake per age groups, diagnostic efforts applied to distinguish clinical forms and vaccine failure type, when coming to any conclusions on disease severity.
IMMUNOGENICITY AND SAFETY OF AN ADJUVANTED INACTIVATED POLIO VACCINE, IPV-AL, IN PRIMARY AND BOOSTER TRIALS IN ASIA, CENTRAL AMERICA AND EUROPE

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Background: Withdrawal of OPV and widespread introduction of IPV is key for the Polio Endgame. Transition from OPV to IPV requires more, and affordable IPV to secure IPV for every child. An aluminium hydroxide adjuvanted inactivated polio vaccine (IPV-Al), with a reduced dose of inactivated poliovirus, can help mitigate global supply and cost constraints of IPV through dose-sparing. Objective: Investigation of immunogenicity and safety of IPV-Al compared to standard IPV.

Methods: Two Phase 3 trials in infants vaccinated at 6,10,14 weeks and 9 months in the Philippines; at 2,4,6 months and 15-18 months in Panama. A Phase 2 trial in Dominican Republic at 6,10,14 weeks. A Phase 1/2 booster trial in Denmark in children and adolescents (10-15 years). Concomitant vaccines were administered according to local recommendations.

Results: Seroconversion rates (an antibody titre ≥4-fold higher than the estimated maternal antibody titre and a titre ≥8) one month after primary vaccination were: polio type 1, 96-98% (IPV-Al) versus 99-100% (IPV); type 2, 94-100% versus 99-100%; and type 3, 98-99% versus 99-100%. Non-inferiority of IPV-Al to IPV (predefined 10%-point margin) was confirmed in trials assessing primary immunogenicity. In infants, robust booster responses were demonstrated following a fourth polio vaccination and post-booster geometric mean titres (GMTs) were higher than post-priming GMTs. In the adolescent trial, robust booster responses were demonstrated following a fifth polio vaccination. All vaccines administered were well tolerated with a safety profile for IPV-Al comparable to that of standard IPV in the three trials.

Conclusions: Results support the applicability of the dose sparing adjuvanted IPV-Al vaccine to help secure a more affordable and stable supply of IPV as part of the Polio Endgame. IPV-Al is safe and well tolerated in concomitant use with other vaccines.

Clinical Trial Registration: NCT03025750, NCT03671616, NCT03032419, NCT02280447.
FREQUENCY OF SAFETY EVENTS OCCURRING ON THE DAY OF VACCINATION WITH 4-VALENT HUMAN PAPILLOMAVIRUS AMONG MALES IN THE UNITED STATES

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Background: The 4-valent human papillomavirus (HPV) vaccine (4vHPV vaccine), Gardasil\textsuperscript{®}, is indicated for the prevention of several HPV-related diseases. In the US, it was licensed for use in females in 2006 and males in Oct-2009. The 4vHPV vaccine is licensed in many parts of the world. The objective was to assess the frequency of pre-specified safety events that occur on the day of 4vHPV vaccination among males.

Methods: Within a US health insurance database, males receiving 4vHPV vaccine were identified. Syncope, epilepsy/convulsions, head trauma, and allergic new events associated with outpatient visit, emergency department visit or hospitalization occurring on the day of vaccination were identified using diagnostic codes. These events were specified based on consideration of temporal and biological plausibility. Event rates (per 10,000 doses) were calculated and compared with those in males receiving a vaccine other than 4vHPV vaccine (Td/Tdap, HepA, meningococcal, or influenza) matched on age and calendar time of vaccination. Separate analyses were conducted for all doses combined, Dose 1 only, and for those receiving concomitant vaccinations.

Results: Between Oct-2009 and Dec-2016, 202,737 4vHPV doses were administered to 114,035 males; 160,867 were matched to comparators. Thirty-one percent of 4vHPV vaccine was received a concomitant vaccine. In the all dose analyses of 4vHPV vaccinations vs. comparators, there were higher rates of allergic events (21.07, 95% CI 18.89-23.44 vs. 11.44, 95% CI 9.84-13.22), lower rates of epilepsy/convulsions (5.66, 95% CI 4.55-6.95 vs. 7.58, 95% CI 6.30-9.06) and similar rates of syncope and head trauma. Similar patterns were observed among Dose 1 only and by number of concomitant vaccinations.

Conclusions: Higher rates of allergic events observed in this study are consistent with the safety profile of 4vHPV vaccination established from previous studies/surveillance programs.

Clinical Trial Registration: This is an observational research study and not a clinical trial.
PASTEURIZATION OF HUMAN MILK INCREASES THE INCIDENCE OF NECROTIZING ENTEROCOLITIS IN PRETERM INFANTS

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Background: Necrotizing enterocolitis - NEC - is a major event which affects newborns and is frequently related to prematurity with negative outcomes. Pasteurized human milk - PHM - in comparison to artificial formula is already known to reduce incidence of NEC. Although, the same benefit for unpasteurized mother’s own milk - uMOM - is yet to be proven.

Methods: A retrospective observational study evaluated impacts of feeding restriction of uMOM to infants born from 27 to 32 weeks GA in three periods (P) with 2 different pasteurization practices. In PI from 2013 to 2015 and PIII from 2017 to 2018, babies born bellow 27 weeks to mothers with positive CMV IgG did not receive uMOM and were fed with PHM or formula. In PII from 2015 to 2017, the same rule was applied to babies born ≤ 32 weeks. NEC rates in babies born under 27 weeks GA served as control.

Results: During the study, 2576 NBs with GA from 27 to 32 weeks were admitted in our NICUs. There were 15 NEC episodes in PI, 41 in PII and 16 in PIII, with significant difference in overall NEC incidence rate between PI versus PII, PIII versus PII and PI+PIII versus PII. In control group, there was no significant difference in overall NEC incidence between the periods mentioned before (graph).
Conclusions: Pasteurization of human milk is known to reduce the concentrations of important biologically active components. Some of these factors are believed to prevent NEC. In the presented study, a statistically significant increase in the rates of NEC was observed when we restricted the feeding of uMOM to a vulnerable population of infants with GA ranging from 27 to 32 weeks.
E-POSTER VIEWING
E-POSTER DISCUSSION SESSION 05: NEONATAL INFECTIONS
10-28-2020 8:00 AM - 7:00 PM

SUSCEPTIBILITY OF COAGULASE-NEGATIVE STAPHYLOCOCCI (CONS) BLOODSTREAM INFECTIONS TO TEICOPLANIN IN NEONATAL INTENSIVE CARE UNIT (NICU)

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Background: As Coagulase-negative staphylococci (CoNS) remain the major pathogens of late onset sepsis (LOS), glycopeptides, including teicoplanin, are among the most commonly prescribed antimicrobials in NICU. There are reports that Coagulase-negative staphylococci (CoNS) population is shifting toward decreased susceptibility to glycopeptides. We assessed the susceptibility pattern of Coagulase-negative staphylococci (CoNS), isolated from blood of hospitalized neonates, to teicoplanin and evaluated its correlation with teicoplanin consumption.

Methods: This was a retrospective analysis of CoNS isolates from BSIs in a 44-bed polyvalent NICU within a 9-year period. Blood cultures were processed using the automated system BacT/ALERT; identification and antimicrobial susceptibility testing were performed by Vitek2. Teicoplanin consumption during 2010-2018 was expressed as defined daily doses per 100 bed-days (DDD/100BD) and was correlated with teicoplanin Minimum Inhibitory Concentration (MIC) during 2011-2019.

Results: 368 positive blood cultures were identified: Staphylococcus epidermidis (71%), Staphylococcus haemolyticus (16%) and Staphylococcus hominis (9%). Geometric mean of teicoplanin MIC ranged from 1.8 to 4.2mg/l, with no significant differences throughout the study. In 18% of CoNS MIC was >= 0.5 mg/l, in 5% MIC=1, in 23% MIC=2, whereas in 54% MIC >2mg/l (in 4% MIC <= 16mg/l). A strong correlation was found between teicoplanin consumption and percentage of CoNS with MIC >2mg/l in the following year (r=0.74, p=0.02). No teicoplanin MIC creeping of CoNS through the years was found.
Conclusions: A considerable percentage of Coagulase-negative staphylococci (CoNS) exhibited increased teicoplanin MIC and CoNS isolates with MIC>2mg/l were significantly correlated with its use. As increased teicoplanin MIC may impose some of the neonates to suboptimal therapeutic exposures, further aggravating emergence of resistance and risk of therapeutic failure, monitoring of local status of teicoplanin MIC and antimicrobial stewardship are needed.
HEARING LOSS IN CMVC SCORE (EAGLE SCORE). A MULTICENTRIC COHORT STUDY ABOUT HEARING LOSS IN CONGENITAL CYTOMEGALOVIRUS INFECTION.


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Background: Congenital CMV (cCMV) is the leading cause of non-genetic hearing loss (HL) in children. Individual risk of developing HL is difficult to establish. We aimed to evaluate risk factors associated with the development of HL in the Spanish cohort of cCMV (REDICCMV) and to build a HL prognostic score.

Methods: A multicentre retrospective study of cases included in a prospective national cohort was performed. The main outcome was HL in any ear at 24 months. We perform a Penalized Regression Model to select the best predictor variables for HL among 40 variables at birth (clinical, blood, image). Children with CMVc diagnosed at in-utero or at birth were included. For continuous variables, optimal cut-offs were selected according to ROC curve. Weights of each variable were calculated with multivariate logistic regression. The score result was calculated with the sum of OR coefficients.

Results: Overall 173 out of 501 patients fulfilled inclusion criteria and were evaluated. Variables included in the EAGLE score were: HL at birth (OR 14.2), ventriculomegaly in MRI (OR=6.2), focal/multifocal white matter abnormalities in cUS (OR= 2.9), lenticulostrate vasculopathy (cUS) (OR=1.6), microcephaly (Z-
score < -2) (OR = 3), weight Z-score < -0.71 (OR = 3.4) and splenomegaly (OR = 3). We obtained two possible cut-off points: > 5.5 points (90 % sensitivity [CI95%: 77.4-97.3], 70% specificity [61.6-77.9]) or > 7.5 points (86% sensitivity [CI95%: 71.5-94.6], 82% specificity [CI95%: 72.3-86.6]). The area under the ROC curve was 0.90 [CI95%: 0.85-0.95].

**Conclusions:** EAGLE score was able to predict HL at 24 months with high sensitivity and specificity. External validation in other cohorts should be addressed.
NEONATAL HERPES SIMPLEX VIRUS: AN UPDATE ON NATIONAL SURVEILLANCE AND A SURVEY OF CURRENT UK PRACTICE

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Background: Neonatal herpes simplex virus (HSV) infection is a rare but dangerous condition. A recent study indicates that the UK incidence is rising. There is currently no national guidance on the initiation of treatment for suspected infection and practice varies between clinicians. Rising incidence may support the wider use of empirical treatment. More information about the burden of neonatal HSV disease, its clinical features, and current management is required.

Methods: (i) Prospective surveillance of neonatal HSV commenced in July 2019 through the British Paediatric Surveillance Unit (BPSU). Paediatricians reporting cases are requested to complete a detailed questionnaire. Case notifications and completed questionnaires from the first 6 months are reported here. (ii) A survey of practice was sent to doctors on BPSU and BPAIIG distribution lists, asking questions regarding empirical HSV treatment of babies presenting with non-specific signs of infection.

Results: (i) 79 case notifications were received. 30 clinicians returned completed questionnaires on 21 cases. 94\% presented at <4 weeks of age, 45\% had disseminated disease, and 40\% died. 80\% had no fever at presentation.
(ii) 87 clinicians responded. Local guidelines were reported to mention HSV as a cause of neonatal infection in 75\%, and recommended empirical treatment in all babies <3 months with suspected infection in 6\%. Deranged clotting and liver function would prompt initiation of aciclovir in 52\% and 77\% of respondents respectively.

Conclusions: More case notifications were received in the first 6 months than predicted. Mortality remains high and presenting features are non-specific. Absence of fever in 80\% of cases demonstrates that HSV should not only be considered in febrile infants. Variation in current UK management may be a result of regional differences in the availability of diagnostic tests or the burden of disease.
THE EFFECT OF SINGLE-ROOM VERSUS OPEN-BAY CARE ON THE INCIDENCE OF BACTERIAL NOSOCOMIAL INFECTIONS IN PRETERM NEONATES: A RETROSPECTIVE COHORT STUDY

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Background: Nosocomial infections (NIs) continue to be a major source of iatrogenic harm in neonatal intensive care units (NICUs). The influence of a hospital’s infrastructure on NIs has thus far not been well-documented. The aim of the present study was to examine the effect of open-bay units (OBU) versus single-room units (SRU) on the incidence of NIs including central-line associated bloodstream infections (CLABSI) in preterm neonates.

Methods: All preterm neonates (<32 weeks gestational age) admitted to our NICU were included. Two study-periods were compared: one prior (May 2015 – May 2017) and one following (May 2017 – May 2019) transition from OBU to SRU. Incidence density (number of infections per 1,000 patient-days) and cumulative incidence (number of infections per 100 neonates) for NI were calculated. CLABSIs were calculated per 1,000 central-line days.

Results: 170 of 707 infants acquired ≥1 NIs. A non-significant reduction in incidence density (14.26 vs. 13.08, p=0.59) and cumulative incidence rate of NI (25.81 vs. 22.12, p=0.29) was noted after unit transition. CLABSIs showed a similar non-significant reduction after the move (15.22 vs. 10.59, p=0.35). Kaplan-Meier estimates for time to infection revealed no statistically significant difference between OBU and SRU (Figure 1). Multivariable cox hazards regression analysis revealed longer duration of invasive mechanical ventilation to be a significant risk factor for NI (HR: 1.03 per day on ventilation, p=0.023). Figure 1.
Conclusions: Single-rooms are not associated with a significant reduction in the acquisition of nosocomial infections in the NICU. This study nevertheless adds observational evidence that could support the recommendation to build single-rooms as part of a larger multimodal infection control strategy. A restricted analysis of the contribution of single-room design alone and its implications for enhanced infection control warrants further investigation.
POSSIBLE SOURCE OF THE PERINATAL LISTERIOSIS

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Background: Pregnant women and infants are in the high risk groups, which could be affected by foodborne invasive listeriosis, caused by Lysteria monocytogenes. The cases of listeriosis are infrequent in Russia, but severity of disease for fetus or newborn baby determines the need for surveillance of this infection. Investigation of pathogens diversity in perinatal listeriosis and searching the sources of the infection was the goal of our project.

Methods: Microbiological methods, MultiLocus Sequence Typing, whole genome sequencing (WGS) and data analysis using the Bacterial Isolate Genome Sequence Database for L. monocytogenes (BIGSdb-Lm) was performed.

Results: Monitoring of listeriosis in Moscow hospitals revealed 8 cases during the nine months from November 2018 to August 2019. There were 3 women with listeriosis, caused by L. monocytogenes ST7, but with different outcomes: recovery and birth of a healthy baby; abortion; premature birth of child with septicemia and pneumonia due to L. monocytogenes ST7. The four more neonates had septicemia: one infant due to L. monocytogenes ST7 and three – due to ST6. WGS of the isolates from the couple of mother and child demonstrated that they belonged to cgMLST1748 and had the closest profile cg-14120 in BIGSdb-Lm. Comparison of clinical and foodborne isolates revealed that L. monocytogenes ST7 from the chilled meat had the same cg-14120 profile that could suggest the acquisition of infection from food. L. monocytogenes ST6 were absent in the foodstuff of the Russian manufacturers.

Conclusions: Autochthonous L. monocytogenes ST7 and imported L. monocytogenes ST6 caused perinatal listeriosis in the control period. The chilled meat could be the source of ST7 infection, but we could not exclude the possibility of environmental L. monocytogenes acquisition.

Clinical Trial Registration: Clinical trial registration:N/A
DEL-1 IS REQUIRED TO MAINTAIN GRANULOCYTOSIS AND CONFER SURVIVAL FROM SEPSIS IN NEONATAL AGE

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Background: Newborns have well described deficits in innate and adaptive immunity that place them at risk for serious infections. Del-1 is a protein that promotes bone marrow granulopoiesis and inhibits leukocytes' ability to adhere to blood vessels. The expression of Del-1 in the neonatal period and its contribution in the development of neonatal sepsis has not been evaluated.

Methods: C57BL/6 WT and Del-1⁻/⁻ mice of neonatal or adult age were used. Sepsis was induced using the cecal slurry polymicrobial peritonitis mouse model. A group of C57BL/6 newborn septic mice were treated with recombinant Del-1 protein fused with human IgG Fc (Del-1-Fc) or recombinant IL10 - Receptor blocking antibody.

Results: Neonate mouse pups exhibited significantly higher Del-1 expression in all vital organs than adult mice and failed to downregulate Del-1 levels in tissues during sepsis. Del-1 levels in septic neonates were associated with reduced IL-17A and elevated IL-10 expression compared to adults. However, septic Del-1⁻/⁻ neonate mice exhibited worse survival rates than WT mice. Del-1⁻/⁻ mice failed to maintain granulocytosis and control bacterial load in blood 12 hours after sepsis and exhibited lower bone marrow neutrophil numbers. Systemic administration of Del-1Fc in Del-1⁻/⁻ mice resulted in enhanced survival from sepsis. Administration of IL-10R blocking antibody downregulated Del-1 levels in the bone marrow in WT mice and mice abrogated blood granulocytosis, bacterial burden and sepsis survival in WT mice.

Conclusions: Newborns, due to reduced numbers of innate immune cells and limited reserves in bone marrow, fail to achieve sustained output of circulating neutrophils in sepsis. Del-1 was found to be important for sepsis survival in neonates since it maintained neutrophil pool in bone marrow and promoted peripheral blood granulocytosis in neonatal sepsis.

Clinical Trial Registration: Not applicable
Background: Neonatal macrophages are considered to have an anti-inflammatory phenotype that renders them less responsive against inflammatory stimuli. However, the molecules that mediate and promote this anti-inflammatory phenotype in neonatal macrophages remain elusive. Del-1 is an anti-inflammatory homeostatic protein, that promotes resolution of inflammation. In this study we aimed to evaluate Del-1 expression and regulation in neonatal macrophages upon both basal and inflammatory conditions.

Methods: Primary thioglycolate elicited macrophages from C57BL/6 WT mice of neonatal (4-8 days old) and adult age (8-10 weeks old) were isolated and placed in culture. Macrophages were stimulated with LPS and treated with recombinant IL-17A and/or IL-10.

Results: Del-1 mRNA levels were significantly higher in murine neonatal macrophages compared to adult ones under normal conditions. During inflammatory stimuli, such as LPS or IL-17A, Del-1 was suppressed in adult macrophages but not in neonatal ones. IL-10 resulted in upregulation of Del-1 levels in unstimulated neonatal macrophages and IL-10 administration abrogated Del-1 suppression upon IL-17A but not upon LPS stimulation. IL-10 upregulated p-STAT3 protein levels and CEBP mRNA transcription in neonatal macrophages and in silico analysis revealed that CEBP beta and p-STAT3 have binding sites on Del1 promoter and are capable to promote Del-1 transcription.

Conclusions: Del-1 is elevated in neonatal macrophages and is upregulated by the anti-inflammatory cytokine IL-10. Since Del-1 is a secreted protein that promotes resolution of inflammation, it may be an essential mediator to inhibit excessive inflammation and maintain homeostasis upon severe inflammatory stimuli in the susceptible neonatal hosts.

Clinical Trial Registration: Not applicable
EVALUATING THE COST-EFFECTIVENESS OF INCLUDING ROTAVIRUS VACCINATION IN THE FRENCH NATIONAL IMMUNIZATION PROGRAM

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Background: Rotavirus gastroenteritis (RVGE) is one of the leading causes of infant hospitalization and infant death. We developed an age-structured deterministic dynamic transmission model specifically adapted to the French context to assess the public health and economic impact of a universal rotavirus vaccination strategy compared to no vaccination.

Methods: The modeled French population is divided into 40 age groups; each age group is further stratified into 43 mutually exclusive compartments defined by the disease stages, up to four histories of infection, and vaccination status. The model also allows breakthrough rotavirus infection after vaccination to occur. Model parameter values were obtained from published modeling and epidemiological literature for rotavirus transmission dynamics, consultation with local experts, and calibration efforts to fit recent French rotavirus incidence reports. Extensive modeling scenario analyses were performed to evaluate the impact of uncertainty around parameters (including analysis perspective, price of the vaccine, discount rates, time horizon of analysis, and vaccine coverage rates) on the evaluation of cost-effectiveness of universal rotavirus vaccination strategy (versus no vaccination program).

Results: In the base case, over the five years after vaccination implementation, a total of 798,093 (89.7% reduction) RVGE cases of children less than five years is expected to be averted. The vaccination program evaluated at the price of €37.08/dose is estimated to be potentially cost-effective from the societal perspective, with an ICER value of €39,721/QALY for a willingness-to-pay threshold of €90,000/QALY. The cost-effectiveness (with ICER values ranging from €8,269 to €45,924) of the universal rotavirus vaccination is consistent across an additional 25 plausible scenarios examined.

Conclusions: Our study suggests that a universal rotavirus vaccination program in France is highly effective and could be considered as cost-effective.

Clinical Trial Registration: This study does not report any results of a controlled trial.
Background: Since 2015, an increase in invasive meningococcal serogroup W disease (IMD-W) was observed in the Netherlands, reaching an incidence of 0.6 per 100,000 and case fatality rate of 23% in 2018. In response, a MenACWY vaccination campaign in 14-18 year olds was executed from October 2018 to June 2019, achieving an uptake of 84%. In addition, MenC vaccination at 14 months was replaced by MenACWY. We describe the IMD-W incidence in 2019 and assess the first effects of the vaccination campaign.

Methods: The Dutch IMD surveillance includes epidemiological and clinical data from mandatory notifications and microbiological data through laboratory surveillance by the Netherlands Reference Laboratory for Bacterial Meningitis. We evaluated IMD-W cases in vaccine-eligible birth cohorts before and after implementation of the campaign.

Results: In 2019, 62 IMD-W cases (0.4/100,000 population) and 9 deaths were reported which was lower than in 2018 (103 cases, 23 deaths, IRR=0.60;95%CI:0.44-0.82). This decrease was due to decreases in vaccinated and unvaccinated age groups. In the vaccine-eligible adolescent birth cohorts (2001-2005), no cases of IMD-W have occurred since June 2019, compared with 9 cases in the same period in 2018 (IRR=0.05;0.01-0.90). In children eligible for 14-month vaccination, two IMD-W cases have occurred since the switch to MenACWY, compared with six cases in a similar period before the switch (IRR=0.34;0.07-1.66).

Conclusions: After four years of increasing incidence of IMD-W, a reduction in cases and deaths was observed in the Netherlands in 2019. The MenACWY vaccination campaign is likely to have impacted the number of cases in the vaccinated birth cohorts, although absolute numbers are low. It is uncertain whether the decrease in unvaccinated age groups is due to herd effects or other effects.
INVASIVE INFECTIONS CAUSED BY GROUP A STREPTOCOCCI IN SWITZERLAND

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Background: Besides mostly mild infections like pharyngitis/tonsillitis or impetigo, group A beta-haemolytic streptococci are also causing severe invasive infections (iGAS). To date, no exact figures are known on the incidence, epidemiology, clinical course, possible risk factors and characteristics of invasive group A streptococci (iGAS) in children in Switzerland. In this study, the incidence and clinical manifestation of iGAS in Switzerland will be assessed.

Methods: Inpatients < 17-year-old with iGAS defined as isolation of GAS from a sterile body site or isolation of GAS from a non-sterile body site plus severe clinical presentation (e.g. toxic shock syndrome) were reported to a national registry, the Swiss Pediatric Surveillance Unit (SPSU). During 2018 a total of 48 cases having a median age of 5 years (range 26 days to 15.3 years) whereof 17/48 (35%) were female were registered. The invasive bacterial strains were stored for later analysis.

Results: Of the 48 iGAS cases, 33 (69%) occurred October to March. The average duration of hospital stay was 10 days (1 - 21). 13/48 (27%) were temporarily intubated and ventilated, in 10/48 (20%) circulatory support with catecholamines was needed and 27/48 (55%) required surgery. In 33/48 (67%) a complete cure and in 11/48 (23%) residuals were reported. One previously healthy infant (age 26 months) died, resulting in a mortality rate of 2%. Risk factors were preceding primary varicella infection in 6 cases (12%), 5 patients (10%) had an underlying disease.

Conclusions: In Switzerland, iGAS shows the typical seasonality mainly during winter and occurs mainly in formerly healthy children. iGAS is a serious disease in about 1/3 of cases, but fortunately seems to be a rare event with minimal mortality. The reason for lower than expected mortality needs further investigation.
AIR POLLUTANTS SHOULD BE CONSIDERED WHEN WE TRY TO UNDERSTAND THE SEVERITY OF HRV INFECTION

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Background: Exposure to air pollution has been associated with asthmatic exacerbations and pneumonia in children. Nonetheless, there is scarce information focused on the effect of weather conditions and air pollution on acute viral respiratory infections. Human-Rhinovirus (HRV) has a poor seasonal pattern of circulation in our setting. The aim of this study is to describe associations between severe respiratory infection by HRV and air pollution levels.

Methods: An analysis of temporal series of weather, environmental exposures and Paediatric-Intensive-Care (PICU) admissions was performed. Daily weather variables and levels of main pollutants (SO2, NOx), were collected from regional stations of a reference area of a pediatric tertiary center in Barcelona. Daily counts of PICU admissions of children <18 year-old with a severe respiratory infection and HRV detection by PCR in nasopharyngeal aspirate were collected among those who were residing in this reference area during 2017-2018.

Results: Thirty-one patients with HRV infection were admitted to the PICU. The average temperature across the 5-days prior to the admission was lower than that of the 5-days when no-admissions were observed (median 12.8°C (intercuartile-range(IQR):10.7-18.7) vs 17.4(IQR:12.5-23.3), p<0.01). No differences in peaks of rainfall or wind-speed were observed. The average levels of NOx during the 5-days prior to the admission were significantly higher than that of those days without admissions (61 µg/m3(IQR:47-83) vs 49(37-64), p<0.01). No differences were observed in SO2 levels.

Conclusions: According to the 2005 WHO air quality guidelines, the NOx levels associated with severe respiratory disease in this study were below the recommended maximum values. Despite this, other studies have observed similar associations with pneumonia or mortality. The NOx level association with severe HRV-caused disease could exist for children. Further studies in other setting with different weather conditions are needed.
ACTIVE NOROVIRUS SURVEILLANCE IN CHILDREN UNDER 5 YEARS WITH DIARRHEA AFTER ROTAVIRUS VACCINE INTRODUCTION IN ARGENTINA (2017-2020).

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Background: Argentina introduced massive rotavirus vaccination in 2015. An increase in Norovirus (NoV) activity worldwide has been described at the expense of a decrease in the prevalence of rotavirus. The aim of this study is to analyze the role of NoV in acute diarrhea cases in outpatient children under 5 years of age and their epidemiological profile.

Methods: A prospective and cross sectional study in <5 years outpatients attended for acute diarrhea (AD) in Children’s Hospital “Dr. Ricardo Gutiérrez” in Buenos Aires, Argentina, between July/2017-January/2020 was conducted. Active epidemiological surveillance was performed. Stool samples were tested for NoV (RT-qPCR).

Results: From a total of 300 AD enrolled, 283 stools samples were tested: median of age was 21.8 months (IQR:11-30), 59% male. The most frequent symptoms were fever and vomiting in 63.3% and 53.8%, respectively; 54.9% had watery diarrhea, 46% moderate according to Vesikari Scale, 22% had a household member with diarrhea and 72% had received rotavirus vaccine (85% full scheme). From samples tested, 24.7% (74) were NoV positive; 20% had a household member with diarrhea. Regarding genetic diversity the most frequent genogroup was GII (79.7%; 59/74) and genotype GII.P16-GII.4 Sydney (49%;22/45). Bacterial coinfections were found in 35.1% (most frequently Campylobacter spp.). The viral coinfection were with Adenovirus(4), Astrovirus(2), Rotavirus(6) and Sapovirus(1). Compared to negative cases, NoV were younger (18 vs 19 months;p<0.001) and were associated with higher prevalence of rotavirus vaccination (84.7% vs 67.3%;p=0.001). No statistically difference was found regarding to gender, clinical outcome and severity.

Conclusions: Norovirus was detected at high frequency in children presenting moderate acute diarrhea, mainly in those whom received rotavirus vaccine. Regarding sporadic acute diarrhea cases in children, it is important to consider NoV as a frequent etiological agent.

Clinical Trial Registration: Not applicable
BRAIN ABSCESES AND SOCIAL DEPRIVATION IN CHILDREN IN THE NORTH EAST OF ENGLAND 2001-2018

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**Background:** The North-East of England has a higher incidence of paediatric brain abscess (BA) than the national average (8.92 per million) but it is unclear why. 24% of children in the North-East live in poverty and 30% in Newcastle city (1) (national average 20%). We hypothesized that the increased incidence of brain abscesses was associated with social deprivation. Our aim was to examine the sociodemographic characteristics and identify any associations between social deprivation and incidence of paediatric brain abscesses in the North-East of England.

**Methods:** This retrospective cohort study looked at 115 confirmed cases of brain abscesses in children and young people aged 0-16 years referred to our tertiary neurosurgical service at the Great North Children's Hospital between 01/01/2001 - 31/12/2018. Patient information was collected from notes or an established database. Patients' postcodes were linked to data from The English Indices of Deprivation 2015. Data for brain abscess incidence and patient outcomes was plotted against deprivation indices.

**Results:** Brain abscesses were over thirty times more common in the most deprived centile compared to the least. Brain abscess frequency had a positive relationship with Health Deprivation index (proportion of people who die prematurely or whose quality of life is impaired by poor health) and Income Deprivation Affecting Children Index (proportion of all children aged 0 to 15 living in income deprived families).
Conclusions: Our findings suggest that the incidence of brain abscesses may be associated with social deprivation in children and young people. This data reflects frequency of brain abscesses across the north east region of England and more research is required to establish which parameters of social deprivation are most significant and to confirm this in subsequent studies in a wider population.
ARTERIAL STIFFNESS IN YOUNG PEOPLE WITH PERINATAL HIV AND HIV NEGATIVE YOUNG PEOPLE IN ENGLAND

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Background: Antiretroviral therapy (ART) has increased life expectancy and consequently the risk of cardiovascular disease (CVD) in HIV positive adults. We investigated predictors of arterial stiffness in young people with perinatal HIV (PHIV) and HIV negative young people (HIV-) in AALPHI (Adolescents and Adults Living with Perinatal HIV).

Methods: 213 PHIV and 65 HIV- (42% siblings of PHIV) had pulse wave velocity (PWV) measurements taken (Vicorder software) from the supra-sternal notch to the middle of the thigh cuff. Average PWV was calculated from the 3 closest readings (≥3m/s and ≤12m/s) within 0.6m/s of each other. Linear regression examined predictors of higher (worse) PWV, including age, sex, PHIV/HIV- and height as a priori, ethnicity, born outside UK/Ireland, alcohol/nicotine/drug use, weight, waist-to-hip ratio, mean arterial pressure (MAP), caffeine 2h before PWV and nicotine on the day of PWV. A separate PHIV model included CD4, viral load, years taking ART and ART regimen.

Results: 128(60%) PHIV and 45(69%) HIV- were female (p=0.18), with median[IQR] age 18[16,20] and 18[16,21] years (p=0.48) respectively. Mean PWV was higher in the PHIV group (6.15(SD 0.83)m/s vs 5.93(0.70)m/s in HIV-, p=0.056). In multivariable analysis, having PHIV, being female, older age, higher MAP and nicotine use on day of measurement, but not ever smoking, were predictors of higher PWV (Table). In the PHIV group, older age, being born outside of the UK/Ireland, higher MAP and longer duration of ART were associated with higher PWV.
**Conclusions:** By late adolescence PHIV had worse PWV in comparison to HIV- peers. In terms of traditional risk factors for CVD, only blood pressure and age were associated with higher PWV scores. Further markers of HIV-related inflammation and infection need evaluating to assess their relationship with cardiovascular changes in PHIV.

**Clinical Trial Registration:** N/A
HIGH PD-1 EXPRESSION ON CD8+ T CELLS OF VERTICALLY HIV-INFECTED ADOLESCENTS IS ASSOCIATED WITH TETANUS AND DIPHTHERIA SUSCEPTIBILITY 2 YEARS AFTER A Tdap BOOSTER

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Background: Studies on the kinetics and factors associated with antibody decay after a Tdap booster in vertically HIV-infected individuals are not available.

Methods: Forty-three adolescents were assessed: 11 vertically HIV-infected ART-treated individuals on virologic suppression, 16 ART-treated without virologic suppression and 16 healthy adolescents. All individuals had a primary scheme with three whole-cell DTP vaccine plus two booster doses and CD4>200 at Tdap booster. Blood samples were collected immediately before, 14 and 28 days, 6 months, 1 and 2 years after Tdap. CD4+ T cells, immune activation (CD38+HLA-DR+) and PD-1 expression on CD8+ T cells were evaluated by flow cytometry at Tdap administration. Tetanus, diphtheria and pertussis toxin antibodies were assessed by ELISA.

Results: After Tdap, one individual from non-virologic suppressed group did not respond to tetanus and 3 individuals, to diphtheria; after 6 months, all 3 were already susceptible to both diseases. Tetanus antibodies were lower in non-virologic suppressed group than in virologic suppressed group after 6 months; diphtheria and pertussis antibodies were lower in the same group at 14 and 28 days, but antibody decay was not faster than in the other groups. PD-1 expression was the only factor associated with tetanus and diphtheria susceptibility as early as 6 months after Tdap (Table).

Conclusions: Most vertically HIV-infected adolescents respond to a Tdap booster. However, non-virologic suppressed individuals respond less efficiently and present a faster decay of tetanus antibodies than other groups. High PD-1 on CD8+ T cells, an immune exhaustion marker, was associated with tetanus and diphtheria susceptibility early after Tdap.
MORTALITY AND VIROLOGICAL OUTCOMES FROM TWO TO FIVE YEARS AFTER EARLY INITIATION OF ANTIRETROVIRAL TREATMENT DURING INFANCY: EXPERIENCE OF THE ANRS-1240 PEDIACAM STUDY (CAMEROON)

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Background: In most studies, the virological response is assessed during the first two years of antiretroviral treatment initiated in HIV-infected infants. However, early initiation of antiretroviral therapy exposes infants to very long-lasting treatment. We aimed to assess the virological response and mortality after two years of antiretroviral treatment initiated early during infancy and identify factors associated with virological success in Cameroon.

Methods: We included children of the Pediacam study still alive after two years of antiretroviral treatment initiated early during infancy. Virological response was assessed after 5 years of antiretroviral treatment. The probability of maintaining virological success between two and five years of treatment was estimated using the Kaplan-Meier model. Factors associated with a viral load < 400 copies/mL in children still alive at five years of antiretroviral treatment were studied using univariate and multivariate logistic regression.

Results: The viral load after five years of early initiated antiretroviral treatment was suppressed in 66.8% of 144 children. Five deaths (3.3%) were recorded during the study period. Among the children with viral suppression after two years of treatment initiation, the probability of maintaining viral suppression after five years was 64.0%. The only factor associated with viral suppression after five years of treatment initiation was achievement of confirmed virological success at least once within the first two years of antiretroviral treatment.

Conclusions: This study reported findings on virological outcomes up to 5 years on ART early initiated during infancy. It highlighted the importance of initial suppression for achieving and maintaining virologic suppression in the long-term in Sub-Saharan countries. It also emphasized the importance of initial suppression for achieving and maintaining virologic suppression in the long-term and the need to provide better formulations for children in health facilities.
2-YEARS OBSERVATION OF LIPID DISORDERS, INSULIN RESISTANCE AND CAROTID INTIMA MEDIA THICKNESS IN HIV INFECTED CHILDREN AND ADOLESCENTS

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Background: Along with HAART introduction HIV infection changed from acute life-threatening into chronic disease. Unfortunately, many serious metabolic side effects appeared with the benefits of longer survival. Aim of the study was to assess the prevalence of lipid disorders, insulin resistance and to measure carotid intima media thickness in HIV infected children. All assessments were performed at baseline and over 2 years.

Methods: The study group consisted of 37 HIV-infected children aged 10,4-17,7 years. In all patients fasting lipid profile was evaluated at baseline and 2 years. Insulin resistance was determined based on value of HOMA-IR (>3,16). Measurement of cIMT was performed in all patients at baseline and in 29 after 2 years. We analyzed correlation between metabolic parameters and cIMT and compare changes at time points.

Results: At baseline, hypercholesterolemia, hypertriglyceridemia, hypoHDL-cholesterolemia, hyperLDL-cholesterolemia and hyper-non-HDL-cholesterolemia was in reported in 18,9%, 64,9%, 27%, 5,4% and 32,4%, respectively. Insulin resistance had 51,4%. Results after 2 years of observation showed that prevalence of hypercholesterolemia was 13,5% (p < 0,05), hypoHDL-cholesterolemia 18,9% (p < 0,05), hyperLDL-cholesterolemia 8,1% (p < 0,05), hyper-non-HDL-cholesterolemia 27% (p < 0,05). Hypertriglyceridemia and insulin resistance did not change significantly. Mean SDS cIMT was 2,21 at baseline and 0,72 at 2 years (p < 0,05). There was no correlation between lipids, HOMA-IR or SDS cIMT.

Conclusions: Metabolic abnormalities are prevalent among children infected with HIV. Majority of lipid parameters improves during long-term observation. Primary results showed high values of SDS cIMT but its decreasing over time may lead to reduce the risk of cardiovascular disease. Thickness of carotid intima media was not correlated with lipid and glucose metabolism disorders, which could serve as surrogate markers in predicting cardiovascular risk.
DIFFERENCES IN LOCATION OF WHITE MATTER HYPERINTENSITIES IN HIV: A COMPARISON BETWEEN CHILDREN AND ADULTS

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Background: Despite effective combination antiretroviral therapy (cART), brain white matter hyperintensities (WMHs) are still observed in children and adults living with Human Immunodeficiency Virus (HIV). To gain more insight in WMHs according to age and mode of HIV acquisition, we compared their presence and location in ongoing cohort studies of perinatally HIV-infected children (NOVICE) and HIV-positive adults (AGEhIV) in Amsterdam, Netherlands.

Methods: Fluid-attenuated inversion recovery (FLAIR) MRI scans obtained at cohort entry were used to assess the volume and location (periventricular vs. deep) of WMHs. WMHs within 10mm of the lateral ventricles were labeled periventricular. For comparison between groups, WMH volume was adjusted for intracranial volume. We compared both groups using the Mann-Whitney U test for continuous, or Fisher’s exact test for categorical data. Logistic regression models were used to assess associations between WMH location and patient or HIV-related characteristics.

Results: At enrollment the median age was 13.8y [11.4–15.9] and 53.4y [48.3–60.8] respectively; 27/31 children(87%) and all adults used cART with a viral load <200 copies/mL. WMHs were seen in 16/27 (52%) children and all adults. Deep WMHs were comparably prevalent: children(100%) vs. adults(96%). Periventricular WMHs were more prevalent in adults(100%) vs. children(56%) (p<0.001). Adults had a higher median WMH volume (1182mm³[425–2617] vs. 109mm³[61.7–625], adjusted p<0.001). We found no significant associations between WMH location and patient or HIV-related characteristics in children.

Conclusions: In line with existing published literature, we conclude that HIV-positive adults had a larger total volume of WMHs compared to perinatally HIV-infected children. Not surprisingly, the prevalence of periventricular WMHs was higher in HIV-positive adults compared to perinatally HIV-infected children. The differences in the location of WMHs observed in adults and children living with HIV might suggest a different underlying pathophysiological mechanism accounting for these WMHs.
E-POSTER DISCUSSION SESSION 07: HIV
10-28-2020 8:00 AM - 7:00 PM

RUBELLA ANTIBODIES IN VERTICALLY AND HORIZONTALLY HIV-INFECTED YOUNG ADULTS VACCINATED EARLY IN LIFE AND RESPONSE TO A BOOSTER DOSE IN THOSE WITH SERONEGATIVE RESULTS

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Background: Very limited data are available on the persistence of rubella antibodies in vertically HIV-infected individuals who were vaccinated early in life.

Methods: Prospective, cohort study on 4 groups of patients: 97 vertically HIV-1-infected ART-treated individuals, 69 horizontally HIV-1-infected ART-treated individuals, 93 healthy controls previously vaccinated for rubella and 20 healthy controls with history of rubella disease. A blood sample was collected and rubella antibodies were analyzed by ELISA. Those with seronegative results (<11IU/mL) were offered an extra MMR vaccine dose and were subsequently tested at least 30 days afterwards.

Results: Regarding time since previous rubella vaccination, both HIV-infected groups and the vaccinated control group were comparable. The number of individuals on ARV treatment and CD4 T numbers were similar between vertically and horizontally HIV-infected groups. Nevertheless, virological suppression was lower in vertically HIV-infected group. Rubella seropositivity was lower in vertically HIV-infected individuals in comparison to horizontally HIV-infected ones. Rubella seropositivity was lower in the HIV-infected groups than the two control groups (Table). After a booster dose of MMR vaccine, 67/69 seronegative individuals (97.1%) responded, with no significant difference among groups.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Vertical HIV (n=97)</th>
<th>Horizontal HIV (n=69)</th>
<th>Vaccinated Controls (n=93)</th>
<th>Controls with history of rubella (n=20)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female gender</td>
<td>56 (67.7%)</td>
<td>56 (61.7%)</td>
<td>76 (81.7%)</td>
<td>16 (80.0%)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Median age in years (01-05)</td>
<td>31 (28-40)</td>
<td>36 (26-40)</td>
<td>27 (19-33)</td>
<td>62 (57-64)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Number of individuals with 0-2 previous rubella vaccine doses</td>
<td>1 dose: 32 (33.0%)</td>
<td>2 doses: 50 (80.0%)</td>
<td>1 dose: 20 (29.9%)</td>
<td>1 dose: 21 (10.5%)</td>
<td>n.a.</td>
</tr>
<tr>
<td>Median time interval between the last MMR vaccine dose and assessment (01-03)</td>
<td>15.0 (8.0 - 18.0)</td>
<td>11.0 (4.5 - 18.0)</td>
<td>11.0 (6.2 - 12.0)</td>
<td>n.a.</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Number of individuals on ART at assessment (%)</td>
<td>41 (42.1%)</td>
<td>58 (85.5%)</td>
<td>n.a</td>
<td>n.a</td>
<td>0.135*</td>
</tr>
<tr>
<td>Median CD4 T cells/mm³ at assessment (01-03)</td>
<td>608 (150-953)</td>
<td>814 (149-784)</td>
<td>n.a</td>
<td>n.a</td>
<td>0.594*</td>
</tr>
<tr>
<td>Number of individuals, virological suppression at study entry (%)</td>
<td>59 (60.8%)</td>
<td>59 (85.5%)</td>
<td>n.a</td>
<td>n.a</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Median virological suppression rate (01-03) at assessment</td>
<td>5.9 (2.5-9.5)</td>
<td>3.0 (1.0-5.9)</td>
<td>n.a</td>
<td>n.a</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Rubella seropositivity at assessment (%)</td>
<td>24/97 (24.7%)</td>
<td>14/69 (20.3%)</td>
<td>84/93 (90.3%)</td>
<td>20/20 (100%)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Rubella seropositivity after an extra MMR dose (%)</td>
<td>25/27 (92.8%)</td>
<td>2/2 (100%)</td>
<td>12/13 (92.3%)</td>
<td>n.a</td>
<td>0.558*</td>
</tr>
</tbody>
</table>

*p value: not available
* CD4 count not available in virological suppression
Conclusions: As vertically HIV-infected individuals reach adolescence and adulthood, assessment of vaccine antibody levels might help identify those who might benefit from an extra vaccine dose. Protection against rubella might be especially important for HIV-infected women who decide to conceive.
INFLUENCING FACTORS ASSOCIATED WITH HIV-RELATED CARDIOMYOPATHY IN PARENTERALLY HIV-TRANSMITTED CHILDREN

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Background: Cardiovascular disorders in HIV-positive children may occur because of infection directly or due to the use of certain antiretroviral drugs, however, the exact mechanism of the pathogenesis is not fully understood. The purpose of the study was to determine the influencing factors which might be associated with the HIV-related cardiomyopathy in HIV parenterally transmitted children receiving treatment in 2010-2017 at the Republican Center of AIDS.

Methods: Among 362 children with HIV-parenteral transmission, 128 informed consents were obtained (mean age 6.3±4.9 years, 69 male and 59 female). In 26(20.3%) children, cardiomyopathy was diagnosed (e.g. dilated cardiomyopathy was in 8 cases, left ventricular diastolic dysfunction was in 11, thickening of the left ventricular wall was in 7 cases). HIV infection was detected by the ELISA method following by Western Blot confirmation. Viral load and CD4 count were determined by PCR.

Results: HIV stage was not correlated with the prevalence of heart lesions, r=0.079, p=0.189, as well as the HIV viral load (r=0.072, p=0.209). The severity of the immunosuppression based on the CD4 counts in children was positively related to the prevalence of cardiomyopathy (the worse the immunosuppression the more likely cardiomyopathy was diagnosed), but not statically significant, Pearson r was 0.143, p=0.053. Similarly, the longer the detected duration of the HIV infection, the more registered cases of cardiomyopathy, but not statistically significant, r=0.138, p=0.059.

Conclusions: Almost 1 of 5 HIV-parenterally infected children developed cardiomyopathy. However, none of the observed factors such as the HIV-stage, viral load, time after HIV detection, the severity of immunosuppression did not show a statistically significant association with the prevalence of cardiomyopathy among observed children. More studies are needed to determine the influencing factors to decrease incidence of cardiomyopathy and the affiliated mortality rate.
EARLY DISCONTINUATION OF EMPIRIC ANTIBIOTIC THERAPY IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA AND FEBRILE NEUTROPENIA

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Background: Febrile neutropenia (FN) is a life-threatening complication for children with cancer. Early administration of broad–spectrum antibiotics has significantly contributed to improved outcome. Often, children with culture negative FN remain hospitalized on treatment until recovery of neutrophil count, resulting in prolonged antibiotic courses and increased length of hospital stay. The aim of this study was to explore the safety of short course antibiotic regimens in children with culture negative FN and ALL.

Methods: A prospective study of children with FN and ALL admitted at the Paediatric Oncology department of Aglaia Kyriakou Children’s hospital (Athens, Greece) between February 2017 and December 2019. All children received empiric treatment with Cefepime or Piperacillin/Tazobactam combined with an aminoglycoside. Children with negative blood cultures regardless of their absolute neutrophil count, had their antibiotics discontinued 48 hours after defervescence. On discharge, children and carers were instructed to return if fever recovers. Daily follow-up visits were scheduled for clinical examination and blood count.

Results: A total of 23 cases of ALL with FN met the inclusion criteria for early discontinuation of empiric antimicrobial treatment. Median age at admission was 5.92 years (IQR=4-10.1) with a predominance of males (62.5%). All children were on intensive chemotherapy. Median neutrophil count at discontinuation was 186.7/mm³ (IQR=100-260/mm³). Early discontinuation resulted in 148 less days of hospitalization (average 6.46 days/case). Average hospital stay was 3.35 days. There were no readmissions due to fever or infection during the stage of neutropenia.

Conclusions: Results from this study encourage the early discontinuation of antibiotics in oncology patients with FN regardless of their neutrophil count. Benefits include reduced exposure to antibiotics and length of stay as well as lower risk for hospital acquired infections.

Clinical Trial Registration: 000000000000000000
ETIOLOGY AND ANTIMICROBIAL SUSCEPTIBILITY PATTERNS OF HOSPITAL-ACQUIRED CONJUNCTIVITIS IN A NEONATAL INTENSIVE CARE UNIT IN CRETE, SOUTHERN GREECE

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Background: Hospital-acquired conjunctivitis (HAC) is one of the most common infections encountered in neonatal intensive care units (NICUs) and a significant cause of ocular morbidity if not adequately treated. The aim of this retrospective study was to determine the etiology and antimicrobial susceptibility of pathogens causing HAC in a tertiary care reference NICU with a mean annual admission rate of 400 neonates over a 3-year period.

Methods: Hospital databases were retrospectively searched for neonates with culture-proven HAC. Antimicrobial susceptibility testing data according to EUCAST guidelines were identified for all isolated microorganisms from January 2017 to December 2019. HAC cases were defined using the ECDC criteria as described in the HAI-Net ICU protocol, version 2.2 after reviewing the patient’s chart. Cultures were not routinely tested for viral pathogens or Chlamydia.

Results: HAC occurred in 151 hospitalized neonates (151/1278, 11.8%). The most common pathogens were gram-positive bacteria (67.3%), followed by gram-negative bacteria (29.8%) and fungi (2.9%). Among gram-positive pathogens, CoNs were the predominant organisms (66.3%), while Enterococcus spp, viridans streptococci, and S. aureus were less frequent (15.0%, 10.7%, and 5.9%, respectively). The most common gram-negative pathogens were Pseudomonas aeruginosa (28.9%) followed by Klebsiella (22.9%) and Enterobacter species (15.7%). Resistance rate to tobramycin, empirically prescribed as 1st line treatment, was significant (58.8%), while none of the isolates were resistant to chloramphenicol.

Conclusions: HAC is common in NICU. Continuous surveillance and physician awareness are required to prevent treatment failure with potentially serious sequelae for neonatal health, especially in premature neonates. Given the observed resistance patterns, tobramycin resistance should be considered in selecting empiric antibiotic treatment. It is worth emphasizing the importance of the implementation of strict infection control measures to prevent the dissemination of resistant strains.
Background: Healthcare-associated infections (HAI) are a major concern in Paediatric Intensive Care Units (PICU) specially those associated to medical devices like catheter-associated urinary tract infections (CAUTI), central line-associated blood stream infections (CLABSI) and ventilator-associated pneumonia (VAP). The aim of the study is to describe the rates of HAI from the PICU participating in the Paediatric-ENVIN-HELICS multicentre registry and to compare 2019 rates with the previous ones.

Methods: Multicentre, prospective and observational study of HAI diagnosed in 26 Spanish PICU from April to June of 2019. The ENVIN diagnostic criteria adapted to paediatrics were used, based on Centre of Disease Control (CDC) recommendations.

Results: 1752 patients were included. The mean age was 5.4 years, the length of stay was 6.13±8.9 days and the mortality rate was 1.4%, similar to previous years. 68 patients (3.88%) had at least one HAI, lower than between 2014-2018. CAUTI (21,25.9%) and CLABSI (21,25.93%) were the most frequent HAI, followed by VAP (13,16.1%) and primary bacteraemia(13,16.1%). The highest infection rate (cases/device days) was observed in CAUTI (5.7/1000), followed by CLABSI (2.34/1000) and VAP (2.3/1000). Compared to 2018, there were higher CAUTI rates (p<0.05) and lower rates of VAP and CLABSI.

Conclusions: Almost the 4% of patients admitted to the PICU presented a HAI. Rates have significantly decreased between 2014-2018 and 2019. Although the CLABSI rate has decreased, the mean device-associated HAI rates are higher than those referred in the international bibliography. Therefore, the HAI prevention measures in the participating PICU must be reviewed and reinforced.
TIME TO SWITCH?

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**Background:** Urinary tract infection (UTI) is a common cause of fever in children. National guidelines on diagnostic work-up and antimicrobial treatment are largely implemented. Resistance of *E. coli* to co-amoxiclav as high as 48% was reported in Ireland's adult population in 2014. Treatment with an ineffective antibiotic can lead to treatment failure. This has prompted us to review our local resistance landscape.

**Methods:** This was a retrospective observational study in the paediatric department of a regional hospital in Ireland. Urinary cultures of paediatric patients (0-16 years) between January 2019 and January 2020 were identified by microbiology department. Repeat samples, multiple organism-growth and no-growth samples were excluded. Organism, panel of antimicrobial sensitivities, patient’s clinical details and antimicrobial therapy prescribed were input into an Excel sheet.

**Results:** Over 90% of UTIs in this study were in children without urinary tract abnormality, previous hospital admission or prolonged antibiotic exposure. *E. coli* was the most common isolate. Seventy-four percent of isolated *E. coli* were resistant to co-amoxiclav, 35% to trimethoprim. There were no ESBL isolates. Majority (82%) of co-amoxiclav-resistant strains were sensitive to first-, second- and third-generation cefalosporins. Antibiotics were switched once sensitivities available regardless of clinical response. No adverse clinical outcome was recorded.

**Conclusions:** Significant pattern of resistance to co-amoxiclav and trimethoprim was identified, reflecting the most commonly prescribed antibiotics in paediatric UTI. Resistance rates were higher than those reported in 2014. No adverse clinical outcome was reported following a delayed switch. Following results of our retrospective audit, a meeting between local microbiology, paediatrics and the pharmacist is scheduled for spring 2020, to discuss possible changes in our guidelines. An ongoing monitoring of local sensitivities of isolates is required, as resistance to other antibiotics was significant and is increasing.
ANTIMICROBIAL STEWARDSHIP INTERVENTION PROGRAM IN A PEDIATRIC INTENSIVE CARE UNIT

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Background: Paediatrics Intensive care units (PICUs) are among the heaviest consumers of antibiotics, with an estimated 70% of patients receiving antibiotics during a stay. Antimicrobial stewardship programmes (ASPs) aim to rationalize antimicrobial use and are effective and safe in reducing and improving prescribing of antimicrobials. We present the results of an audit conducted in a pediatric cardiac intensive care (PCIC) in a tertiary paediatrics hospital.

Methods: Data from January 2015 to December 2018 were extracted from the ASP database to describe the intervention of the ASP team. A weekly ASP team evaluated the patients selected by the PCIC physician. The ASP team intervention was divided in 1) confirmed antibiotic therapy (CAT) 2) modified antibiotic therapy (MAT), de-escalated therapy (DT) and interrupted antibiotic therapy (SAT).

Results: A total of 868 consultations were reported for 251 patients in the four years. The rate of evaluation/100 patients admitted in the PCIC increased from 30 in 2015 to 54 in 2019. The ASP team confirmed the therapy prescribed from the PCIC physician in 43-45% of cases and modified the prescription in 31% of cases. We did not observe a change of these percentages during the years. The analysis showed as well a stable rate of 12-13% for DT and SAT (Fig.1).

Conclusions: In the last few years, an increased request of ASP team consultations was observed, justified by the more complexity of patients and by the increased rate of infections due to multidrug
resistant pathogens, requiring a specialist support. The challenge for the PCIC setting remains the rate of DT and IAT. We believe that implementing ASP programs and enabling physician to take direct responsibilities for their patients about DT and SAT might be a successful strategy.
WHAT MATTERS WHEN MANAGING CHILDHOOD FEVER IN THE EMERGENCY DEPARTMENT? A DISCRETE-CHOICE EXPERIMENT COMPARING PARENTAL AND HEALTHCARE PROFESSIONAL’S PREFERENCES IN THE UNITED KINGDOM.

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**Background:** Fever among children is a leading cause of Emergency Department (ED) attendance and a diagnostic conundrum. However, robust quantitative evidence regarding the preferences of parents and healthcare professionals (HCPs) when managing paediatric febrile illness is scarce. We conducted a discrete-choice experiment (DCE) to elicit the comparative preferences of both parents and HCPs for the management of paediatric febrile illness in the ED.

**Methods:** Nine focus-groups and coin-ranking exercises were conducted with parents, and a DCE conducted with both parents and HCPs, from June-2018 to January-2019. 98 Parents of children aged 0-11 years, and 99 HCPs took part. The DCE asked respondents to choose their preferred option of several hypothetical management scenarios for paediatric febrile illness, with differing levels of; visit time, out-of-pocket costs, antibiotic prescribing, HCP grade and pain/discomfort from investigations.

**Results:** Response rates to the DCE were 94.2% and 98.2% among parents and HCPs respectively. Avoiding pain from diagnostics, receiving diagnostic information faster, and minimising wait-times were major concerns for both groups, with parents willing-to-pay €19.81 (95%CI €9.83-€31.85) for every one-hour reduction in waiting. Both groups preferred treatment by consultants and nurse practitioners over doctors in postgraduate training. Parents were willing to trade-off an additional 24mins of waiting to be seen by consultants, and 46mins to avoid pain from investigations. Reducing antibiotic prescribing was important to HCPs but not parents.
Conclusions: Both parents and HCPs expressed strong preferences for reducing visit times, avoiding pain from investigations and receiving diagnostic insights faster when managing paediatric febrile illness in the emergency department. Advances in diagnostic capabilities, including protein-based or RNA signatures delivered through point-of-care testing, should improve patient and carer experience, and HCP satisfaction considerably when managing paediatric febrile illness in the ED.
INFLAMMATORY BIOMARKERS IN SUSPECTED NEONATAL LATE ONSET SEPSIS AND ASSOCIATION WITH CLINICAL COURSE

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²Erasmus Medical Center, Department Of Clinical Chemistry, Rotterdam, Netherlands

Background: Sepsis is a major health issue in preterm infants. Chemical biomarkers might be useful for early diagnosis and to predict disease severity. The aim of this study was to evaluate the association of interleukin-6 (IL-6), C-Reactive Protein (CRP) and procalcitonin (PCT) levels at onset with subsequent clinical course in preterm infants (gestational age <32 weeks) suspected of late onset sepsis.

Methods: A total of 480 sepsis episodes in preterm infants were retrospectively analyzed. Serum IL-6, CRP and PCT were assessed at the time of sepsis suspicion. We assessed the association between these biomarkers and 7-day mortality and disease severity (Neonatal Sequential Organ Failure Assessment (nSOFA) score, need for inotropic support, invasive ventilation and thrombocytopenia), all analyses were adjusted for gestational age, sex and birthweight.

Results: A total of 24 sepsis episodes (5%) resulted in death within 7 days after the first suspicion. Log IL-6 (adjusted HR: 2.28; 95% CI (1.64–3.16; p < 0.001), and PCT (HR 2.91 ; CI 1.70–5.00; p < 0.001) levels were associated with 7-day mortality. Log CRP levels were not significantly correlated with 7-day mortality. Log IL-6 and PCT levels were also associated with sepsis severity. The AUC with respect to predicting 7-day mortality for IL-6, PCT and CRP were 0.64, 0.74 and 0.52, respectively.
**Conclusions:** Serum IL-6 and PCT levels at time of sepsis suspicion offer valuable information about sepsis severity and mortality risk in preterm neonatal late onset sepsis. The predictive value is superior to that of CRP. As both IL-6 and PCT show a rapid increase at onset of sepsis, it might help to identify patients with imminent severe sepsis, which may lead to more intensive monitoring and help us to personalize therapy.
COMPARISON OF DIFFERENT CRITERIA FOR VENTILATOR ASSOCIATED EVENTS DIAGNOSIS IN CRITICALLY ILL CHILDREN

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Background: Ventilator-associated pneumonia (VAP) is one of the most common health-care associated infections in pediatric ICUs (PICU), but its definite diagnosis remains controversial. A new approach for VAP surveillance includes the Ventilator-Associated Event (VAE) module which has been validated only in adults. The aim of this study was to evaluate three different criteria for diagnosis of VAE in critically ill children.

Methods: This study was conducted in a PICU, from 2017 to 2019. Assessment of “oxygen deterioration” for tier 1 of CDCVAE module was made using 3 different pathways: adult (increase of daily minimum fraction of inspired oxygen-FiO₂>=0.2 or positive end expiratory pressure-PEEP>=3cmH₂O, for 2 days), US pediatric (increase of daily minimum FiO₂>=0.25 or mean airway pressure-MAP>=4cmH₂O, for 2 days) and European pediatric (increase of FiO₂>=0.2 or PEEP>2cmH₂O, for 1 day or increase of FiO₂>=0.15 and PEEP>=1cmH₂O for 1 day) criteria.

Results: Among 361 children admitted to PICU, 312 (86%) received mechanical ventilation (4712 ventilator-days). During study period the incidence rate of VAE according to adult criteria was 5.7 per 1000 ventilator days whereas using the US and European pediatric criteria the incidence was 6.4 and 11.5 per 1000 ventilator days, respectively. Substantial agreement was found between adult criteria and both US (k=0.75) and European (k=0.62) pediatric criteria. In contrast, moderate agreement (k=0.53) was found between US and European pediatric criteria.

Conclusions: This is the first study comparing three currently available definitions for VAE diagnosis in critically ill children. Both US and European pediatric criteria had substantial agreement with adult criteria for VAE diagnosis in pediatric patients. In contrast, moderate agreement was found between the two pediatric VAE algorithms. These findings highlight the need for a unified VAE definition in critically ill children aiming improvement of preventive strategies.
**Background:** To assess whether a diagnostic algorithm for pneumonia that combines lung ultrasonography (LUS) and procalcitonin (PCT) may be useful in indicating antibiotic treatment. To analyse the sensitivity and specificity of LUS, compared to chest X-ray (CXR), for pneumonia diagnosis.

**Methods:** Prospective, randomized, blinded, clinical trial. Patients younger than 18 years old with pneumonia suspicion admitted in the Paediatric Intensive Care Unit from June 2017 to December 2019. Community pneumonia (CP) diagnosis was defined following CDC criteria; nosocomial pneumonia (NP) based on Clinical Pulmonary Infection Score (CPIS). Radiological findings were described depending on randomization group: experimental group (EP) – group 1/LUS; control group (CG) – group 2/ CXR. The images were evaluated by a pediatric investigator (IP) blinded to LUS or CXR, and by a radiologist blinded to clinical signs. LUS results were defined in 4 patterns: interstitial pattern, viral pneumonia, bacterial pneumonia and atelectasis. LUS images were compared between IP and a paediatrician. Statistical analysis was done with SPSS® program.

**Results:** We recruited 194 patients. Randomization is shown in table 1.

<table>
<thead>
<tr>
<th></th>
<th>CP</th>
<th>NP</th>
</tr>
</thead>
<tbody>
<tr>
<td>LUS</td>
<td>72</td>
<td>24</td>
</tr>
<tr>
<td>CXR</td>
<td>69</td>
<td>9</td>
</tr>
</tbody>
</table>

CXR and LUS were done to >98% of cases. The final diagnosis for CP and NP were 58(41.1%) and 38(71.17%) bacterial pneumonia and 41(20.1%) and 4(0.07%) viral pneumonia correspondingly. The interobserver kappa index (KI) (IP and CP) resulted in 0.79 and concordance correlation coefficient was 0.69. Concordance between LUS and CXR was 82%. LUS sensitivity and specificity for pneumonia was 97.6% and 87.1%; and 89.2% and 72.7% for CXR. The diagnosis with LUS was done earlier in 49.9% of patients.

**Conclusions:** LUS shows higher sensibility and specificity for pneumonia diagnosis than CXR. LUS use can lead us to a less radiation to paediatric patient.

**Clinical Trial Registration:** ClinicalTrials.gov NCT04217980
USE OF GROUP A STREPTOCOCCAL RAPID DIAGNOSTIC TEST IN AMBULATORY PEDIATRIC PRACTICES

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¹ACTIV, Biostatistics, Créteil, France, ²AFPA, R&d, Talence, France, ³ACTIV, Association Clinique Et Therapeutique Infantile Du Val De Marne, Creteil, France

Background: Pharyngitis is the second cause of antibiotic prescription in children in France. While the majority of pharyngitis is due to viruses, a large proportion is linked to Group A Streptococcus (GAS). The use of Rapid Diagnostic Test (RDT), recommended in children from 3 years old in France, allows to detect GAS pharyngitis, with a ≈ 90% sensitivity and ≈ 95% specificity.

Methods: By automated data extraction, we daily prospectively collect anonymized data (age, sex, height, weight, daycare attendance, vaccines, diagnosis and prescriptions) of children with infectious diseases in 100 primary-care pediatric offices using the same software (Axi5-Infansoft®, CompuGroup Medical): PARI study (Pediatric Ambulatory Research In Infectious Diseases). The pediatricians of this network have to participate to e-learning and face to face meetings in order to improve their diagnosis and management of infectious diseases.

Results: Between September 2017 and November 2019, data on 10,186 pharyngitis diagnoses were recorded (Figure). RDT were performed for 8,612 pharyngitis (85%) with positive results for 3,716 patients (43%). Before 3 years old, RDT were performed in 50% of cases and among them, 20% were positive. From 3 years old, RDT were almost systematically used (>95%) and detected GAS in 55% of cases. When RDT were negative or not done, no antibiotic was prescribed in 97% and 79%, respectively. For positive RDT, amoxicillin was the main treatment prescribed (93%).
Conclusions: The PARI network showed a screenshot of "real life" daily practice in pediatric ambulatory settings and demonstrated that regular training of pediatricians allows more efficiency in guidelines implementation and a more accurate antibiotic prescription.
Background: There is a lack of consensus on the standard method for collection of urine specimens for culture in children with suspected urinary tract infections (UTI). We examined the reliability of different techniques of paediatric urine culture collection.

Methods: A prospective observational study of children aged 0-18 years in a Paediatric Emergency Department (PED). Children of all ages whose urine sample was obtained for culture during their PED visit during the study period were enrolled to the study. Data were collected from electronic health records. Contamination rates and positive urine cultures rates were calculated and compared for sex, age group and collection technique.

Results: Urine culture samples obtained from 1507 children were included. 284/1507 (18.8%) of cultures were positive with significant growth, and 52/1507 (3.45%) were defined as contaminated. Contamination rates of midstream (MS) urine samples in toilet-trained children was 1.6% (10/609), of midstream clean catch (MSCC) in non-toilet-trained children was 4.9% (17/348), of catheterized specimens was 4.9% (25/515), and of specimens collected via supra-pubic aspiration was 0% (0/35); (p=0.006). Specifically, in non-toilet-trained children, there was no statistically significant difference between the contamination rates in specimens obtained by MSCC versus catheterization in girls across all age groups (Table). In the subgroup of children that was defined as "high index of suspicion for UTI" there were similar rates of positive cultures obtained by the different collection methods. Escherichia coli were yielded in 71.8% of positive cultures, 6.4% of enterobacteriaceae were Extended-spectrum beta-lactamase-producers.
## Conclusions:
Given the high diagnostic value of MSCC as demonstrated by positive cultures rate in the children with high index of suspicion for UTI, and the similarity between contamination rates of MSCC and catheterization, we show that MSCC is non-inferior to catheterization for collecting urine cultures for suspected UTI.

**Clinical Trial Registration:** n/a, prospective observational study

### Contamination rates of urine cultures collected by urethral catheterization vs midstream clean catch in non-toilet-trained boys and girls

<table>
<thead>
<tr>
<th>Age (weeks)</th>
<th>0-12</th>
<th>13-156</th>
<th>&gt;157</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boys</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Girls</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Midstream Clean Catch</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Boys</td>
<td>3.5%</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Girls</td>
<td>14.3%</td>
<td>4.7%</td>
<td>0.0%</td>
</tr>
<tr>
<td>n</td>
<td>7/200</td>
<td>0/32</td>
<td>0/1</td>
</tr>
<tr>
<td>Catheterization</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Boys</td>
<td>12.5%</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Girls</td>
<td>6.5%</td>
<td>3.3%</td>
<td>0.0%</td>
</tr>
<tr>
<td>n</td>
<td>2/16</td>
<td>0/4</td>
<td>0/3</td>
</tr>
<tr>
<td>p-value</td>
<td>0.088</td>
<td>0.791</td>
<td>0.972</td>
</tr>
</tbody>
</table>

**Conclusions:** Given the high diagnostic value of MSCC as demonstrated by positive cultures rate in the children with high index of suspicion for UTI, and the similarity between contamination rates of MSCC and catheterization, we show that MSCC is non-inferior to catheterization for collecting urine cultures for suspected UTI.

**Clinical Trial Registration:** n/a, prospective observational study
INCREASING TUBERCULOSIS NOTIFICATION RATES AND IMPACT OF MIGRATION IN CHILDREN LIVING IN CAMPANIA REGION, SOUTHERN ITALY

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**Background:** With a tuberculosis (TB) notification rate of 6.5/100.000 inhabitants, Italy is classified as a low incidence country. Although authorities reported stable national rates in recent years, the Reference Centre in Campania Region (CRRC) observed an increase in paediatric TB. Contemporarily, Italy is experiencing a raise in migration. Our aim was to assess TB rates, changes in clinical outcomes and impact of migration in children living in Campania.

**Methods:** We conducted a prospective cohort study (January 1st 2009 to December 31st 2018) enrolling children < 18 years who received diagnosis of active TB at the CRRC. TB rates were calculated dividing the number of new cases with the total number of residents < 18 years in Campania. Prolonged or second-line treatment, sequelae or death were grouped as a poor clinical outcome.

**Results:** Overall 146 children (52.1% male, median age 50 months, IQR 96.33) received diagnosis of TB. The annual TB rate increased from 0.44 in 2009 to 1.84/100.000 inhabitants <18 years in 2018. The TB incidence rate and the rate of migrants in Campania were strongly correlated (R² = 0.9272, p < 0.0001). Compared to Italians, foreign patients showed a higher risk of poor clinical outcome in univariable (OR 2.18 95%CI 1.11-4.29, p=0.023) and multivariable analysis adjusted for age, gender, nationality, TB localization, drug-resistance and smear-positivity (OR 2.26 95%CI 1.08 to 4.71, p=0.029).

**Conclusions:** Paediatric TB rate in Campania significantly increased in the last 10 years in parallel with the increase in migration. The use of overall national TB rates may lead to miss relevant differences in local infection trends, limit medical awareness about the problem and dismantle local prevention measures. Foreign children have higher risks of poor outcome and need tailored management programs.
E-POSTER VIEWING
E-POSTER DISCUSSION SESSION 10: MYCOBACTERIA
10-28-2020 8:00 AM - 7:00 PM

QUANTIFERON-TB GOLD PLUS PERFORMANCE IN THE DIAGNOSIS OF TUBERCULOSIS INFECTION IN CHILDREN AND ADOLESCENTS


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Background: Immune-based tests are crucial for the diagnosis of latent TB infection (LTBI), and important adjunctive diagnostic tools in active tuberculosis (TB). The QuantiFERON-TB Gold Plus (QFT-Plus) assay became available in 2016, and includes an additional antigen tube (TB2) intended to detect CD8+ T-cell responses. This study aimed to determine the performance of QFT-Plus assays in children and adolescents at risk of TB in Spain.

Methods: Prospective, cross-sectional study including patients <18 years-of-age who had a QFT-Plus assay performed in one of the participating centres of the Spanish Paediatric TB Network (PTBRED) between September 2016 and November 2019. QFT-Plus results were evaluated
according to the reason for screening and the final diagnosis.
Results: 780 patients were included (49.5% male; median age: 8.7 years), having undergone screening due to clinical or radiological suspicion (n=235), prior to initiation of immunosuppressive treatment (n=216), following TB contact (n=209), or recent migration (n=83). The final diagnoses were: 477 (61.2%) uninfected, 120 (15.4%) LTBI, and 183 (23.4%) TB. Among patients with LTBI or TB (n=303), 86.1% had positive QFT-Plus results; the concordance with tuberculin skin test (TST) results was 81.2% (kappa=0.253; fair agreement). The concordance between TB1 and TB2 tubes was 93.9% (kappa=0.741; good agreement). Eight (2.6%) patients had a TB1+/TB2+ (5 LTBI, 3 TB cases) result constellation and seven (2.3%) a TB1+/TB2- (2 LTBI, 5 TB) constellation. Forty-nine (6.3%) patients had indeterminate QFT-Plus results, which were significantly more common in younger children and those receiving immunosuppressive treatment (p=0.01 and p<0.01, respectively).
Conclusions: Our data suggest QFT-Plus assays are not superior to TSTs, or previous generation interferon-gamma release assays. Concordance between TB1 and TB2 is high, and the second antigen tube only increases assay sensitivity marginally.
Clinical Trial Registration: Approval for pTBred was obtained from the Hospital Carlos III Madrid Ethics Committee (ref.P13/12).
TB LAM IN THE DIAGNOSIS OF TUBERCULOSIS IN INFECTED OR NON-INFECTED CHILDREN BY HIV

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**Background:** TB is one of the main cause of morbidity and mortality in children. Short of number of diagnostic problem in term of equipment and personnel, given its specificities. It is often young children (0-5 years) who pay a heavy price for their immunity. Mycobacterial Lipoarabinomann (AML) in the urine of patient with pulmonary or extra-pulmonary TB through their evidence in HIV-infected patient with low CD4. But, very few studies have been done with young children infected or not. To evaluate the contribution of TBLAM test in the diagnosis of TB in children and adolescent infected or not by HIV

**Methods:** Cross-sectional study with results of TB Lam test performed in HIV-infected or not and adolescent aged between 0.25 and 18 years, followed by Pediatric Kalembelembe Hospital between August and November 2018. Children and ado have a complete record and in the bacterial antigen, Lipoarabinomann has been searched in urine (TBLAM) before the presumptive elements of TB (clinical, paraclinical and Keith Edouard Score) were found in the age

**Results:** 44 children and adolescent were included in the study, 9 (20%) of whom were HIV-infected and 35 (80%) of whom were HIV-free. Of 9 infected with HIV, the mean age was 13.5 years (6-18) and the sex ratio (M/F) was 0.3. TBLAM performed was positive in 4 patients (44.4%), of which 2 (50%) had a CD4 count of 100/mm³. 35 children not infected with HIV, the mean age was 3.9 years (0.25-6) and the sex ratio (M/F) 1.1. The achieved TBLAM was positive in 21 patients (60%) and all were between 0.25 and 5 years old. In this population, the average weight had increased from 10.7 kg to 13.9 kg at the end of treatment

**Conclusions:** TB LAM diagnostic test is a very promising for the diagnosis of TB in HIV-infected or not according to the presumptive signs of TB. Its therefore possible to quickly diagnose and treat the lives of presumed children. However, it would be useful to conduct large-scale studies to determine its sensitivity and specificity in the population of young children infected or not with HIV
FIXED-DOSE COMBINATIONS OF CHILD-FRIENDLY, FIRST-LINE TUBERCULOSIS DRUGS AVAILABLE IN EUROPE: A PAEDIATRIC TUBERCULOSIS NETWORK EUROPEAN TRIALS GROUP (PTBNET) SURVEY

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Background: Fixed-dose combinations (FDCs) of dispersible, palatable and simple-to-administer tablets of first-line tuberculosis (TB) drugs for children have recently become available. In Europe, these FDCs are not licensed and there is lack of knowledge on their use. We aimed to assess the currently available licensed formulations of first-line TB drugs for children and how these are being used in Europe. We also explored knowledge and experience of the new FDCs among European clinicians.

Methods: We conducted a web-based survey among Paediatric Tuberculosis Network European Trials Group (ptbnet) members based in Europe (November-December 2019). Eighty-four individuals from 25 European countries participated, mostly consultants (89%) in university hospitals (75%) and treating yearly 5-20 children with TB (53%) and >20 with latent TB (57%). Rifampicin suspension is the only child-friendly formulation available in Europe (licensed in 38% of countries).

Results: Measures to ease the administration of TB drugs reported were: halving/cutting (80%), crushing (75%) or mixing tablets with food (48%), and omission of fasting before (24%) or after (42%) drug administration. Other than licensed TB drug formulations, 44% used pharmacy suspensions prepared ad hoc, 33% FDCs licensed for adults, 10% unlicensed dispersible tablets and 10% imported formulations. Most respondents (74%) were aware of the new FDCs, 24% had tried to obtain them but only 10% had succeeded (from the UK, Russia, Bulgaria and Austria).

Conclusions: In Europe, rifampicin suspension is the only licensed child-friendly formulation available to treat TB. Currently, ptbnet physicians use several off-label alternatives for TB treatment in infants and children, with unknown effects on treatment outcomes. Child-friendly TB drugs are urgently needed in Europe. Administrative and regulatory issues need to be rapidly overcome for new FDCs to be obtained and used regularly.
EVALUATION OF XPERT MTB/RIF ASSAY FOR THE DIAGNOSIS OF CHILDHOOD PULMONARY TUBERCULOSIS FROM STOOL SPECIMEN AT JIMMA UNIVERSITY MEDICAL CENTER, SOUTHWEST ETHIOPIA

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Background: Diagnosis of tuberculosis (TB) in children often relies on clinical diagnosis because they are usually unable to produce sputum specimens. Gastric lavage can be applied to obtain for microbiological diagnosis. However, these methods are complex, invasive and not feasible in peripheral settings. In this study, we evaluated the performance of Xpert MTB/RIF the diagnosis of childhood TB from the stool specimen.

Methods: Gastric lavage was collected from children (<15 years old) suspected of TB and processed for Xpert MTB/RIF and culture. In addition, stool specimens were collected and tested for the presence of Mycobacterium tuberculosis by Xpert MTB/RIF assay. The diagnostic accuracy of Xpert MTB/RIF (stool versus gastric lavage) was calculated against culture and composite reference standard (CRS). The CRS made of Xpert MTB/RIF, culture, and response to anti-TB treatments.

Results: Of 152 children enrolled, 10 had bacteriologically confirmed TB, 10 had probable TB (bacteriologically negative but positive response to anti-TB treatment) and 132 not TB cases. Stool based Xpert MTB/RIF had a sensitivity of 100% (95%CI: 66.37-100) and specificity of 99.30% (95%CI: 96.17-99.98) compared to culture but the sensitivity was reduced 50% when compared to CRS. Stool Xpert MTB/RIF was negative in all children with probable TB cases. The Xpert MTB/RIF sensitivity from gastric lavage was 77.8% compared to culture and 40% compared to the CRS.

Conclusions: Stool specimens can be a promising specimen for the diagnosis of pulmonary TB by Xpert MTB/RIF assay for children unable to expectorate sputum specimens and can be easily implemented in the peripheral health care system. However, a negative Xpert MTB/RIF may not exclude a diagnosis of pulmonary TB in children and children with strong clinical findings suggestive of TB should be started anti-TB treatment.
Background: Tuberculin skin test (TST) should be performed to all close and community contacts of a pulmonary tuberculosis (TB) patient, with a priority for those children younger than 5 years of age. Our aim was to determine the associated factors to latent TB infection (LTBI) and TB in the childhood contacts of an adult with positive acid-fast bacilli (AFB+) pulmonary TB.

Methods: A population based observational study was performed among all children and adolescents <18 years-old contacts of AFB+ screened for LTBI and TB in Barcelona (Spain) between 2014 and 2018. TB infection was considered if TST ≥ 5mm. Demographic, epidemiological and clinical variables were collected from Public Health Agency electronic database. Logistic regression analysis for repeated measures (GEE) was performed with SPSS v25.

Results: Among 861 children/adolescents contacts of an AFB+ index case, 114/861 (13.3%) had LTBI or TB disease representing 1.75 secondary cases per index case. The median [IQR] age for contacts was 10 [6-15] years; 58.8% male and 64% foreign-born. Significant association for childhood LTBI or TB was for household contacts OR=8.7 (95%CI:3.9-19.3), index case with pulmonary TB cavity OR=1.9 (95%CI:1.05-3.7), male index case OR=2.0 (95%CI:1.03-3.8), and foreign-born children OR=2.8 (95%CI:1.4-5.5). No association with LTBI was found for diagnosis delay in the index case or contact or index case age.

Conclusions: Childhood TB infection in Barcelona was associated with living in the same household, the index case had a pulmonary TB with cavitation or was male, and the contact was immigrant. To perform a contact tracing in children who are contacts of AFB+ case is essential for implementing a TB control at family and community level, and for preventing TB cases in the future.
Background: Paediatric tuberculosis remains a global challenge. There remains a disparity in outcomes across different paediatric age groups. Adolescent period presents a challenging time for treatment adherence and completion in most chronic care settings including TB. This retrospective study describes the outcomes of TB among adolescents at Mulago National Referral Hospital (MNRH) paediatric TB unit.

Methods: We conducted a descriptive retrospective review of all records of children diagnosed and registered at MNRH paediatric TB clinic for the period 2010 – 2015. We excluded records with missing age and outcomes.

Results: We extracted records of 590 children for analysis. The majority of children were male (55%) and mainly HIV negative (82%). The adolescents were those above 9 years and they constituted 12.8% (76/590). There were 415 PTB cases (10% of these were adolescents), and 175 were EPTB (20% of these were adolescents). The treatment success rate was the poorest among adolescents at 67% and they had a high loss to follow up rate (13%) and a high mortality rate (9.2%).

Conclusions: Whereas they generally only represent about 12% of the total population analyzed, adolescents represent 23% of all the lost to follow-ups and 18% of all mortality. These findings represent disproportionate poor outcomes in this age group. These unfavorable outcomes need to be investigated so that this population may be given special attention.
DIPHTHERIA MYOCARDITIS: LESSONS LEARNED FROM DIPHTHERIA OUTBREAK IN JAKARTA AND TANGERANG 2017-2018

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Background: Diphtheria is still a health problem with high mortality in Indonesia, even in the era of immunization. Diphtheria myocarditis is an important complication that can cause death. In an outbreak, awareness of clinical course that may develop into a severe complication should be noticed. The aim of this study is to identify factors those contribute to complication of myocarditis in pediatric with clinical diphtheria during recent diphtheria outbreak in Jakarta and Tangerang 2017-2018.

Methods: This was a cohort retrospective study at five referral hospitals in Jakarta and one in Tangerang district. The study subjects were pediatric 1-18 years old who admitted to hospital during period of 1 January 2017 to 31 August 2018 with discharge diagnosis as clinical diphtheria. The data of epidemiology, clinical appearance and laboratory had been recorded. Between groups comparison was done using Chi-square test for categorical data.

Results: Amongst 283 patients with clinical diphtheria, 45 (15.9%) had complication of myocarditis diphtheria. Stridor (RR 2.120; 95%CI 1.230-3.654; p 0.012), bullneck (RR 2.767; 95%CI 1.648-4.645; p <0.001), administration of diphtheria antitoxin (RR 0.069; 95%CI 0.010-0.493; p <0.001), leukocyte count >15,000 cell/mm³ (RR 7.5; 95%CI 1.625-34.621; p <0.001) and thrombocyte count <150,000 cell/mm³ (RR 35.5; 95%CI 10.08-125.37; p <0.001) were contributed to myocarditis diphtheria. All fatal cases had myocarditis.

Conclusions: Myocarditis is an important cause of death in diphtheria. Severe classical clinical features of diphtheria, as stridor and bull neck, and abnormality of laboratories measures, as leukocytosis and thrombocytopenia, must make us more alert as the patients my have myocarditis diphtheria. Even though our study was failed to proof that immunization status has correlation with severe outcome of diphtheria, this is the important factor of diphtheria outbreak.
Background: Soil-transmitted helminth (STH) infections are one of the most important neglected tropical diseases. School-age children are at the highest risk to acquire the infection leading to delay in physical growth and cognitive development. In North Sumatera province of Indonesia, the prevalence of STH ranges from 55% to 98% in school-aged children. Nevertheless, despite government recommended 6-monthly deworming programme for school-aged children, the re-infection rates remain high.

Methods: This study was an open label clinical trial conducted between March 2019 and March 2020 to compare a single health hygiene education on STH infections and a 4-monthly repeated education. Singkuang and Sikapas elementary schools in in Mandailing Natal district, North Sumatera, Indonesia were randomised to receive a single intervention or a repeated intervention. Three days treatment of albendazole was administered to all children grades 1 to 5. Of those, 426 children negative by Kato-Katz examination after treatment were enrolled to the study. A questionnaire was used to evaluate hygiene habits, sanitation practices, and STH-related knowledge prior to intervention and at follow-ups. Health education intervention was given in a format of a cartoon video. Re-evaluation on all children was done 4-monthly comprised of questionnaire and stool examinations. Infected children were then received repeated albendazole treatment on follow-ups.

Results: Baseline STH prevalences were 76.8% and 87.2% in Singkuang and Sikapas, respectively. Only 54.9% of children had access to toilet in the house, and almost 50% of them defecated outdoor. Reinfection rates at months 4, 8 and 12 will be presented in the meeting.

Conclusions: Health-hygiene education may improve hygiene and knowledge on STH, and protect children from reinfection. The study was funded by TALENTA Universitas Sumatera Utara.

Clinical Trial Registration: NCT04227834
PERSISTENCE OF PLASMODIUM MALARIAE AND P. KNOWLESI INFECTIONS IN NEAR MALARIA ELIMINATION SETTING IN NORTH SUMATERA, INDONESIA

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Background: A substantial reduction of malaria burden worldwide has been seen in the last 2 decades. This reduction has been achieved due to improvement in malaria control efforts including insecticide-treated nets, indoor residual spraying, improved diagnostics, and better access to effective treatment. Indonesia is now approaching malaria elimination goal by the year 2030. Across Indonesia, Plasmodium falciparum and P. vivax were equally contributed as the cause of malaria, although in western Indonesia P. knowlesi has increasingly been reported in Sumatra and Kalimantan.

Methods: The aim of this study is to determine the prevalence of Plasmodium species in North Sumatra province, Indonesia, a low unstable malaria endemic area. A cross-sectional study was conducted in Langkat district in June 2019, obtaining 342 blood samples from individuals in six villages. Samples were screened for malaria by both microscopy and PCR assay targeting Plasmodium 18s rRNA gene and sicavar gene for human Plasmodium species and P. knowlesi identification, respectively.

Results: Of these, one individual (0.3%; 95% CI: 0.0-1.6) was identified as having P. malariae by microscopy with a density of 1160 parasites/μL blood. By PCR, three individuals (0.9%; 95% CI: 0.2-2.5) were positive for Plasmodium mono-infection; two and one as P. knowlesi and P. malariae, respectively. None of these individuals were microscopy positive. All positive individuals were adult female.

Conclusions: The findings show that P. falciparum and P. vivax were not present which may explain that malaria control efforts for P. malaria and P. knowlesi are not necessarily similar to the former two. Therefore, improved efforts need to be made to better understand malaria control of non-falciparum species and screening of malaria should not be restricted to microscopy and RDT but include molecular methods to identify asymptomatic submicroscopic carriers.
BURDEN AND DIFFERENTIAL FEATURES OF CHOLERA AND NON-CHOLERA WATERY DIARRHEA AMONG UNDER-FIVE CHILDREN: A CASE-CONTROL STUDY IN BANGLADESH

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Background: Liquid- or watery-diarrhoea (WD) is a universal health problem among young children. Few of the WD-cases may be cholera who may need antibiotic. Data on differential features of cholera and non-cholera WD are limited, that information would be helpful in proper management of WD to avoid and/or control the unethical use of antibiotic. This study aimed to assess the case load of cholera and non-cholera WD and the differential features between them in under-five children.

Methods: We collected the data between 1996-2014 in a hospital-based Diarrhoeal Disease Surveillance System in the ‘Dhaka-Hospital’ of icddr,b. Relevant information of 21626 under-five children were available who reported with diarrhoea. Of them, 20936 (96.8%) children were shigella-negative in stool or rectal-swab culture, and admitted with features of WD, and their data were analyzed. Variables found significantly associated with cholera-positive cases in bi-variate analysis were used in logistic regression analysis after checking multicollinearity between the independent variables.

Results: Age of the children was 14.8±11.6 months, 40.3% were girl, 2264 (10.8%) children had cholera and the rest 18672 (98.2%) had non-cholera WD. Age >12 months, stool frequency >10/24 hours, and warmer month (April-September) were found as the associated or risk-factors (p<0.05 for all adjusted-odds-ratio) of cholera. However, absence of abdominal pain and predominant breast-feeding during first six months of life were found as the associated/risk-factors (p<0.05 for all adjusted-odds-ratio) of non-cholera WD.

Conclusions: The most common cause (98.2%) of diarrhoeal illness in under five is non cholera WD. The above mentioned associated or risk factors in under five children would help to differentiate non-cholera WD (who does not need any antibiotic) from cholera that would help in reducing the rampant use of antibiotic and appropriate management of diarrhoeal illness in under five children.
THE IMPACT OF STUNTING AND IN-UTERO HIV EXPOSURE (CHEU) ON BODY COMPOSITION IN RURAL ZIMBABWE

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Background: Globally, 150 million children become stunted in response to both nutritional, socio-economic and other factors. Beyond simply measuring linear growth, body composition provides important insights into function and the body’s response to inflammation. Food insecurity makes the body prioritise fat mass for short-term survival, but this increases the long-term risk of metabolic disease. However, inflammation such as in-utero HIV exposure may decrease prioritised fat mass. By contrast, increased lean mass (ie muscle, tissues and organs) ultimately provides better health, physical and cognitive function. The Sanitation Hygiene Infant Nutrition Efficacy (SHINE) trial tested the effects of improved nutrition and water, sanitation and hygiene (WASH) on stunting at age 18 months in rural Zimbabwe.

Methods: Research nurses travelled by motorbike to measure children’s growth at their homestead. Bio-impedance analysis was performed which measured fat and lean mass (BodyStat 1500). The subcutaneous fat layer was assessed using the skinfold thicknesses and tibial growth recorded using knee to heel length, which is important in examining relative growth.

Results: 230 children were measured at age 2 years, of whom 69 were stunted and 36 had a history of HIV exposure in-utero (CHEU). CHEU were enrolled into prevention-of-mother-to-child Transmission (PMTCT) programmes and so were born and remained HIV- negative up to the age of 18 months. Children with stunting had reduced lean mass. Intriguingly, CHEU had both reduced lean mass and subcutaneous fat.

Conclusions: Advanced body composition measurement techniques have been successfully adapted for rural Sub-Saharan settings to provide insight into the adverse effects of stunting and in-utero HIV exposure. Ongoing inflammation is a possible mechanism for the reduced fat mass observed in CHEU. Future work aims to assess the SHINE trial's early-life interventions’ effect on school-age body composition.

Clinical Trial Registration: ClinicalTrials.gov NCT01824940
**COMPARISON OF LYMPHOCYTE SUBSET POPULATIONS IN CHILDREN FROM SOUTH AFRICA, US AND EUROPE: EFFECT OF EVOLUTION OR ENVIRONMENT ON THE PAEDIATRIC IMMUNE SYSTEM?**

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**Background:** Typically, African healthcare providers use immunological reference intervals adopted from Europe and the United States. This may be inappropriate in a setting with many differences including exposure to different environmental stimuli and pathogens. We compared immunological reference intervals for children from Europe and the United States with South African children to explore whether healthy children living in settings with high rates of infectious diseases have different baseline immunological parameters.

**Methods:** Blood was taken from 381 HIV-uninfected healthy children aged between 2 weeks and 13 years from a clinic in an informal settlement in Cape Town, South Africa. Flow-cytometry quantified percentage and absolute counts of the B-cells, NK-cells and T-cells including activated, naïve and memory subsets. These parameters were compared to 3 separate studies of immunophenotyping done in healthy children in Europe and the United States.

**Results:** Healthy South African children demonstrated increased NK-cells, increased activated CD4 and CD8 T-cells and far lower ratio of naïve/memory CD4 and CD8 T-cells than children in resource-rich countries.

**Conclusions:** This is the largest data set to date describing immunophenotypes of healthy children from an African environment. The dramatic decline in the naïve/memory ratio of both CD4 and CD8 T-cells alongside increased activation markers may indicate that South African children are exposed to a wider range of environmental pathogens in early life than children in resource-rich countries. These data have been used to create local reference intervals for South African children and illustrate that reference intervals should be relevant to the population they serve.
E-PAPER VIEWING
E-PAPER DISCUSSION SESSION 12: VACCINE COMMUNICATION
10-28-2020 8:00 AM - 7:00 PM

EVALUATION OF FACTORS ASSOCIATED WITH ADHERENCE TO THE IMMUNIZATION

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Background: The role of vaccination in reducing infectious disease morbidity and mortality is undeniable. Every year vaccination saves millions of lives. The percentage of vaccination coverage in Ukraine is the lowest in Europe. Much has been done in recent years to improve the situation. The aim of the study was to evaluate the parental adherence to the vaccination, and factors that influence on parental perceptions.

Methods: This study included the surveys of 164 children aged 4–11 years from Ternopil region (Western Ukraine). We assessed the effects of some background factors (maternal age, education, residence) and other medical and social factors that can influence on parental perceptions (the fear of side-effects, religious belief, contrindications, etc). The questionnaire also contained questions about sources of information about vaccination that influences parents’ decisions.

Results: Among the children of the respondents a fully immunized according to the National Immunisation Program Schedule were 88 (53.7%), partially vaccinated (missed one or more vaccinas) - 64 (39.0%) and 12 (7.3%) were not vaccinated. The highest percentage of partially and unvaccinated children were among rural populations (54.1%, and 20.8% respectively). The fear of side-effects and mistrust to the vaccine manufacturers were defined as the main factors of vaccination refusal (47.5% and 27.5% respectively), followed by religious beliefs (15%) and false medical contraindications (20%).

Conclusions: The study has determined the improvement of the parental adherence to the vaccination during last years. The main factors that influence on parental perceptions were doctor's recommendations and Internet. Parents, used as main source information from their doctor, were determined as more adherent to the vaccination. The need to raise the awareness of healthcare professionals, especially in rural areas, has been identified,
Background: Vaccine hesitancy threatens to reverse progress made in tackling vaccine-preventable diseases. The WHO SAGE Working Group on Vaccine Hesitancy developed the Vaccine Hesitancy Scale (VHS) to identify and compare hesitancy in different global settings. The objectives of this study were to describe and analyze vaccine hesitancy and to validate the VHS in a population of parents in Buenos Aires City, Argentina.

Methods: Cross-sectional survey in parents of 1-3 and 12-15 years old between June’18-May’19. We collected sociodemographic data, history of refusal and/or delay in children’s vaccination (hesitancy). We administered 10 Likert VHS items (higher scores indicating lower hesitancy) and verified children’s immunization records. We assessed association between: sociodemographic variables and hesitancy; hesitancy and vaccination status for five vaccines. We used Cronbach’s α to determine reliability and factor analysis to confirm survey subdomains. We examined associations between VHS scores, hesitancy and vaccination status.

Results: We included 600 parents and obtained 469 records. 11.5%(n=69) were hesitant. High maternal education level showed significant association with hesitancy (OR:2.66 95%CI:1.20-5.9) in the multiple regression analysis. Hesitancy was significantly associated with incomplete MMR status in children (OR:4.43 95%CI:1.08-8.20) and HPV in adolescents (OR:3.75 95%CI:1.54-9.12). VHS Cronbach’s α was 0.66 and factor analysis identified three underlying constructs: “Benefits”, “Harms” and “Confidence in health providers”. High scores showed association with lack of hesitancy (OR:1.2 95%CI:1.13-1.27) and complete vaccination status (OR:1.07 95%CI:1.02-1.12).

Conclusions: Our study found association between hesitancy and high maternal education level. Children with incomplete MMR and HPV vaccination status were more frequent in hesitant parents. VHS showed acceptable reliability and we identified three underlying constructs. We observed that VHS was a reliable and valid tool in this population, showing association between higher scores and complete vaccination status for specific vaccines.
HOW TO MAKE THE PUBLIC AWARE ABOUT VACCINATIONS NOT (YET) IN THE NATIONAL IMMUNIZATION PROGRAM?

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Background: There are several effective and safe vaccines outside the national immunisation program (NIP). One of these vaccines was maternal pertussis vaccination (MPV) before the introduction in the NIP at the end of 2019 in the Netherlands. We examined if our information materials (i.e. website, posters and flyers through midwifery services) about MPV had reached pregnant women by determining whether women heard or read about the vaccine (i.e. awareness), what their information need was, whether they searched for more information, and if they were already vaccinated.

Methods: In Dec 2018/Jan 2019 a survey was administered, among women who were (recently) pregnant (N = 942). Here, we will focus on pregnant women (N = 358 (38%)). The questionnaire was based on the Precaution Adoption Process Model (PAPM). This model describes how a person comes to a new decision. We adapted it to fit the situation of MPV.

Results:

Approximately 70% were aware of the vaccine (stage 1) and 87.5% thought it was an important topic in their lives (stage 2). Approximately 60% searched for more information (stage 2b) and 43% got vaccinated (stage 3). Midwives were their most used source of information. The RIVM site was used most when searching for more information. Most women thought they were able to make a decision (86.3%).

Conclusions: Midwifery services were the most common used source of information. The RIVM website was important when women wanted to have (more) information. Additional information materials provided through the involved health care professionals (HCP), seems to be an effective strategy to make the public aware of vaccinations not (yet) in the NIP. However, more research should be done into the organization of these materials and the effects within other target groups.
PATHOGENS DETECTED AMONG FEBRILE CHILDREN PRESENTING TO OUTPATIENT DEPARTMENT IN URBAN GAMBIA

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Background: The introduction of effective vaccines against childhood infections and other disease control programmes have led to a shift in the pathogens causing febrile illnesses among children. Detecting the cause of fever in children, however, remains a challenge in Africa.

Methods: Between December 2016 and September 2018, the PERFORM\(^1\) study recruited children between the ages of 1 month and 18 years who presented to outpatient with fever (≥38°C) or suspected infection, and no history of antibiotic use in the previous seven days. Samples were taken for research purposes and the children were treated following local guidelines.

Results: 500 children were included. 163 (32.5%), 190(37.9%) and 148(29.5%) were <2, 2-4 and ≥5 years of age respectively and 237 (47.3%) were female. Only 22 (4.4%) were admitted. A pathogen was detected in 261 (52.2%) of the children, see figure below. Phenotypic diagnosis, using the \(^1\)PERFORM algorithm (clinical and laboratory based) confirmed 39% and 4% of cases as definitive viral and bacterial infections respectively, and 2% had confirmed parasitic infections. The remaining 55% cases had probable or unknown diagnosis. Antibiotics were prescribed for 398(79.4%) of cases.

Conclusions: Viruses were more commonly isolated from febrile children in the Gambia. Though the final diagnosis was uncertain in most cases, most children received antibiotics. A rapid diagnostic test to differentiate viral and bacterial infection would be useful in the management of febrile children.

Acknowledgements \(^1\)PERFORM; Personalised Risk assessment in Febrile illness to Optimise Real-life
Management across the European Union, Consortium MRCG at LSHTM, Serekunda General Hospital

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EPIDEMIOLOGY OF ROTAVIRUS GASTROENTERITIS IN GREECE: COMPARISON BETWEEN EARLY AND LATE POST VACCINATION ERA.

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Background: Rotavirus gastroenteritis (RVG) is the leading cause of viral diarrhea in children. Rotavirus vaccines were licensed in Greece in 2007 and were included in the National Immunization Schedule with partial reimbursement in 2011. Aim of our study is to compare RVG epidemiology between early (2008-2011) and late (2012-2016) post vaccination period in Greece.

Methods: Demographic data and fecal samples were collected from children ≤5 years old with symptoms of acute gastroenteritis who visited emergency units of Pediatric Hospitals in Greece between 01/2008-12/2016. Samples were tested for RV Group A antigen with rapid immunochromatography assay. Positive samples were further G and P typed through RT-PCR and multi-nested PCR using specific primers for the VP7 and VP4 genes respectively.

Results: A total of 3070 children participated in the study with median age 20.5 months (±18.2). Males outnumbered females (54.6%). Most of them were ≤2 years old (60.6%) and lived in urban cities (83.2%). Genotyping was performed in 2642/3070 samples; G4P[8] (46%), G1P[8] (27.1%), G2P[4] (14.5%), G9P[8] (2.3%), G3P[8] (2.2%) and G12P[8] (2%). Mixed, unusual and zoonotic genotypes were identified in 3.8%, 1.2% and 0.8% of the samples respectively. During the late post vaccination period RVG seasonal peak was mentioned earlier in the winter and children with RVG were significantly older (p<0.001). Genotypes G1P[8] and G12P[8] were detected mostly during the early post vaccination period whereas G2P[4], G3P[8], G4P[8], G9P[8] and mixed types were significantly more common during the late post vaccination period (p<0.001).

Conclusions: During the post vaccination period RVG is caused mostly by five genotypes(>92%) , which are included in the vaccines. Although RV immunization coverage is not high in Greece, changes in the epidemiology of RVG are observed and unusual genotypes are detected.
PERIPHERAL FACIAL NERVE PALSY IN CHILDREN WITH ENTEROVIRUS INFECTION – DATA FROM THE GERMAN ENTEROVIRUS SURVEILLANCE

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\textbf{Background:} Enteroviruses (EV) are the leading causes of central nervous system infections, but their causative role in peripheral facial nerve palsy (pFP) is unresolved.

\textbf{Methods:} We retrospectively analyzed data from the German Enterovirus Surveillance (EVsurv), based at the Robert Koch Institute, Berlin, for the time period 2006 through 2019. All children with a documented affection of the facial nerve were included. EV were detected from stool and/or cerebrospinal fluid samples. Strains were consecutively serotyped. We compared children with pFP who were EV positive to those who were EV negative.

\textbf{Results:} Of a total of 35604 patients analyzed within EVsurv 2075 were reported to have pFP. EV testing was positive in 79/2075 (3.8\%) patients. Median age of EV positive patients was 6.8 years (interquartile range 3.8-8.9) compared to 10.4 years (IQR 6.9-14.1) in EV negative children (p<0.0001). The majority of EV positive patients were male (56.4\%). EV diagnosis derived mainly from stool samples (80.8\%). The majority of EV positive patients were diagnosed in the months July, August, and October (52/79). No specific EV serotype was found to be predominant.

\textbf{Conclusions:} EV infection occurs in a small yet quantifiable fraction of children with facial nerve affection within the German Enterovirus Surveillance. Further confirmatory studies are needed to support the role of EV in the aetiology of pFP.
Background: Children with sickle cell disease (SCD) are at high risk of invasive bacterial infections (IBI). Penicillin prophylaxis and vaccination have deeply modified the epidemiology of bacterial infections. Streptococcus pneumoniae remains the leading bacteria. However, most of published studies were monocentric and included small samples. We aim to conduct the first multinational study to provide an epidemiological update in IBI in the post-pneumococcal conjugated vaccine (PCV13) era.

Methods: A multinational retrospective study is designed, including confirmed IBI in SCD patients aged <18 years old, between 2014 and 2018. IBI is defined as a positive culture or bacterial polymerase chain reaction from a normally sterile fluid (blood, cerebrospinal, joint or pleural fluid, deep surgical specimen), excluding urinary tract infection. Data are collected online through REDCap. The study has obtained the approval of a French Ethics Committee.

Results: Nineteen centres from 7 countries (France(8), Belgium(3), Italy(2), Spain(2), United Kingdom(2), Nigeria and Saudi Arabia) participate in the study. All centres have access to culture to diagnose IBI and 12, also to PCR. Three centres have active files of >500 children with SCD. Participating centers for the moment account with about 130 IBI. Inclusions have started in January 2020 and 14 patients have already been included on February 27th.

Conclusions: BACT-SPRING is the first international study describing the epidemiology of invasive bacterial infection in SCD children in the post-PCV13 era. The recruitment of centres is ongoing and the aim is to include 200 patients. This study is a milestone for SPRING and its results will help updating antibiotic management and stewardship for children with SCD hospitalized for an invasive bacterial infection.
BURDEN OF INFLUENZA DURING THE FIRST YEAR OF LIFE

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Background: Every year influenza infects millions of children and causes an enormous burden of disease. Young children are at the highest risk for influenza-attributable hospitalizations. Nevertheless, a vast majority of influenza cases in young children are self-restricted and treated in outpatient settings. Despite the high incidence of influenza in children, the burden of influenza in young children treated as outpatients is poorly defined.

Methods: In this prospective cohort study, 431 infants born in June-August 2017 were followed for 10 months from 1 September 2017 to 30 June 2018. The parents filled out daily symptom diaries and were instructed to bring the children for clinical examination every time they had any signs or symptoms of respiratory tract infection. During each illness, nasopharyngeal flocked swabs were obtained and subjected to a multiplex-PCR assay for 16 different viruses.

Results: A total of 55 episodes of influenza were diagnosed among the 408 actively participating children during their first year of life, which corresponds to an annual incidence rate of 135/1000 children (95% CI 102-175). Excluding five children with double viral infection, acute otitis media developed as a complication of influenza in 23 (46%) children, and 21 (42%) were treated with antibiotics (Table). One (2%) child with influenza was hospitalized. Except for antiviral treatment, there were no differences in any other variables between influenza A and B illnesses.

<table>
<thead>
<tr>
<th></th>
<th>Influenza A (n=26)</th>
<th>Influenza B (n=24)</th>
<th>Total influenza (n=50)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Duration of illness (median, IQR)</strong></td>
<td>8.5 (6.25-15.75)</td>
<td>8 (6-10)</td>
<td>8 (6-11)</td>
</tr>
<tr>
<td><strong>Duration of fever (median, IQR)</strong></td>
<td>2 (1.25-3.75)</td>
<td>3 (1.75-4)</td>
<td>3 (1.75-4)</td>
</tr>
<tr>
<td><strong>Acute otitis media</strong></td>
<td>10 (39%)</td>
<td>13 (54%)</td>
<td>23 (46%)</td>
</tr>
<tr>
<td><strong>Antibiotic treatment</strong></td>
<td>10 (39%)</td>
<td>11 (46%)</td>
<td>21 (42%)</td>
</tr>
<tr>
<td><strong>Antiviral treatment</strong></td>
<td>23 (89%)</td>
<td>14 (58%)</td>
<td>37 (74%)</td>
</tr>
<tr>
<td><strong>Hospitalization</strong></td>
<td>0 (0%)</td>
<td>1 (4%)</td>
<td>1 (2%)</td>
</tr>
</tbody>
</table>

Table. Complications and management of influenza infections.

Conclusions: Although most children with influenza are treated as outpatients during their first year of life, almost half of them develop acute otitis media and receive antibiotics. Because influenza vaccines are licensed only from 6 months of age and protection afforded by maternal antibodies is limited, effective strategies for prevention of influenza in this vulnerable age group are needed.

Clinical Trial Registration: ClinicalTrials.gov N/A
INCREASED GENOTYPING SHOWS BELGIUM INTERRUPTED ENDEMIC TRANSMISSION OF MEASLES VIRUS IN 2018

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Background: Measles has been targeted for global elimination. Nevertheless, in 2017 the disease was still considered endemic in several European countries including Belgium. Endemic transmission is defined as a continuous chain of transmission for ≥ 12 months within a country. We used genotyping, in addition to epidemiological investigation, to enhance identification of chains of transmission for measles in Belgium during 2018.

Methods: Notification of measles cases is mandatory in Belgium. All samples for PCR are analysed at the WHO-accredited National Reference Centre. Every sporadic case and minimum one case per outbreak was selected for genotyping. In-house sequencing of the N-450 target was performed on all samples that were PCR positive. Sequences were uploaded to an international databank (MeaNS) to identify circulating subtypes.

Results: Hundred-seventeen cases were reported throughout all twelve months of the year; 28 sporadic cases and 21 outbreaks. Genotyping was done for 72 cases. One outbreak (two cases) and nine sporadic cases could not be genotyped due to either unsuitable sample type, PCR negative samples or too low viral load. The longest chain of transmission was for genotype D8-4807, which circulated 29 weeks from week 22 until week 50. Four non-genotyped sporadic cases occurred outside this time frame, at weeks 3, 9, 12 and 18.

Conclusions: Based on these findings, the WHO Regional Verification Committee declared Belgium has interrupted endemic transmission. As cases occurred throughout the year and epidemiological links are difficult to establish given the high infectivity of measles, this conclusion could only be reached thanks to genotyping. Possibly, interruption of endemic transmission had already occurred in previous years but went undetected. Therefore, collection of adequate specimens from every suspected case and the availability of sufficient funds for genotyping should be further ensured.
Background: Childhood encephalitis is a severe central nervous system infection associated with high morbidity and mortality. Encephalitis often presents with nonspecific symptoms, making early recognition challenging. The etiology, treatment and outcomes of childhood encephalitis have changed importantly since the start of effective vaccinations. Our study aimed to increase insight on clinical presentation, etiology, and clinical outcome of children with severe encephalitis in the Netherlands.

Methods: We identified patients retrospectively through the Dutch Pediatric Intensive Care Evaluation (PICE) database and included all children with a clinically diagnosed encephalitis < 18 years of age admitted to one of the eight pediatric intensive care units in the Netherlands between January 2003 and December 2013. We analyzed demographic characteristics, clinical symptoms, neurological imaging, etiology, CSF characteristics, treatment and mortality.

Results: We included 121 children with a median age of 4.6 years (IQR 1.3 – 9.8). Headache (82.1%) was the most frequently described clinical feature. In 44.6% of children no causative agent was identified. Viral- and immune-mediated encephalitis were diagnosed in 33.1% and 10.7% of patients. An age of ≥ 5 years at presentation was associated with a lower mortality (OR 0.2 [CI 0.08 - 0.78]). Detection of a bacterial (OR 9.4 [CI 2.18 – 40.46]) or viral (OR 3.7 [CI 1.16 – 11.73]) pathogen was associated with a higher mortality.

Conclusions: Children with encephalitis present with nonspecific symptoms. In almost half of the Dutch children presenting with severe encephalitis a causative pathogen could not be identified, underlining the need for enhancement of improved diagnostic tools. Children< 5 years are at a higher risk of dying from encephalitis than older children. The detection of a bacterial or viral pathogen were associated with a higher mortality.
VARIATIONS IN THE CD40 PROMOTERS PREDICT LONGITUDINAL SUSCEPTIBILITY TO MALARIAL ANEMIA AND ALL-CAUSE MORTALITY IN KENYAN CHILDREN

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Background: Molecular mechanisms which influence pediatric malaria outcome remain partially defined. Investigation of pathways leading different malaria outcomes have the potential to understanding this complex pathogenesis. Cluster of differentiation 40 (CD40) expressed on immune and non-immune cells stimulate inflammatory reactions. Polymorphisms within the CD40 promoter would impact on clinical outcomes of pediatric malaria. The influence of CD40 variations [(-580G/A; rs1800686 and -1C/T rs1883832) at enrolment and longitudinal outcomes were determined in children (n=1,370, aged ≥6 months.)] from Siaya County, western Kenya, a P. falciparum holoendemic transmission area

Methods: Genotypes were generated using Taqman® genotyping. Cross-sectional analysis was done using bivariate logistic regression analysis while longitudinal analysis was done using Cox survival analysis controlling for anemia-promoting covariates such as age at enrolment, sex, Alpha-thalassemia, HbAS, HIV-1 and bacteremia.

Results: Carriage of the -1CT genotype had significantly increased susceptibility to SMA (OR=8.09, 95%CI=2.49-26.21, P<0.001). GC was associated with 79% reduced susceptibility to SMA (OR=0.21, 95%CI=0.08-0.57, P=0.002). Longitudinally, carriage of AC haplotype consistent with its effect at enrolment revealed increase in risk of repeated malaria (OR=1.10, 1.02-1.19, P=0.018). The carriage of -1TT revealed a significantly high hazard of SMA episodes at the end of the follow-up period (HR=2.5, 95%CI=1.17-5.33, P=0.018) and increased risk to mortality (HR=2.12, 95%CI=1.08-4.14, P=0.028). The GC haplotype had an increased survival for SMA episodes (HR=0.55, 95%CI=0.32-0.97, P=0.037). The AC haplotype also revealed significantly decreased survival for malaria episodes (HR=1.09, 95%CI=1.10-1.18, P=0.024).

Conclusions: Collectively, these results demonstrate that CD40 promoter variations influence malaria disease outcomes and all-cause mortality.

Clinical Trial Registration: Not Applicable
THE EFFECT OF MATERNAL HELMINTH INFECTION ON MATERNAL AND NEONATAL IMMUNE FUNCTION AND IMMUNITY TO TUBERCULOSIS

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Background: *M. tuberculosis* and helminth infection each affects one third of the world population. Helminth infections down regulate cell mediated immune responses and this may contribute to lower efficacy of BCG vaccination and higher prevalence of tuberculosis. Hence the aim of this study was to determine the effect of maternal helminth infection on maternal and neonatal immune function and immunity to TB.

Methods: In this cross sectional study, eighty-five pregnant women were screened for parasitic and latent TB infections using Kato-Katz and QFT-GIT tests, respectively. IFN-γ and IL-4 ELISpot on Cord blood Mononuclear Cells, and total IgE and TB specific IgG ELISA on cord blood plasma was performed to investigate the possible effect of maternal helminth and/or latent TB co-infection on maternal and neonatal immune function and immunity to TB.

Results: The mean total IgE value of cord blood was significantly higher in helminth positive than negative women (p = 0.042). Cross placental transfer of TB specific IgG was significantly higher in helminth positive than negative (p = 0.002) in latent TB Infection positive participants. The IFN-γ response of CBMCs to ESAT-6/CFP-10 cocktail (p = 0.018) and PPD (p = 0.02) was significantly lower in helminth positive than negative participants. There was no significant difference in IL-4 response of CBMCs between helminth negative and positive participants.

Conclusions: Maternal helminth infection had a significant association with the IFN-γ response of CBMCs, total IgE and cross placental transfer of TB specific IgG. However, there was no significant difference in IL-4 response of CBMCs between helminth negative and positive participants. Therefore, further studies should be conducted to determine the effect of these factors on neonatal immune response to BCG vaccination.
PROTEIN BIOMARKERS THAT DISCRIMINATE BACTERIAL FROM VIRAL INFECTION IN FEBRILE CHILDREN

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Imperial College London, Paediatrics, London, United Kingdom

Background: The majority of A&E cases involving febrile children are viral in nature but those minority cases caused by bacteria demand immediate antibiotic treatment. Current methods to diagnose bacterial infection are lengthy and/or expensive and require specialist personnel and laboratory facilities. A rapid, easy to use point-of-care diagnostic test that would enable earlier diagnosis of serious bacterial infections in febrile children would lead to better patient outcomes and reduce the administration of unnecessary antibiotics, thus tackling the issue of antibiotic overuse and resistance.

Methods: To identify proteins that discriminate bacterial from viral infection we analysed serum from febrile children presenting to hospitals as part of the IRIS study with definite bacterial (DB, n=18), definite viral (DV, n=47) or indeterminate infection (n=91). For untargeted analysis, sera were analysed on cationic, anionic and IMAC arrays using SELDI-TOF mass spectrometry. Immunoprecipitation was used for protein identification and antibody-based methods for validation. For targeted analysis, a Mesoscale panel of proinflammatory cytokines and chemokines was used.

Results: We identified 80 proteins with significantly different levels (p< 0.05) between DB and DV cases from the untargeted analysis. To identify the smallest number of proteins to distinguish DB from DV, patients were randomly assigned to training (80%) and test (20%) sets and logistic regression variable selection performed. A three protein signature comprised of peaks identified at 6.4[HS1], 8.6 and 10.8kDa showed a combined AUC of 1.0. The targeted analysis identified IL-6, IL-2, IL-17 and INFα 2a as the most significant (p< 0.0001) proteins to discriminate between DB and DV cases.

Conclusions: Proteomic analysis of serum can identify proteins that discriminate between DB and DV infections that may be useful for diagnostic development.

Clinical Trial Registration: Not applicable
TYPE I INTERFERON IN VIRAL AND BACTERIAL INFECTIONS IN CHILDREN

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**Background:** Fever is one of the leading cause of consultation in pediatric emergency department (PED) under the age of 3 years old. Diagnosis of viral versus invasive bacterial infection is challenging. Type I interferons (IFNs) are implicated in antiviral responses. Secreted at femtomolar concentrations during course disease, detection of type I IFN in these patients remains challenging. We hypothesized that type I-IFN, the key cytokines of antiviral response, may represent a new early biomarker of viral infection.

**Methods:** This is an ancillary study of the prospective multicentric protocol ANTOINE. Paxgene® tubes and serum were collected from febrile children, in PED, aged from 7 days to 36 months with proven viral or bacterial infection. We have assessed the performance of IFN score, used in interferonopathies, calculated using Nanostring® technology and plasma IFN-α quantified by digital ELISA technology (Quanterix®).

**Results:** In viral infection compared to bacterial infection IFN-α levels were significantly higher (median [IQR] 7856 [3096 ; 62305] and 406 [68 ; 3708] fg/mL respectively (p<0.001) and IFN score was 30-fold higher (p<0.001). We noticed a very strong correlation between serum IFN-α concentrations and IFN score (r-spearman [IC95%] 0.85 [0.76-0.91]) Both serum level IFN-α and IFN score robustly discriminated (Area Under the Curve [IC 95%] : 0.930 [0.877-0.983] and 0.908 [0.845-0.971] respectively) between viral and bacterial infection in febrile children, compared to CRP (0.829 [0.747-0.910])

**Conclusions:** This preliminary study revealed for the first time, that IFN-α is increased in blood of febrile infants with viral infections. The performance of this promising biomarker needs to be confirmed in a larger cohort of febrile children with suspected and proven infections.

**Clinical Trial Registration:** clinicaltrials.gov (NCT03163628)
Background: Most children with fever without source (FWS) require diagnostic laboratory tests to exclude a serious bacterial infection (SBI), often followed by admission and empirical administration of broad-spectrum antibiotics. As febrile children with a viral infection are less likely to have a concomitant SBI, identifying patients with systemic viral infection could contribute to exclude an SBI. Therefore, we evaluated whether the presence of virus in the blood could be used as a biomarker to rule out an SBI in pediatric FWS.

Methods: Children <3 yo with FWS were prospectively enrolled and had real-time (reverse-transcription) PCR performed on the blood for Adenovirus, Enterovirus, Parechovirus and HHV6.

Results: 20/135 patients had an SBI and 47/135 had one virus detected in the blood. SBI was less likely among patients with viremia (p=0.011). Viremia had a higher sensitivity and negative predictive value (90% and 96%, respectively) to rule out an SBI than CRP (65% and 93%, respectively) and PCT (55% and 90%, respectively). The odds ratio (OR) for having an SBI among non-viremic patients was 5.8 (p=0.0225), compared to 5.5 and 3.7 for CRP³40mg/l and PCT³0.5ng/ml (p=0.0009 and 0.0093, respectively). This remained significant after adjusting for CRP and PCT (OR 5.6 and 5.9 respectively; p=0.03 for both). Area under the curve (AUC) for CRP and PCT were 0.754 and 0.779, respectively. When viremia was combined to CRP and PCT, AUC increased to 0.803 and 0.832, respectively.

Conclusions: The presence of viruses in the blood had a better performance than commonly used inflammatory biomarkers to rule out an SBI. Larger studies should evaluate the role of point-of-care testing of viruses by PCR in the plasma in management algorithms of children with FWS.

Clinical Trial Registration: Clinical trial registration: ClinicalTrials.gov NCT03224026
DIFFERENTIAL GENE EXPRESSION IN CHILDREN WITH SEVERE AND MILD INFECTION

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Background: Of the many children who present with infection only a small number progress to life threatening disease. We used microarray data to identify host gene expression that characterised severe disease, aiming to understand biology and develop expression signatures that allow early identification of those with severe disease.

Methods: Whole blood gene expression microarray data were available from hospitalised febrile children (IRIS study). Samples were collected early in the admission and clinical data were recorded. Bacterial or viral aetiology was assigned after comprehensive case review. Cases admitted to PICU within 24 hours were compared to cases that did not require PICU admission.

Results: There were 53 cases in the PICU group (mortality 4/53 (7.5%)) and 55 in the non-PICU group (mortality 1/55 (1.8%)). The PICU and non-PICU groups had similar phenotypes with 15 and 11 bacterial cases, and 12 and 19 viral cases in the two groups respectively. 150 genes were upregulated and 10 downregulated in the PICU group compared to the non-PICU group, satisfying p≤0.05 and log2 fold change >0.5. Pathway analysis suggested many differentially expressed genes have roles in immune signalling. One of the top genes, IRAK3, remained differentially expressed when analysis was limited to bacterial infection patients, and expression levels were stable over 5 days of PICU admission, suggesting expression may be driven by severity rather than intervention.

Conclusions: Differentially expressed genes between severe and non-severe disease phenotypes can provide insights into the biology of severe infection and have the potential to be developed into tools allowing early patient stratification to facilitate recognition of those with severe disease. Signals identified in this pilot will require validation.

Clinical Trial Registration: not applicable
Background: Leishmaniasis affects about 350 million people in 88 countries, 72 of which are developing countries. The aim was to explore the clinical and epidemiological characteristics of the cases of cutaneous Leishmaniasis, in pediatric population (0 to 17 years) in the endemic region of Lambayeque in northern Peru in South America. There are only 79 publications in pubmed focusing in pediatric Leishmaniasis.

Methods: A descriptive, retrospective study was conducted evaluating a pediatric cases series. Through observational study and protocolised review of medical records in the Leishmaniasis registry during 3 years at the Lambayeque region, 579 cases were included. We used descriptive statistics.

Results: One district called Salas at 190 meters above sea level had the highest amount of cases. The majority of the affected children were male (56.43%). The most frequent anatomic site was upper limb with 36.79%, face with 31.09% and lower limb with 24.18%. Local pruritus (47.15%) and pain (41.85%) were the main symptoms. The single lesion represented 60% of clinical presentation, the ulcerative form being the most reported with 58.01%. The median time to evolution was 4 weeks and the median of the affected body surface was 200 mm².

<table>
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<tr>
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<tr>
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<td>Trunk</td>
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<td>4.53</td>
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<tr>
<td>TOTAL</td>
<td>486</td>
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Conclusions: In this case serie cutaneous Leishmaniasis is reported mainly in boys, with a single, ulcerated, pruritic and painful lesion predominating in the upper extremities, which is different from most adult case series occurring in lower limbs.
WHOLE GENOME SEQUENCING EVALUATION OF LATE ONSET STREPTOCOCCUS AGALACTIAE IN A SPECIAL CARE BABY UNIT AND IMPACT ON INFECTION PREVENTION AND CONTROL

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Background: Invasive Streptococcus agalactiae (Group B Streptococcus) is a common cause of neonatal sepsis. Late onset disease (LOD) develops between 7 days and 3 months of age; this can result from vertical or horizontal acquisition. LOD within a specialist unit can be indicative of hospital acquired infection. Whole genome sequencing (WGS) can identify linkage of strains pointing to a common but undetermined source.

Methods: Streptococcus agalactiae was isolated from blood cultures from two babies residing in the Special Baby Care Unit (SCBU) within a 48 hour period. There was no known maternal Group B streptococcus colonisation in either mother and both babies were in the same room on the unit, 5 days apart. Isolates were serotyped at Public Health England Bacterial Reference Unit. The Scottish Microbiology Reference Laboratory used Illumina MiSeq WGS to provide MLST profiling and genomic comparison.

Results: Both isolates were identified as serotype 1A and MLST type ST-23. Single nucleotide polymorphism (SNP) comparison of genomes was carried out using BioNumerics v7.6 (Applied Maths, Belgium). The isolates were compared with 8 isolates of ST-23 identified in a collection of S.agalactiae from five Scottish hospitals. There were no SNP differences between the two isolates suggesting a common but undetermined source. The affected room was terminally cleaned, hand hygiene audits reviewed and surveillance measures instigated.

Conclusions: Our data suggests a single case of late onset Group B Streptococcus sepsis within a neonatal unit should be considered a potential hospital acquired infection. MLST profiling and WGS should be conducted on all isolates to identify linkage. Prospective surveillance for more cases and investigation of preventable sources of transmission is warranted to avoid further horizontal transmission events within units.
A two-steps score to differentiate viral from bacterial and typical from atypical bacterial pneumonia in hospitalized children


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Background: Establishing the etiology of community-acquired pneumonia (CAP) in children at admission is challenging. As a result, most admitted children with CAP receive antibiotics. We have built and validated a diagnostic tool to sequentially differentiate viral from bacterial CAP, and among bacterial CAP, typical from atypical bacteria. We hypothesized as main outcome that viral, typical bacterial and atypical bacteria could be predicted with a score combining clinical, analytical and radiographic features.

Methods: Observational, multi-center, prospective cohort study conducted in two phases in fifteen hospitals in Spain (April 2012 to March 2015 and December 2017 to May 2019). 495 hospitalized children were enrolled. We collected clinical, microbiological, analytical and radiographic variables. To select variables, a Ridge model was used. The most significantly variables associated with the etiology were searched and the weights of each level and variable were calculated from the odds ratios (OR) in a
multivariable model.

**Results:** Several variables were significantly associated with the different etiologies. A two-step score was built and validated to first differentiate viral from bacterial CAP (first step) and secondly, typical from atypical bacterial CAP (second step) with the most significantly associated variables and the weights of each level and variable (Figures). Bacterial CAPs were classified with sensitivity=97%, specificity=48%, and area under the curve (AUC)=0.81. Typical bacteria were classified with sensitivity=100%, specificity=64%, and AUC=0.90.

Step 1. OR viral vs bacterial CAP. *p<0.050; **p<0.01; ***p<0.001. Step 2. OR typical vs atypical bacterial CAP. *p<0.050; **p<0.01.

**Conclusions:** We succeeded in building a 2-step score to differentiate safely viral from bacterial CAP and typical from atypical bacterial CAP. This tool can facilitate the physician's decision to prescribe antibiotics without compromising patient safety.
SARS-COV-2 INFECTION IN PRIMARY OR SECONDARY IMMUNOCOMPROMISED CHILDREN.

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**Background:** During the SARS-CoV-2 pandemic, specific advice regarding prevention of infection was given to children thought to be more susceptible to SARS-CoV-2 such as those with chronic diseases or receiving immunosuppressive medication. Many parents expressed concerns about SARS-CoV-2.

**Methods:** Children vulnerable to infection, defined as having an indication for an annual influenza vaccination, were identified in 46 centres throughout the United Kingdom. These children/parents were invited to participate in a weekly online questionnaire study, commencing on 16th March 2020. The questionnaire included SARS-CoV-2 test results, symptoms and anxiety level (0=none, 10=high). This cohort will be followed for one year.

**Results:** The cohort size increased over a period of 15 weeks to a total of 1313 patients, mean age 10.3 years, 56% female. A total of 47845 patient days were reported during which 92 patients were tested for SARS-CoV-2, none of whom were positive. In 37% of the reported patient weeks at least one symptom associated with SARS-CoV-2 infection was reported, of which 16% were cough, 4% fever, 5% shortness of breath, 10% sore throat and 17% blocked nose. The modal parental anxiety score was 10/10 for the majority of weeks.

**Conclusions:** In this study no positive tests for SARS-CoV-2 among immunocompromised children were found although symptoms indicative of SARS-COV-2 infection were common. This suggests that either the shielding measures were effective, or that immunocompromised children are less affected by SARS-CoV-2 than adults, as is the case with immunocompetent children. Anxiety about SARS-COV-2 infection is extremely high amongst parents of immunocompromised children.
HOST BIOMARKERS ARE ASSOCIATED WITH SEVERE MALARIA IN MOZAMBICAN CHILDREN: A MATCHED CASE-CONTROL STUDY

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Background: Laboratory parameters easily measurable and associated with a higher severity risk in malaria infection would allow for early screening, risk stratification and better management of this life-threatening disease. The primary objective of this study was to identify biomarkers of inflammation and endothelial activation differentially expressed in cases of severe malaria compared to uncomplicated malaria cases.

Methods: We conducted a case-control study (2014-2016) in a rural hospital recruiting as cases pediatric patients with severe malaria (defined by World Health Organization criteria) and as controls pediatric patients with uncomplicated malaria matched by age, sex, and Plasmodium falciparum parasitaemia. We compared the levels of biomarkers associated with total parasite mass (plasma levels of HRP-2) and host response to infection: Ang-1, Ang-2, ratio Ang-2:Ang-1, sTie2, BDNF, Cys-C, sFlt-1, IL-6, IL-8, IP-10, sTNFR1, sTREM-1, between both groups. We also compared those levels between children with different severe clinical manifestations and scores using the Lambaréné Organ Dysfunction Score (LODS).

Results: Levels of Ang-2, Ang-2: Ang-1 ratio, sTie-2, sFlt-1, IL-6, IL-8, IP-10, TFNR1, sTREM-1 were significantly higher in children with SM when compared with matched controls with uncomplicated malaria. After application of Bonferroni correction for multiple-comparisons Ang-2, sFlt-1 and IL-8 levels were still significantly higher in children with SM. sFlt-1, IL-6 and IL-8 levels were higher among those children with higher LODS scores. HRP-2 levels were not significantly different between severe cases and their matched controls although HRP-2 levels were strongly correlated with levels of Ang-2.

Conclusions: Host biomarkers associated with endothelial activation and inflammation can reliably identify those patients with a greater severity. Ang-2 is the most promising candidate for future clinical applications as it can be used to guide malaria diagnosis and tailor supportive treatment.

Clinical Trial Registration: This is not a clinical trial
SHOULD AMOXICILLIN BE THE PRAGMATIC FIRST-LINE ANTIBIOTIC FOR PAEDIATRIC BACTERIAL PHARYNGITIS?

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Background: The UK National Institute of Clinical Excellence guidelines recommend phenoxymethylpenicillin (pen V) as first-line treatment of bacterial pharyngitis in paediatrics. However, growing evidence suggests amoxicillin may be better tolerated, cheaper and equally effective. Amoxicillin is already a first-line treatment in many healthcare settings. We explored variation in prescribing practice for bacterial pharyngitis nationally across the UK. We also surveyed a cohort of patient families at a tertiary paediatric centre to understand their contrasting experiences of amoxicillin and Phenoxymethylpenicillin administration in suspected bacterial tonsillo-pharyngitis.

Methods: We retrospectively identified 723 consecutive pharyngitis presentations at a UK tertiary paediatric centre and reviewed their notes. We identified those prescribed antibiotics and contacted their families. We completed a short survey related to patient and family experience with each family. We went on to establish national prescribing practice across the UK for paediatric tonsillo-pharyngitis. A total of 155 English emergency departments were consulted by telephone regarding their first line antibiotic choices and rationale for prescriptions.

Results: Whilst compliance was similar for pen V and amoxicillin, patients were most satisfied with amoxicillin (overall satisfaction score 8.9/10 compared to 6.7 for pen V (p=0.0003)). Disagreeable taste, administration challenges, and impractical dosing schedules were reported by families receiving pen V. National prescribing practice varies: eleven units (8%) recommend amoxicillin first-line, four (2.6%) recommend either pen V or amoxicillin and the remaining 137 units recommend pen V. Practice is heterogeneous regarding both course length and rationale. A course of amoxicillin (£1.40) was found to be less expensive than pen V (£5.06).

Conclusions: We believe there is a case for following international precedent and offering amoxicillin as a first-line alternative to pen V for cases of bacterial pharyngitis requiring antibiotics. Amoxicillin could offer superior patient experience at lower cost without sacrificing efficacy.
COMMUNITY-BASED ANTIBIOTIC DISPENSING ATTRIBUTABLE TO RESPIRATORY SYNCYTIAL VIRUS AND OTHER COMMON RESPIRATORY VIRUSES: A POPULATION-BASED STUDY OF YOUNG SCOTTISH CHILDREN, 2009-2017

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Background: Recent research suggests inappropriate antibiotic prescribing, such as that for viral illness, is common in primary care. This is of growing interest given concerns around antimicrobial resistance and harms associated with unnecessary treatment. The objective of this study was to estimate the proportion of community-dispensed antibiotics among children attributable to respiratory syncytial virus (RSV) and other common respiratory viruses.

Methods: We fit time series negative binomial models to predict weekly antibiotic dispensing rates from positive viral pathogen tests rates for the period April 1, 2009 through December 27, 2017 using comprehensive, population-based administrative health data for all children (<5 years) living in Scotland. We used these models to estimate the proportion of dispensed antibiotics explained by the circulation of RSV, influenza, human metapneumovirus (HMPV) coronavirus, adenovirus, rhinovirus, enterovirus, and parainfluenza viruses among children. We stratified our analysis to investigate differences according to age, presence of chronic conditions, and antibiotic class.

Results: We included data on over 6 million antibiotic prescriptions among 762,357 children. Based on our model, an estimated 6.9% (95% CI: 5.6, 8.3), 2.4% (1.7, 3.1), and 2.3% (0.8, 3.9) of antibiotics were attributable to RSV, influenza and HMPV, respectively. RSV was consistently associated with the highest proportion of antibiotics prescribed but particularly among children without chronic conditions and for amoxicillin and macrolides.

Conclusions: Nearly 14% of antibiotics prescribed to children in this study were estimated to be attributable to common viral pathogens for which antibiotics are not recommended, such as RSV. This highlights clear targets for antibiotic stewardship programs and further suggests antibiotic prescribing could be considerably reduced among children once an RSV vaccine is introduced in the coming years.
PEDIATRIC TUBERCULOSIS DISEASE DURING YEARS OF HIGH REFUGEE ARRIVALS: A 6-YEAR NATIONAL PROSPECTIVE SURVEILLANCE STUDY

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Background: In Europe surveillance and monitoring of tuberculosis (TB) remains important, particularly in the light of high refugee influx in recent years. The aim of the study was to analyze demographics, risk factors, clinical, diagnostic and treatment characteristics of pediatric TB in Switzerland.

Methods: Data was prospectively collected through the Swiss Pediatric Surveillance Unit (SPSU) in 33 pediatric clinics from December 2013 to November 2019. Case definition included children <16 years with culture- or molecular-confirmed disease from *M. tuberculosis*, *M. africanum*, *M. bovis*, *M. caprae* or “Mycobacterium complex” or for whom treatment with ≥ 3 anti-mycobacterial drugs had been initiated.

Results: A total of 139 cases were included in the final analysis. The median age was 6.7 years (IQR 1.6 to 13.8 years). A total of 72 (51.8%) cases were Swiss-born. The median TB incidence was 1.8 per 100'000 children, with the highest annual incidence in 2016 with 2.17 per 100'000 children. Incidence rates in Swiss-born children remained stable with a median of 1.0 per 100'000 children and were significantly lower compared to the TB incidence in foreign-born children with a maximum 13.7 per 100'000 children in 2016.

Conclusions: The annual TB incidence varied only among foreign-born children with highest in 2016 associated with high rates of refugee arrivals. The data from Switzerland show high rates of culture or molecular confirmation.
IMPACT OF THE UK QUADRIVALENT MENACWY IMMUNISATION PROGRAMME ON OROPHARYNGEAL CARRIAGE OF MENINGOCOCCI IN ADOLESCENTS

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Background: The UK introduced an adolescent conjugate-MenACWY immunisation programme in 2015 in response to increasing group W:ST-11cc Invasive Meningococcal Disease (IMD). Uptake was 79-86% in the eligible cohort (13-19 year-olds). The impact of a population-level conjugate-MenACWY immunisation programme on carriage and contribution to herd protection has not been reported.

Methods: Comparison of culture-defined oropharyngeal carriage in UK school students (16-19yrs) between two cross-sectional carriage studies conducted pre/post MenACWY introduction: “UKMenCar4” Study (2014/15) and “Be on the TEAM” (2018 - ongoing), a controlled trial evaluating the carriage impact of 4CMenB and MenB-fHbp.

Results: 10625 and 13488 participants were included from the pre-implementation and post-implementation cohorts, respectively. Between 2014/15 and 2018, genogroup Y carriage decreased from 1.61% to 0.50% (OR 0.30, 95% CI 0.23 – 0.40; p<0.001) and genogroup W carriage decreased from 0.33% to 0.09% (OR 0.26, 95% CI 0.14 – 0.50; p<0.001). Genogroup B meningococci carriage did not change (1.26% vs 1.22% p=0.8) and genogroup C remained rare. The percentage of isolates that were sero-groupable, i.e. expressing a capsule, decreased amongst genogroup W isolates from 79% [n=78/99] to 42% [n=5/12] (OR 0.19, 95% CI 0.06–0.64; p=0.005) and genogroup Y isolates from 75% [n=261/347] to 47% [n=31/66] (OR 0.29, 95% CI 0.17–0.50; p<0.001).

Conclusions: The MenACWY vaccine decreases carriage of genogroup Y and W meningococci and the proportion of these genogroups expressing a capsule. This supports the hypothesis that the reduction in MenW IMD in unimmunised age groups since conjugate-MenACWY introduction is a herd immunity effect induced by vaccinating the age-group of peak meningococcal carriage. Funding: “UKMenCar4” NIHR(PS-ST-0915-10015) & Wellcome Trust(087622). “TEAM” NIHR-PRP(Pr-R18-0117-21001). View expressed are authors own and not necessarily those of the NHS/NIHR/DHSC, arms-length bodies or other government departments. MenB-fHbp donated by Pfizer.

Clinical Trial Registration: EudraCT: 2017-004609-42
**Background:** Sparse data are available regarding accuracy of Xpert MTB/RIF (Xpert) and Xpert MTB/RIF Ultra (Ultra) assays for the diagnosis of paediatric pulmonary tuberculosis (PTB) in low TB burden settings. Moreover, no study evaluating the performance of Ultra assay was conducted using gastric aspirate lavage (GLA) specimens, frequently collected in children. We evaluated the accuracy of Xpert and Ultra in GLA samples for the diagnosis of childhood PTB and the detection of rifampicin-resistance, in a low-TB-incidence country.

**Methods:** Data from children consecutively referred to the Infectious Disease Unit, Meyer Hospital, Florence, Italy, for suspected PTB from 2013 to 2019 were retrospectively collected. Three consecutive GLAs were obtained for smear microscopy, culture and Xpert or Ultra assays, and results analysed.

**Results:** Seventy-six children were enrolled (median age: 81.8 months). Xpert and Ultra were performed in 30 and 46 children. Sixty PTB cases were clinically diagnosed. Culture and smear microscopy were positive in 30/60 and 9/60 children, respectively. In culture-confirmed PTB cases, Ultra sensitivity was significantly higher than microscopy sensitivity (84.2%;95%CI:63.3-94.5 vs. 30.0%; 95%CI:16.7-47.9%). Conversely, Xpert and smear microscopy sensitivities were similar (45.5%;95%CI: 21.3-72.0). Xpert/Ultra correctly identified the only rifampicin-resistant child, with 100% correspondence with drug susceptibility test (DST). Three rifampicin-susceptible, mono-resistant PTB cases were evidenced by DST.

**Conclusions:** Ultra assay in GLA samples is a useful diagnostic tool in paediatric PTB, since it allows to increase of the proportion of PTB cases with *M. tuberculosis* detection. Novel assays, able to detect resistance profiles to numerous anti-tubercular drugs, will be strategic.
EFFECTIVENESS AND IMPACT OF THE 4CMENB VACCINE AGAINST GROUP B MENINGOCOCCAL DISEASE IN TWO ITALIAN REGIONS USING DIFFERENT VACCINATION SCHEDULES: A FIVE-YEAR RETROSPECTIVE OBSERVATIONAL STUDY

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Background: Few years after the introduction in Italy of a four-component anti-meningococcal B vaccine (4CMenB), we evaluated, through an observational retrospective study, the effectiveness and impact of vaccination in two regions using different schedules (2,4,6,12 months in Tuscany vs 7,9,15 months in Veneto).

Methods: Vaccination started in 2014 in Tuscany and in 2015 in Veneto; data collected referred to period 2006-2018 for Tuscany and 2007-2018 for Veneto. Cases of invasive meningococcal disease due to N. Meningitidis B were identified by culture and/or realtime-PCR. Effectiveness was calculated with the Farrington’s method.

Results: In Tuscany, pre-vaccine incidence was 1.96 (95%CL 1.52;2.40) and 0.62 (95%CL 0.60;0.64) in post-4CMenB era. In Veneto, pre-vaccine incidence was 1.94 (95%CL 1.92;1.96) and 1.34 (95%CL 1.31;1.38) in post-4CMenB era. In vaccinated children, post-4CMenB incidence were respectively 0.12 (95%CL 0.08;0.15) and 0.53 (95%CL 0.50;0.56). Vaccine effectiveness resulted 93.6% (95% CL 55.4;99.1) in Tuscany and 91.0% (95%CL 59.9;97.9) in Veneto with mean vaccine coverages of 83.9% and 81.7% respectively. The overall impact (evaluating both vaccinated and unvaccinated children) was 0.68 (95%CL 0.10;0.89) in Tuscany and 0.31 (95%CL -0.56;0.69) in Veneto.
Conclusions:

In conclusion 4CMenB appears to have a very high effectiveness in Italy; the impact of vaccination appears greater where the immunization program is started early.

Incidences of Invasive meningococcal disease in children 0-5 years of age pre and post introduction of 4CMenB in Tuscany (A) or Veneto (B).

Crude incidence rate and 95% CI of IMD are shown in blue for the pre-4CMenB era and in orange for the post-4CMenB era for each year of age. In Tuscany, 3 out of 4 cases of IMD and in Veneto 5 out of 7 cases of IMD in post-4CMenB era occurred in non-vaccinated children.

Conclusions: In conclusion 4CMenB appears to have a very high effectiveness in Italy; the impact of vaccination appears greater where the immunization program is started early.
THE IMPACT OF THE MENINGOCOCCAL C CONJUGATE VACCINE ON THE INCIDENCE OF MENINGOCOCCAL DISEASE IN DISTINCT BRAZILIAN REGIONS

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Background: Infections by *Neisseria meningitidis* are a major public health problem, making it necessary to implement the Meningococcal C Conjugate (MCC) vaccine. However, the control of an infection disease is made also with other public health development measures, which differ among regions. We aimed to evaluate the impact of MCC vaccine implementation in the Brazilian population by administrative region.

Methods: A descriptive ecological study and population-based analysis was developed. Data were collected on the DATASUS platform. Diseases and Notifiable Diseases (SINAN) and meningitis from 2002 to 2018 were selected. We searched for cases reported in all age groups from the etiologies: meningococcemia, meningococcal meningitis and both. The vaccine was implemented in 2010, so the pre-exposure period defined from January 2002 to December 2009 was compared to the post-exposure period from January 2011 to December 2018. Linear regression was performed to assess the trend of the incidence coefficient between these periods.
In Brazil, 42,034 cases of Meningococcal Disease cases occurred in all age groups in the period from 2002 to 2018. A declining trend was observed in probability of falling ill due to meningococcal disease, through the incidence coefficient, in all Brazilian regions, with the greatest reduction being observed in Southeast (2.46 to 0.67 notifications/100,000). The downward trend of the coefficient was more pronounced in the pre-exposure period compared to the post-exposure in the North, Northeast and South regions. Linear regression confirmed this tendency, being statistically significant (p<0.05).

**Conclusions:** The MCC vaccine has a different impact in each region. This suggests that control strategies for an infectious disease should be individualized in distinct places and based in multiple public health care measures in addition to vaccine implementation.
Background: Children with Shiga-toxin producing *Escherichia coli* (STEC) infections may develop hemolytic uremic syndrome (HUS). Consequences include acute kidney injury, renal/neurologic sequelae, and death. Risk stratifying children with HUS can guide early intervention and avoid these events. We assessed the ability of an HUS severity score in predicting adverse outcomes among children who initially presented to the emergency department.

Methods: We reviewed records of children <18 years-old with STEC infections, treated in one of 38 participating EDs, from 2011-2015. The severity score was calculated using the first available results, and equals the hemoglobin (g/dL) plus two times serum creatinine (mg/dL). Children with scores >13 were designated as having increased likelihood of adverse outcomes. We assessed score performance to predict severe adverse events (dialysis, neurologic complication, respiratory failure and death) using discrimination, calibration, and net benefit, with subgroup analyses by age.

Results: Of 167 children with HUS, 155 had sufficient data for score calculation. From these 155
children, 60.4% experienced severe adverse event(s). While discrimination was acceptable overall (AUC 0.71; 95% CI 0.63,0.79), it was best for children <5 years of age (AUC 0.77; 95% CI 0.68,0.87). Physicians who could tolerate a threshold probability for adverse events of >26% had the highest benefit, when they utilize the score for risk-stratification rather than treating all children.

Conclusions: In the ED, the HUS severity score was able to distinguish children at high vs. low risk of severe adverse outcomes (especially for children <5-years-old). This score may help clinicians guide resource allocation to those at highest risk. However, utilizing the score would only yield greater benefit than a treat-all approach if a clinician would not intervene unless the probability of a severe adverse outcome was at least 26%.
COMMUNITY MAPPING AND ENGAGEMENT TO CO-CREATE A ONE HEALTH UNDER-5 (U5) INFECTION IN URBAN SLUMS CONCEPTUAL DIAGRAM: THE CHILDHOOD INFECTION AND POLLUTION (CHIP) CONSORTIUM

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\textbf{Background:} Rapid, unchecked urban migration is leading to expanding urban slums creating environments where disease-causing bacteria, viruses and parasites can thrive. Infections are a leading cause of mortality in U5s and the health effects of these infections are exacerbated by increasing antimicrobial resistance (AMR) from poor antibiotic governance, especially where rates of antibiotic consumption and resistance are highest. The Childhood Infections and Pollution Consortium (CHIP) was designed to reduce the burden of childhood infections and AMR in urban slums using One Health and technology-enabled Citizen Science approach.

\textbf{Methods:} Between September-December 2019, we undertook fieldworks and engaged with mothers and key informants in urban slums in Jaipur, Jakarta and Antofagasta. We utilised a geo-tagged action camera in transect walks to observe infection pathways. Social mapping with slum-dwellers produced a detailed map of slum level variables. 1:1 interview, via mobilising with the community, explored the community’s understanding of infections and the social-cultural context in the feasibility of sample collection.

\textbf{Results:} Preliminary data analysis supported the co-production of a conceptual map and interviews explored slum dwellers’ understanding of infections and gave us insight into the feasibility of collecting biological and non-biological samples in the future. The map summarises the complex relationships we are investigating and serves as a roadmap to identifying specific research questions and designing effective SDGs focused interventions.

\begin{center}
\includegraphics[width=\textwidth]{conceptual_diagram.png}
\end{center}
Conclusions: This fieldwork allowed us to observe environmental and living conditions, potential human-livestock interactions, potential pathways to infections for children and to explore the feasibility of sampling procedures that would be acceptable to the individual communities. Participatory GIS, digital footprints for disease tracking using mobile phones, sensors to detect water/air pollution, mould & temperature provide a novel opportunity to continuously facilitate communities to record data throughout the complex intervention design of CHIP.

Clinical Trial Registration: This is not a clinical trial.
C-REACTIVE PROTEIN, PROCALCITONIN AND WHITE BLOOD COUNT TO RULE OUT NEONATAL EARLY-ONSET SEPSIS WITHIN 48 HOURS: A SECONDARY ANALYSIS OF THE NEOPINS STUDY


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**Background:** Neonatal early-onset sepsis (EOS) is one of the main causes of global neonatal mortality and morbidity and initiation of early antibiotic treatment is key. But antibiotics may harm: Increasing resistance due to overuse of antibiotics and alteration of the individual microbiome are the potential downside of unnecessary antibiotic use.

**Methods:** Secondary analysis of NeoPIns, a prospective, multi-centre, randomised controlled intervention study: Primary outcome was the diagnostic accuracy of serial measurements of C-reactive protein (CRP), procalcitonin (PCT), and white blood count (WBC) within different time windows to rule out culture-positive EOS (proven sepsis).

**Results:** We analysed 1678 neonates with 10,899 biomarker measurements (4654 CRP, 2047 PCT and 4198 WBC measurements) obtained within the first 48 hours after start of antibiotic therapy due to suspected EOS. The area under the curve (AUC) comparing no sepsis versus proven sepsis for maximum values of CRP, PCT and WBC within 48 hours were 0.986, 0.921, and 0.386, respectively. The AUC for CRP and PCT increased with extended timeframes up to 36 hours but there was no further difference between start to 36 versus start to 48 hours. Cut-off values at 16mg/l for CRP and 2.8ng/l for PCT provided a sensitivity of 100% for discriminating no sepsis versus proven sepsis.

**Conclusions:** Normal serial CRP and PCT measurements within 36h after the start of empiric antibiotic therapy can exclude the presence of neonatal EOS with a high probability. The negative predictive values of CRP and PCT do not increase after 36 hours.

**Clinical Trial Registration:** Clinicaltrials.gov (NCT00854932)
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Background: Since December 2019, when the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) first appeared in China, has spread rapidly across the world affecting all ages. Even though the fact that the heaviest death toll has been paid by the elderly, pediatric populations have also been affected. Our aim was to present the clinical management of the first 5 neonates and very young infants that have been admitted to the largest tertiary Children’s Hospital in Greece during the first 3 months of the pandemic.

Methods: All pediatric patients with suspected COVID-19 who were hospitalized between February and May 2020 at “Aghia Sophia” Children’s Hospital were tested for SARS-CoV-2. Confirmed cases were defined through nasal and/or pharyngeal swabs positive for SARS-CoV-2 nucleic acid by using real-time reverse transcriptase polymerase chain reaction (RT-PCR) test and were admitted to the dedicated COVID-19 Unit of the hospital.

Results: Five neonates and very young infants were found positive for SARS-CoV-2. All patients were male, with ages ranging from 11 days to 3 months. In all but one infant, at least one family member was tested positive for SARS-CoV-2 but with no symptoms of infection. All infants presented with mild symptoms, non-specific laboratory findings and did not require specific treatment. Three infants presented with neutropenia but none with lymphopenia. Prolonged viral shedding has been detected in nasopharynx up to 35 days after admission.

Conclusions: According to our experience, very young age does not predispose for severe disease but could be a risk for prolonged viral transmission.
MYCOPLASMA PNEUMONIAE-SPECIFIC IFN-Y-PRODUCING CD4+ EFFECOR-MEMORY T CELLS CORRELATE WITH PULMONARY DISEASE

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Background: Mycoplasma pneumoniae (Mp) is a major cause of community-acquired pneumonia (CAP) in children. Lymphocyte responses against Mp have been reported to promote either protection or immunopathology in mice. In humans, intradermal injection of Mp antigen elicited a delayed-type hypersensitivity (DTH) skin reaction in patients with serologically confirmed Mp infection. The size of the induration of the DTH skin reaction depends on CD4+ T helper cell type 1 (Th1) and correlated with the severity of pulmonary infiltrates in those patients. These observations suggest that the pathogen-specific T-cell response contributes to pulmonary disease in Mp CAP.

Methods: This is a prospective longitudinal study of 63 community-acquired pneumonia (CAP) patients and 21 healthy controls (HC), 3–18 years of age, from 2016 to 2017. Mp-specific interferon (IFN)-γ producing peripheral blood mononuclear cells (PBMCs) were measured by enzyme-linked immunospot (ELISpot) assay.

Results: The assay detected IFN-γ released by PBMCs after stimulation with Mp antigen most frequently and pronounced in Mp PCR-positive (Mp+) CAP patients. In contrast, no or very low numbers of IFN-γ spot-forming units (SFU) were measured in Mp- HC (carriers), Mp PCR-negative (Mp-) CAP patients and Mp- HC (P<0.001). The Mp-specific IFN-γ response was long-lasting and also detectable in the convalescent stage. Depletion of CD4+ T cells reduced IFN-γ SFU by 96% upon 24h pre-incubation with Mp antigen. The majority of IFN-γ+CD4+T cells was detected in the effector-memory T-cell (T_EM) compartment. The extent of pulmonary disease reflected by increased chest radiograph (CXR) severity correlated positively with the degree of the specific IFN-γ response (P=0.02, R=0.50).

Conclusions: These data indicate that CD4+ effector-memory T cells form the major population of the pathogen-specific IFN-γ response in children with Mp CAP, and that the presence of these Th1 cells in peripheral blood correlates with pulmonary disease severity. These data further support the hypothesis that host cell-mediated immunity is involved in the pathogenesis of Mp pulmonary disease.

Clinical Trial Registration: NCT03613636
INCREASED SERUM LEVELS OF SCD14 AND SCD163 INDICATE A PREPONDERANT ROLE FOR MONOCYTES IN COVID-19 IMMUNOPATHOLOGY

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Background: Emerging evidence indicates a potential role for monocyte in COVID-19 immunopathology. We investigated two soluble markers of monocyte activation, sCD14 and sCD163, in covid19 patients with the aim of characterizing their potential role in monocyte-macrophage disease immunopathology. To the best of our knowledge, this is the first study of its kind.

Methods: Fifty-nine SARS-Cov-2 positive hospitalized patients, classified according to ICU or non-ICU admission requirement, were prospectively recruited and analyzed by ELISA for levels of sCD14 and sCD163, along with other laboratory parameters, and compared to a healthy control group.

Results: sCD14 and sCD163 levels were significantly higher among COVID-19 patients, independently of ICU admission requirement, compared to the control group. We found a significant correlation between sCD14 levels and other inflammatory markers, particularly Interleukin-6, in the non-ICU patients’ group. sCD163 showed a moderate positive correlation with the time at sampling from admission, increasing its value over time, independently of severity group.

Conclusions: Monocyte-macrophage activation markers are increased and correlate with other inflammatory markers in SARS-Cov-2 infection, in association to hospital admission. These data suggest a potentially preponderant role for monocyte-macrophage activation in the development of immunopathology of covid19 patients.

Clinical Trial Registration: Not applicable
MATERNAL ANTIBODIES IN MILK AFTER VACCINATION; RESULTS FROM THE MAMA STUDY

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**Background:** Despite high vaccination coverage, the incidence of pertussis in high-income countries has risen in recent years. Pertussis vaccination in pregnancy is a strategy employed to protect infants. However, no study has examined the impact of timing of antenatal vaccination on pertussis specific antibody levels in breastmilk postpartum. This pilot study was designed to provide information about this important aspect to inform future work.

**Methods:** We recruited participants who had received the Tdap vaccine in pregnancy. Maternal serum and colostrum samples were collected within 48 hours of delivery and further breastmilk samples collected at two and six weeks postpartum. These were then analysed using ELISA.

**Results:** We recruited 41 women who had received the Tdap vaccination in pregnancy: 20 vaccinated from 16-23+6 gestational weeks (GW), 12 from 24-27+6 GWs and nine from 28-36 GWs. This study was not adequately powered to assess the significance of differences in antibody concentration following vaccination at different time points, however no differences were detected in sIgA (Figure 1) or IgG.
against pertussis toxin (PT) in colostrum and breastmilk of women vaccinated at different gestations.

There was moderate correlation for sIgA against PT between the colostrum sample and the breastmilk sample taken at two weeks \((r=0.63)\) and strong correlation for sIgA against PT between the breastmilk samples taken at 2 and 6 weeks \((r=0.83)\).

**Conclusions:** Our findings show no relationship in the concentration of IgG and sIgA against PT after Tdap vaccination at different gestations. This suggests that the timing of antenatal Tdap vaccination does not significantly alter the level of pertussis-specific passive immunity provided to the breastfeeding infant via breastmilk. This should be considered further in larger studies assessing the timing of pertussis vaccination in pregnancy.

**Clinical Trial Registration:** ClinicalTrials.gov NCT03982732
Background: In the Sched3 trial, children were randomised to receive a reduced ‘1+1’ schedule of PCV13 (given at 3 and 12 months) versus a 2 + 1 schedule (2, 4 and 12 months). We previously reported this reduced schedule resulted in a lower group C meningococcus serum bactericidal antibody (SBA) titres at 1 month following administration of a combination Haemophilus influenzae type b and group C meningococcus vaccine using tetanus-toxoid carrier protein (Hib-MenC -TT) at 12 months. Here we report on whether this influence persisted through the second year of life.

Methods: Blood samples were taken at approximately 2 years of age from children previously enrolled into the Sched3 study, one year following administration of HibMenC -TT at 12 months. Rabbit complement SBA (rSBA) titres against a Men C reference strain were determined.

Results: Seventy-six children had bloods taken between 21 and 33 months of age. The proportions of participants with rSBA titres ≥8 from follow-on bloods were 58.8% (40.7-75.4) in PCV13 2+1 recipients and 33.3% (19.1-50.2) in PCV13 1+1 recipients (p =0.04). rSBA geometric mean titres were 9.4 (5.3-16.7) and 5.0 (3.2-7.8) respectively, p = 0.04.

Conclusions: The introduction of the reduced dose (1+1) schedule of PCV13 in the UK in 2019 may result in an unexpected, and persistent, reduction in MenC rSBA titres. Given these vaccines use different carrier proteins (CRM197 and tetanus toxoid), this highlights the complex and unpredictable nature of polysaccharide conjugate vaccine interactions. While continued use of an adolescent MenC containing vaccine in the UK is likely to maintain herd protection across all ages, ongoing surveillance is required to assess the impact this has on meningococcal C disease incidence in immunised infants. Funded by NIHR Policy Research Programme and Gates Foundation.

Clinical Trial Registration: Assessment of Post Booster Antibody Responses in UK Infants Given a Reduced Priming Schedule of Meningococcal Serogroup B and 13 Valent Pneumococcal Conjugate Vaccines ClinicalTrials.gov identifier (NCT number): NCT02482636
RATES OF CMV SEROCONVERSION IN PREGNANCY AND CONGENITAL CMV INFECTION IN CRETE, GREECE


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Background: Congenital Cytomegalovirus (CMV) infection causes substantial morbidity and neurodevelopmental sequelae and remains a silent global epidemic. However, CMV seropositivity in women of childbearing age and the burden of congenital CMV infection have great variability in different parts of the world. We evaluated the CMV seroconversion in pregnant women as well as the rates of congenital CMV infection in our area.

Methods: Retrospective study, that included demographic and serological data of all pregnant women, who delivered, in four major public hospitals (Heraklion University Hospital, Venizeleion General Hospital of Heraklion, “St. George” General Hospital of Chania and General Hospital of Agios Nikolaos) in Crete, Greece from January 2017 to December 2018. The rates of congenital CMV infection during the same period were also recorded.

Results: A total of 5,485 pregnant women were included. In 4,940/5,485 (90.1%) the CMV serology had been evaluated. Immune to CMV (IgG positive, IgM negative, without evidence of recent seroconversion) were 3,334/4,940 pregnant women (67.5%). Seroprevalence was significantly affected by ethnicity but not by age. Among the non-immune women (IgG negative, IgM negative), seroconversion was noted in 62/1,606 (3.9%) during pregnancy. All neonates with a history of maternal seroconversion during gestation were evaluated postnatally and 7 cases of congenital CMV were detected.

Conclusions: Prenatal CMV screening of pregnant women is widely performed in our area; however it was not universally applied. Seroconversion rates were low by not negligible. Differences were recorded among women of different nationalities. Congenital CMV infection rates were also low; however there is no information on potentially missed cases due to failure to identify prenatally primary CMV infection, reinfeciton or CMV reactivation.
Background: Antimicrobial resistance is a recognized public health danger that limits our ability to treat infections. Surveillance of antibiotic consumption is essential for antibiotic stewardship programs. WHO’s antibiotics “Access, Watch and Reserve” (AWaRe) classification can be used to map the use of antibiotics in children. We aimed to describe the antibiotic consumption in Greece using this classification and to check for trends between two periods.

Methods: Data on antibiotic prescriptions in Greece, for patients aged ≤19 years old between (07/2010-06/2013) and (04/2015-03/2018), were extracted from the Intercontinental Marketing Services (IMS) HealthXponent database which contains a 100% projection of prescribing activity in the community. Antibiotics were grouped based on the classification used in the WHO’s 2017 revision of the Essential Medicines List for children (EMLc). Antibiotics not represented were grouped as ‘Unclassified’. We described trends in prescribing of antibiotics over the two periods. Amoxicillin index was calculated as the number of amoxicillin prescriptions divided by the total. Access-to-Watch index was calculated.

Results: There were 7,005 (x10^3) prescriptions in children for 2010-2013 and 6,323 (x10^3) for 2015-2018. The prescriptions by AWaRe groups can be seen in Table 1. There was an increase in prescribing of ‘Access’ vs ‘Watch’ group in the 2nd period (p<0.001) which lead to a higher Access-to-Watch index, while the Amoxicillin index showed only a small increase by 1.4%. No prescriptions in the reserve group as expected for this population.

Table 1 – Pediatric Antibiotic Prescribing in Greece, grouped by WHO’s Access, Watch, Reserve (AWaRe) Groups, in 2010-2013 and 2015-2018

<table>
<thead>
<tr>
<th>ACCESS</th>
<th>2010-2013</th>
<th>2015-2018</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>34.3%</td>
<td>41.5%</td>
</tr>
<tr>
<td>WATCH</td>
<td>32.4%</td>
<td>26.5%</td>
</tr>
<tr>
<td>RESERVE</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td>UNCLASSIFIED</td>
<td>33.4%</td>
<td>32.0%</td>
</tr>
</tbody>
</table>

Indexes

- Access-to-Watch Index*: 1.06 vs 1.57
- Amoxicillin Index*: 8.5% vs 9.90%

*Amoxicillin index = number of amoxicillin prescriptions divided by the total.
*Access-to-Watch index = the ratio of ‘Access’ to ‘Watch’ prescriptions

Conclusions: Antibiotic consumption in the pediatric outpatient setting in Greece as measured in prescriptions and classified in WHO’s AWaRe groups changed over the years, showing an increase of prescriptions in the ‘Access’ versus the ‘Watch’ group in 2015-2018 when compared to 2010-2013.
Mapping antibiotic use using prescriptions and the AwaRe classification can be a useful tool for the stewardship efforts in Greece.
POLYMICROBIAL GASTROENTERITIS IN CHILDREN

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Background: In some cases of gastroenteritis, a single host is infected by two or more pathogens. Coinfecting pathogens have been associated with more severe diarrhea than infection with a single pathogen; however the causative agents and their potential associations remain elusive. We aimed to determine the rate and the characteristics of bacterial enteropathogens that act synergistically to cause polymicrobial gastroenteritis in children.

Methods: Retrospective cohort study that included all the bacterial enteric pathogens, isolated the last 27 years from 0-18 years old children, with acute diarrhea, in Crete, Greece. Any cases due to viral or parasitic gastroenteritis were excluded. Differences in age, seasonal distribution, hospitalization rates, antimicrobial resistance and pathogen associations were investigated by comparing co-detection and mono-detection frequencies for all pairwise pathogen combinations.

Results: In 53 (2.74%) children, two or more enteropathogens were isolated. Two pathogens were isolated in 52/53 (98.1%) and 3 pathogens in 1/53 (1.9%). Children with coinfection were younger (p 0.0001). Coinfection was more prevalent during summer (p 0.04) but was not associated with higher hospitalization rates. E. coli, especially strain O127:B8, and Shigella spp were significantly more prevalent in polymicrobial gastroenteritis (79.2% vs 12.4% of mono-infection, p 0.001 and 3.7 vs 0.3% in mono-infection, p 0.01 respectively). E. coli was positively associated with Campylobacter spp and Salmonella spp (p 0.001).

Conclusions: E.coli and Shigella spp was most commonly associated, as co-infecting agents, with polymicrobial gastroenteritis in children in our area. A strong interaction of those agents with the intestinal epithelium may explain their ability to co-exist with other pathogens. Pathogens such as Campylobacter spp and Salmonella spp may also interact in a manner that enhances the pathogenicity of several E. coli strains.
HUMAN RHINOVIRUS LOWER RESPIRATORY TRACT INFECTION SEVERITY: THE ROLE OF COINFECTION

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Background: Clinical spectrum of Human rhinovirus (HRV) infection ranges from asymptomatic or mild symptomatic infection to be often the only etiological agent in patients requiring advanced-life-support. Role of viral coinfection is controversial and the diagnosis of bacterial superinfection is often missed in literature evaluating variables associated with severe disease. The aim of this study is to determine the impact of viral and bacterial coinfection in HRV severity.

Methods: Patients <5 year-old admitted to the Paediatric-Intensive-Care-Units (PICU) of a tertiary hospital in Barcelona with LRTI were enrolled. Study period:2018-2019. Patients with comorbidities were excluded, as well as bacterial results of patients receiving antibiotics for >48 hours at the time of respiratory sampling. Nasopharyngeal-aspirate (NPA) samples were collected during the first 48 hours of hospital admission and a PCR for multiple-respiratory-pathogens (Filmarray-RP) and bacterial cultures were performed.

Results: Sixty-four patients. Median age, 2 month-old. In 28, HRV was the unique viral detection. Respiratory-Syncytial-Virus was the most common viral coinfection (41%). Haemophilus influenzae was the most frequent bacterial co-detection (42%) followed by Moraxella (32%) and other gram-negative bacteria (16.1%). Eleven required invasive-mechanical-ventilation, 52 non-invasive mechanical-ventilation. Invasive-ventilation was associated with bacterial coinfection (P=0.02), but neither with viral codetection (P=0.29) nor age (p=0.20). 2/11 did not fulfill analytical-radiological diagnostic criteria of bacterial pneumonia. Gram-negative-bacilli were detected (NPA) in them.

Conclusions: HRV is often found as the unique viral aetiology in very young infants with severe LRTI. Diagnostic criteria of bacterial pneumonia could help to identify high risk patients. Nonetheless, this study shows that detecting bacterial growth in NPA is enough to develop a more severe disease. This could be especially important, when Gram-negative bacilli are detected in NPA, regardless of whether or not the pneumonia criteria are met.
BARRIERS AND FACILITATORS TO INFECTION PREVENTION AND CONTROL IN A NEONATAL UNIT IN ZIMBABWE – A THEORY-DRIVEN QUALITATIVE STUDY PREPARING FOR A BEHAVIOUR CHANGE INTERVENTION

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Background: Hospital-acquired neonatal infection is an increasing cause of morbidity/mortality in low-income settings. Staff behaviour-change interventions may offer long-term, cost-effective methods to improve infection prevention and control (IPC) practices. Aim: To explore barriers/facilitators to IPC in a neonatal unit in Harare, Zimbabwe.

Methods: Setting: An urban hospital in Harare, managing 12,000 births/year, with ~400 admissions/month to the 100-cot neonatal unit. Sepsis is implicated in ~90% of deaths.

Materials/methods: Interviews were conducted with fifteen staff members of neonatal and maternity units alongside ethnographic observations. Data collection and analysis was informed by the Capability/Opportunity/Motivation-Behaviour (COM-B) model of behaviour change and focused on identifying barriers/facilitators to IPC. Potential interventions were identified using the Behaviour Change Wheel (Figure) and discussed with stakeholders (neonatal consultants, matrons, hospital executive) to explore acceptability/affordability/feasibility.

Results: Enablers within Capability (Knowledge) included awareness of IPC, and within Motivation included beliefs that IPC was crucial to one’s role (Identity), and for patient outcomes (Beliefs), alongside concerns about poor IPC (Emotions). Staff were optimistic that IPC could improve, contingent upon resource availability. Barriers across COM-B domains included: Capability (Knowledge): limited knowledge of guidelines, and observed implementation of poor practices; Capability (Behavioural Regulation): no formal feedback or unit-wide performance discussions. Opportunity (Physical), i.e. lack of resources was a key barrier, leading to improvisation and poor habit formation (e.g. intermittent availability of water/handrub prevented handwashing habits). Opportunity (Social) could be limited by the unit’s hierarchy e.g. low engagement of cleaners and parents in IPC. Potential interventions identified included role-modelling, engaging parents and staff across cadres, feedback and flexible protocols (adaptable to water/handrub availability).
**Conclusions:** Most barriers to IPC fell within Opportunity, whilst most enablers fell under Capability and Motivation. Applying this framework identified potential interventions for future evaluation.

**Clinical Trial Registration:** This is not a clinical trial
ANTIBIOTIC USE IN CHILDREN HOSPITALISED WITH PNEUMONIA IN CENTRAL VIETNAM

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Background: Challenges in child pneumonia management in Vietnam and other East-Asian countries are different than in Sub-Saharan Africa, where access to life-saving antibiotics is limited. Excessive use of antibiotics has been noted in children with respiratory tract infections in Vietnam, but antibiotic use in hospitalised children is poorly documented. Antibiotic use and direct healthcare costs in children hospitalised with pneumonia in central Vietnam were assessed in this study.

Methods: We conducted a prospective descriptive study of all children hospitalised with ‘pneumonia’, as diagnosed by the admitting physician, over a 1-year study period (1 July 2017 to 30 June 2018). The Da Nang Hospital for Women and Children is a referral provincial hospital in central Vietnam with 570 paediatric beds (for children <15 years old), with bed occupancy more than 150% (2017).

Results: Of 2,911 children hospitalised with pneumonia, 94.0% were classified as ‘non-severe’ pneumonia. Intravenous antibiotics were given to 12.3% children with ‘non-severe’ and 89.2%. Only 19.3% children on IV antibiotics were stepped down to an oral antibiotic. Cefuroxime was the preferred, but its use was associated with a higher rate of oral to IV switch than amoxicillin or amoxicillin/clavulanic acid (p<0.001). Hospital admission for oral antibiotics in ‘non-severe’ pneumonia was a major cost driver, with an average direct cost of 78.9 USD/patient - accounting for 54.0% of the total hospitalisation cost.
Conclusions: Unnecessary hospitalisation for childhood pneumonia is a major healthcare cost driver in Vietnam; likely also in other East Asian countries. Early step down from intravenous to oral antibiotics is rarely practiced and could further reduce healthcare cost and other adverse effects associated with unnecessary hospital stay. The use of broad spectrum antibiotics is preferred, but generally not associated with improved outcome.
Title of Case(s): Neonatal tuberculosis: an outbreak?

Background: Many women display signs of peripartum sepsis and are treated according to sepsis protocols. In turn their babies are often screened for sepsis. However, most guidelines focus on common and serious causes of peripartum and neonatal sepsis, meaning other diagnoses can be missed. In exceptionally rare circumstances this can result in serious infection control issues.

Case Presentation Summary: A 21-year-old Romanian woman delivered a healthy 37-week-gestation baby after an uncomplicated pregnancy. The baby was screened for sepsis due to suspected maternal sepsis. The baby had a raised CRP, and thus a lumbar puncture, but results were reassuring and she remained well. She received 5 days of antibiotics on the postnatal ward before being discharged. 16 days postpartum the mother presented unwell and febrile. A chest x-ray displayed severe cavitation and widespread shadowing, highly suspicious of pulmonary tuberculosis. Sputum cultures revealed acid-fast bacilli and the woman was referred for tuberculosis treatment. The paediatric team were informed and the baby was admitted. Inflammatory markers, blood culture, repeat lumbar puncture, interferon-gamma release assay, and gastric aspirates were all reassuring. The baby received 3 months of rifampicin, isoniazid, and pyridoxine, after which she remained well and had a negative tuberculin skin test. Unknowingly, this mother spent 5 days in an open 5-bedded postnatal bay whilst unwell with smear positive pulmonary tuberculosis. During this time her close contacts included numerous women and their newborns. This resulted in significant difficulties with contact tracing, along with decisions regarding the investigations and management of those contacts.

Learning Points/Discussion: Not all peripartum fever is due to pregnancy-related sepsis but other, rarer causes can be easily overlooked. Contagious pathogens on a postnatal ward pose significant problems, and guidelines regarding screening and treatment in these situations are scarce.
HOW IRRITABLE IS TOO IRRITABLE?

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**Title of Case(s):** HOW IRRITABLE IS TOO IRRITABLE?

**Background:** Hand foot and mouth disease (HFMD) is a common paediatric presentation to general practice and emergency department. It is caused by a group of viruses of the *Picornaviridae* family, has no targeted treatment and usually has a benign course. In rare cases however, the initial phase of viral exanthema can be followed by severe neurologic complications and life-threatening autonomous instability.

**Case Presentation Summary:** Case: 22-months-old boy presented with a 2-day history of vomiting, irritability, exanthema of his palms, soles and mouth blisters. After an initial improvement, he became encephalopathic, with fluctuating alertness. He had normal deep-tendon reflexes, but little spontaneous movement. He had tremulous eye movements, intention tremor, ataxia, frequent myoclonus and profuse sweating. An MRI brain and spine was consistent with brainstem encephalitis and transverse myelitis. He had CSF pleocytosis. He received 5 days of IVIG and intensive neuro-rehabilitation. He was discharged on day 14 of illness having made full recovery. His rectal swab subsequently identified Enterovirus 71.

**Literature review:** A PubMed search yielded 257 abstracts, that were manually reviewed. Out of those, 28 series and 3 case-reports of complicated HFMD were selected for full review. 22/28 were from Asia. General incidence of neurologic complications varied between 0.1 – 19.8%. Severity of acute presentation correlated with outcome. Enterovirus 71 caused more severe disease. CNS disease without cardiopulmonary involvement had mostly favourable outcome.

**Learning Points/Discussion:** HFMD can have rapid onset, severe and potentially life-threatening complications. Careful clinical assessment of patients will help to identify children at risk of complicated disease and allow for rapid escalation of supportive care or transfer. A multi-center prospective study of the changing landscape of causative agents of HFMD is required in European Countries to allow for appropriate public health measures.
CONGENITAL AND ACQUIRED NEONATAL MEASLES: EXPERIENCE IN CLINICAL CASES

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Title of Case(s): CONGENITAL AND ACQUIRED NEONATAL MEASLES: EXPERIENCE IN CLINICAL CASES

Background: Since 2017, a measles outbreak has been ongoing in Ukraine. Since outbreak’s onset 115,129 people got measles, children were about 70% of them. In the Chernivtsi region, 6438 cases of measles including 76 pregnant women and 7 newborns were registered during the outbreak. Because of the rarity of congenital and acquired neonatal measles international treatment recommendations and practical experience are controversial.

Case Presentation Summary: Seven newborns suffering from laboratory confirmed measles were under observation. One full-term newborn was infected by its mother who became ill after delivery (acquired neonatal measles) and characterized by the presence of coryza, cough, fever, typical maculopapular rash, shortening of the prodromal period, absence of conjunctivitis and Koplik’s spots. Six children were born from mothers with clinical manifestations of measles in childbirth, in these cases symptoms of the disease appeared on 2-6 days of life (congenital measles). Among newborns with congenital measles one child was an asymptomatic, none newborn had Koplik’s spots. One child was born to a woman in the prodromal measles and had fever, minimal coryza and conjunctivitis and maculopapular rash that appeared simultaneously at 6th days old. The other 4 children were born to mothers with measles rash and had a single macular rash with no catarrh or conjunctivitis. All cases were uncomplicated. Symptomatic cases got Human Immunoglobulin IV, vitamin A orally and symptomatic treatment.

Learning Points/Discussion: The case of acquired measles in a newborn had an incomplete clinical picture with some typical symptoms, while cases of congenital measles were characterized by clinical polymorphism as asymptomatic and symptomatic variants with atypical characteristics. For the treatment and prevention of complications of congenital (including asymptomatic cases) and acquired neonatal measles the use of Human Immunoglobulin IV is recommended and justified.
NEW DISCUSSION OF AN OLD CHALLENGE: USE OF IMMUNOSUPPRESSIVE MEDICATIONS AND ACTIVE CMV INFECTION DURING PREGNANCY

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Title of Case(s): New discussion of an old challenge: use of immunosuppressive medications and active CMV infection during pregnancy

Background: Congenital cytomegalovirus (CMV) infection is an important cause of sensorineural hearing loss and neurodevelopment disabilities. The use of immunosuppressive drugs during pregnancy is becoming more frequent and there is limited data on how it affects mother and foetus. We report a case of an active primary CMV infection in an immunosuppressed pregnant woman who gave birth to an uninfected child.

Case Presentation Summary: A 31-year-old primiparous woman was in use of azathioprine and infliximab to treat Chron’s disease since before conception. Between first and second trimester of gestation, she had CMV seroconversion with positive IgM and IgG and low IgG avidity. At 22 weeks of gestational age (GA) an amniocentesis was performed with negative CMV PCR. Obstetric and foetal ultrasounds were normal during all pregnancy. At 23 weeks GA, only infliximab was interrupted. In the beginning of third trimester, maternal serum and urine were collected for CMV PCR and both resulted positive, then oral valacyclovir (8g/day) was started. At 39 weeks GA she gave birth to an asymptomatic baby with negative screening tests for CMV infection, including negative serum antibodies and urine PCR. Mother’s serology was repeated. After 3 weeks, mother’s and baby’s CMV infection status were re-accessed with PCR in breastmilk and newborn’s urine.

- CMV RT-PCR viral load in breastmilk: 52803 IU/mL
- CMV RT-PCR viral load in newborn's urine: 60 IU/mL
Learning Points/Discussion: Congenital CMV infection might be a challenge in terms of diagnosis and management. It can become more difficult as there is scarce information on how monoclonal antibody biologics and other immunosuppressive drugs affect CMV viral and antibodies dynamics during pregnancy. This case suggests an interference of maternal use of immunosuppressive medications in transplacental antibodies transfer. It is also questionable if high doses of antiviral drugs are indicated for immunocompromised pregnant woman with active CMV infection.
Title of Case(s): Unusual occurrence of severe migratory polyarthritis in a child treated with Ustekinumab for Crohn disease

Background: We present very rare and uncommon clinical findings of disseminated mycobacterial infection occurred in a child receiving monoclonal anti-IL12/23 antibodies for inflammatory bowel disease (IBD), in spite of negative purified protein derivative (PPD) test and interferon-γ release assay (IGRA).

Case Presentation Summary: A 12-year-old girl of Tunisian origin affected by Alagille disease with severe cholestasis with concomitant pan-enteric Crohn Disease (CD) and HLA-B27-negative sacroiliitis starting from 9 years of age, was admitted for severe migratory polyarthritis of large and small joints with fever, liver deterioration and spleen enlargement. Six months before she was treated with infliximab plus MTX for CD and one month before presentation she was shifted to ustekinumab due to secondary loss-of-response to anti-TNF therapy. She was vaccinated for BCG and previous IGRAs were negative. At admission, several investigations ruled out neoplastic, rheumatologic and infectious causes of polyarthritis. IGRA and PPD tests were negative as much as chest TC scan and culture and PCR assays for M. Tuberculosis in gastric aspirate, urine, feces and synovial fluid. One month after samples collection, culture for M. Tuberculosis-complex resulted positive from blood and colonic biopsies, leading to a diagnosis of disseminated TB with reactive polyarthritis (Poncet’s Disease). A TB treatment was started along with immediate suspension of anti-IL12/23 therapy. At 6-month follow-up, she was permanently apyretic with clinical improvement except for a persistent and refractory painful polyarthritis, therefore treatment with low-dose TNFi (adalimumab) was associated to anti-TB treatment, leading to clinical response 2 months after.

Key Learning Points: As subjects with inborn errors of the IL-12/23 pathway are at high risk for mycobacterial infections, we hypothesize a main role of ustekinumab in LTBI reactivation and we endorse the need of considering disseminated TB disease in case of persistent fever and migratory polyarthritis, in patients receiving anti-IL12/23 therapy.
A COMMON INFECTION WITH SIGNIFICANT HEALTH BURDEN

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Title of Case(s): A common infection with significant health burden

Background: Globally, infections with bacteria resistant to antibiotics are becoming increasingly prevalent. Yet, in the Netherlands this prevalence is considerably low. This clinical case abstract aims to highlight prolonged comorbidity after a methicillin resistant Staphylococcus aureus (MRSA) pneumonia affecting an otherwise healthy adolescent.

Case Presentation Summary: A 17-year-old girl presented with fever (38.5°C) and a productive cough. She experienced a sharp pain below her left scapula over the last four days. She reported loss of appetite, night sweats and weight loss, however no substance abuse or allergies. One month prior to hospitalization, she took amoxicillin as treatment for a pneumonia clinically diagnosed by her general practitioner. Three months ago she spent her holidays in India during which she had been hospitalized for one night due to a gastro-enteritis. Her physical examination was unremarkable, except for a tachycardia (95/min) and a palpable abscess in the right axilla. A chest X-ray showed a cavitating consolidation in the left lower lobe. We isolated MRSA from sputum, pus from the axillary abscess, and swabs of nostrils, pharynx and perineum. There were no signs of endocarditis. We concluded that our patient had multiple abscesses (in lung and axilla) caused by MRSA. Before the cultures were available, she received ceftriaxone and clindamycin empirically. Subsequently, she was treated with intravenous vancomycin for two weeks followed by oral cotrimoxazole for four weeks. Initially, our patient experienced a swift recovery. She could be discharged from the hospital after one week. However, she still remains MRSA-positive and has recurring abscesses despite several medical and chirurgical interventions during the first year after hospitalization. There was no immunodeficiency (no abnormalities in number and function of any white cell line).

Key Learning Points: Infections caused by antibiotic resistant bacteria challenge health professionals to find tailor made treatments. Once treated, healthy patients can still experience significant comorbidity and protracted medicalization.
ANTIMICROBIAL RESISTANCE OF URINARY TRACT INFECTION IN CAMBODIAN CHILDREN

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Background: Antimicrobial resistance (AMR) is an emerging global public health threat. In Cambodia, community-acquired AMR causes serious bacterial infections in children, due to uncontrolled community antibiotic use. Unlike most Cambodian hospitals, Angkor Hospital for Children has microbiology facilities and is able to design antibiotic guidelines based on local evidence. We aimed to determine the prevalence and type of AMR in bacterial urinary tract infection (UTI) in children presenting to our outpatient department (OPD) over six months.

Methods: A retrospective study was conducted of UTI in children aged 1 month to 16 years presenting to out patient department of Angkor Hospital for Children, Siem Reap, Cambodia over 6 months in 2016. The electronically data bases files of 365 children were diagnosed of UTI with disease code (ICD10: N39.0) between 01 January 2016 and 30 June 2016 were evaluated.

Results: Among of 90 patients, 78.9% were female and 21.1% were male. The mean age of the subjects was 1.5 year (± 1.1). 25 of total 90 cases UTI were culture positive. The most common organism was Escherichia coli (76%) and this demonstrated resistance to all commonly available antibiotics (amoxicillin 100%, cotrimoxazole 77.8%) and 41% were extended spectrum beta-lactamase species. The most common antibiotics to which these UTI were sensitive to were nitrofurantoin (100%) and imipenem (94.4%).

Conclusions: UTI is common in children under years especially among females and infants. The organisms are highly resistant to most of the antibiotics recommended for empiric use in the therapy of UTI. AMR is a significant problem affecting common paediatric serious bacterial infection. The majority of UTI are culture-negative due to prior antibiotic use and the majority of culture positive UTI are not susceptible to commonly available antibiotics.
PEDRIATRIC MELIOIDOSIS: CALL FOR BETTER AWARENESS AND EARLY DIAGNOSIS

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Title of Case(s): Prolonged fever and dyspnea after rice field water submersion

Background: Melioidosis, infection by Burkholderia pseudomallei, is an important but frequently under-recognized cause of morbidity and mortality in Southeast Asia and elsewhere in the tropics where infection is thought to be acquired after environment exposure by ingestion, inoculation or inhalation. The clinical presentation is highly variable and ranges from a mild localized infection to acute fulminant sepsis with widespread bacterial dissemination.

Case Presentation Summary: A 19-month-old girl presented with fever, cough, and runny nose for 7 days, she was diagnosed with pneumonia and prescribed Amoxicillin. The symptoms did not improve, she developed mild dyspnea and abdominal pain. Her parents are farmers and she was submerged in field water a few days before symptoms started. She was previously healthy. She had fever and looked toxic, mild subcostal retraction with crackles bilaterally. Abdominal examination revealed 1 cm hepatosplenomegaly. The lab revealed WBC:11.0x10⁹, Hb:11.3mg/dl, Platelet:236x10⁹, ANC:7.7x10⁹, Na:135mmol/L, K:4.8mmol/L, CRP:157mg/L, ALT:21U/L, AST:61U/L, negative blood culture and Malaria. Her CXR showed bilateral opacity. She was diagnosed with bacterial pneumonia, and treated with IV Ceftriaxone. After 5 days, she still had fever, mild dyspnea and worse abdominal pain. Septic and melioidosis screen were done. They revealed positive throat swab with *Burkholderia pseudomallei* and abdominal ultrasound showed hepatosplenic abscesses. She was treated with 4 weeks ceftacedim, followed up with weekly abdominal US and switched to oral contrimoxazole for another 4 weeks.

Learning Points/Discussion: Melioidosis following aspiration or a near-drowning episode is well recognized especially in Cambodia. Given the high mortality associated with bacteraemic infection, there is an urgent need for greater awareness amongst healthcare professionals in Cambodia and other countries where melioidosis is known or suspected to be endemic area. Empiric treatment guidelines should ensure suspected cases are treated early with appropriate antimicrobials.
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CHANGING FACE OF CANDIDA COLONIZATION PATTERN IN PEDIATRIC PATIENTS WITH HEMATOLOGICAL MALIGNANCY DURING REPEATED HOSPITALIZATIONS, RESULTS OF A PROSPECTIVE OBSERVATIONAL STUDY (2016-2017) IN SHIRAZ, IRAN

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Background: Surveillance of current changes in the epidemiology of Invasive Fungal Diseases as an important component of the antifungal stewardship programs, requires careful regular monitoring, especially in high-risk settings such as oncology centers. This study aimed to examine Candida colonization status and corresponding current changes in children with malignancy during repeated admissions and also investigate the possible epidemiological shifts after the implementation of ASP.

Methods: In this prospective observational study, all eligible patients younger than 18 years were recruited. Totally, 136 patients were enrolled and 482 samples were collected from different sites. Weekly regular sampling was carried out during hospitalization. Candida colonization status and epidemiological changes were monitored during repeated admissions. Samples were cultivated on Sabouraud Dextrose agar medium and identified by Polymerase Chain Reaction-Restriction Fragment Length Polymorphism.

Results: Estimated Candida colonization incidence was 59.9% (82/136) in our patients. Candida colonization was found to be higher in oral cavity and rectum than that in nasal cavity. Among those long-term follow ups and repetitive hospitalizations, a significant number of patients exhibited changes in their colonization patterns (37.7%). Candida colonization did not reveal any significant relationship with age, sex, oncologic diseases and degree of neutropenia. C. albicans (72.0%) was found as the most common Candida species in colonized patients, followed by C. krusei, C. kefyr, C. glabrata and C. parapsilosis.

Conclusions: Our study confirmed that repeated hospitalization in children with malignancy has an important role in changing the face of Candida colonization. We observed some changes to non-Albicans species during hospitalization. Despite observed changes in the pattern of candida colonization and also implementation of non-Azole prophylaxis in high-risk patients, it should be noted that no significant changes have occurred to the burden of candidemia.
A MULTIPLEX ASSAY TO ANALYSE EBV-SPECIFIC ANTIBODY RESPONSES IN PATIENTS WITH INFECTIOUS MONONUCLEOSIS (IM)

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Background: The Epstein-Barr virus establishes lifelong persistent infections in more than 90% of the world population and is associated with several malignant and autoimmune diseases. While primary infection usually occurs in early childhood in a mostly asymptomatic way, delayed primary infection during adolescence often results in Infectious Mononucleosis (IM). IM is a self-limiting disease and commonly associated with tonsillopharyngitis, lymphadenopathy, fever and fatigue, but can sometimes lead to life-threatening complications such as splenic rupture, hepatitis or myocarditis. The project aims to identify biomarkers of severe IM by characterizing the humoral immune response against EBV using a novel multiplex array.

Methods: Sera from 101 IM patients participating in the “Munich Infectious Mononucleosis study (IMMUC) were analysed for EBV-specific IgG antibody responses at disease onset, one and six months later. For this purpose, 81 ORFs of EBV B95.8 and 4 ORFs of EBV AG876 were expressed as C-terminally His6-tagged proteins in HEK293T cells and purified by immobilized metal affinity chromatography. The EBV proteins were spotted onto nitrocellulose membranes and then incubated both with patient sera and a monoclonal mouse antibody directed against the His6-tag. Following hybridization with an IRDye800-coupled anti-human IgG and an IRDye700-coupled anti-mouse IgG secondary antibody, EBV-specific humoral responses as well as the protein levels were quantified.

Results: IM patients developed IgG antibodies against several antigens of the EBV life cycle that are not part of commercial tests. Furthermore, this immunoassay is a first approach to distinguish serologically between EBV virus type I and II infection.
**Conclusions:** While some distinct proteins elicited strong antibody responses in a number of patients, other EBV antigens appeared to be neglected by the virus-specific antibody response during the course of IM.

**Clinical Trial Registration:** non applicable
THE EPIDEMIOLOGY OF CHILDHOOD TUBERCULOSIS IN CAMBODIA

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Background: Paediatric tuberculosis (TB) represents a major public health concern worldwide. Children are important in the epidemiology of tuberculosis as a marker of recent disease transmission and a reservoir for the future. Once infected they have a higher risk of progressing to tuberculous disease. The aim of this study is to identify the epidemiology and investigation of tuberculosis in children in Cambodia where is an endemic country.

Methods: This is a retrospective study. All patients aged 0 to 15 years, who were diagnosed tuberculosis at National Pediatric Hospital (NPH) Phnom Penh, Cambodia from 01 January 2014 to 31 June 2016 were included in the study. There were 166 children eligible for this study. Chart review was done and was recorded in case record forms by focusing on epidemiology and investigation.

Results: Among 166 patients, 60.8% was male and 39.2% was female. The group age from 2 months to 5 years was the most common TB group. Pulmonary TB was 21.1% while extra-pulmonary TB represented 78.9% including cervical lymph node TB 71.7%, intestine lymph node TB 6.6% and vertebra TB 0.6%. 100% of cases revealed positive tuberculin skin test, 21.1% enlargement of hilar lymph node and alveolar opacity, 1.8% was positive gen X pert and only 1.2% was positive of smear microscopic. Almost all case had BCG vaccination 83.7% after delivery.

Conclusions: Childhood TB is commonly in boy than girl and mostly occurred on younger age group who lived close contact with house wholes tuberculosis. BCG vaccination will not 100% protect from TB infection but it decreases severity. Chest radiography and tuberculin testing with or without tissue for culture are still the standard tools for confirming the diagnosis once this is considered.
Title of Case(s): Fever in a neonate

Background: *Neisseria meningitidis* is a well-known and much-feared cause of meningitis and sepsis in the pediatric population, it is an uncommon cause of infection in neonatal period. Timely diagnosis of *Neisseria meningitidis* in this age group is challenging because neonates rarely present with “classic” signs, such as petechial rash. Neonates may present with non-specific signs and symptoms, or asymptomatic until late in the disease course.

Case Presentation Summary: A 26-day-old male presented with fever, irritability and poor feeding for one day without seizure, vomiting or skin rashes. He was a full term and previously healthy neonate. He was active but irritable. There was no fontanel bulging, respiratory distress, hemodynamic instability, hepatomegaly or skin lesions. He was diagnosed with neonatal sepsis and suspected meningitis. The investigation revealed serum WBC:8.3x10⁹/L, Hemoglobin:93mg/dL, Platelet:177x10⁹, Neutrophil:51%, Lymphocyte:42%, CRP:210mg/dL. The CSF showed WBC:9980/mm³, Polynuclear:85%, Mononuclear:15%, RBC:6600/mm³, Glucose:1.7mmol/L, Protein:0.6g/L. Gram-negative diplococci was seen on a Gram-stained smear of CSF. Blood culture reported Gram negative Cocci in 24 hours. CSF and blood culture grew Neisseria meningitidis. Empiric therapy was initiated with intravenous Ceftriaxone. The organism was susceptible to ceftriaxone. The patient received a 7-day course of intravenous Ceftriaxone. Ceftriaxone prophylaxis was given to family members who closed contact. The baby was discharged home and followed up with growth and development.

Learning Points/Discussion: *N. meningitidis* is rare in neonate group, genitourinary colonization of the mother or nasopharyngeal carriage among close relatives must be evaluated. In communities with a high nasopharyngeal carriage rate, contact between neonates and crowded environments must be avoided. During the neonatal period, in cases of sepsis/septic shock that respond poorly despite early, fast, and appropriate treatment, *N. meningitidis* should be considered even if there are no specific clinical findings.
SYMPTOMATIC CONGENITAL CYTOMEGALOVIRUS INFECTION IN AN IRISH TERTIARY NEONATAL UNIT – A RETROSPECTIVE REVIEW.

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Title of Case(s): Symptomatic Congenital Cytomegalovirus Infection in an Irish Tertiary Neonatal Unit – a Retrospective Review.

Background: Congenital Cytomegalovirus (cCMV) infection is under-appreciated as the leading cause of congenital infection worldwide. cCMV has surpassed congenital rubella infection as the commonest non-genetic cause of childhood hearing loss worldwide and is a significant cause of neurodevelopmental delay in children globally. The aim of this case series was to assess presentation, management and outcomes of cCMV infection in our neonatal unit in recent years, and current diagnosis and management strategies.

Case Presentation Summary: Four infants were identified with symptomatic congenital CMV infection over a two year period. Maternal primary CMV infection was suspected in two cases. Two infants were small for corrected gestational age (SGA) and petechial rash was noted in three infants. No infants had CMV retinitis, pneumonitis or seizures. Time taken to confirm of diagnosis with urine CMV PCR was seven days or less (median 4 days), and was confirmed by plasma PCR. One infant had a CMV viral load of >100,000 copies/ml with severe anaemia, thrombocytopenia and neutropenia, requiring multiple blood product transfusions and G-CSF. All cases had abnormal findings on MRI brain, but only two cases had neuro-imaging fully consistent with cCMV infection. Two infants were initially managed with intravenous gancyclovir, with switch to oral valganciclovir. One infant was managed with oral valganciclovir alone. One infant did not receive treatment due to delayed diagnosis of cCMV.

Learning Points/Discussion: This case series highlights the varying severity of symptomatic cCMV infection. Diagnosis can be time-consuming and management challenging. Introduction of simple hygiene and CMV-specific prevention advice may helpful and cost effective in many settings. Development of a safe and efficacious vaccination is likely to be the most powerful method in turning the tide against congenital CMV and its devastating neurodevelopmental consequences.
ROTAVIRUS GASTROENTERITIS AMONG CHILDREN ADMITTED: A PROPOSAL OF DATA COMPARISON BETWEEN DIFFERENT CENTERS TO HIGHLIGHT THE PROBLEM

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Title of Case(s): ROTAVIRUS GASTROENTERITIS AMONG CHILDREN ADMITTED: A PROPOSAL OF DATA COMPARISON BETWEEN DIFFERENT CENTERS TO HIGHLIGHT THE PROBLEM

Background: Rotavirus is the main cause of severe gastroenteritis among children, and an important etiologic cause of hospital admission to gastroenteritis worldwide: it's estimated that about 2 million subjects are yearly hospitalized to severe Rotavirus infection. Aim of this study was to evaluate the impact of Rotavirus among children admitted in pediatric wards and propose a multi country comparison to highlight the importance of this virus in clinical practice and improve prevention.

Case Presentation Summary: In a 4 years retrospective observational data collection, from January 2015 to December 2018, in the Hospital of Magenta (Milan, Northern Italy) 130 patients were admitted to Rotavirus gastroenteritis. They accounted 2.8% of all admissions, and 25.9% of all gastroenteritis admitted during this period. Rotavirus resulted particular endemic during cold Italian months, from January to May (108 of the 130 cases were reported during this period), with a peak on March and no cases at all on December. The same data collection is now in progress in the University of Colima (Coquimatlán, West Mexico): a recent national epidemiological overview revealed hundreds of Rotavirus gastroenteritis admissions each year in the whole country, with an important impact on pediatric and public health.

Learning Points/Discussion: Rotavirus remains an important cause of gastroenteritis, in particular in infants, with an high impact on pediatric admissions worldwide despite two oral live attenuated vaccines are licensed to prevent this infection. A multi-country data comparison could highlight this issue and the impact of Rotavirus gastroenteritis on public health, show seasonal variability through different countries, and sensitize physicians to improve vaccinations.
A RARE BACTERIAL MENINGITIS: A DIAGNOSIS TO CONSIDER EVEN IN AN IMMUNOCOMPETENT CHILD.

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Title of Case(s): A rare bacterial meningitis: a diagnosis to consider even in an immunocompetent child.

Background: Listeria (L.) monocytogones is a Gram-positive bacillus, causing meningitis primarily in immunocompromised individuals, which may be associated with high morbidity and mortality rate. In immunocompetent patients, the diagnosis is frequently underestimated. L.monocytogenes should be suspected in children with bacterial meningitis who fail to respond to empirical antibiotic therapy. We report a rare case of neurolisteriosis in a 7-years-old immunocompetent patient.

Case Presentation Summary: A 7-years-old boy was admitted to the emergency room for fever, vomit and severe headache. Physical examination revealed a meningeal syndrome without purpura. Lumbar puncture showed a cloudy CSF with 700 leukocytes/mm3 (50% neutrophils). Blood exams revealed leukocytosis with neutrophilia, increased CRP and procalcitonin. RT-PCR on CSF was positive for L.monocytogenes. The initial antibiotic treatment included ampicillin and vancomycin. CSF culture (day 4) resulted positive for L.monocytogenes, sensitive to ampicillin. Due to the clinical and biological improvement of the patient, antibiotic therapy was not changed. Vancomycin was discontinued on day 7, ampicillin on day 21. The EEG, performed at the onset and revealing diffuse cerebral dysfunction, improved in following controls. A brain MRI scan (day 15) showed no anomalies. The results of the diagnostic immunological investigation were normal. Retrospectively, no source of infection was clarified in his recent history. The patient was discharged in good condition with normal clinical and neurophysiological outcome 4 months later.

Learning Points/Discussion: Listeria meningitis may rarely occur in previously healthy, immunocompetent children. It should be considered when treating a child with meningitis, especially when appropriate empiric antibiotic therapy fails to cure the disease. The clinical presentation of Listeria meningitis has poor specificity, similar to other viral or bacterial CNS infections. RT-PCR is extremely useful to enable a rapid and appropriate antibiotic treatment with ampicillin.
Background: Central venous catheters are critical for pediatric hematology and oncology patients owing to difficulties in intravenous access and the necessity of safe administration of chemotherapeutics. Catheter-related bloodstream infections (CRBSI) are the most common complication of central lines. Data concerning the effectiveness and safety of antibiotic lock therapy (ALT), especially in pediatric malignancies, have not yet reached sufficient levels of evidence. We aimed to share our center's experience on ALT in pediatric cancer and to investigate the causes of treatment failure.

Methods: All cases with CRBSI and treated with adjunctive ALT in pediatric hematology/oncology patients between January 2015 and May 2019 were reviewed. Patients with only one blood culture positivity for common skin concomitants, with another infection source or with a short-term catheter were excluded. Patients characteristics, laboratory and clinical findings, treatments, outcome of ALT, recurrences and reinfections were recorded. Patients with successful and unsuccessful ALT outcome were compared to identify the risk factors for ALT failure.

Results: Sixteen eligible CRBSI treated with adjunctive ALT were identified. The most common pathogens were coagulase negative staphylococci (50%). Treatment failure was observed in 31.2%. Younger age alone was an independent risk factor for treatment failure (0.9 vs 6.8 years, p=0.038). Recurrence and reinfection rates were 23.1% and 16.7%. Mild bleeding occurred in two cases (12.5%) and occlusion causing catheter removal was seen in one (6.3%).

Conclusions: ALT was found to be a safe modality with a success rate of 68.8% in pediatric hematology/oncology patients at our center. Younger age was an independent risk factor for ALT failure. Identifying groups with low treatment success may lead to changes in the population in which ALT was recommended. Future studies with larger sample size are needed to determine the factors for ALT failure.
ETIOLOGICAL STRUCTURE OF VERIFIED BACTERIAL MENINGITIS

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Background: According to the World health organization, about 1 million cases of bacterial purulent meningitis are registered annually in the world, of which 200 thousand cases end fatally. The incidence of bacterial meningitis has significant fluctuations in different countries of the world and depends on a number of factors: the economic situation in the country, the prevalence of bacterial pathogens, the establishment of vaccination, etc.

Methods: The analysis of the results of the examination of 168 patients under the age of 18 years, who were treated at the municipal children's infectious diseases clinical hospital IN Minsk from 2009 to 2018, was carried out. The age distribution of patients was as follows: up to 1 year-62 (36.9%), 1-3 years-55 (32.7%), 4-6 years- 25 (14.9%), 7-14 – 18 (10.7%), over 14-8 (4.8%).

Results: The analysis was carried out taking into account the age of patients, which allowed to establish that at the age of 1 year the main pathogens were N. meningitidis (28%), Str. agalactia (22%) and Staph. aureus (10%); 1-5 years of age - Str. pneumoniae (25%), N. meningitidis (21%) and H. influenzae (16%), in children 5-10 years – Staph. aureus (27%), N. meningitidis (13%) and E. faecalis (13%), and in children older than 10 years, the most common pathogens of meningitis were: N. meningitidis (17%), staphylococci (17%) and Str. pneumoniae (9%).

Conclusions: The etiological structure of bacterial meningitis has age-related features, with the dominant position occupied by N. meningitidis, Str. pneumoniae, Str. agalactia, H. influenzae and Staph. aureus. This is important because against some infections (meningococcal, pneumococcal, hemophilic) there are opportunities for vaccination. Therefore, the introduction and wider use of vaccination will avoid the development of invasive forms (including meningitidis) of these infections.
Background: Dengue is an endemic disease throughout India with yearly outbreaks. Researchers earlier focused on identifying its serotype specificity for the severity of the disease but studies on serotype specific manifestations in detail are lacking especially in children. This study attempts to find variations in Dengue serotype specific clinical features and hematological parameters in children as well as its serotype prevalence in this part of the world.

Methods: This observational prospective longitudinal study with NS1 positive Dengue cases having fever for ≤ 5 days was conducted from October 2017 to September 2019. Only admitted children between 1 month–12 years of age were included. Dengue serotype determination was done thereafter. These cases were monitored clinically & hematologically till discharge. The findings were then compared among Dengue serotypes using Epi Info ™ 7.2.2.2.

Results: Out of 118 cases, Dengue Virus (DENV) was isolated in 76(64.4%). Prevalence of DENV-2 was 73.7%, DENV-3 15.8% whereas DENV-1 & 4 was 5.3% each. DENV-3 predominated in upper respiratory tract symptoms (66.7%; p value<0.001) & DENV-2 showed preponderance for CNS symptoms(16.1%; p value<0.001). All DENV-3 & DENV-4 patients showed gastrointestinal manifestation (p value<0.001). Dengue hemorrhagic fever(2.63%) was associated only with DENV-2. Regarding Dengue Shock Syndrome(14.47%) no serotype specificity was found. The mean level of LDH increased significantly(p value 0.0011) with the increase in severity of dengue irrespective of serotype.

Conclusions: Certain clinical features or specific system involvement is often the hallmark of an individual Dengue Serotype infection. A significant increase in the prevalence of DENV-3 was noted this year compared to previous year which is also a predictor of the recent outbreak running in this area. LDH levels are a good predictor of severity of Dengue irrespective of the infecting serotype.
VARICELLA VACCINATION IN INDIA’S UNIVERSAL IMMUNISATION PROGRAM – IS IT TIME?

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Title of Case(s): Complicated Vaccine Preventable Disease in Immunocompetent Children

Background: Varicella (chickenpox) is caused by Varicella - Zoster (V-Z) virus. Most infections are benign and self-limiting. Varicella can however, lead to disseminated and deep seated infections. We hereby present 2 cases of disseminated varicella leading to fatal consequences in immunocompetent children highlighting need of varicella vaccination to be considered in India’s universal immunization program (UIP). Also we discuss the therapeutic options including steroids and role of Varicella Immunoglobulin.

Case Presentation Summary: The first child was a 12 years old boy presenting with pneumonia, acute respiratory distress syndrome, shock and encephalitis. The second child was a 7 years old girl presenting with necrotizing fasciitis, septicemia and disseminated intravascular coagulation. Both the children were unimmunised for varicella. There was history of pleomorphic vesicular rash in family members in both cases few days back. Lab investigations revealed severe combined respiratory and metabolic acidosis with anemia, leukocytosis, thrombocytopenia, coagulopathy, D-dimers positive, azotemia. Immunological workup of the children was normal. Both children received mechanical ventilation, ionotropes, acyclovir (20 mg/kg/dose Q8hr) and broad spectrum antibiotics. The children presented to us in the second week of illness and succumbed within 72 hours of hospital stay.

Learning Points/Discussion: Secondary bacterial infection is the most common cause of hospitalisation in varicella. Varicella pneumonia is the most common cause leading to death. Mainstay of therapy is supportive alongwith Acyclovir in complicated cases. Disease is severe in adolescents and household contacts. Since the secondary attack rate for varicella is 90%, effective vaccination is an important weapon to curb case fatality.
SEROGROUP DIVERSITY OF N.MENINGITIDIS ISOLATED FROM CHILDREN UNDER 18 YEARS WITH MENINGITIS

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Background: Meningococcal infection is still actual not only among children infections. Rearrangement mechanisms of meningococcal serogroup structure have been studied not enough. Meningococcal vaccine is not included in the National calendar.

Methods: 81 N.meningitidis isolates were collected from CSF (74.1%), blood (18.5%) and nasopharyngeal swabs (7.4%) of children with invasive bacterial diseases under 18 years from Minsk (44.4%), Brest region (19.8%), Grodno and Mogilev regions (13.6%), Vitebsk region (6.2%), Gomel and Minsk regions (1.2% each) during the period since 2011-2019 years. Cultivation of the strains was carried out on VCNT agar in a CO$_2$ incubator at 37°C and 5-10% CO$_2$ for 20-24 hours. Additional identification, DNA detection in biological samples and serogenotyping, was carried out by real-time PCR (CDC and WHO protocols).

Results: Meningococci, isolated in 2011 - 2019 were distributed among serogroups as follows: MenB - 69.2%, MenC - 21.0%, MenW - 4.9%, MenA - 1.2%, MenY – 1.2%, other serogroups – 2.5%. Group of children from 1 to 5 years old (n=38) the most diversified - MenB – 63.2%, MenC – 15.8%, MenW – 7.9%, MenA – 3.9%, MenY – 3.9%, other serogroups – 5.3%. In children under 1 year old (n=31) the dominant serogroup is MenB - 80.6% and other MenC - 19.4%. In group from 6 till 17 (n=13) MenB - 53.8%, MenC - 38.5% and MenW - 7.7%.

Conclusions: The serogroup structure of meningococci circulating among the population of Belarus is diversified. Men B dominates throughout the country. In recent years, the proportion of serogroup W increased and serogroup A decreased.

Clinical Trial Registration: УДК 616.98:S79.862.083(047.31)(476) № гос. регистрации 20190144
KNOWLEDGE OF MOTHERS ON ACUTE LOWER RESPIRATORY INFECTIONS, MODE OF TRANSMISSION, SYMPTOMS AND INDOOR MICROBIOME

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**Background:** Acute lower respiratory tract infections is a major cause of mortality among under five children in Africa, especially in Nigeria. 

**Methods:** This was a comparative study which recruited mothers aged 19-68 years with under five children who had any form of acute lower respiratory tract infections as cases, and mothers aged 22-46 years with under five children without any form of respiratory infections as controls. A total number of two hundred mothers was the sample size for this study. Data collected was analyzed using statistical package for social sciences and presented using descriptive statistics such as frequency, simple proportion and percentage.

**Results:** The mean age among the study participants was 32.14 ± 7.01 years among the case population and 32.85 ± 5.83 years among the control population. Majority (98.0%) of cases and controls had 1-3 under five children. Results for household size showed that majority (89.9%) of cases and controls had a household size of between 2-5 people. Knowledge of Acute Lower Respiratory Infections, Mode of Transmission, Symptoms and indoor microbiome among mothers was categorized into poor knowledge and good knowledge. Majority (73%) of the case population had poor knowledge of Acute Lower Respiratory Infections, Mode of Transmission, Symptoms and indoor microbiome. A large number of mothers (94.9%) in the control population also had poor knowledge of Acute Lower Respiratory Infections, Mode of Transmission, Symptoms and indoor microbiome.

**Conclusions:** This study revealed poor knowledge of Acute Lower Respiratory Infections, Mode of Transmission, Symptoms and indoor microbiome among the populations studied. Hence, in other the mitigate the menace of under-five mortality due to Acute Lower Respiratory Infections, a lot of awareness needs to be created on the causes and prevention of this deadly disease.

**Clinical Trial Registration:** Not available
LIVER ENZYMES DURING AND AFTER ANTIMALARIAL THERAPY IN NIGERIAN CHILDREN WITH UNCOMPLICATED PLASMODIUM FALCIPARUM INFECTION

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Background: Derangement of liver enzymes could occur during malaria and this has been attributed to drug-induced liver toxicity. However, it remains unclear whether these changes in liver enzyme levels persist upon completion of treatment. We investigated plasma levels of four liver enzymes namely: Alanine aminotransferase [ALT], Aspartate aminotransferase [AST], Alkaline phosphatase [ALP] and γ-Glutamyl transpeptidase [GGT], in children treated for uncomplicated malaria with Artemether-Lumefantrine (AL).

Methods: We examined the records of 102 children with microscopically proven uncomplicated P. falciparum infection treated with AL at recommended age-specific doses in a clinical trial. The main study (clinical trial) was conducted following the principles of Helsinki declaration and good clinical practice. Data on parasite density and liver enzymes (ALT, AST, ALP and GGT) were extracted and subjected to statistical analysis using Friedman two-way ANOVA at p = 0.05.

Results: Median age of participants was 25 month (range =3-119), and 49% were male. The mean ALT (U/L) decreased from 25.8 (95% CI=15.5-36.0), to 23.1 (95% CI=16.4-29.8) on day-3 and 19.1 (95% CI=15.8-22.4) on day-28 (p=0.219), p = 0.219. Mean AST increased from 50.3 (95% CI=36.7-64.2) to 51.0 (95% CI=36.9-65.1) on day-3 and 55.2 (95% CI=37.5-72.9) on day-28; p=0.198. However, ALP decreased from 319.2 (95% CI=287.6, 250.7) to 308.3 (95% CI=279.7-336.8) on day-3 and increased to 373.8 (95% CI=327.9-419.8) on day-28; p=0.042. The GGT increased from 21.1 (95% CI=17.5-24.8) to 22.6 (95% CI=19.3-25.8) on day-3 and decreased to 18.7 (95% CI=1.9-14.9) on day-28; p=0.001.

Conclusions: There was a substantial rise in ALP and GGT which suggest some liver injury during malaria treatment. Considerable rise in plasma levels of liver enzymes indicative of liver injury do occur during malaria illness among Nigerian children but the mechanism by which this happened remains unknown. Further research is needed to identify the underlying mechanism responsible for this drug-induced liver toxicity.
COMPARATIVE EFFECT OF FOUR ANTIMALARIAL TREATMENTS ON HAEMATOCRIT IN CHILDREN IN SOUTHWEST NIGERIA

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Background: Anaemia in malaria has both central (dyserythropoiesis) and peripheral causes (phagocytosis of both infected and uninfected erythrocytes and haemolysis). However, it is often difficult to disentangle the anaemia effect of malaria from its treatments. The aim of this study is to compare the change in haematocrit following four antimalarial treatments which include Artemether-Lumefantrine, Chloroquine, Artovaquone-Proguanil and Artesunate-Amodiaquine among children of microscopically-confirmed Plasmodium falciparum infection.

Methods: Data were extracted from 313 cases forms of children that met the eligibility criteria aged 3-119 months enrolled in antimalarial clinical trials in Southwest Nigeria between 1998 and 2014. Study participants were followed up over a 28 day period according to the WHO recommendation for treatment of malaria research participants. Enrollment criteria included symptoms compatible with acute uncomplicated malaria. Change in haematocrit level from baseline through the treatment period and 28 days post treatment were compared among children treated with artemether-lumefantrine (82), artovaquone-proguanil (41), artesunate-amodiaquine (156) and chloroquine (34). Repeated measures analysis was done by fitting a general linear model (GLM).

Results: The median age of the study population was 25 months and 54% were males. The mean differences (95% CI) in haematocrit from baseline were 4.7 (95% CI = 3.6, 5.8), 4.4 (95% CI = 2.7, 6.0), 3.8 (95% CI = 3.0, 4.7) and 2.4 (95% CI = 0.5, 4.4), for artemether-lumefantrine, artovaquone-proguanil, artesunate-amodiaquine and chloroquine, respectively. Using the general linear model, repeated measure analysis showed that there were significant differences in the mean haematocrit level over the 28-day follow-up among the four treatment groups (p<0.05).

Conclusions: Commonly used antimalarial therapy in Nigeria do not contribute to malaria-related anaemia but cause rise in haematocrit level by day 28. All children experienced increases in haematocrit after treatment, with artesunate-amodiaquine appearing to result in a greater increase in haematocrit than other antimalarial drugs. Artesunate-amodiaquine might be of more benefit to children who are prone to haemolyze more during malaria infection.
SYSTEMATIC REVIEW AND META-ANALYSIS OF DETERMINANTS OF LATE PRESENTATION OF HIV POSITIVE PEOPLE TO HIV/AIDS CARE IN ETHIOPIA

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Background: Though some studies addressed the determinant of late presentation HIV infected people or presented with advanced disease stage to the healthcare, there were conflicting results among such studies. The main purpose of this study was to estimate the pooled prevalence and determinants of late presentation of HIV positive people.

Methods: Systematic review and meta-analysis were carried out from ten articles with a total of 11,329 participants. Articles were retrieved from electronic-based databases such as Google Scholar, PUBMED, Hinari and African Journals Online (AJOL). Articles published in English language were included. There was no exclusion on the basis of study period and study design. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were strictly followed. Data were analyzed using Stata Version11 software. Pooled prevalence and unadjusted odds ratios were reported with 95% CI.

Results: the pooled prevalence of late presentation of HIV infected people to HIV/AIDS care in Ethiopia was 57.81% (95% CI, 44.84 to 70.78). Risk factors were those with high perceived HIV related stigma (OR, 2.07 (95% CI, 1.49, 2.88)), those living in rented houses ( OR, 1.31 (95% CI, 1.03, 1.679)) and those who use khat (OR, 1.44 (95% CI, 1.074, 1.93))

Conclusions: in Ethiopia, three out of five HIV positive people presented late or with advanced disease stage of HIV/AIDS care. Self-perceived stigma, living in rented house and those use substances like khat were an increased risk for late presentation to health care. Therefore, active HIV test provision and stigma minimization strategy need due emphasis to achieve the test and treat goal. Those people found to be at a risk for delay needs also special follow up to optimize the benefit of early engagement in care.

Systematic Review Registration: there is no registration number
INTESTINAL PARASITOSIS IN RELATION TO CD4+ T CELLS LEVELS AND ANEMIA AMONG HAART INITIATED AND HAART NAIVE PEDIATRIC HIV PATIENTS IN A MODEL ART CENTER IN ADDIS ABABA, ETHIOPIA

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Background: Intestinal parasites (IPs) are major concerns in most developing countries where HIV/AIDS cases are concentrated and almost 80% of AIDS patients die of AIDS-related infections. The aim of the study was to determine the prevalence of intestinal parasites in relation to CD4+ T cells levels and anemia among pediatric HIV patients in a Model ART center in Addis Ababa, Ethiopia.

Methods: A cross-sectional study was conducted among pediatric HIV/AIDS patients between August 05, 2013 and November 25, 2013. A total of 180 (79 HAART initiated and 101 HAART naïve) children were included. Stool specimen was collected and processed using direct wet mount, formol-ether concentration and modified Ziehl-Neelsen staining techniques. A structured questionnaire was used to collect data on socio-demographic and associated risk factors. CD4+ T cells and complete blood counts were performed using BD FACScalibur and Cell-Dyn 1800, respectively. P values < 0.05 were taken as statistically significant.

Results: The overall prevalence of intestinal parasites was 37.8% where 27.8% of HAART initiated and 45.5% of HAART naïve pediatric HIV/AIDS patients were infected (p < 0.05). The overall prevalence of anemia was 10% in HAART and 31.7% in non-HAART groups. Hookworm, S. stercoralis, and H. nana were helminths significantly associated with anemia in non-HAART patients (P< 0.05). The prevalence of IPs in non-HAART patients was significantly associated with environmental factors (P<0.05).

Conclusions: The overall prevalence of intestinal parasites significantly differed by HAART status and cryptosporidium species were found only in HAART naïve patients with low CD4+ T cell counts. Anemia was also more prevalent and significantly associated with IPs in non-HAART patients. This study identified some environmental and associated risk factors for intestinal parasitic infections. Consistent public health measures are highly recommended.
Correlation Between Prevalences of Various MDRO Phenotypes and Prevalences of Corresponding Systemic Antimicrobials Used in Pediatric Patients

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Title of Case(s): Correlations between prevalences of various MDRO phenotypes and prevalences of corresponding systemic antimicrobials used in pediatric patients

Background: Aim – exploring relation between multidrug resistant organisms (MDRO) carriage and systemic antimicrobial consumption in children patients in our infectious diseases clinic. Study population included patients screened for MDRO in the first half of 2019 via rectal swab for Extended spectrum beta-lactamase-producing Enterobacteriaceae (ESBL-E), carbapenemase-producing Enterobacteriaceae (CPE) and vancomycin-resistant Enterococcus faecium (VRE) and via faringeal swab for methicillin-resistant Staphylococcus aureus (MRSA).

Case Presentation Summary: Methods: the positive cultures were characterized by morphology, Gram stain and standard biochemical tests; antimicrobial susceptibility was performed using disk-diffusion CLSI methods. Antimicrobials consumption – doses of antimicrobials prescribed to children patients discharged in one calendar month were retrieved from medical charts transformed in Daily Defined Doses (WHO/DDD) and allocated to selected Anatomic Therapeutic Chemical (ATC) classes – percent of each ATC class was calculated from the total DDD counted. From 162 patients screened 4.9 %, 18.5 %, 1.2 % and 1.9 % respectively were confirmed as MRSA, ESBL-E, CRE and VRE carriers. From all 320 DDD of antimicrobials prescribed 9.6 %, 30.0 %, 0.4 % and 1.0 % were classified as Penicillins (J01C), Cephalosporins (J01DD04), Carbapenems (J01DH02) and respectively Glycopeptides (J01XA01). By linear regression we found a strong association between the two series iterated above (R2: 0.99; β: 1.846; F-test:133.4767; p: 0.000273).

Learning Points/Discussion: Lesson learned - By linear regression we found a strong association between the two series iterated above (R2: 0.99; β: 1.846; F-test:133.4767; p: 0.000273). Our results document strong relation between MDRO carriers and systemic antimicrobial consumption - of note comparatively high consumption of Cephalosporins reflected in the also high prevalence of ESBL-E carriers represents a target for antimicrobial stewardship interventions including preauthorization of cephalosporins, antimicrobain treatment audit and feedback.
A RARE CASE OF NEONATAL LIVER ABSCESS CAUSED BY ESBL-PRODUCING E.COLI

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Title of Case(s): A rare case of neonatal liver abscess caused by ESBL-producing E.coli

Background: Neonatal liver abscess is a rare but serious disorder associated with high mortality and morbidity. The disorders can occur both in term and preterm babies. Since 1930, less than 150 cases of liver abscess have been reported in the literature. We recently encountered a case with difficulty in diagnosis of neonatal liver abscess caused by Extended Spectrum Beta-Lactamase(ESBL) producing E.coli.

Case Presentation Summary: A 15-day-old term, girl baby, birth weight 3.5kg, was referred from health center with three days of fever, poor feeding and abdominal distension. On admission to NICU, she had fever (T: 38°C), abdominal distension and hepatomegaly. Empirical Ceftriaxone 80 mg/kg IV was commenced for late onset neonatal sepsis but did not improve. Laboratory data showed leukocytosis, neutrophilia with high C-reactive protein. Cerebral spinal fluid (CSF) result was normal. Abdominal US showed multiple hypoechochogenic in liver, the largest one 13×12 mm, suggesting of multiple liver abscess. On day three, blood culture revealed ESBL-producing E.coli with Meropenem sensitive. We changed Ceftriaxone to Meropenem 20 mg/kg IV every 8 hours. Two day after meropenem, her clinical gradually improved and CRP gradually normalized, and the baby recovered and discharged home after three weeks of meropenem. Regular follow up did not show any recurrence with normal ultrasound at second week after treatment.

Learning Points/Discussion: Neonate liver abscess may be difficult to diagnose. Sign such as septic appearance, fever, feeding intolerance, abdominal distension, and hepatomegaly are non-specific, as are laboratory findings such as leukocytosis with high CRP. Therefore, performing routine abdominal ultrasound to look for a liver abscess in all septic newborns without identifiable septic foci may ensure early diagnosis. Blood cultures also important for multi-drug resistance organism with appropriated antibiotics are curative in most case.
Background: Diarrheal diseases contribute to 14% of under-five mortality, amounting to about 3,34,000 deaths in India annually. Available data indicates that Rotavirus is responsible for nearly 40% of moderate to severe diarrhea which leads to malnutrition and loss of cognitive development potential. As Rotavirus vaccines are introduced into the Immunization Program in India, monitoring their public health impact is a high priority. This study highlights the profile of children under 5 years of age admitted with acute watery diarrhoea over a period of 12 months.

Methods: This was a prospective (multi-centric study) and our centre enrolled 291 children over a period of 1 year. Basic demography, clinical data, vaccination history were captured via a preformed questionnaire. Stool samples were collected and transported as per the prescribed protocol. Rotaviral assay was performed on all stool samples via ROTACLONE ELISA. All ELISA positive samples (strains) were further processed for genotyping via multiplex RT-PCR.

Results: Majority of the cases of diarrhea were in the infantile period (45%). The incidence of Rotaviral diarrhea was 44% (n=125, boys-78, girls- 47) with the maximum burden of the disease in children below 2 years of age (n=99, 84%). G3P[8] was the commonest circulating strain (n=59 50.4%). 46% (n=136) had received Rotaviral vaccines (completed series). Stool rotavirus positivity was lesser in the vaccinated versus the unvaccinated cohort. (36% vs 49%).

Conclusions: Rotaviral diarrhea was the commonest cause of acute watery diarrhea in children below 5 years. It presented at an earlier age than Non-Rotaviral diarrhea and was more common in boys. Maximum occurrence was in cooler months. Vaccinated children had lower rates of stool Rotavirus positivity, lesser incidence of severe diarrhea and reduced duration of hospitalization as compared to the unvaccinated cohort.
MODIFIED PERITONEAL DIALYSIS FOR TREATMENT ACUTE KIDNEY INJURY FROM TROPICAL DISEASE- A CASE SERIES

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**Background:** Some tropical diseases such as wasp sting, snake bite and post streptococcal infection can cause acute kidney injury (AKI) in children. It is a severe complication with high morbidity and mortality. Peritoneal dialysis (PD) is a common renal replacement therapy (RRT) in children. We investigated the efficacy of modified peritoneal dialysis to treat acute kidney injury in low resource setting.

**Methods:** Our PICU admitted four children with AKI caused by wasp sting, snake bite, streptococcal infection and septic shock. This study was conducted between January 2017 and September 2019. All four children were treated with modified PD, using a simple wound drainage tube as PD catheter with dialysate solution containing sodium bicarbonate 40ml, 0.9% sodium chloride 680ml, 5% glucose 280ml, 50% glucose 5 ml and gentamycin 0.1ml. PD cycle were continuous using 5-10 ml/kg of dialysate, 5 minutes fill time, 45 minutes dwell time and 10 minutes drain time.

**Results:** One child died from septic shock complicated by multi-organ failure. Three surviving children returned to normal renal function without complication using the modified PD for seven days. Urine output increase from less than 0.3ml/kg/h before PD to 1-2ml/kg/h following PD. Serum creatinine fell from 300-675 umol/l to 51-81umol/l and urea fell from 30-54 mmol/l to 2-7,4mmol/l. Acidosis, electrolyte imbalance and fluid overload all improved. All three patients were discharged with normal renal function.

**Conclusions:** Some tropical diseases can cause acute kidney injury (AKI) in children. Modified peritoneal dialysis (PD) using a simple wound drainage tube as a peritoneal dialysis catheter and custom-made dialysate with a mixture of simple solution, is a safe and feasible for pediatric acute kidney injury in low resource setting where standard PD sets are not available or not widely use.
THE RELATIONSHIP OF REDUCED ACID SUPPRESSION DRUGS ADMINISTRATION WITH THROMBOCYTOPENIA LEVEL IN PATIENTS WITH DENGUE VIRAL INFECTION

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**Background:** Management of dengue viral infection (DVI) can included some symptomatic therapy, anti-ulcer administration of reduced acid secretion drugs (RASDs) become management for abdominal pain and prophylaxis against gastrointestinal bleeding. H2RA and PPI, included the frequent drug prescribed. Those drugs had been reported able to cause the drug-induced thrombocytopenia event, while thrombocytopenia itself is one hematologic abnormality found in DVI. Thrombocytopenia counted to be an indicator of severity and prognosis in DVI. This study aimed to find the relation of each RASDs with the thrombocytopenia level in DVI patients.

**Methods:** This study was a cross sectional analytical study with retrospective approach from medical records using standardize questionnaire from patient admitted by final diagnosed DF, DHF, DSS period January 1 to December 31, 2015 to 7 major hospital in Bandung. Point biserial analysis was used to find the correlation of each RASDs to thrombocyte count in DVI patients, significant if p<0.005

**Results:** A total of 4005 patients admitted by final diagnosis DF, DHF, and DSS with 2140 patient age between 0-18 years old. 11.0% and 21.1% of them received H2RA and PPI respectively. Patients that given RASDs, 55% for H2RA and 50.8% for PPI showed thrombocyte count <50,000/mm$^3$. Our study indicated a correlation between H2RA (p <0.001;r 0.103) and PPI (p <0.001;r 0.138) with the lower thrombocyte count in DVI patient.

**Conclusions:** The use of H2RA and PPI as RASDs found to be related with lower thrombocyte count in dengue virus infection patients. That why this drug should not be use regularly but with caution and selected cases, especially in dengue virus infection patients who prone to thrombocytopenia. because it may cause further thrombocytopenia that my affect the outcome of the patient.
Background: Survey Background- Acute gastroenteritis is a common childhood illness. In children below 5 years of age, viruses are the commonest etiology. As the disease is self-limiting, antibiotics are not indicated. However, establishing etiology is essential for estimating burden, epidemiological studies and future vaccine development. The aim of this hospital-based surveillance was to summarize the clinical features, identify the common viral etiologies and differences in clinical presentation of individual viruses.

Methods: A prospective observational study was conducted over a period of 1 year at Manipal Hospital, Bangalore (India). All children between 1 month to 5 years of age with acute watery diarrhea were enrolled in the study. Clinical data was captured and analyzed using a structured proforma. Stool samples for PCR analysis (TaqMan assay) were collected as per the required protocol.

Results: Over a period of 1 year, 100 children (79% stool assay positivity) were enrolled in the study with M:F ratio of 1:1 and age distribution between 24-60 months. 84% needed admission while 16% were treated as out-patients. Mean duration of frequency of diarrhea and vomiting was more in children with a positive stool assay (p<0.003 & p<0.01). Rotavirus was the commonest isolate (n-49). Rotavirus and Norvirus were the commonest co-infection (n-7) followed by Rotavirus & Adenovirus (n-5). Patients with co-infection presented with severe dehydration (p<0.001).

Conclusions: Viral diarrhoea was most commonly seen in the 2-5 years age group with equal sex distribution. 60% had moderate, 19 % had severe dehydration respectively and severity was correlated with stool viral assay positivity (p<0.001). Presence of stool RBC correlated with a negative stool assay (p= <0.0001). Rotavirus was the most common etiology and co-infections with Norovirus and Adenovirus presented with severe dehydration.
CONCORDANCE BETWEEN UPPER AND lower RESPIRATORY MICROBIOTA IN CHILDREN WITH CYSTIC FIBROSIS: A SUB-STUDY OF THE MUCOVIB PROJECT

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Background: Inconsistent intra-individual microbiota between upper (throat swabs) and lower respiratory (sputa) niches has been reported among infants with Cystic Fibrosis (CF). We aimed to investigate the concordance between the bacterial community composition of 24 paired throat swabs swabs and corresponding sputa, collected from children with CF above one year of age by using metagenomic analyses, specifically 16Sr ribosomal RNA PCR (16 S rRNA PCR).

Methods: As part of the longitudinal multicentric MUCOVIB project, TS and EXP were collected for bacterial 16 S rRNA metagenomics analyses. Standard V3V4 16S rRNA metagenomics libraries were sequenced on Illumina MiSeq. Reads were processed by an in-house pipeline before being analyzed by dedicated packages in R. Beta-diversity analyses assessed the compositional distance between paired TS and EXP by using the Jaccard and Bray Curtis indices.

Results: 48 paired TS and EXP collected during the same visit were analyzed for beta-diversity. When using the Jaccard distance index, paired TS-EXP samples mostly clustered by patient and by visit in ordination and hierarchical clustering. TS and EXP from the same visit had a shorter average distance (0.505, ± 0.056 95%CI), compared to EXP (0.695, ± 0.017) or TS (0.704, ± 0.045) from the same patient but different visits.

Conclusions: Our preliminary findings reported a good inter-individual concordance of the microbiota in upper and lower respiratory niches, thus suggesting that TS could be used as proxy to measure bacterial biodiversity among children with CF unable to expectorate. Despite a slight but significant difference in microbiota composition between TS and EXP, findings from throat samples might still predict an exacerbation and guide appropriate antibiotic prescription.
THE ROLE OF NON-FERMENTERS IN THE STRUCTURE OF PATHOGENS OF BACTEREMIA

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Background: Bloodstream infections are serious problems that require immediate attention and treatment as it can lead to severe disease and death, especially if they are caused by multidrug-resistant bacteria. The aim of this study was to determine the role of non-fermenters in the etiological structure of pathogens isolated from blood cultures of febrile pediatric patients in order to update the subsequent approaches to empirical therapy.

Methods: Children of both genders who are between the age of one month to 18 years admitted to the pediatric ward with recorded temperature of > 38°C and with a history of fever more than two days and whose blood culture has been sent. A total 656 blood cultures during 2009-2018 were tested.

Results: Gram-positive bacteria (59.5%, n=390) were predominant throughout the study period; gram-negative bacteria were isolated in 33.8% (n=222) cases and fungus – in 6.7% (n=44). Most of the Gram negative isolates in our series were non-fermenter Gram-negative bacteria (n=108; 48.6% of all isolated strains). Among them were dominated Acinetobacter – 50 cases (46.3%, incl. Ac. baumannii – 26 (24.1%); Pseudomonas – 21 cases (19.45%, incl. Ps. aeruginosa – 13 (12.05%), Achromobacter – 13 cases (12.05%) и Stenotrophomonas maltophilia – 9 cases (8.3%). The following gram-negative non-fermenting bacteria were also isolated from the blood: Agrobacterium tumefaciens, Burkholderia spp. (incl. cepacia), Flavobacterium indologenes, Flavobacterium meningosepticum, Ochrobactrum anthropic, Sphingomonas paucimobilis, Sphingobacterium spiritivorum – in 15 cases (13.9%).

Conclusions: Among gram-negative bacteria were leading non-fermentative bacteria (n=108; 48.6%). Pseudomonas species and Acinetobacter species were the two major non-fermenter bacteria isolated between 2009 and 2018.

Clinical Trial Registration: no unique identifying number
ATYPICAL KAWASAKI DISEASE - A RARE CASE WITH PREVENTABLE CAUSE OF VASCULITIS

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Title of Case(s): A RARE CASE OF PREVENTABLE CAUSE OF VASCULITIS AMONG CHILDREN

Background: It is a rare disease with acute vasculitis which occurs primarily in children under the age of 5. The aetiology of the disease is still unknown. Diagnostic criteria are fever and at least four of the five additional clinical signs. Incomplete or Atypical disease should be taken into consideration in case of all children with unexplained fever for more than 5 days, associated with 2 or 3 of the main clinical findings of disease. The diagnosis of this incomplete disease is based on echocardiographic findings indicating the involvement of the coronary arteries. Cardiac complications, mostly coronary artery aneurysm, can occur in 20% to 25% of untreated patients and in 4% of treated patients.

Case Presentation Summary: In this report we present a case of atypical Kawasaki disease in a 4 year old boy who presented with fever for 20 days along with cough and vomiting for 10 days. He had generalised lymphadenopathy and organomegaly and no other typical findings as mentioned in criteria for Kawasaki Disease. But in view of persistent high grade fever CRP-15, ESR-134 ECHO was planned to r/o Kawasaki disease. In ECHO, he had dilatation of the coronary arteries with a Z-score of 3.58. As soon as the diagnosis of Atypical Kawasaki was made, the patient was treated with 2mg/kg/dose of intravenous immunoglobulin. Patient improved and repeat CRP-3, ESR-15 were in decreasing trend, dilatation also reduced on repeat ECHO. The child was discharged with advice about regular follow up.

Key Learning Points: Kawasaki disease is the second most common cause of vasculitis among childhood but preventable if diagnosed at right time and treated, so it should be included in the differential diagnosis for any child with a prolonged unexplained fever. Atypical Kawasaki disease should be considered in cases even when not all clinical criteria are present but laboratory and coronary abnormalities are documented.
MANAGEMENT CHALLENGING OF COEXISTING DENGUE SHOCK AND SEPTIC SHOCK IN CAMBODIAN CHILDREN - A CASE REPORT

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Title of Case(s): Management challenging of shock in pediatric- a case report

Background: Many countries in southeast Asia are reporting increases in dengue fever in 2019 include Cambodia. There is eight times the number of case reported during the same period in 2018. Some patients developed dengue shock syndrome (DSS) which increase mortality in children. Septic shock melioidosis is a severe complication of infection caused by Burkholderia pseudomallei. The mortality rate in our hospital is 74.4%. We reported a case with coexisting dengue shock and septic shock melioidosis focus on challenging of management.

Case Presentation Summary: A seven year old boy was admitted to PICU with a four days history of high fever, chill and headache. In last 2 days, he developed abdominal pain, vomiting and somnolence. On arrival, he had fever, hypotension (BP: 60/40mmHg), weak pulse. Laboratory data revealed leucopenia, thrombocytopenia, hemoconcentration and positive dengue serology which is compatible with DSS. We treated DSS follow WHO guideline. His circulation was a bit improve then collapsed again with active bleeding and severe respiratory distress. The child was intubated and 150 ml of right pleural fluid was removed. Fluid resuscitation for shock was continuously with normal saline, colloid and blood products. Meropenem was started for suspected septic shock and inotrope was infused (adrenaline 0.5 mcg/kg/min with dobutamine 15 mcg/kg/h). Blood culture growth Burkholderia pseudomallei and he passed away on day 3 of admission.

Learning Points/Discussion: Coexisting dengue shock and septic shock melioidosis is a very severe disease with management challenging and high mortality. There is available guideline for the management of DSS and septic shock separately but no available guideline for the management of this coexisting infection. We should develop a guideline for the management of this coexisting dengue shock syndrome and septic shock to reduce morbidity and mortality in children.
ASSOCIATION BETWEEN PRESCRIPTION'S APPROPRIATEDNESS AND DEESCALATION OF MEROPENEM EMPIRIC TREATMENT IN PEDIATRIC PATIENTS OF AN INFECTIOUS DISEASES HOSPITAL

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Title of Case(s): Association between prescription’s appropriatedness and deescalation of Meropenem empiric treatment in pediatric patients of an infectious diseases hospital

Background: Aim – assessing the effects of the appropriatedness of Meropenem empirical treatment provided to patients aged under two months. A total of 142 patients hospitalized between January 2017 and June 2019 were included in a Epi Info 7 data base – data for each patient included age and gender, initial diagnosis, prior hospitalization or/and Ceftriaxon therapy, length of Meropenem cure and existing of in hospital deescalation.

Case Presentation Summary: An appropriated empirical treatment (n: 109; 76.8%) (Class A) was validated in the following cases: escalation to Meropenem after no clinical response to an narrow spectrum antimicrobial, hipersensitivity to Ceftriaxon, history of hospitalization or/and Ceftriaxon treatment in the month preceding the current hospitalization and infections included in first line use of Meropenem (example bacterial meningitis). Absence of prove for at least one of the features from above was automatecly classified as inappropriate Meropenem prescription (n:33; 23.2 %) (Class B). Univariate analysis of the characteristics of the cases from the two classes revealed that only the prevalence of deescalation was significantly statistically higher in Class A than in Class B [ 28.3 % vs 11.1 % ; RR: 2.55 (95%CI: 1.16 – 5.59); p: 0.0155732]

Learning Points/Discussion: Lesson learned In our perception deescalation translates a positive clinical response to the appropriated Meropenem prescription; even more decreased use of Meropenem, a broad spectrum antibacterial, is obviously another important effect of prescription’s appropriatedness of the drug. On this end we like to emphasize that the both positive effects iterate above might be obtained only based on fully implemented and strictly followed guidelines.
Background: Febrile neutropenia (FN) is an oral temperature of > 38.3 °C or two consecutive readings of > 38.0 °C for 2 h and an absolute neutrophil count (ANC) of < 0.5 x 10^9/l, or expected to fall below 0.5 x 10^9/l. In cancer patients, febrile neutropenia (FN) is a serious, potentially fatal condition complicating cancer treatment associated with significant morbidity and mortality.

Methods: A retrospective cross-sectional study design was employed at TASH in 135 pediatric patients with cancer. The data was collected from pediatric patients’ charts who were admitted to the hospital from January 1, 2017 to December 31, 2017 (1 year) using data abstraction tool. The data was entered into Epi-info 7 and exported to SPSS 20 for analysis. Ethical clearance was obtained from the ethical review board and official support letter was written to study site.

Results: Empiric antibiotics therapy (EAT) was given to all patients in which ceftriaxone with gentamycin constituted of 71.8% followed by ceftriaxone monotherapy. EATs were converted to others in 20 (14.8%) and 2 (1.5%) patients for the first and second times respectively, mainly based on poor clinical response without conducting culture and sensitivity tests. These tests were done only for 13 (9.6%) participants and growth was seen in 5 patients. Most of them (70.4%) were treated for FN and 7 of patients died due to all case mortality.

Conclusions: All patients received empric antibiotic therapy for management of febrile neutropenia. Ceftiaxone with gentamycin is the most combination febrile neutropnia. used for management of febrile neutropenia. in study population. The hospital shouldn’t rely mainly only on ceftriaxone with gentamycin as febrile neutropnia. and should do culture and sensitivity test to optimize therapy based on susceptibility result before conversion and modification of therapy.
Title of Case(s): Unusual case of meningitis

Background: Childhood tuberculosis (TB) has a high incidence and prevalence in developing countries like India with tubercular meningitis (TBM) being the most common cause of death. Most cases of TB meningitis are diagnosed late when despite adequate therapy; morbidity and mortality continue to remain high. It commonly affects children between 6 months and 4 years of age.

Case Presentation Summary: 11 month old child was admitted with new onset irritability for the past two months and recurrent episodes of staring spells in the last two months. There was no preceding fever or poor acceptance of feeds or altered sleep. No h/o contact with TB patients. Parental screening was also unremarkable. Only MRI was suggestive of TBM with basal exudates and brainstorm arachnoiditis. CSF analysis for TB done twice was also normal. Serum galactomannan report ruled out fungal meningitis. Child was started on ATT and steroids after which the child improved, repeat MRI on follow up after a month also was near normal.

Key Learning Points: This case is unique because only MRI was suggestive of TB Meningitis whereas other lab reports were negative with no h/o contact with TB patients. Though he was immunised, no failure to thrive, no h/o contact he presented with seizure in the form of staring and few tremors and stiffness of limbs on and off. He improved with ATT. So possibilities should be kept. TB Meningitis can present in healthy, immunised infants. Childhood tuberculosis (TB) constitutes approximately 10%–20% of all TB cases in India, causing almost 8%–20% of TB-related deaths. Twenty-five percent of the paediatric tubercular cases are extrapulmonary, with tubercular meningitis (TBM) being the most common cause of death. TBM is a medical emergency. So timely diagnosing and treating this condition can reduce significant morbidity and mortality.
ASSESSMENT AND COMPARATIVE STUDY OF BIOFILM FORMATION WITH FREQUENCY OF MULTI DRUG RESISTANCE IN STRAINS OF PSEUDOMONAS AERUGINOSA

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Background: Pseudomonas aeruginosa is an opportunistic organism & cause chronic and acute infections in humans. Biofilm plays a role of a barrier that protects organisms from environmental stress & antibiotic treatment is also a stress to these biofilm producers. The aims are isolation, identification of strains of Pseudomonas aeruginosa from hospitals, the environment and find their degree of biofilm production and frequency of multi drug resistance pattern.

Methods: The strains collected for 3 months, from medical equipments, hospital beds & from soil. The strains were identified and isolated using standard microbiology procedures and techniques, which were later subjected to antibiotic susceptibility testing (Six antibiotics) using standardized operative procedures. Biofilm production and detection protocol was done by 3 protocols that are: Tube Method, Congo Red Agar Method and Tissue Culture Plate Method.

Results: 16 isolates of Pseudomonas aeruginosa were isolated. 6 samples from hospital giving a probability of nosocomial infection associated strains, 5 from environment that include bath tubs, sinks, cell phones and 5 from soil. 45% of the isolates were strong biofilm producers, while the rest of the 55% remained weak to moderate biofilm producers. All the strong biofilm producing isolates showed a more resistant pattern in comparison to none-weak biofilm producing strains. The strains resistant to Gentamicin, Tetracycline, Erythromycin and Cephradine have shown to be stronger biofilm producers as compared to rest of the strains. Highest sensitivity was seen to be in Meropenem.

Conclusions: Antibiotic resistance is an important feature of biofilm infections. The ability of Pseudomonas aeruginosa to form biofilm restricts treatments by means of antibiotics and makes them inefficient and thus promotes chronic infections and diseases. As a result of this study infections that are caused by bacterial biofilms are strong and very difficult to treat.

Clinical Trial Registration: No registration I.D. as it was done in a university lab.
DETERMINANTS AND HEALTH CARE SEEKING BEHAVIOUR OF CHILDHOOD ACUTE RESPIRATORY TRACT INFECTIONS IN BANGLADESH: DATA FROM BANGLADESH DEMOGRAPHIC AND HEALTH SURVEY

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Background: Acute respiratory infections (ARIs) are one of the leading causes of child mortality worldwide and contribute significant health burden for developing nations such as Bangladesh. Seeking care and prompt management are crucial to reduce disease severity and to prevent associated morbidity and mortality. This study aimed to investigate the prevalence and care-seeking behaviors among under-five children in Bangladesh and identified factors associated with ARI prevalence and subsequent care-seeking behaviors.

Methods: The present study analyzed cross-sectional data from the 2004 to 2014 Bangladesh Demographic Health Survey. The study follows a stratified, multi-stage cluster sampling design. Bivariate analysis was performed to estimate the prevalence of ARIs and associated care-seeking. Logistic regression analysis was used to determine the influencing socio-economic and demographic predictors. A p-value of <0.05 was considered as the level of significance.

Results: A total of 10,147 ARI children aged < 5 years were included in the study. Approximately 91% of households used drinking water from improved sources, while 51.5% had access to improved toilet facilities, and most household floors were earth/sand (76.9%) and 48.1 had electricity. 89.7% used polluted fuel for cooking, had diarrhea 9.2%. The family who had higher birth order, not electricity in their household had 1.16 (95% CI 1.03-1.30; P = 0.009) and 1.63 times (95% CI 1.43-1.86; P = <0.001) had less chance to receive care.

Healthcare seeking behaviors for ARI children and maternal education
Conclusions: ARIs continue to contribute to a high disease burden among under-five children in Bangladesh. Various factors i.e. age, maternal education, nutritional status, birth order, and household lifestyle factors were significantly associated with ARI prevalence and care-seeking behaviors. Moreover, public, private actions to increase service accessibility for poorer households, and interventions targeting households with low socio-economic status and lower education levels are recommended.
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PREDICTOR FOR OUTCOME OF CHILDREN WITH CRIME CONGO HEMORRHAGIC FEVER

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Title of Case(s): Predictor for Outcome of Children with Crime Congo Hemorrhagic Fever

Background: Crimean Congo hemorrhagic fever (CCHF) is viral zoonotic infection and tick bite is dominating route of infection in children. The disease in endemic in Kosovo, although in recent years due to infection control measures, there were only sporadic cases. Being rare, in the prehaemoragic phase early diagnosis often fails. The benefit of ribavirin remains undetermined. We report the only case during 2019 in a nine year male child.

Case Presentation Summary: The child had foreign body in his ear and following symptoms next three days: vomiting, diarrhea, headache and decreased level of consciousness. On admission he was in stuporous state, hypotensive, with conjunctival injection, intoxicated, meningeal signs positive. For suspected encephalitis, was performed brain CT scan which showed a hypodense zone suspected for intracerebral bleeding. After admission, the patient manifested haematemesis and melena, gingival bleeding, abdominal ultrasound showed presence of free liquid suspected for hematoperitoneum and right side suspected haemorrhagic pleuritis. Blood analyses showed severe thrombocytopenia (21x10^9/mm^3), leukocytosis, elevated enzymes (AST 2042, ALT 692, LDH 8496, CK 4048), electrolyte imbalance. Based on clinical and laboratory findings, probably tick bite in his ear, we suspected CCHF which next day was confirmed by RT PCR. Treatment was based on fluid and electrolyte replacement, platelets suspensions, fresh frozen plasma, low doses of methylprednisolone and oral ribavirin.

Learning Points/Discussion: Late admission with haemorrhagic manifestations especially visceral bleeding and multisystem involvement is associated with poor outcome. RT PCR assay of blood samples is crucial for early diagnosis. Early supportive treatment with replacement of fluids, electrolytes, low doses of steroids and oral ribavirin were crucial. Replacement of blood products especially platelets are essential for successful treatment as bleeding is one of the strongest predictors for unfavorable outcome of children with CCHF.
NEW HORIZON IN THERAPEUTICS: ANTIMICROBIAL ACTION OF DENDROBIUM NOBILE AND PHALAENOPSIS AGAINST PYOGENIC SKIN INFECTION ISOLATES.

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**Background:** Orchids are well-known around the globe as plants of decoration and called as gems in the area of horticulture. The basic idea of research was the assessment of the flower extracts of Dendrobium nobile and phalaenopsis plants.

**Methods:** In vitro for their antibacterial activity against pyogenic skin infection isolates, that is Staphylococcus aureus and Staphylococcus epidermidis by means of agar disc diffusion method. For this intention, strains were isolated from skin acne patients and were identified by conventional methods.

**Results:** The flower extracts of Dendrobium nobile and phalaenopsis showed antibacterial activity against pyogenic skin isolates. In comparable, several antibiotics also tested alongside the isolated organisms.

**Conclusions:** The information demonstrated potential outcome for Dendrobium nobile and phalaenopsis in contrast of five different antibiotics. Moreover, analysis also confirmed that the pyogenic organisms were challenging besides several antibiotics.

**Clinical Trial Registration:** This is basic science study
THE EPIDEMIOLOGY OF THE ACUTE RHEUMATIC FEVER IN CHILDREN IN MOROCCO

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Background: Acute rheumatic fever (ARF) is a major problem of public health in developing countries like Morocco, because of the high prevalence of its main complication, rheumatic heart disease (RHD). No studies have been conducted about the acute rheumatic fever in Morocco. The objective of this study is to find out the clinical manifestations and laboratory features of patients with ARF in Fez city in Morocco.

Methods: A prospective study was conducted from January 2016 to July 2019 in the pediatric ward of the university hospital Hassan II of Fez. We included patients with age between 0 and 18 years. A total of 152 children diagnosed ARF, based on modified Jones criteria, was studied. The data of patient were collected from the medical records and HOSIX software.

Results: The mean age of ARF cases were 13 years. The sex ratio was 0.7. The most represented age class was the class between 5 and 15 years. Urban residence was found in 78.8% of cases and the majority were admitted in winter and autumn. Cases of ARF with carditis was documented in 78.3%. Arthritis was the major criterion most represented and arthralgia was the minor criterion most represented. History of sore throat presented 68%. Penicillin A was the most antibiotic prescribed. Commonest valvular lesions among ARF was mitral regurgitation.

Conclusions: Acute rheumatic fever (ARF) continues to occur in Morocco. Despite the progress made in the socioeconomic development of the country, it’s often associated with severe cardiac involvement. As long as this condition is not well reported, it is the main source of morbidity and morbidity. The significant incidence of misdiagnoses in ARF children during admission to the hospital, especially the interpretation of joint syndrome indicates that physicians need extra awareness.
BOTTOM-UP APPROACH FOR EVALUATION OF VUR AND ITS TREATMENT

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Background: Vesicoureteral reflux (VUR) is diagnosed in 20%–30% of children with a first UTI, that can cause complications like renal scarring, hypertension, eclampsia, and, rarely, end-stage renal failure. Bottom-Up Approach employs RUS and/or VCUG rather than Up-Bottom Approach that employs DMSA before RUS and VCUG. We aim to determine the success rate of Bottom-Up Approach for evaluation of VUR and its treatment (Deflux).

Methods: A retrospective study was performed involving children aged 1 to 14 that presented with hydronephrosis or recurrent urinary tract infection between May 2013 and November 2019. Children with structural causes or abnormalities like UPJ obstruction, posterior urethral valve (PUV), renal stones, trauma or ischemia were excluded. Two radiologists with paediatric imaging experience reviewed imaging findings, and consensus reporting for final diagnoses was made. Percentage estimation for success of deflux therapy was estimated by either regression or resolution of reflux on subsequent imaging.

Results: Of 336 children, 81 had VCUG positive for VUR (24%) and graded as G1 (12), G2 (0), G3 (21), G4(9) and G5 (39) with 78 (96.2 %) had ultrasonography positive for reflux. Nine patients (11.1 %) underwent both Pre procedure (Deflux) radiological VCUG and DMSA Scan which showed positive results and subsequently had treatment (Deflux). Six children (66.6 %) showed complete response while three (33.3 %) showed no response.

Conclusions: Bottom-up approach for investigation of UTI or hydronephrosis in children seems more reasonable practice to select candidates demonstrating VUR as a probable cause. Pre procedure DMSA helps to identify an already present renal damage, and to follow up post-procedure kidney status. Higher reflux grades have been seen to show good response post deflux therapy. Deficient data, single centre study and discontinuous follow ups remain important limitations in our study.
Background: Streptococcus pyogenes, or group A streptococcus (GAS), is a human pathogen that causes a wide spectrum of diseases, ranging from relatively benign infections, such as pharyngitis and pyoderma, to severe invasive diseases. It can also lead to serious non-suppurative sequelae, including acute rheumatic fever and acute glomerulonephritis. In this study we report the Epidemiological characteristics of GAS responsible of throat infections in children in Morocco.

Methods: A prospective study was conducted from March 2017 to February 2018 in a health center in Fez city in Morocco. A throat swab was practiced to children with throat infections aged 5 to 18 years for isolate GAS. GAS identification was based on conventional bacteriological analysis. Emm typing was performed by sequencing the samples of GAS isolated after a PCR reaction.

Results: 188 patients with throat infections were diagnosed. The mean age was 10 years. There was a masculine predominance. The Majority of children presented a fever > 38°C and a sore throat. 149 patients presented headache and 36.7% had a pultaceous tonsils. The culture of the throat swab was a GAS positive in 5.85%. All GAS isolated was sensible to penicillin G. While 1 GAS express a resistance to erythromycin. We sequenced 11 GAS and we identified seven types of emm. The type of emm the most find was emm 90 and emm 89.

Conclusions: This study highlights the low prevalence of streptococcus pyogenes in the throat infections (5.85%) and the variability of the emm types in Morocco like in the other countries (emm 89, emm 90, emm 12 ...). In the world, as well as in Morocco, group A streptococcus is sensitive to penicillin G. This research highlights also the reliability of molecular analysis to identify different groups of streptococci.
THE SHORTAGE OF ANTI-DIPHTHERIA SERUM IN INDONESIA: A PRELIMINARY RESULTS OF QUALITATIVE STUDY

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Background: Anti diphtheria serum (ADS) is one of the main treatments for diphtheria cases. Indonesia had a high number of diphtheria cases since 2011. Since three years ago, the supply of ADS was stopped because of the supply shortage. The government of Indonesia made several anticipation steps to tackle this problem. The aim of this study was to analyze the shortage of ADS in Indonesia.

Methods: This was a qualitative study. An in-depth interview was done to one person at the Ministry of Health, one health officer at the district level, and one clinician at the provincial hospital. The main questions were about the regular supply of ADS, the changing mechanisms of ADS request, the role of the National Expert Committee of Diphtheria, and the problems at the patient level.

Results: From three interviews, some important issues raised, those were: (1) The distribution of ADS took more time; (2) Some of the requests did not approve so the ADS was not given; (3) The decision to receive the ADS was not the responsibility of the clinicians solely, but also the responsibility of the National Committee; (4) Number of suspected patients was reduced significantly; (5) Evaluation of the mechanisms should be done regularly.

Conclusions: The shortage of ADS creates many problems, but the current mechanisms was considered as the best solution. A continuous evaluation has been done to minimize the negative impacts of this shortage. We also encourage the government to produce this important drug by ourselves. At the same time, the effort to minimize the number of diphtheria patients by strengthening the immunization program should be prioritized.
EVALUATION OF SERIOUS ADVERSE EVENTS FOLLOWING IMMUNIZATION IN 2019 IN EAST JAVA PROVINCE, INDONESIA

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Background: Adverse events following immunization (AEFI) should be monitored because of its potency to cause vaccine hesitancy. In Indonesia, the report and evaluation of AEFI are made routinely from the village to the national level. The serious AEFI cases are the top priority. The aim of this study was to evaluate the serious AEFI in East Java Province in Indonesia for the period of 2019.

Methods: The surveillance reports were distributed from the villages to the district, the province, and, lastly, the national level. The source of the report can come from the people in the community, health centers, hospitals, and private practices. Regular evaluation meeting at the provincial level was done once per year. Both Provincial AEFI Committee and Provincial Health Office took responsibility for the final reports of all cases. All kinds of AEFI were reported, but the priority was for serious cases.

Results: In 2019 there were 34 serious AEFI cases from 13/38 districts. All cases were hospitalized, and eight children died. Most diagnoses were febrile convulsion followed by acute gastroenteritis. Most related vaccines were DwPT. Among death cases, three patients had acquired prothrombin complex deficiency, and three others had diarrhea with hypovolemic shock and septicemia. Nine cases were reported as part of the measles-rubella vaccine clinical trial, and all children in that group were survived.

Conclusions: The serious AEFI in East Java Province is underreported. The majority of the cases were febrile convulsion. Eight children died in 2019. Almost all of serious AEFI cases were not related to the vaccination program or the vaccine itself. The AEFI recording and reporting efforts are compulsory work. We encourage the East Java Provincial Health Office to enhance the ability of all health personnel.
Title of Case(s): Recurrent severe respiratory syncytial virus bronchiolitis in a boy with a genetic CD14 deficiency

Background: Respiratory syncytial virus (RSV) infection can cause life threatening bronchiolitis, typically in newborns. Recurrent severe RSV infection is highly uncommon. Here, we report a boy with an unusual course of recurrent RSV infections. The innate immune response against RSV is characterized by the initial production of cytokines by respiratory epithelial cells, followed by the influx of innate myeloid cells such as neutrophils and macrophages. Pattern recognition receptor (PRR) CD14 has been proposed to mediate the innate immune response against RSV.

Case Presentation Summary: A nine month old boy was admitted to the pediatric intensive care unit with respiratory failure caused by RSV. He was re-hospitalized at the age of 14 and 22 months with RSV bronchiolitis. As an incidental finding we discovered an absence of CD14 on the patient’s monocytes via flow cytometry. Sanger sequencing showed a homozygous frameshift mutation in the CD14 gene resulting in an early stop. Also, soluble CD14 in plasma was undetectable. Nasopharyngeal swabs were negative for RSV between episodes. Blood analysis showed normal routine immunophenotyping and vaccination response. Moreover, he showed normal seroconversion of RSV antibodies before and after RSV infections, with normal antibody avidity. Peripheral mononuclear cells were not capable of responding to TLR4/CD14 ligands, nor RSV-F protein.

Learning Points/Discussion: Altogether, we identified and described the genetic, clinical and immunological characteristics of the first ever reported genetic human CD14-deficiency. Clinical and in vitro experimental data indicate an essential role for CD14 in the defense to RSV. –CD14 seems redundant in protection against pathogens outside the respiratory tract –We predict that other loss of function mutations in the CD14/TLR4 signaling pathway, are associated with severe and recurrent RSV infections.
ASSOCIATION BETWEEN NUTRITIONAL STATUS AND SHOCK IN HOSPITALIZED DENGUE HEMORRHAGIC FEVER CHILDREN IN INDONESIA

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¹Tanah Abang General Hospital, Child Health Department, Jakarta, Indonesia, ²Faculty of Medicine, Indonesia University, Department Of Pediatrics, Jakarta, Indonesia

Background: In southeast Asian countries including Indonesia, dengue infection is an indication for hospitalized and one of main cause of death in children. Several virus serotypes, complex pathogenesis and various clinical manifestations in diverse area make doctors difficult to predict course of disease, even the child admitted in early. Several factors including nutritional status have been studied to find the association with dengue shock syndrome (DSS).

Methods: This was a retrospective study using medical records of children age below 18 years old with WHO fulfilled grade 1 and 2 DHF diagnosis from January 2013-December 2016 in Child Health Department of Dr. Cipto Mangunkusumo Hospital, Jakarta. Independent variables were severe malnourished, moderate malnourished, good nutritional status, overweight and obesity. Shock was dependent variable. Analysis was done by using bivariate analysis.

Results: There were 98 DHF subjects, 5 subjects became DSS during hospitalization. DSS subject characteristics were age of >5 years old, female, severe malnourished 2%, moderate malnourished 30.7%, good nutritional status 40.8%, overweight 9.2% and obesity 15.3%, hemoconcentration ≥20%, leucocyte ≥5,000 mm³ and thrombocyte <100,000 mm³, abdominal tenderness and petechiae. Statistic analysis showed severe-moderate malnutrition was not a significant factor of DSS with p = 0.048 (p<0.05, OR 8.40 (CI 95% 0.900-78.434))
<table>
<thead>
<tr>
<th>Characteristics</th>
<th>n (%)</th>
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<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
</tr>
<tr>
<td>0 - &lt;1 years old</td>
<td>8 (8.2)</td>
</tr>
<tr>
<td>1 - &lt;5 years old</td>
<td>69 (70.4)</td>
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<tr>
<td>5-10 years old</td>
<td>38 (38.8)</td>
</tr>
<tr>
<td>&gt;10-&lt;18 years old</td>
<td>41 (41.8)</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>54 (55.1)</td>
</tr>
<tr>
<td>Female</td>
<td>44 (44.9)</td>
</tr>
<tr>
<td><strong>Nutritional status</strong></td>
<td></td>
</tr>
<tr>
<td>Severe malnourished</td>
<td>2 (2.0)</td>
</tr>
<tr>
<td>Moderate malnourished</td>
<td>32 (32.7)</td>
</tr>
<tr>
<td>Normal</td>
<td>40 (40.8)</td>
</tr>
<tr>
<td>Overweight</td>
<td>9 (9.2)</td>
</tr>
<tr>
<td>Obesity</td>
<td>15 (15.3)</td>
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<tr>
<td><strong>Abdominal tenderness</strong></td>
<td>69 (70.4)</td>
</tr>
<tr>
<td><strong>Bleeding manifestations</strong></td>
<td></td>
</tr>
<tr>
<td>-Petechiae</td>
<td>52 (53.1)</td>
</tr>
<tr>
<td>-Epistaxis</td>
<td>12 (12.2)</td>
</tr>
<tr>
<td>-Gum bleeding</td>
<td>7 (7.1)</td>
</tr>
<tr>
<td><strong>Pleural effusion</strong></td>
<td>13 (13.3)</td>
</tr>
<tr>
<td><strong>Expanded Dengue Syndrome (EDS)</strong></td>
<td>12 (12.2)</td>
</tr>
<tr>
<td>-Encephalopathy</td>
<td>3 (25.0)</td>
</tr>
<tr>
<td>-Acute kidney injury (AKI)</td>
<td>1 (8.3)</td>
</tr>
<tr>
<td>-Increased liver enzymes</td>
<td>6 (50.0)</td>
</tr>
<tr>
<td>-Hyponatremia</td>
<td>2 (16.7)</td>
</tr>
<tr>
<td><strong>Hemoconcentration (increased hematocrit ≥20%)</strong></td>
<td>53 (54.1)</td>
</tr>
<tr>
<td><strong>Leucocyte (μL)</strong></td>
<td></td>
</tr>
<tr>
<td>&lt; 5,000</td>
<td>47 (48.0)</td>
</tr>
<tr>
<td>≥ 5,000</td>
<td>51 (52.0)</td>
</tr>
<tr>
<td><strong>Thrombocytopenia (μL)</strong></td>
<td></td>
</tr>
<tr>
<td>&lt;100,000</td>
<td>82 (83.7)</td>
</tr>
<tr>
<td>100,000-150,000</td>
<td>16 (16.3)</td>
</tr>
</tbody>
</table>
**Conclusions:** Severe-moderate malnutrition was not a significant prognostic factor of Dengue Shock Syndrome in children patients although p value was less than 0.05. Because Confidence Interval level exceeded number one so it became not significant. It was not stated too that other nutritional condition (good-overweight-obese) was a significant prognostic factor. In the future, it need more subjects and improvement to find any association between nutritional status and Dengue Shock Syndrome in children patients.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group</th>
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<tbody>
<tr>
<td></td>
<td>Shock, n (%)</td>
<td>Non Shock, n (%)</td>
<td>p</td>
<td>OR (CI 95%)</td>
<td></td>
</tr>
<tr>
<td>Nutritional status</td>
<td>4 (11.8)</td>
<td>30 (88.2)</td>
<td>0.048</td>
<td>8.40 (0.900-78.434)</td>
<td></td>
</tr>
<tr>
<td>Severe-moderate malnourished</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal-overweight-obesity</td>
<td>1 (1.6)</td>
<td>63 (98.4)</td>
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</tr>
</tbody>
</table>
ARTESUNATE TREATMENT OF SEVERE PEDIATRIC MALARIA

B. Bua, M. Martino, P. Costenaro, D. Dona'
Department for Woman and Child Health, Division Of Pediatric Infectious Diseases, Padova, Italy

Title of Case(s): Artesunate treatment of severe pediatric malaria: efficacy, safety and clinical implications

Background: Pediatric patients with imported severe P.falciparum malaria should receive intravenous artesunate, however limited data are currently available on its use and potential post-treatment effects in pediatric patients in non-endemic settings.

Case Presentation Summary: A 15-month old child presented with high fever five days after a recent trip of 9 months in Nigeria. Antimalarial prophylaxis was never administered to the child and his mother reported that he was treated for malaria (with unknown drugs) while being in Nigeria. At admission, blood tests were performed showing thrombocythemia (16000/mmc),Hb 9.5 g/dL, increased C-reactive protein (160 mg/L) and increased liver function tests. Peripheral blood smear confirmed a diagnosis of P. falciparum malaria with very high parasitaemia (17%).The child was pyretic, well appearing without any neurological sign, physical examination was normal except for a mild spleen and liver enlargement. On DAY 1, due to the very high parasitaemia, intravenous artesunate was administered (3 mg/kg for 5 doses,0-12-24-48-72 hours),with a rapid decrease of the parasitaemia (1-3% after the first dose and negative after the second dose).A concomitant resolution of fever was observed within the next 48 hours, with transient recovery of platelets and stable haemoglobin level (9.2 mg/dl) (DAY 4).During follow-up visits patient presented: on DAY 7 we observed a haemoglobin decrease, up to 7.7 mg/dl with 12.10% reticulocytes, MCV 71.7 fl, MCH 21.8 pg and haptoglobin <0.08 g/L.On DAY 14 child presented stable level of Hb (7.9 mg/dl) but severe neutropenia (230/mmc).On DAY 21 gradual resolution of anaemia (9.2 mg/dl) and normal neutrophils count (4110/mmc) were observed.

Learning Points/Discussion: Intravenous artesunate is highly effective and safe in children with imported severe P.falciparum malaria,however clinicians should be aware that transient moderate/severe anemia and neutropenia may occur even few weeks after treatment.
ENLARGEMENT OF A SUBMENTAL LYMPH NODE.

E. Gowin
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Title of Case(s): Enlargement of a submental lymph node.

**Background:** Enlargement of cervical lymph nodes is a common symptom in children, but those in submental area are not frequently affected. There are many reasons for cervical lymphadenopathy and most of them are benign and require no medical intervention. Tuberculosis is an important disease, which is still present in developed countries. Doctors must think of TB in immunocompetent patients without risk factors.

**Case Presentation Summary:** A 18-year-old girl was admitted to hospital with a nodular swelling in the submental region, which appeared 3 months prior to the admission. She has also noted a recent increase in cough. She reports no fevers. She has been diagnosed with chronic thrombocytopenia at the age of two, and with asthma as a teenager. In November 2018 she had pertussis. On admission in the submandibular area several firm, mobile, non-tender lymph nodes about 1 cm in diameter were palpable and one bigger in submental area.

Results of initial laboratory tests revealed microcytic anemia, mild thrombocytopenia. In ultrasound examination: a single enlarged node with central necrosis in submental region and some smaller satellite lymph nodes were found.

Her chest x-ray showed inflammatory consolidation on the base of the left lobe with blunting of the left costophrenic angle. Quantiferon test and sputum test for acid-fast bacilli - both were positive. She was diagnosed with tuberculosis and put on antituberculous treatment.

**Learning Points/Discussion:** Tuberculosis should be included in differential diagnosis of enlarged cervical lymph nodes also in immunocompetent patients without risk factors. Patients with chronic cough or asthma not responding to treatment should be screened for TB. TB diagnosis should be based on microbiological tests (sputum smear and culture). Serological diagnostic tests for pertussis are not very useful in previously vaccinated children.
Title of Case(s): BCG ADENITIS – WHAT NOT TO MISS?

Background: Bacillus Calmette-Guerin (BCG) is a live vaccine recommended by the WHO to reduce the risk of tuberculosis complications. Underlying immunodeficiencies can be missed in patients presenting with adverse reactions to this vaccine. Chronic granulomatous disease (CGD) is a rare primary immunodeficiency, caused by a defective NADPH oxidase. It is inherited in an autosomal or X-linked recessive manner and mostly occurs in males.

Case Presentation Summary: We present a girl with distant BCG adenitis, who received this vaccine when she was 3-weeks old. She had been treated for neonatal sepsis, multiple febrile illnesses and oral thrush. Her relevant family history is that her brother died of X-linked neonatal ornithine-transcarbamylase deficiency. At 6-month of age she developed a nonhealing BCG ulcer, an abscess in her supraclavicular node and inflamed axillary nodes. She was febrile and had night sweats. In addition, she had spreading, necrotic skin lesions throughout her body, that were diagnosed as ecthyma gangrenosum. She was found to be a carrier for X-linked CGD. She had an abnormal nitroblue-tetrazoliun-test, GP91 deficiency and 20% activity on dihydrorhodamine-1,2,3 test. She was treated with a long course of multiple anti-tuberculous medications. She improved and was discharged after a month-long hospital admission with ongoing anti-tuberculous medication. Due to her severe infection a haematopoietic stem cell transplant (HSCT) is being considered.

Learning Points/Discussion: This case highlights the importance to consider underlying immunodeficiencies in children presenting with BCG adenitis and not to administer this vaccine to children at risk of immunodeficiencies. This case also reminds us that CGD can occur in females with X-linked CGD, if non-random X-inactivation occurs. Finally, this case demonstrates the difficult and lengthy treatment options and that for some a HSCT, that offers a cure, is the best option.
SCORE TO PREDICT DEVELOPMENT OF CORONARY ANEURYSMS IN KAWASAKI DISEASE: PROPOSAL FROM A MULTICENTRE SPANISH NETWORK


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**Background:** Coronary artery aneurisms (CAA) are the main concern with Kawasaki disease (KD). There are studies that aim to identify risk factors, but there are no established scores to predict the development of CAA. We aimed to create a score to predict risk of developing CAA in patients with KD.

**Methods:** Between May 2011- June 2016, the Kawa-Race network collected retrospectively data from 625 patients diagnosed of KD in 84 Spanish hospitals. A penalized regression model was used to select the variables for the score. Optimal cutoffs for continuous variables were selected according to ROC curve. Weights of each variable were calculated with multivariate logistic regression. Score was validated with data from 98 patients collected prospectively within the Kawa-Race network, from January 2018-December 2019.

**Results:** Eight variables were selected with different weight for each: masculine sex (+1.7 points), age at diagnosis <4 months (+2.9), ≥10 days of fever (+2.8), adenopathy (+1), creatinine ≥0.3 mg/dL (+3.5), C-reactive protein ≥13.6 mg/dL (+1.1), haemoglobin <10 g/dL (+1.3) y sodium <130 mEq/L (+2.4). A score ≥8 points, meant a higher risk to develop CAA with a sensitivity of 48%, specificity 81%, and an area under the curve (AUC) of 72.5% Validation in the prospective cohort showed: sensitivity 22%, specificity 75% and AUC 60.2%.

**Conclusions:** A score able to predict the development of CAA will facilitate initial treatment for children with KD. Validation of this score in other cohorts will allow generalization of its use, selecting those patients with higher risk of CAA for a more aggressive therapy since the beginning.

**Clinical Trial Registration:** N/A (it is not a clinical trial)
MULTIPLE ANTIBIOTIC RESISTANT URINARY TRACT INFECTION IN PRIMARY IMMUNODEFICIENCY

A. Pandey
Great Ormond Street Hospital, Infectious Diseases/immunology/bmt, London, United Kingdom

Title of Case(s): Multiple Antibiotic Resistant Urinary tract Infection in an immunocompromised Child

Background: Ectodermal Dysplasia with NFKB1A inhibitor mutation is very rare disease with Autosomal Dominant inheritance. It’s associated with severe Primary immunodeficiency and life threatening infections, where only definitive treatment is Haematopoietic Stem Cell Transplant. Our patient presents with multiple episodes of multi-antibiotic resistant Gram Negative urinary tract infection and renal abscess since 1 year. This being one of the major factors delaying HSCT.

Case Presentation Summary: 7 year old girl with Ectodermal Dysplasia on treatment for BCGiosis was hospitalised on 18/11/19 with recurrent Urinary tract infection, initially treated with piperacillinTazobactum, Amikacin. Urine cultures showed growth of Oxa 48 carbapenemase and NDM metallocarbapenemase gene producing Klebsiella Sensitive only to Fosfomycin. Urinary tract Ultrasound shows multiple renal abscess. A Renal biopsy was inconclusive with negative cultures. Hence owing to Extensive resistant micro-organism we decided to treat only culture positive UTI with multiple drugs (Ceftazidime + Avibactum, colistin, Fosfomycin, Meropenem) instead of only Fosfomycin to prevent development of resistance. She has received 4 courses of treatment, December 2018 and April 2019 x 2 weeks, July 2019 and October 2019 x 6 weeks each. Repeated cultures have shown it is still sensitive to Fosfomycin and a novel drug Cefiderocol, which is not available in UK at present but we are in process of its procurement. We are also in process for initiating Bacteriophage therapy soon.

Learning Points/Discussion: Multiple antibiotics can be used simultaneously for treatment of highly resistant microorganism and prevention of development of drug resistance. But in such situations its worth exploring newer drugs with different mechanism of action like Cefiderocol which enters into bacterial cells by binding to iron using bacteria own iron transport mechanism. Approved in USA for treatment of multi drug resistant UTI on 14th nov 2019.
A RARE CASE OF MASKED IMMUNE THROMBOCYTOPENIC PURPURA (ITP)

J. Rajendran, R. Kullu
PONDICHERRY INSTITUTE OF MEDICAL SCIENCES, Paediatrics, PONDICHERRY, India

Title of Case(s): Bleeding disease - A masked case

Background: Idiopathic Thrombocytopenic Purpura (ITP) is a hematologic disorder, characterized by acute onset of thrombocytopenia in an otherwise well child is (autoimmune) idiopathic thrombocytopenic purpura (ITP). The major causes of accelerated platelet consumption include immune thrombocytopenia, decreased bone marrow production and increases splenic sequestration. Around 70% to 80% of children experience the acute form of the disease and recover within few weeks or months after diagnosis, whereas most adults have the persistent form and require therapy. The bleeding in ITP is mucocutaneous, manifesting as petechiae, purpura, easy bruising, epistaxis, gingival bleeding and menorrhagia.

Case Presentation Summary: 6 year old female child with complaints of cough and rhinitis associated with petechiae, purpura over lower extremities, ecchymosis over bilateral thigh and bleeding gums had 2 episodes of hospitalisation both with severe thrombocytopenia and fever found to be positive scrub IgM responded to doxycycline. At discharge still had thrombocytopenia which persisted after 7 days of discharge so plan was to monitor thrombocytopenia on follow-up. This 3rd time investigation showed severe thrombocytopenia (platelets 11,000) and CRP was negative. Dengue and Scrub typhus serology found to be negative so it was thought to be of viral fever triggered thrombocytopenia. Platelet transfusion was given as it was <10000 for bone marrow. Child did not have any new bleeding spots. Bone marrow showed cellular marrow with trilineage haematopoiesis and megakaryocytic hyperplasia and biopsy showed small megakaryocytes with foci of clustering suggestive of Immune thrombocytopenia. Repeat platelet count was found to be 247000 with no fever spikes and patient was discharged.

Key Learning Points: The clinical course and prognosis of pediatric ITP differs from adult ITP. ITP in young children usually presents with acute bleeding symptoms, often after an infection. So if there is persistent thrombocytopenia not explained by infection, ITP should be kept as possibility and not missed. Intravenous immunoglobulins (IVIGs) should be used for heavy bleeding, and additional platelet concentrates for very heavy bleeding, because this achieves a faster rise in platelet counts than corticosteroids alone.
Title of Case(s): Human herpes virus 6 infection of central nervous system in an immunocompetent infant

Background: Human Herpes Virus 6 is ubiquitous in nature. It is usually associated with an undifferentiated febrile illness, although a subset of children exhibit the classic manifestations of roseola infantum. The most common complication of primary HHV-6 infection is febrile seizure. The virus has been implicated as a cause of encephalitis in transplant recipients, but has occasionally been reported as a cause encephalitis in immunocompetent individuals.

Case Presentation Summary: A 21-months old male, previously healthy, admitted to the University Hospital Center of Tirana for fever without a focus. He had a history of a fourth day fever 39°C, on physical examination appeared relatively well. His blood count was remarkable for a leukocyte count of 16200 cells/mm³. On the second day of hospitalization the case was complicated with a generalized tonic-clonic seizure that lasted over 20 minutes followed by fever 40.6°C. The seizure was not controlled with rectal diazepam so continuous therapy with phenobarbital was initiated for 24 hours. CSF studies found 3 leukocytes/mm³, glucose 63 mg/dL, total protein 0.2g/dL. PCR identified HHV-6 DNA in CSF, whereas PCRs of CSF for HSV and enteroviruses and bacterial cultures of CSF, blood and urine were negative. On the third day occur two others generalized seizure of 2-3 min duration. The patient recovered spontaneously without sequelae, phenobarbital was continued orally for 1 month. Diagnosis at discharge was HHV-6 encephalitis.

Learning Points/Discussion: Infection with HHV-6 is very common. After primary infection, the virus remains latent and persists at low levels in cells and tissues like lymphonodes, kidney tubule endothelial cells, salivary glands, and CNS tissues where viral gene products have been localized to neurons and oligodendrocytes. Not usually associated with disease in the immunocompetent, HHV-6 infection is a major cause of opportunistic viral infections in the immunosuppressed.
PREVALENCE OF EAR INFECTIONS IN FIRST YEAR CHILDREN OF PRIMARY SCHOOLS IN A WESTERN UGANDAN COMMUNITY.

K. Peter, M. Fracis
Mbarara University of Science and Technology, Medical Laboratory Science, P.O BOX , Mbarara, Uganda, Uganda

Background: Ear infections in the United Kingdom were reported at a prevalence of 90% in children aged 0-6 years peaking at six years, the commonest age for Ugandan children to start primary school. This study was done to determine the prevalence of ear infections in primary one children, identify commonest ear infections, the causative pathogens isolated and their antibiograms and compare the prevalence of ear infection in urban and rural schools.

Methods: A cross-sectional study was carried out among three urban day schools and three rural day schools randomly chosen in Mbarara district. History was taken using a data collection form and examinations were done using an otoscope. All pus swabs from infected ears were inoculated on Blood agar, Chocolate agar, MacConkey Agar plates before smears for Gram staining were made. Identification of the pathogen was through biochemical tests and API system. Sensitivity tests to antibiotics were set on Mueller Hinton Agar using the disc diffusion technique of Kirby-Bauer.

Results: Otoscopy was done on 600 children, 8.0 % (48) showed signs of ear infections. The commonest ear infection was otitis externa. Staphylococcus aureus species showed the highest prevalence with 75% (6). Staphylococcus aureus species showed 100% sensitivity to gentamicin, 80% sensitivity to ciproflaxin. Serratia marcescens also showed 100% sensitivity to ciproflaxin. The ratio of male to female was 26:22 with more males affected than females.

Conclusions: The prevalence of ear infection was 8.0% among children in primary one in Mbarara district in a cross-sectional study. The use of eardrops containing ciprofloxacin and gentamicin should be encouraged. They have been proved to be effective first-line topical antibiotic in the treatment of chronic suppurative Otitis Media. Increased health sensitization about the possible risk factors of ear infection should be encouraged.
Title of Case(s): A complicated acute mastoiditis

**Background:** Acute otitis media (AOM) is the most common bacterial disease during childhood, acute mastoiditis (AM), defined as an infection of the mastoid air cells, is the most frequent intratemporal complication of AOM. *Fusobacterium necrophorum* has been reported as an emerging aetiological agent and is associated with a high complication rate such as extracranial and intracranial abscesses, sinus vein thrombosis and osteomyelitis.

**Case Presentation Summary:** A 10-month-old infant was admitted to our hospital for fever, otorrhea and swelling behind the right ear. The laboratory tests showed a white blood cell count of 11,860/mm$^3$ and elevation of C-reactive protein (CRP) 15.76 mg/dL (normal value < 0.5 mg/dL). Computed tomographic (CT) scan revealed a bilateral mastoiditis, multiple abscesses in the right pre-auricular area, thrombosis of the right sigmoid sinus and of the right transverse sinus, right temporal pachymeningitis. The patient was submitted to a subtotal right mastoidectomy with drainage of the subperiosteal abscesses, which culture resulted positive for *Fusobacterium necrophorum* and *Haemophilus Influenzae*. On admission, an antibiotic treatment with Ceftriaxone was introduced, replaced with a combination of Meropenem plus Vancomycin continued for a total of 6 weeks with a normalization of the CRP and an improvement of clinical conditions. The sinus thrombosis was managed with subcutaneous low molecular weight heparin administrated for 3 months. The imaging performed six months later revealed an almost complete resolution.

**Learning Points/Discussion:** Although AM occurs in less than 1% of children who suffer from AOM, it can be complicated by other severe conditions. Among the otopathogens, the *Fusobacterium necrophorum* should always be considered because it causes infections that, if left untreated, could be severe and associated to complications which necessitate surgical intervention and a longer hospital stay in comparison to other aetiological agents.
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**Background:** Pertussis illness requiring admission to the PICU is referred as critical pertussis. This study was planned to discover the demographic data and outcome of infants with Critical Pertussis admitted in PICU of a developing country. Malignant pertussis is a rapidly evolving combination of pneumonia, cardiopulmonary failure, severe leukocytosis, neurologic involvement, severe pulmonary hypertension and can lead to death despite intensive therapeutic measures. **Study Design:** Retrospective Observational Study

**Methods:** This study was conducted in PICU of a tertiary care centre of Punjab State, India over a period from 2010-2018. Pertussis was diagnosed clinically as per WHO guidelines. Patient’s demographics, clinical and laboratory findings were recorded via structured data collection form. Appropriate statistical methods were used to identify independent risk factors for mortality. A total of 26 critical pertussis infants (69% < 3 months years old; Male: 58 %; preterm birth: 31%) were reviewed. **Results:** Complications seen in critical pertussis cases were apnea (92%), respiratory failure (77%), hypotension (54%), cyanosis (35%), cardiac arrest (27%), severe anemia needing packed cell transfusion (50%), seizures (35%), pulmonary hypertension (19%), leucocytosis >50,000 cells per cumm (15%). Mechanical ventilation was required in 77% cases. Cough more than 2 weeks, leucocytosis >50,000 cu mm$^3$, cardiac arrest, need for high frequency ventilation were predictors of increased mortality. Overall mortality was 30 % in our study. **Conclusions:** Critical Pertussis carry a high risk of morbidity and mortality in infants in developing countries. In the study, cough more than 2 weeks, leucocytosis more than 50,000 per cumm, cardiac arrest, need for high frequency ventilation were seen to be predictors of mortality. Prevention with effective vaccination and early detection and treatment of pertussis are important to prevent morbidity and mortality in this group of children.
 Title of Case(s): Morning bites - they are deadly!

Background: Dengue fever or Break bone fever is common in tropical zones of Asia which is transmitted by mosquitoes called Aedes Aegypti and Aedes Albopictus has 4 serotypes; DEN1, DEN2, DEN3, and DEN4. The incubation period is 4 - 7 days after infection. The symptoms may vary from mild to hemorrhagic fever to dengue shock syndrome (DSS). Dengue fever is a viral disease characterized by fever, headache, aching bones and joints, myalgias and rash. Management is usually supportive. Complicated cases might need Intensive Care management.

Case Presentation Summary: 6 year old female child admitted with fever, chills for 2 days and on examination had hepatomegaly and gave history of traveling and mosquito bite in the morning hours. Blood investigations showed normal counts with CRP negative (4mg/dl) and thrombocytopenia (45,000), PCV (43.3). Serum electrolytes showed hyponatremia. Probable diagnosis of dengue fever was suspected and sodium correction was done. USG abdomen and pelvis was taken in view of persistent abdominal pain and decreased air entry on right side which showed edematous gall bladder wall showing honeycomb pattern with moderate ascites and moderate bilateral pleural effusion. Dengue NS1 and IgM serology showed positive and treated appropriately.

Key Learning Points: Many protective measures including increase awareness about the disease in endemic areas, wearing long covered dressings to cover areas liable for the bites, especially during morning, precautions in hospitals treating patients with DF, eliminating infectious sources as water containers such as flower pots, water storage containers and discarded tires. Suspicion of such diseases should be high whenever a travelling history is suggestive while dealing with cases of fever in travellers. In the era of globalization and wide movement of immigration, an increase awareness of the health professionals about tropical and endemic diseases would improve our ability to diagnose and improve the outcome of different conditions and this will save our health resources by avoiding unnecessary investigations. Health care providers should think outside the box, especially while dealing with traveller patients.
CONGENITAL CYTOMEGALOVIRUS INFECTION IN CHILDREN WITH SENSORINEURAL HEARING LOSS: A 5-YEAR CLINICAL AUDIT

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Background: Our hospital routinely offered outpatient clinic appointment to children with sensorineural hearing loss (SNHL) for comprehensive assessment to determine the cause of SNHL. An audit was carried out to determine presence of abnormal clinical findings and investigation results consistent with congenital cytomegalovirus infection (cCMV) among SNHL children diagnosed in the last 5 years. We expected minimum 10% of SNHL cases were caused by cCMV.

Methods: Data of children with SNHL over 5-year period between May 2014 and April 2019 were obtained from electronic systems (Badgernet Neonatal, Newborn Infant Physical Examination and Sunquest Integrated Clinical Environment). Information on aetiologies responsible for SNHL, presence of physical signs, abnormal laboratory and neuroimaging results suggestive of cCMV were collected. This audit study was registered and approved by the trust’s Clinical Audit Department (Reference no. 9958).

Results: Of 96 children with SNHL, there was no documented cause in 62.5% (60/96). Median age of SNHL confirmation was 33.5 days (range 5 days-132 weeks). CMV tests were performed on 55 patients at a median age of 19 weeks (range 1-207 weeks) but none were tested positive. 98% (54/55) were tested outside 21 days old. 22% (12/55) had inappropriate diagnostic cCMV test. There was no statistically significant association between CMV testing among SNHL patients and presence of abnormal clinical signs or investigation results.
Conclusions: Our audit suggests that the current practice of investigating for cCMV as a cause of childhood SNHL in our centre is ineffective and has poor yield. This can be improved by adopting cCMV targeted screening programme for infants who fail initial Newborn Hearing Screening Programme. Neurological complications of cCMV can potentially be averted by accurate and early diagnosis followed by prompt treatment when indicated.
Risk for Asthma Following Pneumonia in Infancy – A Nationwide Family-Based Cohort Study

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Background: Asthma is a chronic pulmonary disease that attributes to significant morbidity. Few studies have assessed the risk for asthma following pneumonia exposure in infancy. We aimed to assess the association between pneumonia exposure in infancy and subsequent asthma at 4 years with adjustments for important confounding factors.

Methods: A register-based cohort study of all Swedish citizens born 2001-2010 was performed. The main exposure was pneumonia diagnosis and primary outcome was asthma. Both were defined using registers held by the National Board of Health and Welfare (NBHW). Further data were retrieved from Statistics Sweden. Odds ratios (ORs) and 95% confidence intervals (CIs) for asthma following pneumonia exposure were calculated using logistic regression, adjusted for important confounders. To further adjust for shared environmental and genetic confounding on the association, sibling analyses were performed, i.e. analyses comparing siblings with different exposure.

Results: Of n=948,043 children included in the study, 60,671 (6.4%) had asthma at 4 years. Children exposed to pneumonia were significantly more likely to have asthma at 4 years as compared to unexposed (19.0% vs 6.1%, crude OR 3.63 (95% CI: 3.51-3.76), adjusted OR 3.38, (95% CI: 3.26-3.51)). The OR for asthma at 4 years following pneumonia in infancy was 2.88 (95% CI: 2.65-3.14) in the sibling analysis.

Conclusions: Pneumonia in infancy was associated with a highly increased risk for subsequent asthma even after adjustments for important environmental and genetic confounding.
MEASLES OUTBREAK IN SAO PAULO BRAZIL 2018-2019

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Background: During 2019, São Paulo city has experienced a measles outbreak that reached over 50,000 suspected cases with more than 14,000 confirmed. A measles mass immunization campaign was initiated including children and young adults between age 6 months and 30 years old. We present data on pediatric patients with confirmed measles and admitted to 3 medical centers in the North-Central region of Sao Paulo, Brazil.

Methods: All children and adolescents with suspected measles were included. The primary diagnosis was based on clinical evaluation and included fever, conjunctivitis, respiratory symptoms, and exanthema. The immunization chart was revised when available. The diagnostic was confirmed by RT-PCR in urine, blood and/or saliva. Among the 343 suspected cases evaluated in three hospitals (135 cases under 12 months; 145 cases between 12-59 months; 58 cases over 60 months).

Results:

<table>
<thead>
<tr>
<th>Age (months)</th>
<th>suspected</th>
<th>confirmed</th>
<th>hospitalized</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 12</td>
<td>135</td>
<td>74 (53%)</td>
<td>15 (20 %)</td>
</tr>
<tr>
<td>12-60</td>
<td>145</td>
<td>13 (11%)</td>
<td>5 (38%)</td>
</tr>
<tr>
<td>&lt; 60</td>
<td>58</td>
<td>6 (10%)</td>
<td>0</td>
</tr>
</tbody>
</table>

A total of 93 cases were confirmed and 20 required hospitalization (Table 1). From the suspected patients, 88 have been vaccinated with at least one measles dose, 44 have not been vaccinated, and in 160 the information was not available. All patients had fever and rash. The predominant clinical symptoms were cough associated with a runny nose (44/91). There were no deaths recorded.

Conclusions: Measles is a reemergent disease although immunization is widespread. The rate of infections was higher in the group younger than 12 months. Even with immunization reaching the infants between 6 and 12 months most of the admitted cases were in this age. There were not death cases in these patients and most of the admissions were due to respiratory disease.
4-YEAR-OLD CONGOLESE BOY WITH AN UNSPECIFIC RASH

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Title of Case(s): 4-year old Congolese boy with an unspecific rash

Background: The incidence of monkeypox (MP) is increasing worldwide. Smallpox vaccination has cross-protective effects against MP, and the rise in the incidence of MP may be explained by reduced immunity to poxvirus after the cessation of smallpox vaccination, as well as increased interhuman transmission may play a role. MP remains a diagnostic challenge due to lack of diagnostic tools and data collection in endemic areas.

Case Presentation Summary: A 4-year-old boy presented to a hospital in the Northern DR Congo with general malaise, tp 37.9°C, rhinitis, conjunctivitis, cough, severe left-sided cervical lymphadenitis, and a non-itchy vesiculopapular rash with elements sized 5 - 10 mm covering his truncal area and face. He was alert with HR 115 bpm and RR 30/min. He was previously healthy and had received no vaccinations. The child was admitted on suspicion of complicated chickenpox or measles and started on i.v. amoxicillin-clavulanic acid, retinol tablets, antibiotic eye drops, paracetamol, and i.v. maintenance fluids. Over the next week the rash grew and penetrated 3-4 mm into his skin and spread to cover his entire body surface – including palms, foot soles and mucous membranes. He was changed to i.v. ceftriaxone, and pain management was intensified. The child passed away on admission day 12. Sufficient diagnostic tests were not carried out, however the patient was recognized as a case of monkeypox.

Learning Points/Discussion: MP often remains a clinical diagnosis due to limited laboratory facilities, as well as lack of efforts put into data collection in endemic areas. Smallpox vaccination gives crossprotection against MP. Reduced immunity to poxvirus after the cessation of smallpox vaccination may explain the rise in MP. Increased interhuman transmission driven by migration due to climate change and war may be another contributor.
Background: Pertussis and influenza vaccination has proven effective in protecting pregnant women and newborns against these immunopreventable diseases. Despite this, there is a lower coverage of influenza vaccination comparing to pertussis in pregnant women in the third trimester of pregnancy. The aim of this study is to describe the differences observed between influenza and pertussis vaccination in pregnant women in the third trimester of pregnancy during the 2018-2019 influenza season in the Valencian Community (VC).

Methods: Retrospective observational study. Data for pregnant women in the third trimester of pregnancy who received pertussis and influenza immunization during influenza vaccination campaign (from 43/2018 to 5/2019 epidemiological weeks) in the VC were obtained from the Immunization Information System (IIS), the computerized nominal registry of immunizations of Valencian Community. Study variables: influenza and pertussis vaccination date (epidemiological week), age and nationality.

Results: 9420 women received pertussis immunization. Of these, 6394 (67.8%) were vaccinated against influenza. While 69.3% of influenza vaccinations were conducted between epidemiological weeks 43 and 46, pertussis immunization was constant throughout the period. The 25-29 age group presented the highest level of compliance with influenza immunization (69.1%) comparing to pertussis vaccination. Significant differences were observed between Spanish women who received influenza vaccination (68.7%) and other nationalities (62.9%), with differences between countries ranging from 57.3% (Romania) to 73.4% (Colombia).

Conclusions: Pertussis vaccination coverage is higher than influenza vaccination coverage in pregnant women in the third trimester of pregnancy during influenza vaccination campaign. The majority of influenza vaccinations were conducted during the first weeks of the study period, while pertussis vaccination distribution was constant. The 25-29 age group and women with Spanish nationality presented the highest level of compliance with influenza immunization comparing to pertussis vaccination.
PROLONGED FEVER IN A WELL CHILD

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Title of Case(s): Prolonged fever in a well child

Background: Brucellosis is a zoonotic disease with high reported incidence in the Middle East countries that can present with prolonged fever and non-specific symptoms. *Brucella* species can be transmitted through contaminated environment, inhalation of aerosols or consumption of unpasteurized dairy product. We present a case of a young child who was admitted for prolonged fever and her blood culture returned positive for *Brucella* species.

Case Presentation Summary: A well-looking 16-month-old girl presented with 13 days of fever and no localising symptom. Hepatosplenomegaly, bicytopenia and raised transaminases were present. There was no reported significant travel or exposure history. She was empirically started on intravenous ceftriaxone for presumed salmonellosis, but blood culture returned positive for *brucella* species at 48 hours. The *brucella abortus* and *melitensis* serology were also positive at 1:640. Parents then revealed that the patient had travelled to Syria, Iraq and Lebanon 5 months prior although there was no animal contact or consumption of unpasteurized dairy products. She was started on oral rifampicin and bactrim. Repeat blood culture returned negative and fever subsided on day 3 of treatment. On outpatient review, she completed 6 weeks of antibiotics with improvement in the biochemical markers. However, three microbiology laboratory staff had exposure to *brucella* species. They were given 3 weeks of doxycycline and rifampicin with serial serological monitoring for 24 weeks post exposure.

Learning Points/Discussion: As *brucella* species have long incubation period, an extended travel and exposure history have to be taken in patients presenting with prolonged fever. *Brucella* can be transmitted in the contaminated environment in countries with high incidence even if there is no reported direct exposure. The microbiology laboratory needs to be informed of cases of brucellosis so that appropriate precautions can be taken.
INFLUENZA IMMUNIZATION AMONG PREGNANT WOMEN IN THE THIRD TRIMESTER DURING 2018 INFLUENZA SEASON IN THE VALENCIAN COMMUNITY: A DESCRIPTIVE STUDY.

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Background: Pregnant women have an increased risk of severe complications in case of influenza disease, especially in the third trimester and if they suffer from chronic pathology. The aim of the study is to describe the pregnant women in the third trimester vaccinated against influenza during the 2018 influenza season in the Valencian Community (VC) and to analyse the prevalence of chronic pathology in the subgroup of women that were vaccinated the previous season.

Methods: Descriptive observational study of pregnant women in the third trimester of pregnancy that were vaccinated against influenza in the VC during the 2018-2019 influenza vaccination campaign. Age, immunization date, nationality and vaccination record were obtained from the Immunization Information System (IIS). Active diagnoses (ICD-9) of those conditions where influenza vaccination is recommended were obtained from the Ambulatory Information System (AIS).

Results: 6394 pregnant women in the third trimester were vaccinated. 81.6% of vaccines were administered between epidemiological weeks 43 and 47 (2018). The peak incidence of influenza cases occurred in week 6 (2019) (1454 cases/100,000). Mean age of pregnant women was 34.2 ±0.14 years. The 35-39 age group presented the highest proportion of vaccinees. Of 397 (6.2%) pregnant women who were vaccinated the prior season (2017), 196 (49.3%) were diagnosed with a chronic pathology. Of these, 8.6% were non-Spanish. Chronic respiratory diseases (27%) and anaemia (26%) were predominant.

Conclusions: There was a time lag of 10 epidemiological weeks between the peak incidence of influenza cases and the time when the majority of influenza vaccines were administered. The highest proportion of vaccinees was observed in the 35-39 age group. Chronic respiratory diseases and anaemia were the prevalent conditions in pregnant women vaccinated against influenza during the prior influenza vaccination campaign.
Background: Neonatal sepsis is common in sub-Saharan Africa and a major reason for admission to neonatal intensive care units in developing countries which often lead to neonatal mortality in low income communities. Evidence regarding its risk factors can be useful for clinical practice and prevention strategies. This survey was designed to assess the prevalence and risk factors associated with neonatal sepsis among new-borns at a Primary Health Centre, Akure, Ondo State, Nigeria.

Methods: This facility-based cross-sectional retrospective study involved 270 children, consisting of 225 delivered over a period of twelve(12) months in February 2018 to January 2019 at the Orita-Obele Primary Health Centre Akure and forty-five(45) children delivered at home but brought to the health facility 24 - 48 hrs after birth. Hospital records of each child was used as data source. Data collected was collated and analysed using SPSS version 22. Binary and multiple logistic regressions was used to observe the association between independent and dependent variables.

Results: This study found that 35% of the total neonates presented with signs and symptoms suggestive of neonatal sepsis at birth and/or 24 to 48 hrs after birth while over 80% of those that were delivered at home had sepsis. Factors such as unhygienic cord care, birth asphyxia, premature rupture of membranes, prematurity and low-birth weight were significantly associated with neonatal sepsis.

Conclusions: This study revealed high rate of neonatal sepsis especially amongst those neonates delivered at home. It is recommended that emphasis should be placed on preventive actions such as good cord care, breast feeding under hygienic conditions while skilled birth attendance should be promoted, as critical intervention for reducing the incidence of neonatal sepsis. Home delivery should be discouraged through aggressive sensitisation and provision of incentives.
Background: Scrub typhus is an acute febrile zoonotic disease, caused by Orientia tsutsugamushi. The clinical features are diverse ranging from a mild, self-limiting illness to varied complications like meningoencephalitis, acute respiratory distress syndrome, hepatitis, acute kidney injury, myocarditis leading to heart failure and at times, multi organ dysfunction. This study attempts to report the various presentations and the complications of scrub typhus encountered in the paediatric age group.

Methods: A prospective observational cross sectional study on 56 cases of scrub typhus, was done from October 2018 to September 2019 at R. G. Kar Medical College and Hospital, a tertiary care centre in Kolkata. Both inpatient and outpatient department cases were included. Scrub typhus was diagnosed by IgM ELISA and confirmed by more than fourfold increase in titre subsequently. Statistical analysis was done using Epi Info™ 7.2.2.2.

Results: Incidence of scrub typhus was significantly higher (p < 0.001) in the rainy season (57.1%). All the cases presented with fever (100%), with a mean duration of 10.5 days. Headache (46.4%) and myalgia (46.1%) along with hepatomegaly (58.9%) and lymphadenopathy (41.1%) were the significant (p<0.05) symptoms and signs at presentation. Among these, 21.4% of the cases required intensive care management. Every 2 out of 5 cases (39.2%) developed complications. Central nervous system (17.9%) and gastrointestinal (10.7%) complications dominated and were significantly higher (p<0.05) than the rest. Other complications observed were nerve palsies, acute disseminated encephalomyelitis, Kawasaki disease, cerebellitis, hepatitis, myocarditis and pericardial effusion.

Conclusions: High index of suspicion is needed for the diagnosis of scrub typhus. Any case of prolonged febrile illness, suspected to be a case of scrub typhus, warrants immediate empirical therapy with anti rickettsial antibiotics to prevent further deteriorations. Despite life threatening complications in a few cases, there was excellent response to doxycycline or azithromycin, resulting in reduced morbidities and better prognosis.
RNA TRANSCRIPTOMIC IN DISTINGUISHING ADENOVIRUS INFECTION FROM BACTERIAL INFECTION IN CHILDREN

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**Background:** Human adenovirus (HAdV) is one of the most common respiratory viruses worldwide. Despite wide range of clinical manifestations, HAdV is often difficult to distinguish from bacterial infection, due to high CRP and WBC. Furthermore, HAdV may co-infect bacterial cases. We hypothesized that the host blood transcriptome can distinguish patients with HAdV-driven disease, from those with bacterial infection with or without co-incident HAdV detection.

**Methods:** Febrile children presenting to participating hospitals in United Kingdom, Spain, Netherlands and the United States during 2009-2013 were prospectively recruited, compromising the discovery and validation groups. After microbiological investigations, each group was classified as definite bacterial, viral or uncertain. A set of genes distinguishing definite HAdV mono-infection from bacterial infection was identified in the discovery group and applied to ambiguous cases.

**Results:** The discovery group comprised of 8 HAdV, 18 bacterial infections, and 47 healthy controls. A 12-transcript signature comprising of transcripts that exhibited the highest discordance in terms of expression between HAdV and bacterial cases was identified. When the 12-transcript signature was implemented as a disease risk score (DRS) in the validation group (12 HAdV and 11 bacterial infections), 10 of 11 patients with microbiologically confirmed bacterial infection were classified as bacterial (specificity, 90.91% [95% CI, 72.73%-100%]) and all 12 with definite viral (HAdV) infection were classified as HAdV (sensitivity, 100% [95% CI, 100-100%]). When the DRS was applied to HAdV-positive cases of uncertain bacterial or viral status, 4 of 6 were classified as HAdV aetiology; of these 3 had CRP>100mg/L.

**Conclusions:** This study provides the preliminary data of RNA transcriptome in distinguishing ambiguous cases with features of both viral and bacterial infection. Further studies are needed to validate the clinical utility of this signature.

**Clinical Trial Registration:** St. Mary Research Committee (REC09/H0712/58 and EC3263), Ethical Committee of Clinical Investigation of Galicia (CEIC ref 2010/015), UCSD Human Research Protection Program No. 140220, Academic Medical Center University of Amsterdam (NL 41846.018.12 and NL34230.018.10)
A CLINICAL AND DEMOGRAPHIC ANALYSIS OF HOSPITALIZED CHILDREN WITH INFLUENZA A (H1N1) IN A TERTIARY CARE PEDIATRIC HOSPITAL SETTING IN SOUTH INDIA

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Background: Influenza A (H1N1) strain causes significant morbidity and mortality in the pediatric population. The disease spectrum ranges from self-limiting viral illness to severe disease necessitating PICU care. Over the past 2 years (2017-2019) there have been 82,258 confirmed cases (adults and children) and 4611 deaths in India. There is paucity of pediatric data in India necessitating studies to assess the burden and impact of H1N1.

Methods: This was a retrospective analytical study that included all confirmed cases of H1N1 (RT-PCR) who were hospitalized over a period of 2 years. They were categorized as B1,B2,C as per published guidelines for managing children with H1N1. Their case records were analyzed for demography, clinical features, flu vaccination, co-morbidities, radiological findings, antibiotic usage, duration of stay, PICU stay and disease outcomes.

Results: Over a period of 2 years, 102 children with PCR confirmed H1N1 were hospitalized (M:F 1.69:1). 51 children (50%) were under 2 years of age. Majority of the cases belonged to category B1 (n=76, 74.5%). Bronchial asthma (n=22, 21.6%) was the commonest co-morbidity. The Mean duration of hospitalization and antibiotics received was longest in category C (8.69 days) (p=0.0018) and (7.77 days) (p=0.0049) respectively. 9 children (8.8%) needed PICU care. 90 children (88%) and 8 children (8%) recovered without and with sequelae respectively and 4 children (4%) succumbed.

Conclusions: Our study of the hospitalized children of H1N1 showed that while a majority of the children had an uncomplicated course and recovered without sequelae, 8.8% PICU admissions and a 4% mortality indicates the need for prevention and further research to improve outcomes. Empirical antiviral therapy in selected cases is prudent as it may improve outcomes. Vaccination and isolation of cases are equally important as preventive and containment care.
ISONIAZID AND RIFAMPICIN SUSCEPTIBILITY TESTING USING LINE PROBE ASSAY GENOTYPE MTB DR PLUS VERSION 2.0 DIRECTLY FROM RESPIRATORY SAMPLES OF CHILDREN WITH PULMONARY TUBERCULOSIS

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Background: In high burden countries like India, childhood tuberculosis is estimated to contribute 15-20% of all the Pulmonary Tuberculosis cases and is one of the leading causes of childhood mortality. WHO has recommended line probe assays for drug susceptibility testing only in smear positive and MDR TB cases. In the present study we evaluated the diagnostic role of commercially available line probe assay for direct use in smear negative pulmonary tuberculosis cases diagnosed by Xpert MTB/RIF(CBNAAT) in children.

Methods: Children ≤ 12 years with clinical suspicion of Pulmonary Tuberculosis and who tested positive for Mycobacterium tuberculosis complex by GeneXpert (CBNAAT) assay were included in the study over a period of six months. Samples like sputum / induced sputum or gastric aspirate or bronchoalveolar lavage were collected from the suspected patients and processed for Line Probe assay along with Ziehl-Neelsen staining.

Results: A total of 35 Children testing positive by CBNAAT were recruited in the study. Majority of cases were Smear Negative (30, 85.8%) Amongst 30 smear negative cases, Mycobacterium tuberculosis band using line probe assay was observed in 25(83.3%) cases. CBNAAT showed Rifampicin resistance in 1 isolate (3%) whereas line probe assay showed 100% susceptibility to Rifampicin. Results of Line Probe Assay showed majority of cases were Isoniazid sensitive (25, 83.3%) and five were Isoniazid resistant (5, 20%) with commonest mutation at INH WT1.

Conclusions: Although WHO recommends use of Line Probe assay in smear positive cases only but according to our study it can be used directly on smear negative sample and can also be used in detecting monoresistance to Isoniazid and Rifampicin in comparison to CBNAAT. Hence Line probe assays can be used in smear negative cases for preliminary evaluation as well as drug susceptibility
CYTOKINE RESPONSE IN CHILDREN WITH ASEPTIC MENINGITIS

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Background: Aseptic meningitis is one of the most common inflammatory disorders of the meningitis of the central nervous system. The vast majority of aseptic meningitis cases are viral infections with most caused by non-polio enteroviruses, which account for more than 85% of cases. The levels of proinflammatory cytokines in CSF are successfully used in early diagnosis as well as in differential diagnosis of bacterial and aseptic meningitis in children.

Methods: 68 children, aged 1–18 y. treated in the Department of Pediatric Lviv Infectious Diseases Clinical Hospital with preliminary diagnosis of aseptic meningitis were kept under observation. Clinical peculiarities of the cytokine profile of CSF and blood (based on the results of determining of IL-1b, IL-4, IL-10, TNF-α levels) and procalcitonin in children were revealed, meningitis severity were estimated by AMSS score.

Results: It was found that in the majority of patients (73%-89%) with aseptic meningitis, the levels of IL-1b, TNF-α and IL-10 in CSF were increased and exceeded the serum cytokines levels. The severe course of meningitis was characterized by significantly higher concentrations of IL-1b and TNF-α in CSF, which was confirmed by positive correlation between AMSS score and IL-1b concentration ($r = 0.46, p <0.01$), IL-10 ($r = 0.32, p <0.01$), TNF-α ($r = 0.62, p <0.05$). The IL-10 / TNF-α ratio was - 17.8.

Conclusions: Increasing of anti-inflammatory cytokine levels in aseptic meningitis contributes to preventing of excessive inflammatory/immune responses in the brain. This can cause a longer disease course and a longer recovery period. This can indicate active production of cytokines in the central nervous system due to intrathecal inflammation and activation of immune responses caused by viral infection, but not its penetration to CSF from the blood.
HUMORAL IMMUNITY TO BORDETELLA PERTUSSIS INFECTION IN THE FIRST YEAR OLD CHILDREN

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Background: In Ukraine, despite the fact that 70-85% of children are vaccinated against pertussis annually, the infants pertussis rates is still high and diseases has not been eradicated and has recently reemerged as a major public health threat.

Methods: 60 children aged 1-12 mon. with pertussis witch were treated at the Lviv Infectious Diseases Hospital were kept under observation. Diseases symptoms, serum cytokine (IL1β, IL2, IL10, INF-γ) levels were studied, pertussis severity were estimated by M.-P. Preziosi, E. Hallora score. PCR test for B. pertussis detection were made.

Results: In infants with severe diseases (according to pertussis severity score) the intensive production pro-inflammatory (IL1β, IL2, INF-γ) cytokines were established, its level was 3 – 4,5 times higher than in healthy children. Simultaneously, we observed the increased levels of anti-inflammatory cytokines – IL10 (38,65±4,22 pg/ml), that was more than three times higher than control groupe. In patient with mild diseases levels pro-inflammatory and anti-inflammatory cytokines was also higher compare to control groupe, but levels INF-γ and IL1β was significantly lower than in patient with severe diseases (INF-γ – 33,90±5,15 pg/ml; IL1β – 8,37±1,44 pg/ml).

Conclusions: Our results suggest about a strong relationship between diseases severity and pro-inflammatory cytokine levels, anti-inflammatory cytokins levels was increase regardless of the pertussis severity

Clinical Trial Registration: N/A - not registered
PERFORMANCE OF A POINT-OF-CARE-TEST IN PAEDIATRIC BRONCHIOLITIS PATIENTS DURING THE 2018-2019 WINTER PERIOD.

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Background: Bronchiolitis is a common lower respiratory tract infection and caused by respiratory syncytial virus (RSV), parainfluenza and influenza A and B viruses. These are highly contagious and the condition is responsible for the biggest cause of paediatric emergency admissions. Point-of-care-tests (POCTs) are an alternative to traditional laboratory methods to identify these patients and their use can enhance patient flow pathways for the management of this condition.

Methods: We conducted a retrospective observational diagnostic study to report on sensitivity and specificity of the BD Veritor POCT which detects RSV and influenza A or B. The study was conducted in a single paediatric centre in the East Midlands in the winter period between November 2018 and March 2019. Data was collected using case notes and electronic records. Statistical analysis was performed using Microsoft Excel.

Results: A total of 152 patients (children aged 0-16 years old) fulfilled the inclusion criteria. 32 patients were subsequently excluded due to insufficient and incomplete data. Patients were tested on the POCT using nasopharyngeal aspirates (NPAs). The sensitivity and specificity for the detection of influenza A was 78.6% and 98.9 % respectively. The sensitivity and specificity for the detection of RSV was 82.3% and 98% respectively. There were no influenza B infections in this population during this study period.

Conclusions: Bronchiolitis is a common and serious condition, seen frequently in children over the winter period. Our results demonstrated that the BD Veritor system had a high degree of sensitivity and specificity to detect both Influenza A and RSV in children aged 0-16 years old presenting with coryzal and flu-like symptoms. Our results demonstrate and validate the use of the BD Veritor system in the diagnosis, management and isolation of affected patients.
Background: Respiratory tract infections (RTI) are the commonest diagnoses among children seeking medical attention accounting for a vast number of antibiotic prescriptions in India. Empiric antibiotic treatment is common among children with RTI, despite infections being predominantly viral. Poor diagnostic tools for viruses and concern about bacterial etiologies lead to inappropriate antibiotic use. We attempted to look into the epidemiological, clinical profile, antibiotic exposure and outcome in children hospitalised with respiratory tract infections.

Methods: A prospective, observational study was conducted in a pediatric hospital from October 2019 to Jan 2020. Respiratory samples from children hospitalised with suspected acute respiratory tract infections were sent for PCR analysis (FilmArray). Nasopharyngeal aspirates were sent for suspected upper and pleural fluid for lower respiratory tract infections (URTI) & (LRTI) (pneumonia with effusion) respectively. Clinical and demographic data was gathered via a preformed questionnaire.

Results: A total of 26 children (M:F 2:1) were enrolled and samples (NPA- 21, Pleural fluid-5) were sent for PCR analysis. The mean age of children was 46.6±49 months. The commonest pathogen isolated from NPA was Rhinovirus in 6(28%) followed by M. pneumoniae in 5 (23.5%) children. S.pneumoniae (n-3, 60%) was the commonest pathogen isolated from pleural fluid. After the diagnosis of viral infection antibiotics were completely stopped in 4 (15.3%) and de-escalated to a narrower spectrum in 3 (11.5%) children respectively. De-escalation was observed in 4 (80%) children with bacterial pneumonia.

Conclusions: Diagnosis with PCR (Film-array) encouraged antibiotic stewardship practices and helped in isolation of cases leading to containment of infection. It also aided in early administration of antivirals and macrolide antibiotics where indicated. After establishing a PCR diagnosis we observed lesser events of inappropriate antibiotic escalation. We recommend PCR analysis on a case to case basis to aid in holistic management.
Title of Case(s): Kawasaki disease: epidemiological, clinical, cardiological and treatment aspects in 2 private hospitals in Buenos Aires, Argentina.

Background: Introduction: Kawasaki disease (KD) is one of the most frequent vasculitis in children. It causes a variety of cardiological disorders (coronary arteri aneurysms, cardiomyopathy, heart failure), which increase the morbidity and mortality. Methods: a retrospective, descriptive study of 36 hospitalized patients diagnosed with KD, according to the American Heart Association criteria, describing epidemiological, clinical, cardiological, echocardiographic and treatment data, within 05-2013 to 10-2019.

Case Presentation Summary: 36 children, 25 male (M). Median hospitalization: 6.5 d, median age: 38.5 months. Age <6 m: 1, 7-24 m: 12, 25-60 m: 19. Axillary temperature> 38ºC: 36. Average duration with > 38ºC: 6.9 days. Generalized maculo papular rash: 26, lateral cervical adenopathy: 21, conjunctival injection 24, extremities desquamation: 24, extremities edema: 11, cheilitis: 25, bcgitis: 9. 25 were typical KD. Laboratory: median WBC: 17830 (10/9 L), neutrophils: 69%, platelets: 598,000mm3, quantitative PCR: 73mg / dl VSR: 88mm / h, Serologies were performed,Electrocardiogram and echocardiogram were done. EKG PR prolonged: 1, QTc prolonged: 2. No ST involvement or arrhythmia were detected. Echocardiogram: some abnormality: 10, coronary artery ectasia: 6, mild dilation: 2, severe dilation: 1. All patients received immunoglobulins (IVIG) 2mg / kg / day. All received aspirin (80 mg / kg / day) until 48/72 h afebrile, continued for 6 weeks (3-5 mg / kg /day).

Learning Points/Discussion: Discussion:The aeteology of this disease (KD) remains unknown, innumerable theories about its origin are described. immunologic response (KD is a systemic, inflammatory illness that particularly affects medium-sized arteries, especially coronary arteries) In Argentina, where the BCG vaccine is part of the National immunization programme, BCGItis is a relatively frequent sign in this disease. Similarity was observed in clinical, laboratory and electrocardiographic data compared to the literature.
MYCOBACTERIUM BOVIS INFECTIONS IN IMMUNOCOMPROMISED PEDIATRIC PATIENTS: A CASE SERIES AND LITERATURE REVIEW

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Title of Case(s): MYCOBACTERIUM BOVIS INFECTIONS IN IMMUNOCOMPROMISED PEDIATRIC PATIENTS: A CASE SERIES AND LITERATURE REVIEW

Background: Tuberculosis (TB) diagnosis and management in immunocompromised host patients is challenging. The incidence of mycobacterial infections is higher in solid-organ transplant recipients and patients with hematological malignancies than in the general population, due to immunosuppressive drugs and chemotherapy. Mycobacterium bovis (M. bovis ) is a member of the Mycobacterium tuberculosis complex (MTBC), the diagnosis of M. bovis should be considered in the setting of an MTBC isolate with pyrazinamide (PZA) monoresistance.

Case Presentation Summary: We report a case series of five immunocompromised pediatric patients with Mycobacterium bovis infections between 2013 and 2017. The first case was a 12-year-old, boy post deceased donor renal transplant (DDRTx) secondary to infantile nephrotic syndrome. Three cases were 9, 7, and 6 years old, with acute lymphoblastic leukemia (ALL) on maintenance chemotherapy. Fifth case 8 years old, female with ALL just ended her chemotherapy. Mycobacterial cultures of sputum and gastric aspirate confirmed the diagnosis of pulmonary TB in four cases; and cerebrospinal fluid (CSF) culture confirmed TB meningitis in one case. TB genotyping confirmed M. bovis in all the cases. Tuberculin Skin test (TST), and interferon-gamma release assays (IGRAs) were negative in all the cases. M. Bovis was susceptible to first-line anti-TB drugs except for pyrazinamide (PZA). The duration of therapy was individualized. Recovery was full for all the cases with no relapse after a year of follow-up.

Learning Points/Discussion: Interpreting a negative TST or IGRAs needs a high level of caution since those patients may be skin test anergic, and the presence of indeterminate or negative IGRAs was observed with low lymphocyte counts. In conclusion a high clinical index of suspicion, early diagnosis and prompt treatments essential in limiting morbidity and mortality from mycobacterial infections in an immunocompromised host.
FOUR CASES OF INFECTIVE DERMATITIS IN BAMAKO, MALI

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Title of Case(s): Four cases of infective dermatitis in Bamako, Mali

Background: Infective dermatitis is the major pediatric manifestation of HTLV1 infection. This diagnostic difficulty is responsible for the wandering of cases and exposes to complications. Affected subjects are at risk of developing malignant tumours several years later. Diagnosis and case surveillance are made more difficult in the context of resource-limited countries.

We report the first 4 cases described in our country Mali.

Case Presentation Summary:
Case 1: A 17-month-old girl, breastfeeding and with a history of protein-energy malnutrition, presented with erythematouskeletal lesions on the trunk, and axillary folds. Exulcated and crusted lesions around the eyes, nostrils and scalp. HTLV1 serology was positive. Undetected mother.
Case 2: An 18-month-old boy with oozing ulcerative lesions around the eyes, nostrils and ears. Scaly lesions on the trunk and shoulders. Mother and child tested positive for HTLV1.
Case 3: A 4 year old boy, breastfed until 24 months of age, followed for congenital heart disease, had pruritic vesicular lesions localized to the trunk and limbs for 7 months, treated for eczema. On examination, papules, on the chest and perinarinarinarin erosion were noted. Mother and child tested
positive for HTLV1.  
Case 4: A 9-month-old boy, breastfed, presented with erythematous-squamous lesions on the face and trunk with chronic rhinitis. Unsuccessfully treated for seborrheic dermatitis. Mother and child tested positive for HTLV1. All cases were successfully treated with sulfamethoxazole-trimethoprim

Learning Points/Discussion: They are the first reported cases in Mali. The viral infection appears to be of maternal origin. a. Our cases are peculiar in the proportion of boys (3/1) contrary to the data in the literature which report a predominance of females. And by the young age of the patients, in Subsaharian Africa, infective dermatitis should be discussed for any recurrent pyodermatitis in children.
OSTEOARTICULAR TUBERCULOSIS: A GREAT MIMICKER

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Title of Case(s): Osteoarticular Tuberculosis: A great mimicker

Background: Children with TB have historically been neglected by clinicians and policy makers because being paucibacillary it is thought to be non-infectious from the public health perspective. In Europe and North America, considered low burden regions, pediatric incidence rates vary from 1 to 15/100,000/year. Skeletal tuberculosis occurs in around 5% of pediatric extrapulmonary tuberculosis patients, Approximate distribution of the skeletal TB are spine (50%), hip (20%), knee (10%), ankle and foot (5%), hand and wrist (3%), elbow (2%), shoulder (1%), bursal sheaths and other bones (8%).

Case Presentation Summary: In this communication we report five cases of Osteo-articular (OA) tuberculosis presenting to the Orthopedics Department of Lady Hardinge Medical College and associated Hospitals. Clinical details have been summarized in the Table-1. Age ranged from 4-12 years. Duration of symptoms varied from 3 weeks to 4 months before the definitive diagnosis could be made. Usual complaint were pain and swelling. In one patient (case-1) underlying condition masked the symptoms. All but one case mimicked congenital lesion or dysplasia. Radiologic examination (X-ray and CT) could provide diagnosis in two. Histopathologic confirmation was available in three cases. Surgical intervention was required in three patients. All cases recovered completely with standard anti-tubercular treatment.
Learning Points/Discussion: OA tuberculosis may mimic congenital lesions or dysplasia in children. Once suspected, diagnosis can be made reliably on clinical and radiological examination. CT and MRI demonstrate the localization and extent of bone and soft-tissue lesions. Whenever there is doubt, it is best to prove the diagnosis of TB by biopsy of the diseased tissue (granulations, synovium, bone, lymph nodes, margin of ulcers or sinuses).
Background: In August 2015, the German Standing Committee on Vaccination (STIKO) changed the pneumococcal conjugate vaccination (PCV) schedule for term infants from a 3+1 scheme (2, 3, 4, and 11-14 months of age) to a 2+1 scheme (2, 4 and 11-14 months of age). It was expected that a reduction might lead to a higher acceptance of vaccination. The study aim was to assess vaccination rates and timeliness for PCV after the change of recommendation based on real world data.

Methods: A Retrospective claims data analysis using InGef research database containing an age and gender representative sample of the statutory health insured population in Germany was conducted. The study population consisted of all term infants in this database born in 2013 (last birth cohort completely under 3+1 recommendation) or in 2016 (first birth cohort completely under 2+1 recommendation) with an individual follow-up of 24 months.

Results: After follow-up of 24 months, 90.9% (91.2%) of the 2016 (2013) cohort received at least one dose PCV. At the same age, 67.7% of the 2013 cohort received a booster dose according to the 3+1 schedule and 75.6% of the 2016 cohort received a booster dose according to the 2+1 schedule (71.7%) or 3+1 (3.9%) schedule. Of those receiving the booster dose, only 46.3% (2016) and 45.1% (2013) received the booster dose on time as recommended.

Conclusions: So far, there is no clear evidence that the reduction of the vaccination schedule for PCV induced a higher acceptance of PCV vaccination. Although the rate for the booster dose slightly increased, nearly 25% of the infants born in 2016 did not receive a booster dose. Furthermore, vaccinations were often still delayed and the rate of unvaccinated infants remained constant.
HEPATITIS A REVEALING HIV INFECTION IN A TEENAGE BOY

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Title of Case(s): Coinfection in a teenage boy

Background: In 2017 an outbreak of hepatitis A was announced in Europe. Most cases are men between 15 and 45 years and MSM (men who have sex with men) are the most affected group. In high-income countries the prevalence of anti-HAV antibodies in the general population is low. The high proportion of susceptible individuals among adults allow transmission, which is limited by personal hygiene.

Case Presentation Summary: In July 2017 a 17-year-old boy was admitted to hospital because of jaundice. For the previous few days he complained of abdominal pain. He had no comorbidities, lived in Poland, did not travel abroad. On admission he was jaundiced, total bilirubin level was 7.52 mg/dl; of which 7.08 mg/dl was conjugated, alanine aminotransferase activity was 1731U/l, but INR remained normal (1.19). Ultrasonography revealed a slightly enlarged liver. Diagnosis was based on the detection of serum HAV-specific IgM antibodies along with elevated liver enzymes. During anamnesis he admitted to have had unprotected sex with several partners – sexually transmitted diseases (STDs) screening was performed and as a result he was diagnosed with HIV infection. One month later his sister was admitted to hospital with jaundice – diagnosed as hepatitis A; fortunately HIV testing was negative in her case.

Learning Points/Discussion: Transmission of hepatitis A virus can occur from any sexual activity with an infected person and is not limited to the fecal-oral contact. That is why patients diagnosed with hepatitis A should also be screened for HIV and other STDs. What is more, it is important to remember about asking during anamnesis about sexual activity even in the younger population.
Title of Case(s): Extensive Lymphadenopathy in an adolescent girl.

Background: Tuberculous lymphadenitis is one of the most common presentations of extrapulmonary TB. In one study, lymph node TB occurred in 30 percent of children with TB. Drug resistant TB is commonly seen in those previously treated for TB or those failing ATT or those with a contact of TB. Multidrug resistant forms of TB lymphadenitis are rare in children. We present a 11 year old girl with Pre-XDR TB lymphadenitis who improved on treatment.

Case Presentation Summary: A 11 year old girl presented to us with two large swellings - left cervical region and in the right axilla with abdominal pain. Both swellings were increasing in size over the last six months. Her younger sibling had a history of TB Lymphadenitis. The child was diagnosed to have TB lymphadenitis six months back and was started on first line anti-tubercular treatment then. In view of increasing size of the swellings and abdominal pain despite being on treatment, she was referred to our hospital. A biopsy lymph node sample confirmed tuberculous etiology, culture isolated Mycobacterium tuberculosis complex and drug sensitivity testing confirmed resistance to first line drugs and fluoroquinolones. She was treated with ATT drugs based on drug sensitivity results and improved subsequently.

Learning Points/Discussion: In conclusion, multi drug resistant is on the rise in developing countries like India. A high level of suspicion is needed to diagnose MDR-TB. Early initiation of treatment leads to improved outcomes. Regular monitoring and follow up are needed to ensure compliance and manage adverse drug reactions. Treatment for MDR TB for non-severe disease is given for 9 – 12 months and that of severe disease is for 12 – 18 months depending on the clinical progress.
Pyrexia of Unknown Origin in an Adolescent Returning from Somalia

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Title of Case(s): Pyrexia of Unknown Origin in an Adolescent Returning from Somalia

Background: Brucella must be considered in travellers with non-specific febrile illnesses, lymphadenopathy, and/or undefined musculoskeletal pathology returning predominantly from Central Asia, the Middle-East, and North-Central Africa.

Case Presentation Summary: Patient A, a 16 year-old boy recently returned from Somalia, was admitted to hospital after presenting with 7-10 days of fever, rigors, muscular pains, and retro-orbital headaches. The patient had travelled to Somalia with his family for approximately 5 weeks over the summer. Symptoms started within 1 week of return to the UK. Patient A did not seek pre-travel advice; he did take Malarone prophylaxis albeit sporadically, and did not receive pre-travel vaccines, although he was up-to-date with vaccinations as per the UK vaccination schedule. He remained well throughout his summer trip visiting family and friends. There were no sick contacts, no fresh water exposures, he was bitten by mosquitos. His fever did not abate despite 3 days of high-dose ceftriaxone although his headache and myalgias improved. Given persistence of fever doxycycline was added on day 3 of admission. Routine bloods demonstrated a CRP of 68, neutropaenia (0.8), lymphopaenia (0.6), thrombocytopaenia (106) and mild transaminitis (ALT: 155). On day 4 blood cultures grew brucella melitensis. It was then revealed by the patient that he and his three siblings had consumed raw camel milk on several occasions whilst in Somalia.

Key Learning Points: Recognition of brucellosis as an important aetiology of disease in returning travellers is essential as it has implications pertaining to: laboratory handling/safety, management of exposed individuals, and requires lengthy antibiotic treatment. This case exemplifies the importance of ruling out concurrent brucella meningitis and endocarditis given their differences in antibiotic management. In particular, the case embodies the importance of post-exposure prophylaxis in both exposed laboratory personnel as well as management of the three exposed siblings whom drank the same unpasteurised camel milk as the patient.
THE ROLE OF LUNG ULTRASOUND FOR THE AETIOLOGICAL DIAGNOSIS OF COMMUNITY-ACQUIRED PNEUMONIA IN CHILDREN

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Background: The aetiology of community acquired pneumonia (CAP) in children is difficult to be established. Chest X-ray has failed in this issue. In recent years, lung ultrasound (LUS) has proved to be an excellent diagnostic tool for CAP. Aim of the study is to analyse the usefulness of LUS in determining the etiology (bacterial, atypical bacteria and viral) of CAP in children.

Methods: Prospective study of children aged 2-months to 17 years. All children with a clinical diagnosis of CAP underwent LUS, nasopharyngeal swab for the detection of respiratory virus, bacteria and genome research of M. pneumoniae. Blood tests and chest X-ray were performed only if considered clinically useful by the evaluating physician. We excluded patients with the immune deficiency, neurological impairment, chronic lung (except asthma) or heart disease, genetic disorders, CAP already on treatment, or any other chronic condition which can predispose to pneumonia. Aetiology definition: Bacterial CAP if leukocytosis and alveolar infiltrate(s) on CXR, positive blood cultures; atypical pneumonia if M. pneumonia genome was positive on nasopharyngeal swab and compatible with clinical diagnosis; viral if positive nasopharyngeal swab and compatible with clinical diagnosis.

Results: We included 171 children with CAP (96 male, 73 female). 66 had probable/confirmed bacterial CAP. 68 had probable/confirmed viral CAP. 37 patients had M. pneumoniae CAP, 6 of them had viral co-infection. Children with bacterial pneumonia had more frequently larger consolidations with air and fluid bronchograms and complicated pleural effusion; viral pneumonia had multiple, bilateral subcentimetric subpleural consolidations, without bronchograms; children with atypical pneumonia had more frequently one to two small consolidations a characteristic perilesional interstitial syndrome with or without simple effusions. Differences were statistically significant.

Conclusions: LUS seems a promising tool in discriminating CAP aetiology.

Clinical Trial Registration: not registered
NEW BIOMARKERS FOR TUBERCULOSIS DIAGNOSIS AND TREATMENT MONITORING: LESSONS FROM A 3-YEAR-OLD CHILD WITH SEVERE POTT’S DISEASE AND NEGATIVE MICROBIOLOGICAL RESULTS

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Title of Case(s): New biomarkers for TB diagnosis and treatment monitoring: lessons from a 3-year-Old Child with severe Pott’s Disease and negative microbiological results

Background: Spinal tuberculosis (TB), or Pott's disease, although uncommon in young children, can cause severe vertebral destruction in this age group, leading to structural kyphotic deformity and neurologic deficits. Achieving definitive microbiological diagnosis can be challenging, since the best approach (surgical vs conservative) is not defined particularly in young children. Therefore, new biomarkers to achieve Tb diagnosis and treatment monitoring are needed

Case Presentation Summary: CLINICAL PRESENTATION 3-years-old boy with 3-months history of non-traumatic, kyphotic deformity of the upper back associated with spastic paraparesis and bladder incontinence. MRI showed destruction of C6-D4 vertebrae with calcified abscess compressing spinal cord, esophagus, lung and vessels. MICROBIOLOGY gastric aspirates yielded negative results. A multidisciplinary meeting with neurosurgeons and vertebral surgeons determined that a surgical approach was not feasible at time of presentation. IMMUNOLOGY TST was positive. Quantiferon-Plus (QTF-Plus) was positive with the following interferon-g values: TB1: 5.88 UI/ml; TB2: 7.20 UI/ml; Mitogen: 9.54 UI/ml. T-cell stimulation performed with the Mtb antigen HBHA was negative (<0,05 UI/ml). A positive QFT-plus associated with a negative response to HBHA in a T cell stimulation assay is associated with active TB disease. The higher interferon-g value obtained with TB2 compared to TB1 lends further support to an active TB disease.

Learning Points/Discussion: obtaining microbiological diagnosis of tuberculosis can be challenging in children with Pott disease if gastric aspirates are negative and a surgical approach to perform biopsy is not safe - conservative treatment with “Halo Vest”, a rigid bust fixed to the skull, was well tolerated and helped the child recovering bladder and lower limbs control and is now walking - HBHA-based IGRA is useful to support TB diagnosis and monitoring of TB therapy in children, particularly for those without microbiological confirmation.
CHARACTERISTICS AND CASCADE OF HIV CARE IN CHILDREN WITH PERINATALLY ACQUIRED HIV IN THREE RUSSIAN CLINICS

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Background: Perinatal HIV transmission has decreased in Russia but progress of the paediatric HIV care continuum in children with perinatally acquired HIV is not well described. We assessed characteristics and cascade of care in children with HIV in Russia.

Methods: Children aged <18 years at perinatal HIV diagnosis, from three Russian centres in the European Pregnancy and Paediatric Infections Cohort Collaboration (EPPICC) were followed from enrolment until death, loss to follow-up (LTFU), or transfer to adult care until 1/10/2016. Among children in care for ≥12 months and seen in 2015-2016, we summarized proportions of children who initiated ART, were virally suppressed (viral load <1000 (<200) copies/ml) and had good (none/mild) WHO immune status at last visit.

Results: Of 749 children included, 396/749(53%) were female, 93/749 (12%) ever had an AIDS diagnosis, 4/749(0.5%) ever diagnosed with tuberculosis, and 41/559(7.3%) were HCV PCR positive. Median [IQR] age at diagnosis was 1.4[0.5-2.6] years which declined over time along with new diagnoses. 694(93%) initiated ART at median age of 2.2[0.9-4.9] years; the median time from diagnosis to ART initiation was 2.0[0.3-16.3] months. Overall, median duration of follow-up was 6.3 [3.5-9.5] years, 15(2%) were LTFU, 53(7%) transferred to care in other clinics, 7 (0.9%) transferred to adult care, and 25 (3.3%) died. Among 626 patients followed-up in 2015-2016 (age at last visit 9.6 [6.1-13.2] years), 592/626 (95%) initiated ART, of whom 491/592 (82%) had viral load <1000 copies, (434/592 (73%) at <200 copies) and 581/591(98%) had good immune status at last visit. This corresponds to 95%, 79% (70%) and 93% of all children in follow-up, respectively (Figure1).
Conclusions: In this Russian cohort, 95% of children initiated ART, of whom 82% were virally suppressed, which is close to the 90% UNAIDS 2020 target

Clinical Trial Registration: Not a trial
DID TETANUS, DIPHTHERIA AND ACELLULAR PERTUSSIS IMMUNISATION DURING PREGNANCY INDIRECTLY IMPACT CARRIAGE OF SPECIFIC PNEUMOCOCCAL SEROTYPES IN BELGIAN CHILDREN?

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Background: Following the switch in the Belgian paediatric pneumococcal vaccination programme from a 13-valent (PCV13) to a 10-valent (PCV10) pneumococcal conjugate vaccine, a nasopharyngeal carriage study has started in 2016 to monitor changes in the proportions of pneumococcal serotypes in children between six and thirty months of age, attending day-care. A significant increase (p<0.001) in the carriage proportion of serotypes 6C (from 0.9% to 5.8%) and 19A (from 0.4% to 7.0%) was observed in 2016-2018. A blunting effect that diminishes the pneumococcal vaccine response in the infant’s first year of life and after the booster dose in the second year of life has been reported after maternal tetanus, diphtheria, and acellular pertussis (Tdap) vaccination in pregnancy which might possibly affect child pneumococcal carriage of specific (vaccine) serotypes. Therefore, we studied serotype-specific pneumococcal carriage according to maternal Tdap vaccination status.

Methods: One nasopharyngeal sample per child and a questionnaire on the child’s demographic and clinical characteristics were collected since 2016; a question on maternal Tdap vaccination status was added from 2018 onwards. Presence and serotype of pneumococci was determined by culture and Quellung-reaction. Statistical analyses were based on Chi²/Fisher’s Exact Test.

Results: Among 635 completely PCV-vaccinated children of whom maternal Tdap status was known, we compared children of Tdap-vaccinated mothers with children of Tdap-unvaccinated mothers, and noted a higher carriage proportion of 6C (p=0.016) in the children of Tdap-vaccinated mothers (20.6%, 61/296 vs 10.1%, 12/119), whereas the carriage proportion of 11A was lower (p=0.002) in these children (3.7%, 11/296 vs 12.6%, 15/119). For 19A, similar carriage proportions were observed in all children (Figure).
**Conclusions:** Tdap-immunisation during a mother’s pregnancy was thus unexpectedly associated with carriage of non-vaccine serotypes 11A and 6C in her PCV-vaccinated child.

**Clinical Trial Registration:** Clinical trial registration: None
RAPID INCREMENT IN NON-VACCINE SEROTYPES CAUSING INVASIVE PNEUMOCOCCAL DISEASE IN ARGENTINA AFTER THE PCV13 INTRODUCTION.

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Background: PCV13 have significantly reduced the burden of invasive pneumococcal disease (IPD) caused by vaccine serotypes. Considering that this vaccine targets 13 of the more than 90 serotypes, there have been concerns that the non-vaccine serotypes (NVTs) may increase and, therefore, reduce the benefits of the vaccination. Here we describe impact of the 13-valent pneumococcal conjugate vaccines on IPD in Argentina after the incorporation to the National Immunization Program in January 2012.

Methods: Using national IPD surveillance data between January 2010 to December 2018, 2116 sterile Spn isolates (169 Hospitals/24 provinces) from pediatric patients <5 y.o were received at the National Reference Laboratory (NRL). All Spn isolates were serotyped by Quellung reaction (Gold Standard Method). The study was divided into two periods: Period pre-PCV13 (2010) and Period post-PCV13 (2018), the years in between were consider transition periods.

Results: Of 2116 isolates, 56.2% corresponded to <2 y.o. The number of isolates causing IPD in <2 y.o decreased, from 224 (189 PCV13 serotypes cases and 35 Non-PCV13 serotypes) in 2010 to 78 (16 VTs cases and 62 NVTs cases) in 2018, this represented a reduction of 91.5% of PCV13 serotypes, mainly at the expense of serotypes 14, 23F and 5. Non-PCV13 serotypes increased to 77.14%, mainly due to serotypes 24 (1.78% / 15.38%) and 12F (4.46% / 19.23%).

Conclusions: A decrease in PCV13 serotypes was observed, parallel to a statistically significant increase in Non-PCV13, mainly associated with serotypes 24 and 12F was observed. The increase in Non-PCV13 serotypes, especially the emergence of serotype 24 associated with MDR, is of particular importance in the Post-PCV13 era about future PCV products. Continued surveillance will be key to monitor the trends of emerging NON-PCV13 serotypes and to inform decisions about future vaccines.
NEONATAL CARBAPENEM RESISTANT ACINETOBACTER BAUMANNII SEPSIS IN AN UNDER-RESOURCED SETTING

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**Background:** Carbapenem-resistant *Acinetobacter baumannii* (CRAB) Blood Stream Infections (BSI) is increasingly being observed and is associated with significant morbidity and mortality in newborns. Numerous outbreaks of carbapenem resistant *Acinetobacter baumannii* have been reported from hospitals in both developed and developing countries. In this study, we determined the clinical epidemiology, bacteriological and antimicrobial spectrum of CRAB infections in neonates in a resource limited setting.

**Methods:** The records of all neonates admitted in the neonatal unit of the national tertiary hospital with positive blood cultures were collected for the period between 1 January to 31 December 2016. All cases with *Acinetobacter baumannii* BSIs were selected. Demographic data, clinical, laboratory findings, their microbiological data, treatment and outcome details were retrospectively reviewed. Data was evaluated and presented using descriptive statistics.

**Results:** During the period, 10 neonates developed *Acinetobacter baumannii* BSI; 9 isolates were CRAB at an incidence of 20% (9/44). Majority of these were female neonates presenting with apnea and feeding intolerance. CRAB infected neonates were born prematurely with low birth weight. Majority of the neonates were inborn and had late onset sepsis. All isolates of CRAB were sensitive to colistin. The all-cause mortality rate for CRAB BSI was 11.5% (3/26) of all deaths and 30% (3/10) of all *Acinetobacter* BSIs. All died from septic shock.

**Conclusions:** *Acinetobacter* bacteremia in neonates was not common but had a high mortality especially for CRAB. Serious therapeutic problems arise, as the choice of antibiotics in resource limited settings are limited. Presence of susceptible patients, potentially colonized, selective pressure from antimicrobial use and poor infection control practices may be certain causes for the rising infections. Continuous surveillance for microbial flora, rational use of antibiotics and better strategy of antibiotic cycling maybe needed reduce CRAB BSIs.
TODDLER PRESENTING WITH BILATERAL LOWER LEG PAIN AND WEAKNESS

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Title of Case(s): Toddler presenting with bilateral lower leg pain and weakness

Background: Potts disease or spinal tuberculosis occurs most commonly in children and young adults and is much more common in the undeveloped world. It causes bone destruction, spinal deformity and neural complications. Multidisciplinary team management is crucial to confirm the diagnosis, eradicate the infection, achieve a decompression of the spinal canal material and correct or prevent spinal deformity and possible sequelae and to provide rehabilitation.

Case Presentation Summary: A 2 years old boy presented with difficulty walking for 2 weeks associated with progressive symmetrical, bilateral lower leg pain and weakness but no back pain. He didn’t have bowel or urinary incontinence. He had no preceding history of trauma. His father had history of pulmonary tuberculosis and child didn’t receive Isoniazid Preventive Therapy (IPT). He was cachetic with a slight kyphosis. Examination revealed reduced muscle tone in the both lower limbs with areflexia. Investigations revealed a raised CRP of 31.9 and ESR of 40mm with thrombocytosis. CSF was negative for Japanese Encephalitis. Electrolytes were normal. Stool for Acute Flaccid Paralysis was negative. CK-MB and ALP were both raised. Tuberculint test was negative. MRI scan of lumbar spine demonstrated enhancement of epidura and pre and paravertebral regions of L4 and L5 with significant disc obliteration. Diagnosis of tuberculous spondylitis was confirmed and patient improved on Anti Tubercular Therapy.
Learning Points/Discussion: Due to the insidious nature of symptoms of spinal tuberculosis in children, diagnosis is often delayed. Complications can be crippling because of bone destruction, spinal deformity and paraplegia. Early diagnosis and intervention can eradicate the infection, ensure a good recovery from any neurological deficits with minimum residual spinal deformity. Isoniazid Preventive Therapy for children is important to reduce the risk of TB in children under 5 years.
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Cambridge University Hospital, Infectious Diseases, Cambridge, United Kingdom

Title of Case(s): A sixteen year old with six days of epigastric pain, fever and rigors

Background: The diagnosis of myocarditis is difficult when the electrocardiogram is normal but it needs to be urgently considered, especially as the therapeutic window is very short. The high C-reactive protein can reflect severe tissue injury. Working in infectious diseases can bias one's clinical judgement away from other diagnoses. The value of intravenous immunoglobulin for the treatment of myocarditis is controversial.

Case Presentation Summary: A sixteen-year-old woman presented with six days of epigastric pain, four days of nausea, two days of rigors and and twelve hours of neck pain. Twelve hours before she had received penicillin V. She was febrile, tachycardic, had neck stiffness, a murmur and epigastric/costovertebral angle tenderness. She was hyperflexible. She had a single petechia. Chest X-ray, full blood count, liver and kidney function, electrocardiogram and urine dip were unremarkable. C-reactive protein was 232 mg/dl (0-5 mg/dl). She was treated with Ceftriaxone high dose and investigations focused on excluding intraabdominal disease and pyelonephritis. On the second day the "murmur" had disappeared and was retrospectively diagnosed as a pericardial rub. High sensitivity troponin returned at 3293 ng/l (0-3) and a diagnosis of posterior myocarditis was made and proven via cardiac echo and cardiac MRI. The patient made a full recovery with antibiotics and antiinflammatories. HHV6 was detectable on blood by PCR. She did not receive intravenous immunoglobulins because of the uncertainty regarding their efficacy.

Learning Points/Discussion: Myocarditis can present with a normal electrocardiogram or an electrocardiogram that evolves over a few days. Very high C-reactive protein levels are specific for bacterial illnesses but can also reflect tissue injury. The use of IVIg for myocarditis remains controversial and further guidance is needed. The significance of the positive HHV6 PCR is unclear. The role of HHV6 in myocarditis needs to be further elucidated.
A NOVEL TTC7A MUTATION IN THE REPUBLIC OF IRELAND

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Title of Case(s): A Novel TTC7A Mutation in the Republic of Ireland

Background: Efficient whole-exome sequencing had identified an autosomal recessive variant of TTC7A gene in patients presenting with combined immune deficiency and multiple intestinal atresias (CID-MIA), an extremely rare condition with death occurring before 2 years of age. Case reports are still very limited to offer us full understanding of the mutation of TTC7A gene either on immunology or gastrointestinal systems. Here, we report a novel TTC7A mutation discovered in the Republic of Ireland.

Case Presentation Summary: A 35 weeker baby was diagnosed with small and large bowel obstruction antenatally. Exploratory laparotomy revealed multiple atretic bowel sections which required extensive resection. Liver wedge biopsy at 2 months, confirmed total parenteral nutrition (TPN) associate liver disease. By the age of 3 months, he had undergone three laparotomies with similar histological findings; a complete loss of luminal continuity and ongoing inflammatory process with mucosal disruption. Persistent lymphopenia associated with multiple episodes of Escherichia Coli sepsis and line-related Staphylococcus epidermidis sepsis triggered a question of possible immune dysfunction. Works of literature which were reviewed bared the correlation between multiple intestinal atresia and immune deficiency. Primary immune deficiency work-up and specific molecular genetic analysis for TTC7A gene were requested. Genetic analysis showed a novel homozygous variant of c.192delT; p.Phe64Leufs*15, NM_020458.4, rs1476031758 in the TTC7A gene.

Learning Points/Discussion: At present, treatments have been commenced to support his immune system with intravenous immunoglobulin and prophylaxis antibiotics. TTC7A gene should be evaluated in patients with gastrointestinal manifestations and immunodeficiency. We need to decode the function of TTC7A gene on intestinal health and how the deficiency results in T-cell and B-cell lymphocytopenia. A research continuum is vital in understanding the pathobiology of TTC7A gene in developing effective therapies for these patients.
PREVALENCE OF VIRULENCE GENES IN ENTEROAGGREGATIVE ESCHERICHIA COLI ISOLATES FROM YOUNG CHILDREN FROM RURAL SOUTH AFRICA

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Background: In this study, we report on the prevalence of 19 virulence genes in EAEC isolates from northern South Africa.

Methods: Stool samples obtained prospectively from 97 children from 1 to 12 months of age were analyzed and EAEC (Enteroaggregative Escherichia coli) isolates were confirmed based on the presence of aaiC or aatA genes. We investigated 177 EAEC isolates for the prevalence of virulence genes using multiplex polymerase chain reaction.

Results: The chromosomal gene aaiC was detected at higher frequency (48.02%) compared to aatA (25.98%). The gene encoding the open reading frame Orf61 was the most prevalent putative virulence trait detected among the isolates (150/177; 84.7%). None of the genes was statistically associated with diarrhea (p>0.05). Detection rates were higher during 7-12 month of life with an association observed for the pic gene and the age group 7-12 month (P = 0.04). Winter was the season with the highest detection rates.

Conclusions: Our data reveal a high prevalence of Orf61, Orf3 and astA in South African EAEC isolates. Specific genes may provide additional markers for study of disease associations with age and season of sample collection.

Clinical Trial Registration: This is a basic science study and not a clinical trial.
REFERRAL OF PEDIATRIC TUBERCULOSIS CASES TO DOTS CENTRE: AN OBSERVATIONAL STUDY IN FIVE MAJOR DISTRICTS OF PUNJAB STATE OF INDIA.

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DAYANAND MEDICAL COLLEGE AND HOSPITAL, LUDHIANA, PUNJAB, Pediatrics, LUDHIANA, India

Background: Many doctors do not refer their Tuberculosis (TB) patients to DOTS centre for treatment and many lack good knowledge and proper practice in management of their TB patients. This operational research was done to assess the referral of TB cases by Pediatricians to DOTS centre in five districts of Punjab, India. Study design: Observational cross-sectional study. Period of study: One year.

Methods: Material and Methods: The study was conducted in five major cities, i.e. Ludhiana, Jalandhar, Amritsar, Patiala and Bathinda, inhabiting approximately half of the urban population of Punjab. Pediatricians were selected by random selection by computer generated randomization method. The data collection was done using a pre-tested, structured questionnaire containing information about age, sex, qualification, experience of Pediatricians and assessing knowledge of TB and its management. Pediatricians were divided into two groups, referral group: who referred their patients to DOTS centre for treatment and non-referral group, those who did not.

Results: Total of 139 pediatricians participated in the study, 69% were male. Overall 64% of Pediatricians referred TB cases to DOTS centre for treatment. Only 20% doctors had adequate knowledge about Treatment of TB. Majority had adequate knowledge of TB Disease and Case suspicion, 87% had adequate knowledge of TB Diagnosis. This knowledge gap of TB Treatment was more in non-referral group (82% vs 18%) (p value=0.025).

Conclusions: Overall 64% of Practicing Pediatricians referred TB cases to DOTS centre for treatment. Approximately 90% doctors had adequate knowledge of TB Disease and Diagnosis. Only 20% doctors had adequate knowledge regarding TB treatment, more in non-referral doctors. Improving the treatment knowledge of paediatricians by regular sensitizing them can go a long way in improving referral of cases to DOTS centre.
Background: Maternal and neonatal infections are an important cause of morbidity and mortality in low- and middle-income countries. Barriers to aseptic procedures and hand hygiene (HH) include lack of running water or HH supplies, inadequate knowledge of guidelines, and overwhelming patient volume. Since many deliveries occur at primary health facilities globally, studying the impact of infection prevention and control (IPC) interventions in this setting may be important.

Methods: A quasi-experimental study was conducted at five rural health facilities in Southern Province of Zambia from December 2018 to August 2019. Implemented low-cost intervention bundle included IPC education, alcohol hand rub (AHR) provision, and SMS reminders. Direct healthcare worker (HCW) observation was used to score IPC practices and HH during childbirth pre- and post-intervention. Post-study survey was performed to assess HCWs’ attitudes towards the interventions.

Results: 12 pre-intervention and 12 post-intervention delivery observations were collected across the five health facilities. Mean observation score for IPC practices during pre- and post-intervention were 18.4 and 25.4 out of 38 points (p=0.08). Labor and delivery practices improved from 3.8 to 5.1 out of 7 points (p=0.06). There was no change in use of protective barriers and gloves. Pre-intervention HH compliance was 35% (56 HH actions/160 opportunities), while post-intervention compliance was 24% (32 HH actions/135 opportunities) (p=0.41). HCWs found the intervention bundle and AHR useful but barriers to IPC included the AHR formulation being too sticky and HCW forgetfulness.

Conclusions: Despite some improvement in IPC practices during childbirth and favorable HCW response to the IPC interventions, there was no improvement in HH compliance. Successful interventions to improve HH and IPC practices should target acceptability of new supplies and adaptation into existing workflow in addition to education on best practices.

Clinical Trial Registration: Clinical trial registration: ClinicalTrials.gov NCT03809741
Title of Case(s): 5 years old child presenting with left chest deformity after a fall

Background: Hydatidosis is a parasitic infection of lungs and other organs caused by the larval stage of the tapeworm *Echinococcus*. Majority of children with lung lesions are asymptomatic because of a weaker immune response and the relatively higher elasticity of the lung parenchyma. The common presentations are cough, hemoptysis and chest pain. However, rarely children can present with chest wall deformity.

Case Presentation Summary: A 5 year old boy presented with a left chest deformity after fall from a height. On further inquiry he had a underlying history of intermittent low grade fever. He had no other complaints of dyspnea, cough or hemoptysis. Both parents are farmers. The child was underweight and stunted. He was pale and had visible clubbing. Bulging of the left chest wall was noted. Trachea was deviated towards the right with reduced respiratory sounds and dull percussion on the left side. Heart sounds were better heard on the right hemithorax. CXR revealed a large well-defined homogeneous mass occupying the left hemithorax. A contrast enhanced CT showed multiloculated collection with collapsed consolidation of left lung. Sputum AFB and tuberculin tests were negative. Hydatid cyst-specific immunoglobulin (Ig) E was positive. Blood showed eosinophilia (580/mm3) and raised ESR (120). Abdominal ultrasound was normal. Lung infection was treated with aspiration and intravenous antibiotics. Albendazole was started and lobectomy performed subsequently.
Learning Points/Discussion: The immune system and the relatively higher elasticity of the lung parenchyma in children allows for the rapid growth of cysts without any symptoms. Giant hydatid cyst of the lung is more prevalent in children, though presentation with chest deformity can rarely be the only symptom. As a result, in endemic regions, Cystic Ecchinococcus should be suspected when children present with chest wall deformity.
OSTEOMYELITIS IN A CHILD WITH STAPHYLOCOCCUS AUREUS SEPSIS AND CONCOMITANT PARVOVIRUS B19 INFECTION

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Title of Case(s): Osteomyelitis in a child with Staphilococcus aureus sepsis and concomitant Parvovirus B19 infection

Background: Parvovirus B19 (B19V) is known to be causative agent of different clinical pictures: transient aplastic crisis, erythema infectiosum, hydrops fetalis, acute polyarthritis. We describe a case in which a Staphylococcus aureus sepsis and osteomyelitis has been probably trigged by B19V. In literature, the possible role of B19V as activator of infection and in pathogenesis of osteomyelitis has never been described.

Case Presentation Summary:

A previously healthy 14-year-old boy presented with “slapped cheek”, fever, pharyngodynia, pain, bilateral swelling of feet, lasting from a week. Blood tests suggested a virosis. Discharged with diagnosis of reactive arthritis probably due to B19V (confirmed by serology), after 48 hours he came back because of persistent symptoms and high fever with shaking chills. Blood cultures detected a methicillin-resistant Staphylococcus aureus (MRSA) sepsis. Recent medical history revealed two abscesses: the first, appeared a month before on right gluteus, was treated with drainage and one-week antibiotic therapy (amoxicillin/clavulanic acid); the second appeared two weeks before admission on controlateral thigh and
was only drained. An MRI and a PET-CT were performed showing osteomyelitis on right foot, involvement of soft tissues at homolateral metatarsus and bilateral involvement of inguinocrural lymph nodes, suggesting an inflammatory process. Patient was successfully treated with vancomycin and rifampicin for 2 weeks and then with cotrimoxazole and rifampicin for other 6. Follow-up at 3 months showed complete resolution.

**Learning Points/Discussion:** To our knowledge, this is the first case of osteomyelitis caused by concomitant *Staphylococcus aureus* and B19V ever reported in literature. This unusual presentation might have been a consequence of the presence of B19V related arthritis. In particular, we suspect that B19V may have played a role in activating a latent *Staphylococcus aureus* infection, although the precise mechanism is still unknown.
E-POTER VIEWING
E-POSTER VIEWING - ALL OTHER TOPICS
10-28-2020 8:00 AM - 7:00 PM

TUBERCULOUS OSTEOMYELITIS IN SINGAPOREAN CHILDREN: RETROSPECTIVE CASE REPORTS AND LITERATURE REVIEW

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Title of Case(s): Tuberculous Osteomyelitis in Singaporean Children: Retrospective Case Reports and Literature Review

Background: Tuberculosis (TB) is prevalent in many parts of the world. Extra-spinal osteoarticular TB is uncommon, affecting about 2-5% of all TB cases and systemic symptoms are usually absent. Radiological findings are also non-specific and tissue samples are required for definitive diagnosis. In this retrospective study, we are reporting the clinical, biochemical, radiological and microbiological characteristics of two children with extra-spinal TB osteomyelitis admitted to KK Women's and Children's Hospital, Singapore.

Case Presentation Summary: Case 1 was a 9-month-old Chinese boy who presented with fever and left lower limb swelling for 1 month. X-ray showed a heterogenous lucent lesion in left proximal tibia metaphysis. His initial AFB (Acid Fast Bacilli) smear was negative and eventual AFB culture returned positive for mycobacterium tuberculosis. Case 2 was a 4-year-10-month old Malay girl who presented with fever and right hand swelling for 14 days. X-ray showed features of spina ventosa involving the first right metacarpal bone. The AFB smear was positive but eventual AFB culture returned negative. Both patients were immunocompetent with no evidence of pulmonary and joint involvement. Infective markers were not significantly elevated in both patients. Both patients received anti-TB therapy and no sequelae was observed on subsequent follow-up.

Learning Points/Discussion: The diagnosis of osteoarticular TB can be challenging because of the absence of classical symptoms of pulmonary TB and infective markers may not be raised. AFB smears are often negative, leading to a delayed diagnosis while waiting for the culture result. The incidence of chronicity, deformity, and disability is substantial thus a high index of suspicion is warranted. More time critical investigations like histopathological examination and PCR can be used guide diagnosis and early anti-TB therapy.
SEASONAL TRENDS IN ADMISSIONS DUE TO RESPIRATORY SYNCYTIAL VIRUS INFECTION AT NINE HOSPITALS IN HYOGO PREFECTURE, JAPAN, FROM 2016 TO 2019

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Background: Although patients with respiratory syncytial virus (RSV) infection have been presenting to outpatient departments in Hyogo Prefecture earlier in the season during the last few years, it is unclear whether there has been a similar seasonal shift in the timing of hospital admissions due to RSV infection. We conducted a retrospective survey to determine the seasonal trends in admissions due to RSV infection from 2016 to 2019.

Methods: We reviewed the medical records of children under 15 years who had been admitted to nine hospitals in Hyogo prefecture, Japan, with RSV infection from 2016 to 2019, and constructed epidemic curves of weekly RSV admissions to the study hospitals over the study period. We compared the timing of the start, peak, and end of each RSV infection season using the Kruskal-Wallis test. If the difference in timing was statistically significant, we also compared the timing of admissions using the Mann-Whitney U test.

Results: The number of admissions of children with RSV infection started to rise and peaked significantly earlier in the 2018/2019 season than in the 2016/2017 and 2017/2018 seasons. The onset of the rise and the peak in admissions due to RSV infection also occurred significantly earlier in the 2017/2018 season than in the 2016/2017 season, thus confirming a shift in the seasonality of RSV admissions.

Conclusions: Based on the number of hospital admissions, the onset and peak of the RSV epidemic period occurred earlier each year over three consecutive years, mirroring the trend in the number of RSV outpatient consultations; therefore, the timing of seasonal prophylactic palivizumab administration should be reconsidered in the prefecture, and vulnerable children should start taking palivizumab earlier in the autumn of each year.
PREVALENCE OF MEASLES ANTIBODIES IN HEALTHCARE WORKERS IN ESTONIA

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Background: Since 2018, significant increase of measles cases in the WHO European Region has been reported. After years of no cases, measles are back in Estonia, albeit incidence remains low (0.1-2.0 cases / 100 000 yearly in 2014-2019). Immunisation rates of measles are 94.7% for 1 and 82.5% for 2 doses. However, we are worried about the risk of an outbreak because of the uncertain quality of vaccines used in the Soviet Union. We studied healthcare workers (HCWs) for measles antibody concentrations, determining the seropositivity rate depending on their immunisation programme.

Methods: From January to June 2019 in two level 2 hospitals all HCWs were invited to participate in the study. Specific measles IgG antibody concentrations were measured by commercially available ELISA (Alegria®, Orgentec, Germany) with seropositivity cut-off at >250 mIU/ml in local laboratories. Data were analysed in four age groups based on the vaccination schedule in their birth cohort: prior to measles immunisation (born <1964), one-dose immunisation with low coverage (1964-1979), two-dose with low coverage (1980-1994) and two-dose with high coverage (>1994). Soviet Union vaccines were used in 1964-1994.

Results: A total of 1083 blood sera were analysed. Significantly more subjects had IgG antibodies above cut-off level in the first birth cohort than in the other birth cohorts (Table 1). The younger birth cohorts had lower seroprevalence (Goodman-Kruskal gamma -0.484, 95% CI -0.56…-0.407). There was no gender difference in IgG concentrations.
**Table 1. Seroprevalence of measles IgG antibodies in different birth cohorts of medical workers in Ida-Viru Central Hospital and Viljandi Hospital**

<table>
<thead>
<tr>
<th>Birth Cohort</th>
<th>Seronegative (&lt;200 mIU/ml) N; % (95% CI)</th>
<th>Indeterminate (200-250 mIU/ml) N; % (95% CI)</th>
<th>Seropositive (≥250 mIU/ml) N; % (95% CI)</th>
<th>Total number of subjects (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1964</td>
<td>19; 5.5 (3.2-8.3)%</td>
<td>7; 2 (0-4.8)%</td>
<td>318; 92.4 (90.1-95.2)%</td>
<td>344</td>
</tr>
<tr>
<td>1964-1979</td>
<td>111; 26.1 (21.9-30.8)%</td>
<td>26; 6.1 (1.9-10.8)%</td>
<td>288; 67.8 (63.5-72.5)%</td>
<td>425</td>
</tr>
<tr>
<td>1980-1994</td>
<td>83; 29.7 (24-35.7)%</td>
<td>29; 10.4 (4.7-16.4)%</td>
<td>167; 59.9 (54.1-65.8)%</td>
<td>279</td>
</tr>
<tr>
<td>&gt;1994</td>
<td>14; 40 (25.7-58.1)%</td>
<td>2; 5.7 (0-23.8)%</td>
<td>19; 54.3 (40-72.4)%</td>
<td>35</td>
</tr>
<tr>
<td>Total</td>
<td>227; 21.0 (18.4-23.6)%</td>
<td>64; 5.9 (3.3-8.6)%</td>
<td>792; 73.1 (70.5-75.8)%</td>
<td>1083</td>
</tr>
</tbody>
</table>

**Conclusions:** We found measles antibody concentrations below the ELISA cut-off point among a significant number of HCWs born after 1964. High seroprevalence in those born in the prevaccine era is likely due to long-lasting immunity following wild-type measles. Further population-based studies on seroprevalence using WHO recommended tests are warranted prior to taking further actions.
THE IMPACT OF CHRONIC SOIL-TRANSMITTED HELMINTH INFECTION ON THE INCIDENCE OF ALLERGY IN CHILDREN

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Background: Soil-transmitted helminth (STH) infections present primarily in tropical and sub-tropical countries with affecting children and people with poor hygiene and inadequate sanitation. The low prevalence of allergy in this population has been associated with exposure to STH infections. Cross-sectional studies have reported a reduced prevalence of skin prick test (SPT) reactivity among school children infected with STH. In this study we evaluated the impact of children who received repeated albendazole for the treatment of recurrent STH infection on the occurrence of allergy or allergic disease.

Methods: The study was a case-control study conducted from January until April 2020 in North Sumatera province, Indonesia. Cases were children resided in Mandailing District, an STH high endemic area, with recurrent STH infections in the past year as determined by Kato-Katz examination; controls were children resided in Medan city who were STH negative. Ten common allergens in Southeast Asia were tested on 40 children in each group using SPT.

Results: Our pilot study showed the prevalence of STH infections among school-aged children in Singkuang subdistrict, Mandailing Natal district ranged between 76.8% and 87.2% in December 2018. These children were prospectively followed up and assessed for their STH status four-monthly until up to a year. Follow-up on controls were not performed. At 12 months of follow-up, SPT was evaluated on all cases and control children.

Conclusions: Protective effect of STH infection against allergy has been previously reported in several studies, here we will discuss the impact of treated recurrent STH infections on the occurrence of allergy or allergic disease as determined by SPT reactivity in children. The comparison of the impact between STH recurrences and STH-free on SPT reactivity in children will be presented in the meeting.
CLINICAL SPECTRUM OF INFECTIOUS FEMALE GENITAL LESIONS.

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**Background:** Genital dermatoses are common but neglected problems worldwide. These diseases are influenced by personal habits and surroundings. Female are more prone to infectious genital lesions. Pediatric female genital diseases are less explored and should be regarded as separate entity from adult because of differences in physiology, presentation and treatment. This study was carried out to describe the clinical characteristics of pediatric female infectious genital lesions.

**Methods:** This was hospital-based, prospective, cross-sectional study conducted in department of dermatology of a teaching hospital in Kathmandu, between June 2016-May 2017. Ethical approval was taken prior to the commencement of the study. Non-probability, purposive sampling was used in female patient below 15 years. All the patients fulfilling the inclusion criteria were enrolled in study after informed consent. Any lesions in genitalia were defined as genital dermatoses. The recorded details were analyzed using Microsoft Excel.

**Results:** Thirty patients were enrolled in study. The age ranged 0.5 to 15 years. Majority of the patients were of low socio-economic status. Ten types of dermatoses were encountered and classified into infections (14), inflammation (13) and benign variants (3). Among infections, candidiasis was common followed by scabies. We encountered single case of staphylococcal scalded skin syndrome and echthyma gangrenosum. Among non-infectious, lichen sclerosus was exclusive. The average duration of the infections was 3 days. Common sites for dermatoses was pubic region and labia.

**Conclusions:** Various types of infectious and inflammatory diseases were present in genitals of female child. They pose considerable concern in parents and treating physicians. They also differ in the patterns and clinical presentations from adult due to various intrinsic and extrinsic factors. Our study suggests the need for health education, proper sanitation and better nutrition for both the parents and children.
Title of Case(s): Evaluation and Management of Two Newborns Exposed to Maternal Tuberculosis in In-Vitro Fertilisation (IVF) Pregnancy- Need for Heightened Screening?

Background: Congenital tuberculosis (TB) is rare, with high mortality if untreated. Paucity of fetal symptoms and non-specific delayed presentation make early diagnosis difficult. Singapore is a high-income Asian country with intermediate TB burden. We present 2 babies conceived by IVF in Singapore, born to mothers treated for active pulmonary TB in pregnancy, that highlight challenges faced in newborn evaluation and management.

Case Presentation Summary: A term boy was born to a Vietnamese mother on anti-tuberculous therapy (ATT) from 36 weeks gestation after 2 months respiratory illness. A girl was born to a Chinese mother diagnosed with miliary TB at 12 weeks after 1 month of systemic symptoms; mother’s ATT had multiple interruptions due to hepatotoxicity. Both babies had no clinical manifestations of congenital TB. Extensive initial investigations including CXR and nasogastric aspirates for TB PCR and AFB smears were unremarkable. The boy received BCG vaccine at birth before TB evaluation. Isoniazid for latent TB prophylaxis was started at 1 week old and changed to rifampicin at 3 weeks old for 4 months due to maternal isoniazid resistance; tuberculin skin testing (TST) at 6 months old is planned. The girl received BCG vaccine on day 4 after a negative TST at birth. Empiric combination ATT started at birth was changed to isoniazid prophylaxis on day 6. Breastfeeding with appropriate cough hygiene was recommended for both.

Learning Points/Discussion: Risk assessment of vertical transmission in pregnant mothers with delayed TB diagnosis or suboptimal treatment is challenging, and requires detailed maternal history with thorough newborn evaluation whether or not the baby has symptoms at birth. After exclusion of congenital TB, decisions must be made on treatment regimes and BCG vaccination. Pre-IVF TB screening may be considered in certain high-risk populations.
Background: The precise urinary tract infection (UTI) diagnosis has been commonly missed during the physical examination due to the non-specific symptoms and signs of both infants and children. Our aim in this study is to develop a new type of the in-vitro detection devices associated with the diaper, allowing us to monitor the pH value, and both nitrite and leukocyte concentrations in urine (i.e., biomarkers for urinary tract infection).

Methods: To evaluate the performance of diaper-based detection devices, we spotted the serially diluted proteins and nitrites onto the test zones (made through using a piece of paper) of the diaper-based detection devices, and photographed the colorimetric reactions of these two biomarkers through using a smartphone camera.

Results: The test zones changed colors from yellow to blue (protein) and white to purple (nitrite) respectively. The distinguishable color intensity was observed in various concentrations (e.g., 0.156, 0.312, 0.625, 1.25, 2.5 and 5 μM), via the test zones integrated with the diaper. The diaper-based detection device has two main advantages; 1) it detects multiple clinical targets simultaneously through just one step while using it, carrying out the lower possibility of clinical sample contaminations; 2) it is easily integrated with the diapers (what we have done and love to share it during the poster session), resulting in a new diagnostic system for infants.

Conclusions: The results have indicated that our currently developed diagnostic tool is a useful one-step device for detecting multiple clinical targets related to UTI. In conclusion, our diaper-based detection device combined with the smartphone-based image analysis has a great potential of becoming a commercial homecare diagnostic device, i.e., total solution of the UTI diagnosis for children.

Clinical Trial Registration: This study does not reports the results of a controlled trial.
Background: Pneumonia and malnutrition are leading causes of death in low and middle-income countries (LMICs). Although prior studies have evaluated clinical risk factors, prognostic markers of mortality within 30 days of hospital admission remain understudied in young children with severe acute malnutrition (SAM), in particular those presenting with severe pneumonia.

Methods: During April 2015- March 2017, we conducted a cohort study of children aged 0-59 months admitted to the Dhaka Hospital, International Centre for Diarrheal Disease Research, Bangladesh (icddr,b) with SAM and severe pneumonia and enrolled 191 children to observe death within 30 days of hospital admission.

Results: Mortality within 30 days of admission was 6% (14/191). Bivariate analysis factors associated with death were female [OR: 4.60 (95% CI: 1.36, 15.34); p=0.007], hypoxemic [OR: 4.53 (95% CI: 1.39, 14.69)] and severely malnourished <4 LAZ [OR: 3.70 (95% CI: 1.15, 11.84)] children, increased biomarkers as procalcitonin [OR: 1.01 (95% CI: 0.99, 1.02)], C-reactive protein [OR: 1.11 (95% CI: 1.03, 1.21)] and polymorph percentage [OR: 1.06 (95% CI: 1.02, 1.11)]. After controlling the co-variates and other factors by using multivariate logistic regression, independent factors associated with death were female [aOR: 5.80; (95% CI: 1.34, 25.19)], LAZ <4 [aOR: 6.51; (95% CI: 1.49,28.44)] and polymorph percentage (>6.0x10⁹ /L) [aOR:1.06; (95% CI: 1.01, 1.11)]. Using sex, LAZ, and polymorph percentage, we used random forest and linear regression models to achieve a cross-validated AUC of 0.83 for prediction of 30-days mortality.

Conclusions: Female sex, severe malnutrition <4 LAZ and polymorph percentage were predictable risk factors for 30 days mortality. Prospective studies need to design to detect children at higher risk of mortality based on biomarker levels on admission and develop improved strategies to prevent mortality.

Clinical Trial Registration: Not applicable
Title of Case(s): STERNAL OSTEOMYELITIS WITH STAPHYLOCOCCUS AUREUS SEPSIS IN A NEONATE: A CASE STUDY

Background: Primary staphylococcal osteomyelitis is uncommon in neonates, and can lead to destructive bone loss and further complications. This can be associated with immunodeficiency, prematurity and central catheters. Staphylococci have a range of resistance mechanisms which further complicates medical and surgical treatment. The prevention of central line associated blood stream infections (CLABSIs) such as staphylococci is a priority in neonatal infection control.

Case Presentation Summary: A preterm MCDA twin male born by cesarean section due to abnormal dopplers required surfactant and non-invasive ventilation. Parenteral nutrition was commenced via a central line. On day 9, he developed tachypnoea, temperature instability, redness and swellings involving the distal sternum and left thenar eminence with a rising c-reactive protein and white cell count. He was commenced on ceftazidime and vancomycin and his line removed. His blood and line tip culture grew penicillin-resistant Staphylococcus Aureus, and Panton-Valentine Leukocidin negative. Flucloxacillin was added. Lumbar puncture and echocardiography was unremarkable. An ultrasound demonstrated an increasing abscess extending the depth of sternum with mediastinal extension. Further antibiotics cover was expanded with gentamicin and rifampicin. Surgical debridement was performed with removal of capsular abscess from sternum. He had low B lymphocyte count, a normal nitroblue tetrazolium test and normal phytohemagglutinin response. Flucloxacillin continued for 6 weeks and Rifampicin for 4 weeks with full clinical and radiological recovery.

Learning Points/Discussion: Staphylococcal sepsis related to central lines can lead to rare and severe complications like sternal osteomyelitis and if untreated can lead to mediastinal extension. This complication can be avoided with timely initiation of appropriate antibiotics, early removal of long lines and prompt surgical intervention. Research and guidance on the timing of long line removal in the context of sepsis is needed.
RABIES EXPOSURE PROPHYLAXIS PRACTICES AMONG CLINICIANS AT A REGIONAL REFERRAL HOSPITAL

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Background: Rabies is a fatal but preventable zoonotic disease. Significant public health problem in developing countries. It is endemic in the southern regions of Bhutan. Rabies post-exposure prophylaxis (PEP) is a key preventive measure of human rabies. Information about the appropriate use of this expensive resource has not been evaluated so far. This study was conducted to assess and evaluate the epidemiology of rabies PEP as well as assess the compliance of clinicians’ decision with the National Guidelines.

Methods: A prospective evaluation of the clinicians’ compliance to the national rabies post exposure treatment guidelines. It was conducted at a regional referral hospital in southern Bhutan. Patients attending the outpatient department with animal exposures were included. Standardized forms were used to collect information available from clinicians’ notes in patients’ prescriptions. Assessment of wounds were done to evaluate the compliance with guidelines.

Results: 45 cases of animal contacts were reported in the two months. 60% were females (p = 0.400). Majority were between 10-19 years. Exposure to dogs were the most common. Exposure categorization was poor with an observed agreement of 17 (k = 0.013). Compliance of PEP administration was fair as (k = 0.38) and (SE of k = 0.272). The false positive rate was 75%. None of the category III cases were administered Rabies immunoglobulin (RIG). 9 were misclassified. 80% didn’t have wound washing advices.

Conclusions: Correct exposure categorization to avoid misclassification and better compliance with guidelines will help reduce unnecessary PEP administration and expenditure. This would increase correct PEP use which is essential to avoid PEP failure and its overuse. Clinician education on proper classification in accordance with national PEP guidelines, complete and proper documentation and public awareness could help in appropriate use of PEP.
ABDOMINAL PAIN IN AN ADOLESCENT WITH ADVANCED PAHIV.

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Title of Case(s): Abdominal pain in an adolescent with advanced PaHIV

Background: Mycobacterium sherrisii is an opportunistic infection which can cause disseminated disease in immunocompromised hosts and has a mortality >50%. It was identified as a novel species in 2011 and is a genotypic cousin of M. simiae, with only a handful of cases reported.

Case Presentation Summary: A 16-year-old living perinatally acquired HIV-1 infection (PaHIV) recently arrived from Tanzania with five days of left-sided abdominal pain, cough, jaundice and lethargy with 5 months of malaise and cachexia. He had tender hepatomegaly with an ultrasound showing gallbladder wall thickening. He had raised inflammatory markers, an obstructive hepatitis and conjugated bilirubinaemia. His bacterial blood cultures were negative. Despite empirical cholangitis treatment (Tazocin, ceftriaxone, ursodeoxycholic acid) he continued to spike fevers. The MRI and MRCP confirmed multiple lymph nodes of the porta, around the pancreas, aorta and mesentery. Blood and sputum cultures for mycobacterium revealed AAFB, subsequently confirmed as Mycobacterium simiae. Empiric treatment with moxifloxacin, amikacin, clarithromycin and ethambutol was commenced. Due to extensive dual class HIV-1 resistance mutations he commenced second-line therapy with darunavir, ritonavir, dolutegravir, tenofovir and emtricitabine achieving sustained viral suppression (<20c/ml) from 8 weeks. CMV viraemia was suppressed with valganciclovir. He developed features of MAI-IRIS and received 12 weeks of steroids. His immune reconstitution was poor with disease progression clinically. Imaging at 5 months was suggestive of abdominal malignancy, however a mycobacterial spindle cell pseudo tumour with Mycobacterium sherrisii was found at laparotomy. After 2 months of amikacin he developed significant high frequency hearing loss. The resistance profiles prompted a switch to azithromycin, clofazamine, and moxifloxacin, bedaquiline. His ART was simplified to Symtuza and dolutegravir. At 18 months, he shows sustained clinical improvement with immune reconstitution to CD4 282 cells/ul.

Key Learning Points: Investigative persistence including for novel species and resistance patterns is key in PaHIV to enable both the correct diagnosis and treatment.
EVALUATING ROUTINE DATA COLLECTION METHODS OF PAEDIATRIC CLABSI RATES IN A UK CHILDREN'S HOSPITAL

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Background: Central line-associated bloodstream infections (CLABSI) increase morbidity, mortality, length of stay and hospital expenditure. Rates of adult CLABSI have decreased following research and development of evidence-based prevention strategies. This has not been reproducible in children. Collection of CLABSI data in paediatrics is not mandatory in the UK. We evaluated the quality of readily available CLABSI data in a UK tertiary Children's Hospital.

Methods: We compared CLABSI data collected through the antimicrobial stewardship (1) and infection control databases (2). Database 1 includes all antibiotic prescriptions with their indications. Data are collected by the antibiotic stewardship team twice weekly. For this study we selected all patients with CLABSI (proven, probable or possible) as the main antibiotic indication. Database 2 includes data from children with positive blood cultures with central lines at the time of culture (proven). The data are originated by the microbiology laboratory and checked against patients records by an infection control nurse.

Results: Over a 2 year time period there were a total of 104 CLABSI recorded. 52 events were identified through database 1 and 69 through database 2. However, only 17 events were recorded in both databases. This shows neither method to be complete. Neither database used line days as a denominator. Database 1 also collected the total inpatient number at the time of database collection.

Conclusions: Although a significant amount of time is spent in data collection, the lack of a strict definition or use of a meaningful denominator limits their use for internal and external benchmarking. We advocate the use of a real-time data collection method, using the CDC CLABSI definitions and collecting line days as part of the routine data collection to drive quality improvements.
CLINICAL CHARACTERISTICS OF VARICELLA INFECTION IN PREGNANT WOMEN

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Background: Varicella is mainly a selflimiting illness, but may cause complications including bacterial superinfection of skin, pneumonia, severe diseases of the central nervous system. There are studies, representing the high risk of complications in immunocompromised patients with varicella. Pregnancy is considered to be a natural immunodeficiency status. Varicella may also cause fetal varicella syndrome (FVS) and varicella infection of the newborn, which includes congenital varicella syndrome and neonatal varicella.

Methods: The pregnancy is considered a natural immunodeficiency status. The aim of the study was to describe the clinical characteristics of pregnant women, hospitalized with varicella and to estimate the risk of complications due to pregnancy. A surveillance was conducted retrospectively based on pregnant women with varicella hospitalized in 2015-2018 years in Yerevan, Armenia. A total of 50 pregnant women with varicella were included.

Results: 78% pregnant women were 20-29 years old, 6% were younger than 20 years old, and 16% were 30 years and older. 14% of women with chickenpox were in the first trimester of pregnancy, 48%- in the second, and 38%-in the third trimester of pregnancy. 80% of all cases had a mild form of disease without any complication, and only 20% had a complications including bacterial infection of skin (16%), pneumonia (14%), 1 woman with cerebellitis. We identified 26 pregnant women with cervical and occipital lymphatic nodes, 19 women with enanthema.

Conclusions: 28% of all cases had a normal temperature, which emphasizes the lack of pyrogen production during pregnancy. All cases with complication were in the third trimester of pregnancy so pregnant women during the third trimester of gestation are vulnerable to complications with chickenpox due to natural immunodeficiency. Varicella vaccination should be considered for women who are seronegative for VZV IgG.
COMMUNITY USE OF DIGITAL AUSCULTATION TO IMPROVE DIAGNOSIS OF CHILDHOOD PNEUMONIA IN SYLHET, BANGLADESH

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Background: The WHO IMCI algorithm for childhood pneumonia diagnosis has high sensitivity but low specificity. Thus, the algorithm frequently misdiagnoses children as having pneumonia, resulting in antibiotic overuse. This study aims to evaluate whether the use of automated lung sound classification through digital auscultation may improve the accuracy of pneumonia diagnosis in first-level facilities.

Methods: In a cross-sectional design, Community Health Workers (CHW) record lung sounds using a novel digital stethoscope (Smartscope) of 2426 under-5 children with possible pneumonia at first-level facilities in Bangladesh. A standardised paediatric listening panel is classifying the recorded sounds into different categories, e.g. normal, crackle, wheeze, crackle and wheeze, or uninterpretable, to serve as the reference standard. A mobile app containing the Smartscope analysis system is also classifying the sounds and comparing with the reference paediatric panel’s classification.

Results: As of 31 December 2019, 1957 children screened, 1070 eligible cases identified and 1029 enrolled (32.67% had IMCI pneumonia). The results of the data collected during the first six months will be presented. These results will describe CHWs ability to record quality lung sounds and agreement between human and machine interpretation.

Conclusions: Auscultation and correct interpretation of lung sounds are often not feasible in the first level facilities due to a shortage of skilled healthcare providers. Even when providers are available, the interpretations are not consistent due to the inter-observer variability. Incorporation of the auto-classification of the Smartscope recorded lung sounds within the current WHO IMCI pneumonia diagnostic algorithm may improve the accuracy of the diagnosis of childhood pneumonia at first-level facilities in LMICs.

Clinical Trial Registration: NCT03959956
Background: We aimed to determine serotype distribution and antimicrobial susceptibility patterns of pneumococci causing pediatric invasive pneumococcal disease (pIPD) after PCV13 introduction in the National Immunization Plan (NIP) to determine the impact of PCV13 on pIPD.

Methods: 196 *Streptococcus pneumoniae* isolates recovered from pIPD cases in 62 hospitals between July 2015 and June 2019 were characterized by serotyping and antimicrobial susceptibility testing. In 96 cases with culture-negative CSF or pleural fluid samples, real-time PCR identified and serotyped *S. pneumoniae*.

Results: Most pIPD cases were caused by serotypes not included in PCV13 (55%, n=161), with serotypes 8 (n=19), 10A (n=20) and 15B/C (n=13) being the most frequent. Among PCV13 serotypes, serotype 3 was the most frequent (27%, n=78) followed by serotypes 14 (5%, n=15) and 19A (4%, n=12). Other PCV13 serotypes detected included 19F (n=8), 6B (n=6), 1 (n=5), 23F (n=4) and 18C (n=3). Comparing with the period prior to the inclusion of PCV13 in the NIP, serotypes 1 and 7F showed significant decreases, while the opposite was true for serotypes 3, 8 and 33F. Susceptibility to penicillin and erythromycin was found in 75% of the isolates, while 10% were simultaneously resistant to erythromycin and penicillin non-susceptible (MIC>0.06 mg/L). 17% of the isolates were penicillin non-susceptible and 18% were resistant to erythromycin, mostly associated with serotypes 14, 19F, 33F and 6B.

Conclusions: Despite universal vaccination with PCV13, serotype 3 is still the dominant serotype in pIPD while other PCV13 serotypes decreased significantly, suggesting that vaccination is not equally effective against all serotypes. The increase of non-vaccine serotypes such as serotypes 8, 33F and 10A, is of concern because NVTs may begin to erode the benefits of vaccination.

Clinical Trial Registration: Not applicable

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Background: The introduction of pneumococcal conjugate vaccines (PCVs) into routine infant immunization programs led to significant changes in serotype distribution and antimicrobial susceptibility patterns of pneumococci causing IPD in Portugal, but little is known about the epidemiology of non-invasive pneumococcal pneumonia (NIPP) in children. Given this, we aimed to characterize the pneumococcal population causing NIPP in children (<18 years) after the inclusion of PCV13 in the National Immunization Plan, by serotyping and antimicrobial susceptibility testing.

Methods: A total of 190 Streptococcus pneumoniae isolates recovered from NIPP cases in 62 hospitals in Portugal between January 2015 and December 2018 was characterized by serotyping and antimicrobial susceptibility testing.

Results: The majority of the NIPP cases were caused by serotypes not included in any PCV formulation (68%), with serotypes 11A (n=23), 23B (n=17) and 21 (n=19) being the most frequent. Among PCV13 serotypes, serotype 19F was the most frequent (n=19) followed by serotypes 3 (n=15) and 19A (n=10). Other PCV serotypes detected included 14 (n=7), 23F (n=2) and 4, 6A, 6B and 18C (n=1 each). Susceptibility to penicillin and erythromycin was found in 61% of the isolates, while simultaneous expression of erythromycin and penicillin non-susceptibility was found in 15% of the isolates. Overall, 21% of the isolates were penicillin non-susceptible and resistance to erythromycin was expressed by 23% of the isolates.

Conclusions: Despite PCV7 use for more than 15 years, serotype 19F is still an important serotype in pediatric NIPP in Portugal. In recent years, pediatric NIPP was mostly caused by serotypes not included in any conjugate vaccine, contrarily to the situation in pediatric IPD, suggesting a different impact of the vaccine in non-invasive pneumonia.

Clinical Trial Registration: Not applicable
CHOICE OF VACCINES AND THE STUDY OF PHARMACOVIGILANCE AT THE INTRODUCTION OF VACCINE AGAINST ROTAVIRUS IN THE DRC

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Title of Case(s): Choice of vaccines and the study of pharmacovigilance at the introduction of vaccine against rotavirus in the DRC

Background: Le programme étendu de vaccination a sélectionné le vaccin ROTASIL sur la base des résultats des souches circulantes détectées en RDC (les souches de rotavirus communément détectées par RT-PCR sont: G1P [8], G2P [6], G1P [6] et G2P [2]), associée à d'autres souches dont l'ampleur est négligeable. We based our study on the adverse effects of other rotavirus vaccines, the

Case Presentation Summary: Le programme étendu de vaccination a sélectionné le vaccin ROTASIL sur la base des résultats des souches circulantes détectées en RDC (les souches de rotavirus communément détectées par RT-PCR sont: G1P [8], G2P [6], G1P [6] et G2P [2]), associée à d'autres souches dont l'ampleur est négligeable. We based our study on the adverse effects of other rotavirus vaccines, the most cruel being intestinal intussusception in children under 5 years. We conducted a retrospective study over the last 6 years on the intussusception cases in Kalembe Lembe Pediatric Hospital in children under 5 years of age.

Learning Points/Discussion: From 2012 to 2017, out of a total of 1,240 cases received in surgery, 115 cases of acute intestinal intussusception (9%), were notified (with 107 surgical procedures and 46 deaths or 40%). Although this vaccine is not on the vaccine calendar, it is marketed in the DRC. The reported causes of intestinal invaginations are: washing of the intestines with indigenous products (41 cases with 13 deaths); congenital malformation (16 cases with 8 deaths); food causes (34 cases with 11 deaths); typhoid fever; other cases whose causes remain unknown.
Background: A previous study from Portugal revealed the dominance of serotype 3, and a considerable number of vaccine failures, during 2010-2015 in pediatric complicated pneumococcal pneumonia (PCPP). We aimed to characterize the serotypes causing PCPP after the introduction of PCV13 in the National Immunization Program (NIP).

Methods: From January 2016 to October 2019, the pediatric departments of 62 hospitals were asked to submit pleural fluid, or the pneumococci isolated therefrom, of all PCPP suspected cases. Pneumococcal isolates were serotyped by Quellung. Real-time PCR targeting lytA, wzg and capsule specific genes was performed in culture-negative cases.

Results: A total of 160 samples was submitted, of which 8 were culture-positive (5%). Among the remaining 152 pleural fluid samples, pneumococci were identified in 85 (53%). The main serotype was serotype 3 (n=64, 69%). Other serotypes found included serotypes 8 and 14 (n=5 each), serotype 19A (n=3), serotype 1 (n=2) and serotypes 11A/11D, 15A and 6B (n=1 each). In 11 samples, it was not possible to determine the serotype (12%). An increase in serotype 3 and a decrease in serotype 1 (p<0.001 in both) were noted relative to 2010-2015. We also identified 26 vaccine failures among age appropriately vaccinated children, mostly due to serotype 3 (n=21), but also involving serotypes 14 (n=3) and 19A (n=2).

Conclusions: Despite the inclusion of PCV13 in the NIP increasing the vaccination coverage, serotype 3 still dominates in PCPP, being responsible for a considerable number of vaccine failures and suggesting a lower efficacy of PCV13 against PCPP caused by this serotype. The data also reinforces the importance of using molecular methods in order to improve diagnosis and gain a better knowledge into the epidemiology of PCPP.

Clinical Trial Registration: Not applicable
Background: Community-acquired pneumonia (CAP) is a common cause of consultation and antibiotic prescription in pediatric practice. Published guidelines recommend high dose amoxicillin for most children with uncomplicated CAP, yet macrolides and broad-spectrum antibiotics are widely prescribed. It is mandatory to reduce the misuse of antibiotics through antimicrobial stewardship programs. A local clinical pathway based on antibiotic therapy guidelines may help to reduce inadequate antibiotic prescription.

Methods: We conducted an observational study at the Pediatric Department of “SS. Annunziata” Hospital, Savigliano. All patients admitted and diagnosed with moderate-severe CAP between January 1, 2019 and December 31, 2019 were included in the study. Children with complex chronic conditions, interhospital transfers or recent hospitalization were excluded. Antibiotic prescription was made according to a local clinical pathway, based on national and international guidelines.

Results: 109 cases (M/F 54/55, mean age 3,5 years; range: 3 months–11 years) were analyzed. Antibiotics used in children hospitalized with CAP were high-dose amoxicillin (18,8%), oral macrolide (1,8%), amoxicillin-clavulanate i.v. (44,4%), amoxicillin-clavulanate i.v. + oral macrolide (16,6%, mean age 6,7 years), ceftriaxone i.v./i.m. (12,9%), ceftriaxone i.v./i.m. + oral macrolide (5,5%, mean age 6,6 years). Amoxicillin-clavulanate i.v. was administered in pretreated patients and/or more severe cases, ceftriaxone i.v./i.m. in complicated CAP. Oral macrolides were used mainly in patients older than 5 years. Local pathway was followed in 96,3% of cases.

Conclusions: This study shows a strict adherence to a local clinical pathway based on national and international guidelines; following such clinical pathway can be an effective instrument for antimicrobial stewardship, allowing to narrow the antibiotic spectrum. However, it would be desirable to improve such tool in order to increase in our Pediatric Department the use of high-dose amoxicillin for patients with uncomplicated CAP.
KEYPOINTS IN PEDIATRIC KIDNEY TRANSPLANT IN CHILDREN LIVING WITH HIV: A CASE REPORT

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Title of Case(s): Keypoints in Pediatric Kidney Transplant in Children living with HIV: A Case Report

Background: End-stage renal disease in HIV patients has multifactorial etiologies, from drug adverse reaction to sepsis and direct effect of the virus. Solid organ transplantation (SOT) in adults living with HIV is rapidly evolving, but experience with children is still limited. Antiretroviral suppressed receptors have similar survival rates than HIV-negative adults, but more complications concerning immunosuppression, prophylaxis, drug interaction and organ rejection.

Case Presentation Summary: We report a case of a 16-year-old girl with perinatally-acquired HIV infection and chronic renal disease caused by septic shock and segmental and focal glomerulosclerosis. She was on dialysis for five years. HIV viral load was undetectable with a second line treatment with darunavir/ritonavir, enfuvirtide and raltegravir after virologic failure due to poor adherence. In January 2017, she was submitted to renal transplant from a deceased donor who was IgM-positive for toxoplasmosis. Our patient was IgG-positive for cytomegalovirus and had previously treated tuberculosis. Induction was made with thymoglobulin and immunosuppression with prednisone, tacrolimus and mycophenolate-mofetil. Dialysis was maintained for three days after surgery. Prophylaxis was with ganciclovir and trimethoprim-sulfamethoxazole. Her tacrolimus trough level was elevated and hard to adjust. It was eventually changed for everolimus. Other complications were urinary tract infection, cellulitis, cytomegalovirus reactivation and a decrease in CD4-cells despite undetectable viral load. She is currently well and with adequate graft function after three years.

Learning Points/Discussion: Drug interactions are one of the complications of SOT in HIV-patients. We saw a protease inhibitor increasing the level of tacrolimus. When prescribing adequate prophylaxis after SOT it is important to consider the use of immunosuppresant drugs as well as the CD4 level and previous infections. Antiretroviral suppressed adolescents can have favorable outcome after SOT. Poor adherence and graft infection can worsen survival rates.
RADIOLOGICAL PATTERNS IN PULMONARY FUNGAL DISEASE IN IMMUNOSUPPRESSED CHILDREN: HOW TO INTERPRET NON-TYPICAL FINDINGS?

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Background: Invasive Fungal Infections (IFI) are an important cause of morbidity and mortality in immunosuppressed children. The most frequent agents are Aspergillus sp. and Candida sp. Clinical signs are not specific, therefore diagnosis relies on radiological imaging, biomarkers and risk factors. There are few studies evaluating radiological findings in children with IFI. They show less typical images (halo-sign, air-crescent sign and cavities) and more nonspecific findings.

Methods: We reviewed the medical records and thoracic CT-scans from 40 patients with malignant diseases and possible, probable or proven IFI in a Brazilian hospital from 2008 to 2014. We analyzed demographic characteristics, risk factors, clinical presentation and outcomes. Radiological images were interpreted by two independent radiologists. Patients were divided into two groups according to the presence or absence of typical findings in the CT-scan.

Results: We evaluated 76 CT-scans from 40 patients. Twenty-nine children had typical radiological images (halo-sign n=27, 67%; cavity n=7, 17%; crescent-sign n=0) and eleven (27%) had only nonspecific findings (nodules n=2; pleural effusion n=4; masses n=7; ground-glass n=10). The group with typical CT-scan was older (123 vs 77 months, p=0.03) and had more days of neutropenia before the IFI (15 vs 11 days, p=0.04). Other characteristics were similar between the groups. Ten patients had proven disease (Aspergillus n=4, Candida n=5, Fusarium n=1) and one had probable aspergillosis. Galactomannan was not performed.
Conclusions: We found a 67% incidence of halo-sign, which is high comparing to other pediatric studies. All patients with proven/probable Aspergillosis had halo-sign. Nonspecific findings were present in 27% of patients. It is important to consider the diagnosis of IFI in children with the presence of risk factors and abnormal chest CT-scans, even if they are not typical findings of IFI.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Patients with typical CT-findings</th>
<th>Patients with nonspecific CT-findings</th>
<th>P value</th>
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<tbody>
<tr>
<td></td>
<td>n=29</td>
<td>n=11</td>
<td></td>
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<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td></td>
</tr>
<tr>
<td>female</td>
<td>15 (51)</td>
<td>7 (64)</td>
<td>0.47</td>
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**Underlying Condition**

- ALL: 9 (31) vs 3 (27), P=1
- AML: 13 (45) vs 4 (36), P=0.72
- RR: 11 (38) vs 2 (18), P=0.28
- Autologous BMT: 2 (7) vs 1 (9), P=1
- Allogeneic BMT: 1 (3) vs 1 (9), P=0.47
- Medulloblastoma: 1 (3) vs 0, P=1
- Other*: 6 (21) vs 4 (36), P=0.45

**Age**

- Median: 12 (5 months) vs 7 (7 months), P=0.03
- 0-4 years: 6 (25) vs 6 (55), P=0.32
- 5-12 years: 9 (31) vs 5 (45), P=0.3
- ≥15 years: 12 (41) vs 0, P=0.01

**Neutropenia**

- Time of neutropenia before diagnosis: 15 days vs 11 days, P=0.04

**Broad spectrum antibiotics**

- 29 (100) vs 11 (100), P=0.24

**Chemotherapy and Invasive devices**

- 28 (97) vs 9 (82), P=0.17
- 15 (99) vs 10 (91), P=0.64
- 25 (97) vs 6 (55), P=0.24

**Symptoms and Signs**

- Fever: 20 (100) vs 10 (91), P=0.37
- Median duration of fever: 9 days vs 5.5 days, P=0.2
- Respiratory distress: 16 (55) vs 6 (55), P=1
- Pleural effusion: 1 (3) vs 0, P=1
- Hemodynamic instability: 6 (21) vs 6 (55), P=0.08
- Skin lesions: 0 vs 1 (9), P=0.29

**ICU Admission**

- 10 (34) vs 8 (73), P=0.08

**Antifungal Prophylaxis**

- Fluconazole: 17 (99) vs 6 (55), P=1
- Itraconazole: 7 (24) vs 0, P=0.15
- Voriconazole: 3 (10) vs 1 (9), P=1
- Micafungin: 5 (17) vs 4 (36), P=0.58

**Treatment**

- Median time of treatment: 21 days vs 22 days, P=0.2
- Fluconazole: 1 (3) vs 0, P=1
- Itraconazole: 5 (17) vs 0, P=0.29
- Anfotericin B: 12 (41) vs 9 (82), P=0.03
- Anfotericin B + Fluconazole: 0 vs 1 (9), P=0.27
- Anfotericin B + Voriconazole: 11 (38) vs 1 (9), P=0.12

**Outcome**

- Cure: 14 (48) vs 7 (64), P=0.48
- Deceased because of IFI: 3 (10) vs 2 (18), P=0.6
- Deceased for other causes: 9 (31) vs 2 (18), P=0.69
- Lost to follow-up: 3 (10) vs 0, P=0.54

**Radiological Findings in chest CT-scan**

- Halo-sign: 27 (91) vs 2 (18), P=0.002
- Masses: 12 (41) vs 7 (63), P=0.29
- Air crescent sign: 0 vs 0
- Saccular: 7 (24) vs 0, P=0.15
- Nodules: 1 (3) vs 2 (18), P=0.17
- Ground-glass: 10 (34) vs 10 (91), P=0.23
- Pleural effusion: 10 (34) vs 4 (36), P=1
- Other: 29 (100) vs 11 (100)

ALL: acute lymphoblastic leukemia; AML: acute myeloid leukemia; BMT: bone marrow transplant; ICU: intensive care unit; IFI: invasive fungal infection; RR: refractory or relapsed. *Other: neuroblastoma (n=4); osteosarcoma (n=2); adenocarcinoma (n=11); hepatocellular carcinoma (n=3); sarcoma (n=2); pinealoblastoma (n=1); neuroblastoma (n=1). **Four patients had 1 finding; five patients had 2 findings; the other patients had ≥3 findings.
ATYPICAL MYCOBACTERIAL INFECTION IN A CHILD WITH MONOCYTOPENIA AND LYMPHOPENIA

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Title of Case(s): Atypical mycobacterial infection in a child with monocytopenia and lymphopenia

Background: GATA2 mutation leading to MonoMAC syndrome is a relatively newer entity. MonoMAC syndrome presenting with monocytopenia and atypical mycobacterial infection is one of the commonest clinical phenotypes. In recent times, Different types of mutations are reported to cause MonoMACsyndrome. This is the first case from India and the mutation in our patient is different from those described in the literature.

Case Presentation Summary: A 14 year-old-boy had weight loss, cough, loss of appetite, low-grade fever, oral thrush, and intermittent diarrhea. During this time, he also developed varicella pneumonitis and H1N1 pneumonia. On arrival, he had left pneumothorax and respiratory failure. Laboratory investigations revealed anemia (lowest hemoglobin 50 gm/L), thrombocytosis (platelets 787x 10^9/L), persistent monocytopenia (all differential count values less than 1%, with maximum absolute count of 50), raised ESR (59 mm in 1st hour), absent B lymphocytes (with 79% CD3+ T-cells and 6% CD56+ natural killer cells), normal Immunoglobulin profile and low post-vaccination antibody levels. HIV serology was non-reactive. Chronic granulomatous disease was ruled out on basis of flowcytometric assay with dihydrorhodamine123 (DHR). He had hypoproteinemia, altered albumin globulin ratio and deranged coagulation parameters. Bone marrow aspirate revealed reactive changes. Sputum showed acid fast bacilli. Mycobacterial polymerase chain reaction test was also suggestive of a nontubercular mycobacterial infection. Genetic study showed deletion in exon2 of GATA2 gene (GATA2 Exon2 XM_005247344.1:c.199_208delCGGGCGCGCX XP_005247401.1:p.Arg67SerfsTer10)

Learning Points/Discussion: 1. Persistent monocytopenia, B-cell lymphopenia, and atypical mycobacterial infection are strong clues for MonoMac syndrome (GATA-2 deficiency). 2. The presence of a history of concomitant viral and fungal infections further strengthens the possibility. 3. MonoMAC syndrome presenting with monocytopenia and atypical mycobacterial infection is one of the commonest clinical phenotypes. 3. Our patient had a novel frameshift mutation in the GATA2 gene.
FUNGAL BRAIN ABSCESS IN A CHILD WITH CHRONIC GRANULOMATOUS DISEASE

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Title of Case(s): Fungal brain abscess in a child with Chronic Granulomatous Disease

Background: Chronic granulomatous disease (CGD) is a primary immunodeficiency disorder with a defect in the nicotinamide adenine diphosphate hydroxyl (NADPH) oxidase enzyme complex. *Aspergillus nidulans* (*A. nidulans*) is a filamentous fungus, which is increasingly being reported as one of the virulent fungus to cause invasive Aspergillosis in immunodeficient patients. We present a case of CGD who had a biopsy-proven *A. nidulans* brain abscess.

Case Presentation Summary: A 5 year-old-boy had been referred to us for recurrent skin and respiratory infections. Dihydrorhodamine 123 (DHR) assay were consistent with a diagnosis of chronic granulomatous disease (CGD). Genetic analysis showed a mutation in the *CYBB* gene encoding for gp91phox protein. While on prophylaxis, he developed headache, lethargy and 3 episodes of focal seizures. He had papilledema and limb rigidity. Laboratory investigations revealed hemoglobin 100 gm/L; total leucocyte count 1.1x10⁹/L (Polymorphs 82%, lymphocytes 12% and monocytes 6%); platelet count 386x10⁹/L; ESR 76 mm in the first hour and C-reactive protein 186 mg/L. Blood culture showed growth of *Escherichia coli*. Brain imaging revealed bilateral nodular enhancing lesions in the fronto-parieto-occipital cortex with significant mass effect. He underwent right fronto-temporal-parietal decompression hemicraniectomy. Potassium hydroxide (KOH) mount of brain tissue showed presence of septate hyphae. Sabouraud dextrose agar culture showed the presence of biseriate conidial heads, , and globose, rough-walled conidia, thick-walled Hülle cells, and cleistothecia identifying the isolate as *A. nidulans*.

Learning Points/Discussion: 1. *A. nidulans* is an important fungal pathogen in patients with CGD, especially in the context of osteomyelitis, pneumonia, and abscesses. 2. It causes significant mortality in these patients. Because of this unique agent-host interaction and high fatality, *A. nidulans* infection is one of the major threats to patients with CGD. 3. CGD and *A. nidulans* have unique agent-host interaction.
ASSESSMENT OF THE CHANGES IN PREVALENCE OF ORAL HUMAN PAPILLOMAVIRUS IN PEDIATRIC PATIENTS WITHIN A MULTI-ETHNIC PEDIATRIC CLINIC POPULATION

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Background: Human papillomavirus (HPV) is a cancer-causing virus most commonly associated with cervical cancers. Less common HPV-related cancers, like oropharyngeal cancer, have also gained increasing attention in recent years. Over the last decade, researchers at the University of Nevada, Las Vegas – School of Dental Medicine (UNLV-SDM) have collected a large number of saliva samples, analyzed them for the presence of HPV, and published these findings. The objective of this study was to assess any changes in prevalence of oral HPV among the pediatric patients sampled from this multi-ethnic clinic population.

Methods: This retrospective analysis involved n=403 pediatric patients (n=403) for analysis. Each saliva sample was processed and screened for both high-risk HPV16 and HPV18 strains. Only basic demographic data, such as Sex, Age and Ethnicity were available for this analysis.

Results: These data demonstrated that the overall prevalence of oral HPV among all samples was 9.1% (n=37/403). However, subgroup analysis also revealed that the prevalence of oral HPV within each sample cohort increased in each of the three sequential studies. The initial study (2012) demonstrated oral HPV prevalence of 2.5% (n=3/118), while the subsequent studies (2018, 2019) demonstrated oral HPV prevalence of 9.2% (n=19/187) and 15.3% (n=15/98) respectively. This represents a greater than 6-fold increase between 2012 and 2019 within a pediatric population that is primarily composed of minority (non-White) and low income individuals.

Conclusions: Although a thorough comprehensive evaluation of all pediatric patients within this clinic was not possible, these individual studies provide some evidence to suggest that oral HPV infection in children may be of significant value to dental, medical and oral health professionals seeking to determine successful vaccination strategies in order to protect the pediatric population in early childhood.

Clinical Trial Registration: Not applicable
FACTORS ASSOCIATED WITH THE ROLE OF PARENTS FOR THE PREVENTION OF HUMAN PAPILLOMAVIRUS IN MEXICAN ADOLESCENTS

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Background: The role of parents is key for the prevention of HPV in adolescents however there are factors that can facilitate or inhibit its performance. The purpose of this study was to explore factors influencing the role of parents for prevention of HPV among their adolescent children.

Methods: A descriptive correlational study design included a convenience sample of 582 Mexican parents, whose son or daughter was in either the second or third year of high school. Data analyses included multiple linear regression.

Results: Factors related to role of parents included HPV knowledge ($r_s = 0.180$, $p < 0.01$), perceived risk to contract HPV ($r_s = 0.148$, $p < 0.01$), self-efficacy for sexual communication with adolescents ($r_s = 0.507$, $p < 0.01$) and attitude toward prevention of HPV ($r_s = 0.272$, $p < 0.01$). Self-efficacy for sexual communication with adolescents and attitude towards prevention of HPV positively influenced role of parents, explaining 28.8% of variance ($F[4,577] = 59.80$, $p < 0.001$).

Conclusions: Our findings indicate that when parents have positive attitudes regarding prevention of HPV and perceive self-efficacy to communicate sexuality issues to their adolescent children, they develop a preventive role to reduce the risk of HPV infection. These findings compel development of strategies that consider these aspects and contribute to empower parents to transition to an active role in HPV prevention. Interventions are indicated to enhance the ability of parents to transmit information concerning sexuality to their adolescent children and reinforce a positive attitude for prevention of HPV as these two aspects influence HPV prevention in adolescents. It is also important to educate parents concerning the need to transition to an active role in HPV prevention, whereby they are the primary source of information and prevention for their children.

Clinical Trial Registration: No Clinical Trial
MENINGITIS CAUSED BY MENINGOCOCCUS OF SEROGROUP Y AS A DIAGNOSTIC CLUE FOR COMPLEMENT FRACTION C6 DEFICIENCY

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Title of Case(s): Meningitis Caused by Meningococcus of Serogroup Y as a Diagnostic Clue for Complement Fraction C6 Deficiency

Background: The complement system has a decisive role in innate immune defenses against invasive meningococcal disease. Deficiency in components of the alternative and terminal complement pathways highly predisposes patients to invasive and often recurrent meningococcal infections. C6 deficiency in particular is usually reported in African Americans and South Africans. We report a case of complement fraction C6 deficiency diagnosed after a single event of meningitis by meningococcus serogroup Y.

Case Presentation Summary: We report the case of a 12-year-old boy, African descendant, with no medical or family history, who was brought to our emergency department with fever, headache, lethargy and vomiting that started two days prior to admission. Physical examination showed drowsiness and nuchal rigidity, but no other meningeal signs and no neurological or cutaneous alterations were present. Significant elevation of the serum inflammatory parameters was found, along with neutrophilic pleocytosis, elevated protein levels and decreased glucose in cerebrospinal fluid. Empirical treatment with ceftriaxone and vancomycin was initiated, and later changed for monotherapy with ceftriaxone after isolation of Neisseria meningitidis serogroup Y in blood and cerebrospinal fluid cultures. Complementary investigation showed absent C6 fraction and low CH50. There were no complications or sequelae. Meningococcal vaccines against serogroup B and A, C, Y, W were administered, and long-term prophylactic antibiotic therapy with penicillin was initiated with no recurrence of infection within one-year follow-up.

Learning Points/Discussion: The increased risk of developing invasive meningococcal disease, adding to the severity of the diagnosis and the possibility of prophylaxis point out the necessity of a systematic screening of complement deficiencies in cases of Neisserial infection. This case reinforces the importance of investigating these disorders even after a first episode in situations where the causative agent belongs to a less frequent serogroup.
PECULIARITIES OF THE COURSE OF RESPIRATORY INFECTION AMONG CHILDREN WITH α-1-ANTITRYSIN DEFICIENCY.

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Title of Case(s): Peculiarities of the course of respiratory infection among children with α-1-antitrypsin deficiency.

Background: α-1-antitrypsin deficiency (A1AD) is the reason of orphan disease among children which is elucidated only in single publications. In the childhood the pulmonary form of the diseases manifests in the form of reinfection of respiratory tract, also it can occur in the form of a recurring syndrome of wheezing which is followed by the transformation into bronchiectasis and emphysema in adults.

Case Presentation Summary: A 6-year-old child is under our supervision from the age of 3 years. Recurrent respiratory infections (bronchitis, pneumonia) and wheezing syndrome (3-4 times a year). Positive dynamics was observed only after the appointment of antibacterial therapy. Increasing of body temperature to 38, BMI 10.4, severe respiratory failure, deformation of nails by “watch glasses” and fingers in the form of “drum” wands was noted during the last hospitalization. The clinical blood test showed accelerated ESR and leukocytosis. The sputum test leukocytes up to 50 were observed, the bacterial diagnostic showed the presence of *St. Pneumonia* and *St. Haemolyticus*. Chest CT scan showed cylindrical bronchiectasis, in the reed segments on the left, in the middle lobe on the right of the lungs. The spirometry results - 1st degree obstruction. SpO₂ - 88%. AAT and ALAT were 2 times higher of the age norm. Blood α-1-antitrypsin was 0.38 g/l (with a norm of 0.78-2.0 g/l). α-1-antitrypsin deficiency and cylindrical bronchiectasis were diagnosed.

Learning Points/Discussion: The pulmonary form of A1AD cannot be diagnosed for a long time and it can leak under the guise of respiratory tract infections. Diagnostic search for A1AD should pass in children with repeated bronchitis, pneumonia, recurrent wheezing syndrome, respiratory failure and persistent microbial state of sputum. A1AD is a rare disease and it is important to create the international registries of such patients.
COMPARISON OF AUTOMATED LIQUID CULTURE AND LINE PROBE ASSAY IN PAEDIATRIC PULMONARY TUBERCULOSIS, INDIA

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Background: It is estimated that childhood Tuberculosis constitutes 10–20% of all in high-burden countries. At Present conventional/Automated cultures are gold standard but the sensitivity still remains low as it needs 10-100 live bacilli to give significant results. Line Probe assays are newer molecular techniques which not only detects the presence of bacilli (dead or live) but also detects resistance to Isoniazid and Rifampicin respectively.

Methods: Children ≤ 12 years with clinical suspicion of Pulmonary Tuberculosis and who tested positive for Mycobacterium tuberculosis complex by GeneXpert (CBNAAT) assay were included in the study. Appropriate Samples were collected from the suspected patients and processed for Line Probe assay along with automated Liquid culture using Mycobacterium growth indicator tube (MGIT). Demographic and clinical details of the patients were also noted.

Results: Majority of cases in the study were Smear Negative (30, 85.8%) and only five cases were smear positive. Amongst the 30 smear negative cases, culture was positive for 18 (60%) cases and Mycobacterium tuberculosis band using line probe assay was observed in 25 (83.3%) cases. Comparison of Line probe assay with MGIT culture (gold standard) showed Sensitivity of 100% (85.1 - 100), Specificity of 41.6% (15.1 - 72.3), Positive predictive value of 76.6% (67.07 - 84.1) and Negative predictive value of 100%.

Conclusions: Although culture is gold standard but in this study it missed few smear negative Pulmonary Tuberculosis patients in comparison to Line Probe Assay which could identify upto 83% of cases with 100% sensitivity rate. Even in culture negative cases line probe assay could detect Mycobacterium tuberculosis cases and hence can be used for early detection and treatment. Therefore further studies should be including larger population to compare the above techniques.
VARICELLA ZOSTER VIRUS ENCEPHALITIS IN VACCINATED PATIENT: A CASE REPORT.

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Title of Case(s): Thinking the disease in the vaccinated patient

Background: In immunocompetent patients, the most frequent complications of varicella zoster virus (VZV) are: cutaneous superinfections (42%), neurological (9%), and pulmonary (0.6%) affections, even in vaccinated patients. Among the neurological affections, the most prevalent one is the acute cerebellar ataxia (1/4000), with favorable prognosis and, less frequently, the viral encephalitis (1.7 / 100,000) that can cause sequelae in 10-20% of the cases.

Case Presentation Summary: 5-year-old male, vaccinated according to local schedule, admitted due to postictal state after afebrile convulsive episode without relevant personal history. Evidence of generalized skin lesions in a crusty stage with no signs of superinfection, corresponding to the 6th day of chickenpox evolution. Admission laboratory with low-risk blood count, metabolic acidosis, discretely increased lactate and normal chest x-ray. Within the first hour of admission he presented a new convulsive episode with adequate response to lorazepam. Normal CT brain scan, negative blood cultures and cerebrospinal fluid (CSF) culture are taken, prior to starting treatment with Ceftriaxone (CTX) and Acyclovir. With normal CSF analysis but positive PCR for VZV, CTX is suspended and continues with acyclovir for 14 days total. Normal EEG and brain MRI are performed. He resolved without sequelae, in clinical follow-up by paediatrician and neurologist.

Learning Points/Discussion: It is known that VZV infection is potentially severe and neurological complications require longer hospitalization time, however, these have decreased in the postvaccinal era. In Argentina, since 2015, is mandatory to vaccinate with single dose of Varicella vaccine (OKA) to 15-18 months-old toddlers according to the national immunization program. In other countries, this scheme have changed to double dose of the vaccine due to continued Varicella outbreaks in children with favorable results.
EFFICACY OF ANTIBIOTIC CONTAINING OINTMENTS FOR NEONATAL OCULAR PROPHYLAXIS FOR THE PREVENTION OF CHLAMYDIAL CONJUNCTIVITIS

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**Background and Objective:** Routine neonatal ocular prophylaxis with silver nitrate drops, while effective for prevention of gonococcal ophthalmia, does not prevent neonatal conjunctivitis due to *Chlamydia trachomatis* (CT). The efficacy of erythromycin or tetracycline ophthalmic ointment for prevention of neonatal chlamydial conjunctivitis has not been established. The objective of this study was to examine the published literature to determine whether antibiotic containing preparation are efficacious for prevention of neonatal chlamydial conjunctivitis.

**Methods:** We conducted a narrative literature search of MEDLINE and EMBASE. Articles were selected if their content included four key criteria: (1) Prospective study. (2) Prenatal screening of the mothers for CT. (3) Follow-up of infants born to chlamydia-positive women. (4) Infants followed at regular intervals and tested for CT in the eye and NP. Exact logistic regression was used to estimate exact odds ratios (ORs) with 95% CI and to compute exact 2-sided tests of the null hypothesis that OR=1.

**Learning Points/Discussion:** Initial search yielded 159 studies; 12 were selected for review, nine were excluded; only 3 addressed the 4 key criteria. The rates of CT conjunctivitis in infants who received silver nitrate was 20-33%; positive NP, 1-28%; pneumonia, 3-8%. The rates of CT conjunctivitis in neonates who received erythromycin or tetracycline prophylaxis did not differ significantly from that seen with silver nitrate; 0-15% and 11%, respectively, who received erythromycin or tetracycline developed CT conjunctivitis; 4-33% and 5% of infants who received erythromycin or tetracycline, respectively, had positive NP cultures; 0-4% developed chlamydial pneumonia. Prophylaxis with antibiotic ointments did not consistently reduce the rates of CT conjunctivitis and respiratory infection compared with silver nitrate. Universal screening and treatment of pregnant women for CT is the most effective approach for prevention of perinatal chlamydial infection.
Title of Case(s): INDOLENT PNEUMONIA : A high index of suspicion

Background: This problem is very rare in childhood. There are few cases in pediatrics described in the literature. The clinical diagnosis is difficult and is often delayed because the symptoms are nonspecific, prolonged and indolent. The infection can simulate malignancy, tuberculosis and lung abscess. With proper therapy, the prognosis is usually very good, achieving healing in a high percentage of cases.

Case Presentation Summary: 12-year-old indigenous girl; 20 days of constitutional symptoms, dry cough and fever, without respiratory distress. Examination was notable for cachexia, pale; pain on superficial palpation and dullness, hypoventilation and pectorilochia in the left hemithorax, the remainder of the examination was normal. Leukocytosis and neutrophilia, anemia, thrombocytosis and elevated C-reactive protein, radiography of thorax: massive left pleural effusion that involves 2/3 lower hemithorax without caverns or nodules. The diagnostic of Community-acquired Pneumonia complicated with left pleural effusion vs Pulmonary Tuberculosis is performed, empirical Ceftriaxone and Clindamycin were administered. Thoracostomy and pleural decortication is performed. Stains and cultures of bacteria, fungi and mycobacteria were negative. Report of biospia pathology: liquefactive necrosis, abundant mixed inflammatory tissue predominantly neutrophils and histiocytes accompanied by basophilic bacterial colonies of cottony aspects compatible with Actinomyces spp. Crystalline penicillin and clindamycin were administered intravenously and once the clinical condition of the girl was satisfactory continuous with amoxicillin for 6 months. Studies to rule out primary immunodeficiency were indicated.

Learning Points/Discussion: Actinomycosis is an infection that must be taken into account in the differential diagnosis of an inflammatory collection of cervical-facial or abdominal or thoracic location, especially if it has a chronic course and / or poor response to treatment. In general, cervical infection responds well to antibiotics. In some cases drainage of large thoracic, abdominal or soft tissue abscesses is required.
Background: Recently, the number of parents who refuse to vaccinate their children or present the so-called hesitant behaviors has increased in many developed countries. The study aimed to analyze the completeness and timeliness of vaccinations against hepatitis B and tuberculosis in neonates in a single maternity hospital in Warsaw (Poland). These two vaccine are obligatory and should be conducted in the first days of life.

Methods: We analyzed 14,785 medical records of children born in the second level hospital in Warsaw between 1st January 2015 and 31st December 2017 and calculated the proportion of newborns not vaccinated on time according to the National Immunization Programme against tuberculosis (TBC) and hepatitis B (HBV). Newborns remained unvaccinated because of parental refusal (refusers) or decision for a delay (hesitants) or medical contraindications.

Results: The percentage of unvaccinated newborns was similar in the analyzed years: 7.3% in 2015, 6.7% in 2016 and 10.1% in 2017. Parental decisions rather than medical contraindications caused non-immunization (4.3% vs. 2.9% in 2015, and 4.7% vs. 2% in 2016, 7.5% vs. 2.6% in 2017). Most parents refused both vaccinations (67.3% in 2015, 74.8% in 2016, 68% in 2017). Among parents who refused only one vaccination, TB vaccination was refused more often than HBV (9.2% vs. 7.1% in 2015, 8.3% vs. 5.7% in 2016, 5.9% vs. 2.7% in 2017).

Conclusions: The increase in the number of newborns who are not correctly vaccinated just after birth due to their parents' decision should be considered non-gradual, both for hepatitis B and tuberculosis. It is necessary to implement effective educational and informative measures targeted at future parents to reinforce positive attitudes towards vaccinations and to dispel doubts about them among parents who are hesitant.
Background: Group A rotaviruses are the major viral agent of acute gastroenteritis and severe diarrhea in children <5 years old. The World Health Organization (WHO) recommends surveillance of circulating strains before and after introduction of vaccination in countries. However, the diversity of circulating strains in developing countries is a major challenge to the vaccination programs. This study, carried out in furtherance of the sentinel surveillance, aims to identify the different genotypes circulating before and after the introduction of the Rotavirus vaccine.

Methods: All children with acute gastroenteritis aged 0 to 5 years, admitted in one of the sentinel surveillance collection sites were included in the study. The study period was from January 2010 to December 2018. Rotavirus was detected in stool specimens by enzyme-linked immunosorbent assay (ELISA). Rotavirus G and P types were determined by real-time polymerase chain reaction (RT-PCR).

Results: A total of 1472 stool samples were collected before introducing vaccination and 430 after. During the first period, 31.8% of the stools were rotavirus positive by ELISA test. G1 was predominant with 39.6% followed by G12 (27%). P [8] was 50.4%. The predominant genotype combinations were G1P [8] with 26.1%; G12P [8], 15%; G1P [6], 11.3% and G12P [6], 10.8%. After introducing vaccination 17.5% of the stools were positive by ELISA test. G1 was predominant with 52.9% followed by None typable (NT) strains (25.4%).

Conclusions: Genotyping of circulating rotavirus strains is important in monitoring strains before and after the introduction of the vaccine. With previous observations, these findings will contribute to baseline data to further monitor the impact of rotavirus immunization in Côte d'Ivoire.

Clinical Trial Registration: no clinical trial registration
MISSED OPPORTUNITIES FOR THE PREVENTION OF HIV-1 MOTHER TO CHILD TRANSMISSION: DATA FROM THE EUROPEAN PREGNANCY AND PAEDIATRIC HIV COHORT COLLABORATION (EPPICC) STUDY GROUP


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Background: HIV-1 vertical transmission (VT) has reached very low levels across Europe, with rates of less than 1% in the West. We aimed to identify and describe missed opportunities for prevention of VT in infants in Europe among a group HIV-1 infected despite receipt of maternal ART and/or infant prophylaxis through a pooled analysis of individual patient data across 11 European countries.

Methods: We included live-born infants with confirmed HIV infection and exposure to any maternal treatment or neonatal prophylaxis born between 2002 and 2014. Missed opportunities were defined as HIV diagnosis (>28 weeks gestation); late antenatal care booking (≥13 weeks gestation); no antenatal ART; late ART start (>28 weeks); vaginal delivery with documented VL >50 copies/ml; no intra-partum intravenous ZDV when necessary; no neonatal prophylaxis; breastfeeding.

Results: Of 254 mother-infant pairs included; 84% (172/204) of mothers acquired HIV heterosexually and 153 (60%) were diagnosed during pregnancy (65 [43%] in third trimester). Ten women conceived on ART, 142 started ART during pregnancy (79 [56%] >28 weeks gestation) and 91 received no antenatal ART. Most infants (92%) received neonatal prophylaxis, half receiving ≥2 drugs. Breastfeeding was rarely reported (n=13); 23% infants were preterm. Missed opportunities for VT prevention were documented for most mother-infant pairs, with 76, 65, 47 and 17 having one, two, three or ≥4 missed opportunities respectively.

Conclusions: In this population of infected infants born in Europe, one or more missed opportunity for preventing VT was identified in 80%. Lack of maternal ART in pregnancy was the most frequent missed opportunity documented. In particular, barriers to timely maternal HIV diagnosis and access to and/or engagement with antenatal HIV care need to be addressed even in settings where VT rates overall are low.
Background: Determining the host molecular genetic characteristics of childhood bacterial pneumonia may inform the development of new clinical interventions for the disease. We performed a genome-wide association study to identify the genes associated with bacterial pneumonia.

Methods: DNA collected from healthy Nepalese children and children admitted to Patan Hospital, Kathmandu with clinician diagnosed pneumonia were genotyped using Illumina Global Screening Arrays. Children admitted with pneumonia were categorised as having bacterial pneumonia if they had a positive blood culture or had both a CRP greater than 60mg/L and end-point consolidation on chest x-ray. DNA array data underwent QC and filtering before undergoing imputation using the HRC R1.1 2016 reference panel. Association analysis was performed using PLINK 1.9.

Results: Following filtering, 103 children with bacterial pneumonia (cases) and 2121 healthy community based children (controls) were analysed. Nine variants were found to be moderately associated with bacterial pneumonia (p<10^{-5}), with five of these variants located within the SGK1 gene (for the lead variant, p=1.7x10^{-6}, MAF cases 0.14 vs MAF controls 0.05, OR=3, 95% CI 1.9-4.6).

Conclusions: We identified host genetic variants in SGK1 associated with bacterial pneumonia. Further studies confirming this association and its biological role in bacterial pneumonia are needed.

Clinical Trial Registration: ClinicalTrials.gov/N/A
BACTERIEMIA AND MENINGITIS BY HAEMOPHILUS INFLUENZAE SEROTYPE A. REPORT CASE.

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Title of Case(s): Considering less prevalent serotypes.
Background: Haemophilus Influenzae (Hi) is a Gram-negative coccobacillus with many serotypes known and exclusive to men. The bigger risk of disease is between 6 and 12 months old, over than 85% invasive disease occurs in children under 5 years old, and over than 65% in children under 2 years. The national immunization program includes, since 1997, vaccination with Hi serotype B component at 2,4,6 and 18 months-old children with remarkable decrease in nasopharyngeal carriers and invasive Hib disease. Other strains in vaccinated individuals should be suspected with invasive disease and meningitis.

Case Presentation Summary: 15 months old female toddler, with vaccination scheme up to 12 months age and personal history of epilepsy in study on treatment with phenobarbital. Admitted due to febrile state, vomiting, diarrhea and moderate dehydration signs, assumed as acute gastroenteritis of 24 hours of evolution. Admission laboratory with WBC 30000/m3 (80%neutrophils), ESR 52 mm/h, CPR 141 mg/dl. Parenteral hydration is indicated. Within the first 12 hours of admission, she presents meningeal signs and sensory deterioration. Normal CT brain scan is performed, as well as negative urine culture, blood and cerebrospinal fluid (CSF) cultures with positive results to Haemophilus Influenzae A (HiA), CSF pathological analysis. Antibiotic treatment with Cefotaxime 300 mg/kg/d (IV) for 10 days. She recovered without sequelae and continues currently under follow up by paediatrician, neurologist and immunologist.

Learning Points/Discussion: Haemophilus influenzae serotype A has emerged as an important serotype to consider in invasive disease in children, due to the widespread use of the Haemophilus influenzae B vaccine. This case and other Hi serotypes should be consider in future events, specially in children less than 2 years old and capsulated bacterias due to the higher risk of infective and neurological complications.
IMPORTED PATHOLOGY IN THE PEDIATRIC EMERGENCY DEPARTMENT OF THE TORREJóN HOSPITAL, MADRID. SPAIN

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Background: The increase in recent years of migratory movements and travelers to countries with limited-resources, has produced a rebound in the incidence of rare infectious-diseases(ID) in our environment. Many of them are in special risk situation due to multiple factors as irregular situation, difficulty for medical access. In addition, there is an important group of travelers who travel to visit their relatives in their country of origin(VRF), who do not usually consult before trip to perform preventive measures

Methods: A retrospective study was conducted between 2013 and 2019. Were included children under 16 years attended in the pediatric emergency department of the Hospital de Torrejón, with international travel history 3 months before the emergency visit. Demographic and clinical data were collected. The objective of the study was to describe the characteristics of patients to identify infections that progress/worsen quickly, treatable or transmissible

Results: During the study period there were 87,000 visits to the service of pediatric-emergency. 80 children were included. The median age was 4 years (IR: 2-9 years). Forty-nine (61%) were women. Twenty nine (36%) were VRF. Seventy-one children flew to Africa. Nineteen (24%) were diagnosed with malaria, 16 (20%) respiratory infections. Other diagnoses were HIV-infection, amoebic-liver abscess, chikungunya virus infection, meningitis due to meningococcal-W, pyelonephritis, pneumonia. No children died. The evolution of all the children was good.

Conclusions: Malaria was the most frequent cause of fever after an international trip. In our study the initial symptoms of potentially fatal imported diseases were indistinguishable from banal infections. The majority of children included in our study had not taken measures preventive during the trip, being lost opportunities of the health system to prevent diseases. The active search for HIV-infection in children immigrants can allow to diagnose the infection in the initial stages of the disease
Background: Maternal Zika virus (ZIKV) infection has been associated with congenital microcephaly and other neuro-developmental abnormalities. The long-term impact of these conditions can be severe for children and their families; however, there is little published research on the effect of maternal ZIKV infection in an European country. We aimed to describe the outcomes of pregnant travelers who were diagnosed as ZIKV-infected in Spain, and their exposed children.

Methods: A three-year multicenter prospective observational cohort study was conducted in nine Spanish health centers. The study enrolled pregnant women who travelled to/from ZIKV-endemic areas or whose sexual partners visited an endemic area within six months before the date of conception. Newborns of ZIKV-infected mothers were enrolled at birth and followed up for a maximum of three years.

Results: There were 163 pregnant women with ZIKV infection; 24 (14.7%) had confirmed ZIKV, 70% asymptomatic. Among 143 infants included in the analysis, 9.8% (95%CI: 5.5-15.9%) had adverse outcomes during follow-up: three cases of congenital Zika syndrome, and 11 with other potential Zika-related outcomes; representing an incidence rate of 135 cases (95%CI: 78.3-232.2 cases) per 1000 livebirth-year. The overall incidence of CZS was 2.1% (95%CI: 0.4-6.0%), but among infants born to ZIKV-confirmed mothers, this increased to 15.8% (95%CI: 3.4-39.6%).

Conclusions: The study found a nearly 10% overall risk of neurologic and hearing adverse outcomes in ZIKV-exposed children born to ZIKV-infected pregnant women who travelled to or from ZIKV-endemic areas. Longer-term follow-up of these children is needed to assess whether there are any later-onset manifestations.

Clinical Trial Registration: not applicable
TRENDS IN CHARACTERISTICS OF CHILDREN NEWLY DIAGNOSED WITH HIV IN THE UK AND IRELAND BETWEEN 2000 AND 2018

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**Background:** In recent years, UK/Ireland vertical HIV transmission (VT) has declined to <0.3% among pregnant women diagnosed with HIV. An increasing proportion of children living with HIV are either, born to women undiagnosed by delivery, or born abroad. We explore the changing characteristics of children diagnosed with HIV and seen for care in the UK/Ireland in 2000-2018 using two observational population-level surveillance datasets.

**Methods:** All children aged <16-years at HIV diagnosis are reported to the Integrated Screening Outcomes Surveillance Service and followed up longitudinally in the Collaborative HIV Paediatric Study throughout their paediatric HIV care. Descriptive statistics summarise characteristics of 1606 children diagnosed with HIV between 2000-18 at first diagnosis in UK/Ireland by place of birth (domestic versus abroad) and calendar year of diagnosis.

**Results:** Diagnoses peaked at 150 (2003-04) declining to 20-50 (2012-18) (p<0.001). Proportion born abroad increased from 63% (2000-04) to 73% (2012-18) (p<0.01). Median [IQR] diagnosis age declined from 2.4y[0.3,4.9] <2005 to 0.3y[0.1,1.6] in ≥2010 among domestic-born, versus 9.2y[5.9, 12.3] and 3y[2.3, 4.5] in children born abroad, respectively. Proportion with AIDS at diagnosis declined from 32% (2000-04) to 12% (2015-18) among domestic-born, and 20% to 15% among children born abroad, respectively. An increasing proportion of children born abroad were diagnosed abroad: 9% (2000-04), to 62% ≥2015 (p<0.001), 60% received ART abroad.

**Conclusions:** Declines in new paediatric HIV diagnoses reflect the success of prevention of VT domestically and globally. An increasing proportion of children born abroad now arrive already diagnosed and on treatment. In later calendar years children were diagnosed at younger ages with less advanced disease stage, irrespective of place of birth. Paediatric HIV surveillance remains vital in ensuring this vulnerable population receives high quality specialist care and optimal health outcomes.
PRETERM, CHALLENGES AT THE POINT OF CARE AND OUTCOME IN A POOR RESOURCE SETTING

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Background: Challenges of managing preterm babies in our facility are huge with background harsh economic situation. This is worsened by regular power outages. Antibiotics for treatment of neonatal infection are expensive and parents/care givers are reluctant to purchase because they have little confidence in the survival of their preterm babies hence, no financial commitment. Incubators and phototherapy machines are also few amongst other infrastructures.

Methods: We looked at the total number of deliveries in our facility and at the total number of preterm admissions into our SCBU from September, 2018 to August 2019. Information documented include the socio-demographic data, cause(s) for the admission and parents/care givers occupation. We took note of the challenges encountered during the study period and we also noted the outcome of babies managed.

Results: Total was 1,081 admissions, 396 were preterms with burden of 36.6%; Most are at GA of < 34 weeks (61.6%). Majority, 234 (59%) were VLBW. Singleton were 198 (48.7%) while, 208 (51.8%) were of multiple gestation, 234 (59%) were not booked, and home deliveries were 123 (31.1%). Major cause of admission was jaundice and prematurity (258; 65.2%). Forty-two (10.6%) died. The major challenges include; incubators/phototherapy machines were not enough for the number of babies that need it, worsened by repeated power outages. Antibiotics were expensive.

Conclusions: More than 10% of our preterm babies were born between 28-32 weeks requiring intensive care and, we dont have it in our facility. Parents perceive the deaths of preterms as inevitable and therefore abandoned them. Challenges include limited infrastructures, frequent power outages, reluctance of parents to pay for investigations, treatment and procedures. There is the need for government political will, partnership with private organization participation and commitment from Stake holders.
Title of Case(s): CYTOMEGALOVIRUS REACTIVATION RESPONSIBLE OF CONGENITAL INFECTION ACCIDENTALLY DISCOVERED THROUGH NEWBORN SALIVA SWAB: A CASE REPORT

Background: The gold standard to diagnose congenital CMV is the presence of viral DNA in urine. Saliva swab has a good sensitivity, but false positives are reported due to contamination. In a multicenter prospective study, all newborns were tested for CMV through a saliva swab with the aim to determine the sensitivity of this test. We describe a case report of a pregnant immune to CMV who delivered a newborn congenitally infected.

Case Presentation Summary: Male, born at term with normal anthropometric parameters. No significant signs/symptoms were reported during pregnancy, and he looked well and health. Mother was immune to CMV in the first trimester, with high IgG avidity. CMV-DNA screening through saliva swab came positive, so the baby was tested for urine (positive) and blood (negative), whether CMV-DNA dosed on maternal milk 5 days after delivery came positive. The newborn undergo all tests to evaluate a possible CMV localization (brain ultrasound and magnetic resonance, abdominal ultrasound, ear test, eye and neurologic specific consultation): all these tests were normal, and the baby did not presented signs/symptoms of congenital CMV during the first six months of follow-up. Retrospectively, maternal sera stored from other blood tests were analyzed: the sera stored at 33 weeks of gestation was positive, and all others (14, 20 and 40 weeks of gestations) negative.

Learning Points/Discussion: Congenital CMV is the more common congenital infection in industrialized countries. Even if is estimated that 60% of all congenital CMV newborns are due to maternal reactivation in immune pregnant, a primary maternal infection is more dangerous to the fetus than reactivations. Saliva swab is a good screening test to newborns at risk of congenital CMV, but with a low specificity due to the possible saliva contamination.
NEONATAL SEPSIS IN A SECONDARY LEVEL NEONATAL UNIT OF NORTHERN ITALY IN THE LAST SEVEN YEARS

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Title of Case(s): NEONATAL SEPSIS IN A SECONDARY LEVEL NEONATAL UNIT OF NORTHERN ITALY IN THE LAST SEVEN YEARS

Background: Despite significant improvements in perinatal care in the last years, neonatal sepsis is currently one of the most serious problems affecting infants in their first month of life. Early onset sepsis (EOS) is the insurgence of infection in the first 72 hours of life; others are called late onset sepsis (LOS). The main causes of neonatal sepsis are Group B Streptococcus Pneumoniae (GBS) and Escherichia coli (E. coli). In a seven year retrospective data collection, all case of neonatal sepsis, both EOS and LOS, with positive blood culture were reviewed.

Case Presentation Summary: From 2013 to 2019, 11 newborns with positive blood culture sepsis were admitted to the Neonatal Pathology Unit of our Hospital: 8 EOS and 3 LOS. Considering newborns with EOS, 4 of them (50%) had E. coli infection, 2 GBS, 1 Klebsiella pneumoniae and 1 Staphylococcus haemolyticus, with an average onset in the first day of life (0-3 days). Among the three patients with LOS, 2 had GBS and one E. coli infection, with an average onset at 25 days of life (22-28 days). The average length of admission was 12.5 days (14.8 days for EOS and 11.3 for LOS) and the average duration of intravenous antibiotic treatment (mainly ampicillin+sulbactam) was 11.2 days (13.2 days for EOS and 10.3 days for LOS).

Learning Points/Discussion: Despite GBS is still considered the most common cause of neonatal sepsis worldwide, the role of gram negative bacteria, in particular of Escherichia coli, is progressively increasing in preterm and term newborns. An early recognition of septic signs and symptoms, in particular in patients at high risk of infection, is very important to reduce mortality, possible severe sequelae and to start an adequate antibiotic treatment.
INFANTS EXPOSED TO COINFECTIONS IN PREGNANCY AMONG WOMEN LIVING WITH HIV IN THE UK

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Background: Sexually-acquired and blood-borne coinfections are frequent among people living with HIV. Infants born to women living with HIV (WLWH) who also have coinfection during pregnancy may be at increased risk for adverse outcomes, including vertical/congenital infection requiring increased management and monitoring. We describe the current picture of infants born to WLWH with coinfection in pregnancy using observational population-level surveillance data.

Methods: The Integrated Screening Outcomes Surveillance Service (ISOSS) conducts active surveillance of all pregnancies in WLWH and their children in the UK, including data on coinfections screened for in pregnancy (HBV and syphilis) and Hepatitis C (HCV). Descriptive statistics summarise infants born to WLWH in 2009-2018 with information on maternal coinfection (for 8832 of 10675), reported to ISOSS by December 2019.

Results: Overall 7.2% (636/8832) of infants were coinfection-exposed: 4.7% (413/8832), 1.4% (126) and 1.4% (120) to HBV, HCV and syphilis respectively. Twenty were exposed to ≥1 coinfection: 4 HBV/HCV, 10 HBV/syphilis, 5 HCV/syphilis, 1 to all. Among coinfection-exposed infants: 19% were born to mothers diagnosed with HIV during pregnancy, most to mothers born abroad (92% v 84% in non-exposed (p<0.001)) and 15% of infants were born <37 weeks (vs 12% non-exposed, p=0.048). Congenital infection was reported in 0.8% infants: syphilis (3), HBV (1), HCV (1); 0.3% (2/621) infants were HIV-infected.

Conclusions: One in 14 infants born to WLWH in the UK are exposed to coinfections, underscoring the importance of monitoring sexual health in pregnancy, to allow for appropriate management of mother and infant and to prevent congenital infection and/or other adverse pregnancy outcomes. As ISOSS expands to monitor other infectious diseases in pregnancy, greater insights are expected into outcomes and the factors driving these to further inform guidelines and policy.
PARVOVIRUS B19 AMONG HEALTH PREGNANTS IN AN URBAN AREA OF NORTHERN ITALY AND IMPACT ON NEWBORNS: A RETROSPECTIVE STUDY

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Title of Case(s): PARVOVIRUS B19 AMONG HEALTH PREGNANTS IN AN URBAN AREA OF NORTHERN ITALY AND IMPACT ON NEWBORNS: A RETROSPECTIVE STUDY

Background: Parvovirus B19 infection in pregnant women is generally asymptomatic. This infection can be transferred from mother to fetus, particularly during the first and second trimesters of gestation, in 17-51% of cases, due to the presence of a globosidic placental receptor. In a retrospective study from February 2017 to January 2018, 1893 sera stored from pregnant women were tested for IgG and IgM against Parvovirus. IgM positive samples were confirmed with Immunoblot and all the positives were tested for Parvovirus B19 DNA.

Case Presentation Summary: Sera stored from 1893 pregnant women were enrolled in the data collection: 60.8% on first trimester, 16.6% second and 22.6% on the third trimester of gestation. 1315 of them (69.5%) were positive to IgG, 21 (1.1%) to IgM, and 578 (30.5%) were IgM and IgG negative. Considering the 21 women with IgM positive, 15 (1.3%) were in the first trimester, 3 (1.0%) in the second and 3 (0.7%) in the third. 15 of these 21 were confirmed positive with Immunoblot test (10 of them were DNA-B19 positive), 1 resulted indeterminate (DNA-B19 positive) and 5 negative (all DNA-B19 negative). No clinical signs were reported from all these pregnant women, and no difference between hemoglobin level between positive and negative patients were found. Considering neonatal data of the 9 pregnant women who delivered in our hospitals, no clinical data or laboratory abnormalities were reported.

Learning Points/Discussion: The prevalence of Parvovirus B19 immune pregnant women (69.5%) was one of the highest reported in Europe during a non-epidemic period. The presence of IgM (confirmed with Immunoblot) doesn’t mean acute infection, since these antibodies can remain positive for different months: it’s important to confirm the acute infection with molecular biology tests. Acute Parvovirus B19 infections weren’t related with fetal damages.
VALIDATION OF BIOMARKERS BY A MULTIPLEX PROTEIN ASSAY TO DISCRIMINATE BETWEEN BACTERIAL OR VIRAL INFECTION IN CHILDREN WITH FEVER

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Background: Infection is the major cause of death in children under 5 years. The most common symptom is fever. Diagnosis in the clinic if febrile children based on clinical grounds is still challenging. As a small number of bacterial infections lead to life-threatening disease patients are often treated with broad-spectrum antibiotics while most of the febrile illnesses in pediatrics are caused by viruses. Hence, there is an urgent need to improve diagnostics in distinguishing between bacterial and viral infections.

Methods: A discovery and validation cohort of both 150 patients was measured using a multiplex protein assay panel of 28 markers including markers for neutrophil and macrophage activation, interleukins and lymphocyte-derived granzymes. We also included CRP and HNEαAT1c by ELISA. With logistic regression models the most optimal combination of markers was found to set up a prediction model. Results: CRP, S100A12, CD163, MPO, IL2r, G-CSF, Lipocalin-2, HNEαAT1c, ST2 and Proteinase-3 showed significant increase in bacterial compared to viral infections in both cohorts. We were unable to validate the combination of TRAIL and IP10 as viral markers and did not find any other significant marker for these infections. Logistic regression and LASSO was performed to select the most optimal combination with resulting in a model with CRP and neutrophil-derived Lipocalin-2. A ROC of these combined markers showed an AUC of 0.93 in our discovery cohort, which was validated with an AUC of 0.91 in our validation cohort.

Conclusions: Combining the different biomarkers from plasma CRP and lipocalin-2 enabled us to discriminate bacterial from viral disease in both cohorts. To improve the model even further more selective biomarkers to indicate viral disease are needed.

Clinical Trial Registration: Study is no clinical trial
E-POTER VIEWING
E-POSTER VIEWING - ALL OTHER TOPICS
10-28-2020 8:00 AM - 7:00 PM

EPIDERMOLYSIS BULLOSA IN A NEWBORN SEEN AT USMANU DANFODIYO UNIVERSITY
TEACHING HOSPITAL, SOKOTO, NIGERIA

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Title of Case(s): A rare Skin disorder seen at a Teaching Hospital-Case report
Background: This is a rare skin disorder referred to our health facility; the incidence is 2.12 cases per 1
million live births (prevalence is 1.5), however, the management remains conservative and, the disease
remain incurable except control of symptoms. The skin is extremely tender, walking difficulties are
experience due to pressures on the soles of the feet. Life expectancy is poor, survivors hardly exceed
the first five years of life.

Case Presentation Summary: Baby AI, a term female neonate delivered to a 38-year-old woman
(P7+0 A5) at term. She was not booked for ANC but delivered in the hospital. The mother had non formal
education. This is the first reported case in our facility in Sokoto, North-Western Nigeria. The neonate was
a product of consanguineous marriage in a polygamous home; no sibling with similar illness. On
examination, baby IA was pale, irritable, febrile with temperature of 38.7°C but, not dehydrated. Had
ulcers on the right lower limb including the toes, right and left fingers with discrete blisters on the fingers,
toes and plantar surface of the right foot. No mucosal lesions. Other systemic examinations were normal.
The baby was managed conservatively with antibiotics and I/V fluids but, signed against medical advice
(SAMA) after 5 days and was lost to follow up.

Learning Points/Discussion: Epidermolysis Bullosa (EB) is a rare group of inherited blistering disorders
that share the common feature of blister formation in response to mechanical trauma caused by
mutations in structural proteins that are responsible for maintaining the integrity of the skin's basement
membrane zone. It is inherited in either an autosomal dominant or recessive fashion. Major types include;
Epidermolysis Bullosa Simplex (EBS), Junctional Epidermolysis, Bullosa (JEB), Dystrophic Epidermolysis
Bullosa (DEB) and Kindler syndrome.
GASTROENTERITIS IN A PEDIATRIC WARD DURING 2015-2018: A RETROSPECTIVE OBSERVATIONAL STUDY

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Title of Case(s): GASTROENTERITIS IN A PEDIATRIC WARD DURING 2015-2018: A RETROSPECTIVE OBSERVATIONAL STUDY

Background: Gastroenteritis is an important cause of hospital admission worldwide, and possible cause of severe morbidity and mortality in particular in developing countries. Rotavirus is the main cause of severe gastroenteritis among children, even if oral live attenuated vaccine is available. In a retrospective study from 2015 to 2018, all clinical files of patients admitted to gastroenteritis in the pediatric ward of the Hospital of Magenta (Milan, Italy) were reviewed, focusing on the etiologic causes.

Case Presentation Summary: During the 4 year retrospective survey, 502 patients were admitted to gastroenteritis (10.7% of total admissions to medical diagnosis): 279 male, 223 female, mean age 4.4 years (0.04 – 17.9). On these patients, stool test were performed in 422 of them, and Rotavirus resulted the main etiologic cause found (130 patients, 25.8% of all patients with gastroenteritis, 30.8% of all patients with stool test available). Adenovirus was the only other viral test performed from our laboratory, and positive in 23 patients (4.5% of all gastroenteritis). Considering bacterial cultures, Salmonella sp. was positive in 63 patients (12.5%), Campylobacter in 40 (7.9%) and Escherichia coli in 4 (0.8%). Rotavirus resulted endemic from January to May (108/130), with a peak on March and no cases at all during December. Bacterial gastroenteritis resulted quite constant during years, with more cases during warm months (July and August), October-November and January.

Learning Points/Discussion: Acute gastroenteritis has an important impact on public health and yearly admissions on pediatric wards (in our study 10.7% of total admission due to medical problems). Viral gastroenteritis remains the main etiologic cause, in particular due to Rotavirus and during cold months. Salmonella and Campylobacter are important bacterial causes of enteritis during the whole year. Rotavirus vaccination should be implemented worldwide.
Title of Case(s): Teenager's associated streptococcal infection (PANDAS syndrome and rheumatism)

Background: Streptococcal infection plays a significant role in the pathogenesis of various lesions of CNS, such as Sydenham chorea (small chorea) with rheumatism, children's autoimmune neuropsychiatric disorder associated with the streptococcal infection (PANDAS syndrome). PANDAS syndrome is an obsessive and compulsive behaviour after streptococcal infection (autoimmune cerebral vasculopathy). Single cases of combined course of acute rheumatic fever and PANDAS syndrome were reported.

Case Presentation Summary: 12-years-old boy complained about psycho-emotional excitability, speech and gait disorder, changes in handwriting, aggressiveness; T-38°С; both swelling and pain in the right hand and polyarthralgia were observed. Convulsions were noted up to 1 year, an Arnold-Chiari anomaly was detected. Up to 11 years the psychological development was in the accordance with his age. Transient cerebrovascular accidents were observed twice. He was often sick with tonsillitis. Objectively: BMI-24.5, swelling of the joints of the right hand. At the projection point of aortic and mitral valves there was diastolic murmur. Neurological status: deviation of the tongue to the left, muscular dystonia. Laboratory: ESR-50 mm/hour, antistreptolysin-O-1600 units/ml, PSA-positive. CEC up to 280 (norm 40-85), IgG to herpes-2.44 wholesale unit (norm up to 0.55). Doppler - regurgitation on the aortic valve of the stage, mitral -Idg., valves of pulmonary artery -Idg. Low amplitude EEG, hypersynchronous type, signs of paroxysmal activity. Diagnosis: acute rheumatic fever, endocarditis, arthritis. PANDAS-Syndrome. Arnold-Chiari anomaly. Treatment: penicillin, streptococcal bacteriophage, aspirin - effective.

Learning Points/Discussion: In the given clinical case, chronic streptococcal infection led to the development of an autoimmune disease with the development of cerebral vasculopathy and rheumatism against a background of congenital anomaly of Arnold-Chiari and complicated family anamnesis of vascular pathology. There are still discussions about the interrelation of PANDAS syndrome, acute rheumatic fever and chorea with a single pathogenetic development mechanism.
Background: Although indwelling catheters are increasingly used in modern medicine, they can be a source of microbial contamination and hard-to-treat biofilms, which jeopardize patients’ lives. Due to its bactericidal properties, 70% ethanol is sometimes used as a catheter-lock solution. However, high concentrations of ethanol can result in adverse effects and in malfunction of the catheters.

Methods: Ethanol was tested at a concentration range of 0.625 to 80% against laboratory and clinical isolates of P. aeruginosa for various time periods (2-48 hours). The following parameters were evaluated following ethanol exposure: prevention of biofilm formation, reduction of biofilm metabolic activity, and inhibition of biofilm regrowth.

Results: Exposing P. aeruginosa to twofold ethanol gradients demonstrated a significant biofilm inhibition at concentrations as low as 2.5%. Treating pre-formed biofilms of P. aeruginosa with 20% ethanol for 4 h caused a sharp decay in the metabolic activity of both the laboratory and clinical P. aeruginosa isolates. In addition, treating mature biofilms with 20% ethanol prevented the regrowth of bacteria encased within it.

Conclusions: Low ethanol concentrations (2.5%) can prevent in vitro biofilm formation of P. aeruginosa. Treatment of previously formed biofilms can be achieved using 20% ethanol, thereby keeping the catheters intact and avoiding complications that can result from high ethanol concentrations.

Clinical Trial Registration: Not a controlled trial
PREDICTORS OF OUTCOME IN CHILDHOOD PLASMODIUM FALCIPARUM MALARIA

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Imperial College London, Infectious Diseases, London, United Kingdom

Background and Objective: *P. falciparum* accounts for the vast majority of global childhood malarial deaths. Classification of malaria, as uncomplicated or severe, helps determine clinical management. Severe malaria (SM) is defined by the presence of one or more features associated with adverse outcome, however, the predictive value of these features is variable. We critically evaluate the usefulness of clinical and laboratory features of SM as predictors of mortality and long-term complications in childhood *P. falciparum* malaria and assess the potential of molecular biomarkers and other approaches to improve the accuracy of prediction.

Methods: Publications were identified through keyword searches of the PubMed database; specific to each sub-section of the review. Additional publications were identified from our own bibliographies and from references in articles identified through Pubmed. We did not exclude any studies based on study size. Wherever possible we report confidence intervals for estimates of risk or association, which indicate the precision of these estimates, in part determined by the study size.

Learning Points/Discussion: The most consistent predictors of death appear to be coma, markers of metabolic derangement (acidosis and hypoglycaemia), and renal failure. Many studies have combined these features into prediction models or scoring systems, which has improved predictive accuracy and ease of use. Numerous molecular biomarkers have also been proposed to predict outcome in SM, including PfHRP2 and angiopoietins 1 and 2. However, challenges include: implementation in clinical settings and identifying universal thresholds. It is clear that prognostic indicators specific for distinct SM syndromes hold promise and may result in better prediction of adverse outcomes than general indicators. There is still a need for a systematic meta-analysis of the impact of all these features on prognosis prediction accounting for the heterogeneity between studies.
A RARE INFECTION IN CHILDREN RETURNING FROM VACATION IN SOUTHERN EUROPE

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Title of Case(s): A rare infection in children returning from vacation in southern Europe

Background: Visceral leishmaniasis (VL) is a vector-borne infection caused by the parasite Leishmania. The infection is endemic in subtropical and tropical areas and listed as one of WHO’s neglected tropical diseases. Only two cases was reported 1996-2016 in Sweden but in 2019, three children were treated at Astrid Lindgren Children’s Hospital in Stockholm. They had all been infected during vacation in Southern Europe.

Case Presentation Summary: After a chickenpox infection with subsequent streptococcal sepsis, a 15-month-old boy developed anaemia and hepatomegaly. Bone marrow aspirate to rule out leukaemia displayed characteristic amastigotes. Serology and PCR were positive for *Leishmania infantum*. The family visited Spain 18 months earlier. A 2,5-year-old boy developed high fever while on holiday in Mallorca. They had visited mainland Spain 18 month earlier. Pancytopenia caused suspicion of acute leukaemia. Bone-marrow revealed no abnormalities. At the hospital in Mallorca, leishmania PCR was performed and was positive for *Leishmania infantum*. A 16-month-old boy presents to the ER with recurring fever episodes and fatigue. The family had been to Italy a year earlier Blood samples revealed anemia and elevated transaminases. Abdominal ultrasound revealed enlarged lymph nodes and hepatosplenomegaly. Bone marrow analysis ruled out malignancy. No amastigotes were seen, PCR was negative, but serology was slightly positive. Spleen aspirate PCR confirmed *Leishmania infantum*. All three recovered after treatment with Amphotericin B.

Learning Points/Discussion: With these cases, we want to raise awareness of VL in travellers returning from vacation in Southern Europe. The incubation period was more than one year for all three cases, highlighting the need for careful travel history in patients with haematological abnormalities and fever. No analysis for leishmaniasis is 100% sensitive, so if suspicion persists, repeat or use different mode of analysis.
E-POSTER VIEWING - ALL OTHER TOPICS
10-28-2020 8:00 AM - 7:00 PM

TORCH (TOXOPLASMOSIS, RUBELLA, CYTOMEGALOVIRUS AND HERPES SIMPLEX VIRUS)
SCREENING AMONG FULL-TERM SMALL FOR GESTATIONAL AGE NEWBORNS IN BELARUS

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²Belarussian state medical university, Children's Infections Diseases, Minsk, Belarus, ³Republican research and practical center «Mother and child», Clinical Diagnostic Laboratory, Minsk, Belarus

Background: Congenital infection can lead to IUGR during fetal development and can manifest as SGA (body weight <10%) at birth. Common practice is screening for toxoplasmosis, rubella, cytomegalovirus (CMV) and herpes simplex virus (TORCH) in small for gestational age (SGA) newborns. Objective: to evaluate the results of TORCH screening by TORCH serology and ultrasound examination of the brain of full-term small for gestational age newborns in Belarus.

Methods: We retrospectively examined 118 SGA newborns (75 girls, 43 boys), born in the perinatal center "Mother and child" from 2015 to 2019, and analyzed gestational age (38.1 ± 0.8 weeks), Apgar scores, anthropometric parameters (body weight 2354 ± 202 g, body length 47 ±1.8 cm), genetic studies and morbidity,. The physical development of children was assessed using INTERGROWTH-21 standards. Maternal factors included maternal diseases, fetal sonography. TORCH screening was performed in 84 (72%) children using serum IgM and IgG and sonographic examination of the brain.

Results: None of the tested newborns were positive for Toxoplasma gondii IgM, rubella, cytomegalovirus, and herpes simplex virus. Calcifications were detected on one cranial ultrasound, but CMV and toxoplasmosis IgM titers were negative. The Z-score of newborn body weight was -1.9 ± 0.5. Percentile of body weight 4.2 ± 3.7%. Head circumference at birth was 32.5 ± 1.3 cm. None of the tested newborns were positive

Conclusions: Congenital TORCH infection in full term SGA newborns is rare. Given the low prevalence and risk of TORCH in Belarus, it is advisable to screen for specific diseases based on a mother’s history and clinical symptoms of the newborn. As for CMV, which may be asymptomatic, routine screening may be useful in cost-benefit analysis.

Clinical Trial Registration: no unique identifying number
THE "CRAG" HEAD

M.C. Quek
AGA KHAN UNIVERSITY, Department Of Peadiatric And Child Health, NAIROBI, Kenya

Title of Case(s): The CRAg Head

Background: Cryptococcal meningitis (CM) is a very lethal and common fungal infection of the central nervous system. It is notorious to cause meningitis among the immunocompromised children either who are HIV-exposed, immunosuppressed due to various reasons. Therapy of cryptococcal meningitis often includes amphotericin B which can cause renal dysfunction in neonates. However, the prevalence of CM among the healthy, non- HIV exposed neonates is unknown.

Case Presentation Summary: A sixteen-day-old baby presented with seizure, irritability, and fever for two days. He was born via spontaneous vaginal delivery uneventfully. He was discharged on day three of life. The next day, his mother noticed yellow discoloration of the conjunctiva and brought the baby back to the hospital. The diagnosis of neonatal sepsis and neonatal jaundice was made. The baby received intravenous ceftazidime for 7 days. His cerebral spinal fluid (CSF) analysis shows a positive cryptococcal antigen (CRAg), WBC > 1000/HPF, low glucose, high protein. His Serum CRAg was positive and HIV status is negative. CT scan of the head reviewed communicating hydrocephalus with interventricular septae. His mother's serum CRAg and HIV status are negative. An impression of cryptococcal meningitis was made. We started him on amphotericin B and ceftriaxone. He recovered remarkably after starting the treatment. He was discharged after the completion of therapy. Currently, he is stable on fluconazole, and continue to follow up for hydrocephalus.

Learning Points/Discussion: CM among healthy neonates is not well documented. Physicians should take cryptococcal infection as a possible pathogen into consideration when diagnosing neonatal meningitis. CSF CRAg is recommended as part of routine CSF analysis. Can neonatal meningitis cause an immunosuppressive state that opportunistic infection occurs is a question worth study. The prevalence and outcomes of CM among the neonatal period should be explored further.
STUDY OF GENETIC CHARACTERIZATION OF THE PHOSPHOPROTEIN (PCV) GENE OF MEASLES VIRUS STRAINS (H1, B3 AND D4) PREVIOUSLY CIRCULATED IN IRAN

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²Vac Center for Communicable Diseases Control, Vaccine Preventable Diseases Department,, Tehran, Iran

Background: Measles is a highly contagious and serious disease caused by a measles virus. Before the 1980s, when vaccination against measles is widely launched, it causes an estimated 2.6 million deaths every year. Measles remains a major cause of mortality especially among children throughout the world. According to the recent studies as well as WHO protocols, more accurate molecular information from the measles virus genome is very important during measles elimination and eradication phases.

Methods: RNA was extracted from infected cell lysate (B3, H1, D4 genotypes) and vaccine strain (genotype A) using Roche kit. RT-PCR amplification was performed using new designed primers to amplify measles Phosphoprotein (PCV) gene. Also partial nucleoprotein gene segments of measles virus were amplified using previously described primers. Sequence data were analyzed using Bioedit-7 and phylogenetic analysis were performed using Mega-X software. Molecular analysis including nucleotide and amino acid mutations was performed on recently circulated strains in Iran (B3, H1, D4) comparing to the vaccine, reference strains and strains from different parts of the world.

Results: The amplified products were sequenced and compared with the WHO Edmonston virus and Iran vaccine strains. Our results confirmed the importance of phylogenetic tree based on the nucleotide sequences of the PCV gene compared to the N-450 gene. Sequence analysis revealed that PCV gene of wild-type measles viruses has important nucleotide and amino acid substitutions.

Conclusions: Our phylogenetic trees confirm that strains with identical N-450 sequences were separated into different variants on the basis of PCV gene sequences. The results of this study suggest that genotyping based on the PCV and NP-450 gene as well as hemagglutinin gene are necessary for countries involved in measles elimination and eradication strategies.

Clinical Trial Registration: Not included in this study
HEALTHCARE-ASSOCIATED INFECTIONS AMONG PEDIATRIC ONCOLOGY PATIENTS IN A DEVELOPING COUNTRY

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The Children’s Hospital and Institute of Child Health Lahore, Pediatric Hematology Oncology, Lahore, Pakistan

Background: It was a prospective survey. The purpose of this study was to determine the incidence, etiology, antimicrobial resistance and outcome of Health-care associated infections among immunocompromised pediatric oncology patients being treated in a developing country. Despite major improvements in the survival of pediatric cancer patients, infections remain a significant complication of treatment and are associated with noteworthy morbidity and mortality.

Methods: Over 6 months study period, 83 pediatric patients of cancer, with culture proven healthcare-associated infection according to the definitions set by the United States Centers for Disease Control and Prevention/National Health Care Safety Network Guidelines were included. After informed written consent relevant clinical data was noted and analyzed in SPSS 16.0. Outcome was measured in terms of discharge or expiry.

Results: Total 101 HAI’s identified in 83 infected patients. Blood stream infection found in 49.5% (n=50), Respiratory tract infections in 16.83% (n=17), Urinary tract infections in 14.85% (n=15), Skin infections in 9.9% (n=10), Otitis media in 5.94% (n=6), Septic arthritis in 1.98% (n=2) and meningitis in 0.99% (n=1). Gram negative organisms were isolated in 69.30% cases. Klebsiella species was most common HAI (18.81%, n=19). Panresistance encountered in 25.74% (n=26), Carbepenam resistant Enterobacteriaceae in 15.95% (n=16), Vancomycin resistant Enterococci in 2.97% (n=3) and Methicillin resistant Staphylococcus Aureus in 1.98% (n=2). Mean hospital stay was 20.22 days and 39.75% patients (n=33) expired.

Conclusions: Healthcare associated infection is an additional challenge in the management of pediatric oncological diseases in a developing country. It is associated with significant morbidity and mortality. Gram negative pathogens are more common in our setup with substantial number being Pan-resistant. Improved supportive care measures for infection prevention and control must be taken. Awareness programs for healthcare professionals of the country for antibiotic stewardship are the need of time.
INFECTION IN THE PEDIATRIC SURGERY DEPARTMENT OF THE ALBERT ROYER CHILDREN'S HOSPITAL, DAKAR, SENEGAL.

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¹Albert Royer children's hospital, Pediatric Surgery, Dakar, Senegal, ²cheikh anta diop university, Pediatric Surgery, Dakar, Senegal

Background: The rise in use of antibiotics and vaccines has changed the prognosis of infections in children. However, infections are still common in our daily living. The immaturity of the immune system is responsible for higher mortality in pediatric population. The aim of this survey is to get an overview of the epidemiological, diagnostic, and prognostic factors regarding infections in our department.

Methods: This is a prospective and descriptive study. It involved patients from age 0 to 15 years admitted in our department for the management of an infection between January 10, 2019 and July 10, 2019. The parameters studied were frequency, age, gender, diagnostic tools, therapeutic methods, morbidity and mortality. Data was collected from patient records, entered into Sphinx software and processed in Excel.

Results: During our study period, 104 patients were admitted for the management of an infection, which represented 18.5% of all the patients admitted. These were mainly infants (34.6%) with a male predominance. Eighty nine patient had a community acquired infection (85.6%). Osteoarticular infections were in the foreground (21.2%). Nosocomial infections mainly involved patients admitted for thermal burns (73.3%). Microscopy culture and sensitivity of pus samples was done for 40.4% patients. Staphylococcus aureus was the most implicated bacteria (38.1%). We counted a total of 9 deaths (8.7%).

Conclusions: Infections in the pediatric surgery unit occurred most often in male infants and are mainly community acquired in origin. They is a clear predominance of osteo-articular infections and staphylococcus aureus is the most common bacteria. The mortality rate is high and involves mainly nosocomial infections. Improving the prognosis of infections in our department therefore requires the implementation of a strategy to fight nosocomial infections, and an improvement in the technical platform.
CHARACTERISTICS OF CHILDREN HOSPITALIZED FOR INFLUENZA IN A PEDIATRIC DEPARTMENT OF A TERTIARY HOSPITAL IN PIRAEUS, GREECE.

A.-E. Sfetsiori, C. Karakos, E. Xenou, G. Triantafyllidis, I. Panagiotou
General Hospital of Piraeus "Tzaneio", Pediatric Department, Athens, Greece

Background: Seasonal influenza is a vaccine-preventable disease associated with significant morbidity and mortality in the pediatric population each year worldwide. Preschool children (especially those under 2 years of age) are at higher risk for hospitalization and severe influenza-related complications. The aim of this study was to evaluate epidemiological characteristics of children hospitalized due to influenza in a pediatric department of a tertiary hospital.

Methods: An epidemiological study of demographic and clinical features of children with laboratory-proven influenza hospitalized in our department during last year’s flu season (1/12/2018-31/3/2019) was conducted retrospectively. A rapid immunoassay chromatographic test or/and a rapid PCR-based test was used for the virus detection. Statistical analysis was performed using IBM SPSS software 25.0. Individual patient data was coded in order to maintain confidentiality.

Results: Thirty seasonal influenza episodes were analyzed. Type A Influenza virus was detected in 100% of cases. Sixty percent of patients were under 5 years of age. Only in 3.3% of episodes children had been vaccinated, whereas in 50% of episodes prior close contact with other patients was recorded. In 10% of episodes, unvaccinated patients had an underlying chronic disease (100% asthma). Clinical features of patients are described in table 1. Complications were recorded in 46.7% of episodes; Pneumonia (35.7%), Myositis (21.4%), Acute Otitis Media (21.4%), Tonsillitis (14.3%) and Respiratory Distress (7.1%). No death was reported among our population.

Table 1. Clinical characteristics of children hospitalized for influenza (median duration of hospitalization; 4 days)

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<tbody>
<tr>
<td>Malaise</td>
<td>73.3%</td>
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<tr>
<td>Severe cough</td>
<td>73.3%</td>
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<tr>
<td>Rigor</td>
<td>40%</td>
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<tr>
<td>Gastrointestinal symptoms</td>
<td>40%</td>
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<tr>
<td>Rash</td>
<td>10%</td>
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Conclusions: Predominance of type A influenza virus was observed in previous year’s flu season in the city area of Piraeus in Greece. Pneumonia was the most common complication observed followed by myositis and acute otitis media. Among hospitalized children due to influenza, the majority was totally unvaccinated highlighting the need for raising public awareness towards the importance of annual influenza vaccination of children at higher risk of severe influenza.
ANALYSIS OF THE ORDER OF ROTAVIRUS IN STOOL SAMPLES (SS) IN A PRIVATE HOSPITAL IN BUENOS AIRES, AFTER INTERVENTION WITH ADJUSTED INCLUSION CRITERIA.

A. Ellis, M. Estraviz, M. Romé, S. Osler, C. García Roig, A. Aupy, A. Eguren
Sanatorio Mater Dei, Pediatria, Buenos Aires, Argentina

Background: Rotavirus has historically been the most important cause of gastroenteritis among children, worldwide. Clinical manifestations include vomiting, watery non bloody diarrhea and fever. In Argentina, classified in the middle-income countries, where the vaccine is included in the National Immunization Program since 2015, the number of hospitalized cases has decreased substantially. However, the request for Rotavirus testing has not been modified.

Methods: Analytical, retrospective and cross-sectional study. We studied the applications of RV in stool samples of children between 0-17 years old, from 01-01-2018 to 31-12-2019. We used the Rotavirus / Adenovirus Montebio® method. Study period March-December 2019/2018. The objective of our study was to analyze the application of Rotavirus in stool samples, in children with gastroenteritis, adjusting them according to established criteria to optimize costs in medical care.

Results: 339 applications were documented in 2018 and 202 in 2019. Comparing both periods, the applications decreased (40.4%). Although the request for studies decreased in 2019, the difference was not significant either comparing outpatient or hospitalization 120/82 (2019) and 226/113 (2018), and the inclusion criteria for applications in winter respect to summer in EC 4/21 vs. 5/38 or in 24/16 internment vs. 23/19. The percentage of positivity was 8.5% and 25% each year. Analyzing 2019, it was more frequent in winter than summer (OR: 2.35 (1.3-4.26) p = 0.0047

Conclusions: There was a reduction in orders in 2019, with a decrease in costs. There was no significant difference in the reduction of applications in the outpatient clinic vs. hospitalized children and in the application criteria in winter or summer, both in the EC neither hospitalized children. There was a significant difference in the percentage of positivity between winter and summer.
ARE CHILDREN RECEIVING THE MMR VACCINE ON TIME?

F. Curmi, M. Mifsud, D. Pace
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Background: Decreased or delayed uptake of the measles, mumps and rubella (MMR) vaccine, as a result of the unfounded concerns on autism, have resulted in recent outbreaks of measles in Europe. We investigated if children were receiving the first and second doses of the MMR vaccine at the recommended ages of 13 months and 3-4 years in Malta, a country with around 4000 births annually.

Methods: A sample of 375 children was taken biannually, from 2007 to 2017, from the birth register using computer-generated randomisation numbers. Information on vaccination was retrieved from national immunisation records. Inclusion criteria included complete MMR vaccination records, children who were still alive and who lacked any contraindications to receiving live vaccines. The two-sample t test was used to compare the ages of MMR vaccination between the years.

Results: Out of 2250 eligible children, 2170 met the inclusion criteria. Uptake rates for the first and second MMR vaccinations were 94.1% (2042/2170) and 88% (1502/1805; excluding 2017 birth cohort) respectively. Children born in 2007 received the first MMR vaccine very late at 24.1 months (95%CI: 16.6-31.5). Significant reductions in age of vaccination were noted in those born in 2011 (16.0 months; 95%CI: 15.2–16.7, p=<0.001) and in 2017 (14.6 months; 95%CI: 14.3-14.8, p=0.004). A sequential significant decrease in the age of the 2nd MMR vaccination was noted for all years except in 2013; p=<0.001.

Conclusions: Although there has been improvement in immunising children against measles, mumps and rubella on time, the harm done to the MMR vaccination programme following the discredited link with autism published in 1998 still persists despite its subsequent withdrawal in 2010. There is still the need to address parental concerns appropriately and to emphasise the benefit of timely MMR vaccination.
HIGH PREVALENCE OF SOIL TRANSMITTED HELMINTH IN SCHOOL AGE CHILDREN LIVING IN A SEMI-URBAN COMMUNITY OF SOUTH WESTERN NIGERIA

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¹Achievers University, Medical Laboratory Science, Owo, Nigeria, ²Ladoke Akintola University, Medical Microbiology And Parasitology, Ogbomoso, Nigeria

Background: Nigeria is the most populous country in Africa and was ranked as the number one country in the World still practicing open defecation according to a UNICEF report. In addition, Nigeria’s tropical climatic environment and weak public health infrastructure favor the transmission of helminth parasites. Helminthiasis such as soil transmitted helminths infection is a neglected tropical disease (NTD) that affects people, living in developing countries, most of whom are poor. The World Health Organization (WHO) recommends regular deworming of people living in endemic areas to reduce the burden of soil-transmitted diseases.

Methods: After obtaining informed consent from parents, this cross-sectional study examined the prevalence of soil-transmitted helminth infection among 213 randomly selected school children living in a semi-urban community in South-West, Nigeria. A direct wet mount faecal examination and formol-ether concentration technique was used for parasite detection. The data was analyzed using Chi-square test and univariate analysis at a significant level of 5%

Results: The participants were between ages 1 to 12years. One hundred and fourteen (53.5%) of the total number of participants examined were infected with one helminth or the other. The prevalence of Ascaris lumbricoide (AL) was 53(24.8%), Hookworms(HW) was 31(14.6%), Enterobius vermicularis (EV) was 8 (3.8%), Schistosoma mansoni (SM) was 6(1.4%) and Strongyloides stercoralis (SS) was 8(3.7%). Multiple infections occurred in 25 children (11.7%).

Conclusions: The prevalence of intestinal helminths of over 50% is worrisome and shows that there is still a wide gap between existing effective interventions and the people who need them the most. There is a need to carry out implementation research in the study areas to understand the barriers to uptake of effective interventions and to proffer community-based solutions to the barriers.

Clinical Trial Registration: This is not a clinical trial
PROFILE OF CHILDREN ADMITTED WITH SUSPECTED DENGUE FEVER IN A TERTIARY CARE CENTER OF NEPAL

S. Adhikari
Chitwan Medical College, Paediatrics, Bharatpur, Nepal

Background: Dengue fever is a common vector borne disease in Nepal and there is a rise in the incidence each year since 2004 when the first case was reported. Chitwan district in central part of Nepal is classified as an endemic area. Children are equally vulnerable as adults and presentation is variable ranging from mild fever to serious life threatening hemorrhage and shock.

Methods: Paediatric inpatient records of Chitwan Medical College were reviewed for the clinical diagnosis of dengue fever, dengue haemorrhagic fever and dengue shock syndrome among children aged less than 15 years from 1st January 2019 to 31st December 2019. All cases with positive dengue virus non-structural protein (NS1 antigen), IgG antibody and IgM antibody tests were included. Demographic details, haemoglobin, haematocrit, complete blood count, differential count and serum transaminases were retrieved.

Results: Of total 2646 admitted children, 34 (1.28%) tested positive for dengue virus. Twenty nine (85.29%) had NS1 antigen positivity and 22 (64.70%) were IgM antibody positive. Mean age of presentation was 9.4±4.17 years and mean duration of hospital stay was 4.35±1.74 days. Two children (5.88%) presented with shock and none had haemorrhagic manifestations. Haemoglobin and haematocrit values were 12.17±2.13 gram/dl and 35.8±11.90% respectively. Platelet count was 1,75,000±1,42,000/mm$^3$ while total leucocyte count was 5147±3077/mm$^3$. Mean aspartate and alanine transaminase values were 39.59 and 24.33 U/L respectively.

Conclusions: NS1 antigen and IgM antibodies helped in the establishment of diagnosis in clinically suspected dengue fever cases. All the children presented with non hemorrhagic manifestations and only two had shock requiring pediatric intensive care. Haemoglobin and haematocrit values were also normal in most children. The most common laboratory abnormality was leukopenia while thrombocytopenia was uncommon. Serum transaminase level was normal in most of the patients.
Background: Fluconazole is a first choice drug for neonatal cerebral candidiasis and for prevention of invasive candidiasis in preterm neonates. Pharmacokinetic (PK) research is needed to optimize dosing. We performed a prospective PK study in preterm neonates who received fluconazole either prophylactically or therapeutically, with the aim to evaluate attainment of the therapeutic target area under the curve of 400 mg*h/L.

Methods: Data from 2 cohorts were combined: cohort 1 was a retrospective TDM cohort in which plasma samples were collected at 24 hours after a fluconazole dose. In cohort 2, samples were collected on multiple occasions at different time points. Available patient characteristics were bodyweight, birthweight, postnatal age (PNA), gestational age (GA), postmenstrual age, gender, and of 26 patients plasma creatinine concentrations (CREAT) were available. Population PK modelling and simulation was performed using NONMEM V.7.3.

Results: In 41 preterm neonates (median (range) GA 25.3 (24.0–35.1) weeks), 146 plasma samples were collected. Median PNA during treatment was 14.5 (0.2 – 67.8) days and median bodyweight 0.87 (0.50-2.20) kg. Clearance of fluconazole (0.0147 L/h (RSE 4 %, interindividual variability 16.6%) for a patient of 0.87 kg with a CREAT of 60 µmol/L) was estimated to increase with 0.002 L/h per 0.1 kg increase in bodyweight. With every unit decrease in CREAT, clearance was estimated to increase with 0.0002 L/h when postnatal age was above 1 week. Volume of distribution was estimated 0.844 L (RSE 6%), and increased linearly with bodyweight. Applying the dosing regimen for term neonates to preterm neonates results in unequal exposure throughout the treatment period (Figure).
Conclusions: Dosing of fluconazole in preterm neonates can be optimized by adjusting for both bodyweight and CREAT for preterm neonates with a PNA above 1 week.

Clinical Trial Registration: ClinicalTrials.gov Identifier: NCT02421068
OFF-LABEL DRUG USE IN HOSPITALIZED CHILDREN: A PROSPECTIVE OBSERVATIONAL STUDY AT GONDAR UNIVERSITY REFERRAL HOSPITAL, NORTHWESTERN ETHIOPIA

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University of Gondar, Clinical Pharmacy, Gondar, Ethiopia

Background: The majority of medications that are currently used for the treatment of childhood diseases are either not licensed or being prescribed outside the terms of the product license (off-label prescribing). In Ethiopia, there is a paucity of data on the nature and magnitude of the problem. This study aimed at determining the extent of unlicensed and off-label drug uses and associated factors in children hospitalized at Gondar University Referral Hospital, Northwest Ethiopia.

Methods: An institution-based prospective cross-sectional study was employed from April 15 to July 15, 2016. A total of 243 pediatric patients admitted to Gondar university referral hospital were included in the study using a simple random sampling method. Data were collected using a structured questionnaire, and the data collected were entered and analyzed using Statistical Packages for Social Sciences (SPSS) version 20.

Results: Of the total of 800 drugs prescribed, 607 (75.8%) were off-label. Off-label medicine use was frequently observed in antimicrobials (60.6%) followed by central nervous system drugs (14.3%). The extent off-label prescribing was highest in the age group of 6–13 years (30%). Inappropriate dosing and frequency (42.3%) were the most common reason for off-label medicine use. Having other variables controlled, age group and undergoing surgical procedure remained to be significant predictors of off-label prescribing in the multivariate regression analysis.

Conclusions: The magnitude of off-label prescribing is considerably high. Dosing and frequency discrepancy were identified as the main contributor to off-label prescribing, which predisposes children to the harmful effects of drugs. Particularly for antibiotics, the development of resistances is fostered when low doses/subtherapeutic doses are given. Implementing evidence-based prescribing by generating more quality literature on the safety profile and effectiveness of off-label would improve the injudicious use of drugs in the pediatric population.
PURPURIC RASH IN AN ADOLESCENT WITH FEVER, PANCYTOPENIA AND AN HLH LIKE SYNDROME DUE TO PARVOVIRUS B19

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Title of Case(s): Purpuric rash in an adolescent with fever, pancytopenia and an HLH like syndrome due to Parvovirus B19

**Background**: Human parvovirus B19 infection is common worldwide and across the age spectrum. Most of the times affected patients are asymptomatic whereas typical exanthems consist of erythematous rash on the face and a lacey like rash on the trunk and the extremities. Here we present an adolescent with an atypical erythematous rash with purpuric lesions and HLH-like syndrome associated with human parvovirus B19 infection.

**Case Presentation Summary**: A 15-year-old previously healthy boy was admitted to our clinic after a 3-day course of persistent fever, an expanding hemorrhagic rash and malaise. On admission, a confluent erythematous rash with haemorrhagic lesions occupying the inguinal regions bilaterally and additional purpuric rash in the armpits and the extremities including the dorsal areas of the palms and soles were evident. He was started on vancomycin and ceftriaxone as in sepsis. In the days following, haemorrhagic lesions were expanding, and the patient became pancytopenic with a prolonged INR and hepatosplenomegaly. Very high ferritin levels were also found. A course of IVIGs 1 gr/kg was given and thereafter the patient became afebrile and started improving. Final diagnosis was made on the 4th day of hospitalization with PCR Parvo B19 DNA positive in serum and bone marrow and positive IgG and IgM abs in serum. He left hospital in excellent condition after completing a 10-day antibiotic course.

**Learning Points/Discussion**: Here we present a rare case of Parvovirus B19 infection associated with fever and hemorrhagic rash. The virus also caused a more severe course of disease manifested as an incomplete HLH syndrome. All the above denote an atypical manifestation of the infection. Parvovirus B19 should be included in the evaluation of febrile purpura and in HLH like syndrome with fever and purpuric rash.
OFF-LABEL ANTIBIOTIC USE AMONG PAEDIATRIC IN-PATIENTS; A PROSPECTIVE, OBSERVATIONAL STUDY AT A TERTIARY HOSPITAL IN SOUTHWESTERN UGANDA.

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Background: Off-label drug use refers to the use of a marketed drug outside the terms of the market authorization regarding the recommended therapeutic indication, dose, frequency, patient age and the route of administration. The purpose of this survey was to determine the incidence and predictors of off-label antibiotic use in children under 5 years admitted at Mbarara regional referral hospital in Southwestern Uganda.

Methods: A prospective drug utilisation study was conducted among in-patients at the general paediatric ward of MRRH from May 20 to June 29, 2019. Prescriptions and clinical notes of patients were reviewed daily. Patient demographics, clinical characteristics and details of prescribed antibiotic regimens were recorded. Off-label status of all prescriptions was determined. data entry and analyses were performed using Epi-data (version 4) and STATA, version 12 respectively.

Results: A total of 165 patients aged 0-59 months were enrolled and received a total of 366 antibiotic prescriptions; 7 prescriptions were excluded from analysis due to incompleteness. Of the analysed prescriptions, 18.9% were off-label. The most common reasons for the off-label categories were dosage and frequency. Ampicillin was commonly prescribed at off-label frequency (57.3%) and ceftriaxone at off-label dose (8.8%). Infants received the highest proportion of off-label antibiotics (47.1%) compared to neonates (27.9%) and children (25%). On regression analysis, age group was significantly associated with off-label antibiotic use.

Conclusions: The findings from this study provide an insight on the extent of off-label antibiotic use in children in southwestern Uganda and demonstrates that the practice is common in paediatrics. Drug regulatory authorities should strive to ensure that sufficient data from clinical trials is made available to support emerging “well-founded” off-label uses of antibiotics in children thus promoting evidence-based medicine practice and rational antibiotic use.
THE STUDY OF EPIDEMIOLOGICAL SITUATION OF VARICELLA AND ITS COMPLICATIONS IN ALBANIAN CHILDREN

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Background: Varicella zoster is a common infection disease in children. Varicella may lead to severe cases and the resultant hospitalization and death. Its serious problems are reduced after introduction of the varicella vaccine. Albania does not currently implement universal varicella vaccination in childhood. The aim of this study was to show the epidemiological data, risk factors, complications and the tendency of this disease.

Methods: In the study we have included all children with varicella aged 1 month to 14 years old presented in the pediatric emergency department of the University Hospital Center:” Mother Theresa” during the period January 2018- December 2018. Epidemiological data analyzed were sex, age, origin, the monthly spreading, risk factor and complications. We followed all complicated cases after being admitted to the hospital and collected all the data.

Results: 671 children were presented with signs of varicella. 593 (88.3%) were uncomplicated cases, 78(11.6%) were complicated from which 34(43.5%) hospitalized. Age group most affected was 13-month-5 years old with 386 cases (57.5%) followed by age group 6-14 years with 232 cases (34.5%) and age group 1 month-12 month with 53 cases (7.8%). 317 cases (47.2%) were female, 354 (52.7%) were male. Most of the patients 442 (65.8%) came from urban zone. Some of the complications we found were: skin and soft tissue infections, pneumonia, etc, 4 varicella cases plus measles, and one death. We observed risk factor such as leukemia, atopic dermatitis etc.

Conclusions: In our service we note a increasing number of varicella cases, year after year, potentially requiring medical visits or hospitalizations and occasionally leading to long-term sequelae or even death. The results of this study can contribute to evaluate the possibility of the universal varicella vaccination introduction in order to minimize the health care burden of varicella in Albania, as the WHO recommend.
BILATERAL FACIAL PALSY - A FORM OF NEUROBORRELIOSIS PRESENTATION IN PEDIATRIC AGE

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Title of Case(s): Bilateral Facial Palsy - A rare entity in pediatric age

Background: Bilateral facial palsy is a very uncommon entity, particularly in the pediatric age. It presents as a manifestation of systemic diseases like borreliosis, Guillain-Barré syndrome, sarcoidosis and HIV infection. Despite its several etiologies, *Borrelia burgdorferi* should be suspected in children presenting with acute neurological disease of unknown cause. We present a case of bilateral facial palsy as the presenting form of borreliosis.

Case Presentation Summary: A 7-year-old male, previously healthy, presenting with bilateral facial palsy with preserved ocular motility and no other neurological abnormal findings, fever or other symptoms. He lives in a rural area in Portugal and travelled in a caravan through the South of Spain a few weeks earlier, staying also in rural areas. He had no previous history of tick bite or cutaneous rash. Full blood count and C-reactive protein were within normal limits. Cerebrospinal fluid (CSF) showed 0.8 cells/mm³ lymphocytes, normal glucose and protein levels, without oligoclonal bands. Brain MRI revealed “signal enhancement in both facial nerves”. Electroencephalogram was normal. The *Borrelia burgdorferi* specific antibodies were positive by ELISA and immunoblot (anti-Borrelia Euroline RN-AT, Euroimmun) with serum-specific bands on IgM (OspC Bg, p39 and p41) in serum and negative in CSF. Other infectious and autoimmune diseases were excluded. He had treatment with ceftriaxone for 21 days, prednisolone for 5 days followed by tapering and physical therapy with gradual improvement.

Learning Points/Discussion: In this patient, peripheral bilateral facial palsy occurred in the context of borreliosis. In the evaluation of a child who presents with these symptoms, history has the highest role in the diagnosis. Given the rarity of this entity, this case is particularly interesting, especially in a country like Portugal, where borreliosis prevalence is one of the lowest in Europe (3.3-7.3%).
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VALUE OF INTRAOPERATIVE CEREBRO-SPINAL FLUID SAMPLING DURING VENTRICULO-
PERITONEAL SHUNT FOR CONGENITAL HYDROCEPHALUS

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Background: ventriculo-peritoneal shunt is the definitive management for congenital hydrocephalus and it is one of the commonest surgical procedure in Neurosurgery. However, shunt related infection is a significant issue in pediatric clinical practice. This creates a massive burden to the patient as well as the health care system due to its considerable morbidity, mortality and the cost of care. Therefore preventive strategies are always followed during shunt procedures.

Methods: Intraoperative CSF sampling as a baseline investigation is practiced by most surgeons during shunt procedures. The objective of this study is to describe the value of intraoperative CSF sampling for microbiological evaluation in ventriculo-peritoneal shunt for congenital hydrocephalus. 50 neonates and infants who underwent VP shunt insertion for congenital hydrocephalus over a period of one year were included in the study. Pyogenic culture of intraoperatively sampled CSF was reviewed.

Results: Escherichia coli, Staphylococcus aureus and Staphylococcus epidermidis were isolated from 4, 1 and 1 samples respectively. Only two of these patients developed shunt related infections, one with meningitis caused by Klebsiella pneumoniae and one with wound infection by Staphylococcus aureus. 12 patients out of 44 who had negative CSF cultures developed shunt related infections during the follow up. There seems to be no association between intra operative CSF culture positivity and shunt related infections in congenital hydrocephalus.

Conclusions: This study shows that the routine intraoperative CSF sampling for pyogenic culture during ventriculo-peritoneal shunt have no practical value in clinical practice. This practice is an additional work burden for the surgical team as well as the laboratory, and creates a significant cost to the health care system. Therefore this practice needs to be discouraged to prevent unnecessasary clinical work load and expences.
Background: Neurogenic bladder (NB) and recurrent urinary tract infections (UTIs) are the main causes of morbidity and mortality in children with spina bifida (SB). Poor drainage from the bladder leads to infections that spread to the kidneys and cause damage. The aim of the study was to determine the frequency of UTIs in children with spina bifida and the ways to reduce them.

Methods: A survey and clinical examination of 35 children with SB were conducted. Oral consent was obtained from all the parents or caregivers. All children were divided into 2 groups. Group 1 included 25 children with open forms of SB, whose average age was 7.4 ± 4.6 years; group 2 - 10 children with closed forms, whose average age was 11.3 ± 3.3 years.

Results: Urinary tract disorders were detected in 31 (88.6 %) of children with SB. There was no difference in the incidence of urinary incontinence between groups of patients. Recurrent UTIs (cystitis and/or pyelonephritis) were observed in 18 (51.4%) of patients. UTIs were detected more frequent in group 1 (68.0% vs 10.0%, p<0.05). Clean intermittent catheterization (CIC) was recommended for 18 (51.4%), was conducted in 16 (45.7%). Absence of UTIs after CIC was observed in 9 (25.7%), decreased of incidence - in 5 (14.3%), without change - in 2 (5.7%) of cases.

Conclusions: Urinary tract infections are often complications of neurogenic bladder in children with spina bifida which lead to chronic kidney disease and kidney failure. In our study urinary tract infections were detected in 51.4% of patients with spina bifida. Clean intermittent catheterization is an effective method which allows to achieve the main goals of treatment, reduce the use of antibacterial therapy, and save the kidneys.
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¹Pulderbos Rehabilitation Centre, Department Of Paediatrics, Zandhoven, Belgium, ²Antwerp University Hospital, Department Of Paediatrics, Edegem, Belgium, ³Antwerp University Hospital, Department Of Paediatric Neurology, Edegem, Belgium, ⁴Antwerp University Hospital, Department Of Neurosurgery, Edegem, Belgium

Title of Case(s): Infliximab as immunosuppressive agent for a child with tuberculomas compressing the brain stem

Background: Paradoxical reaction (PR) during tuberculosis treatment is defined as clinical or radiological worsening or emergence of new lesions during adequate treatment. It is a phenomenon first described in HIV patients, referred to as Immune Reconstitution Inflammatory Syndrome (IRIS). Historically, thalidomide has been used for PR not responding to steroids, but newer agents like infliximab (tumor necrosis factor alpha antibodies) have the theoretical advantage of more selectively suppressing the tuberculosis immune response. Clinical experience is however limited.

Case Presentation Summary: A 21-month-old girl presented with tuberculous meningitis treatment failure due to emerging isoniazide resistance after 11 months of standard treatment. Possible explanations included relatively low dosing of tuberculostatic drugs, pyridoxine overdosing, and vomiting. After four months of rifampin, pyrazinamide, levofloxacin and linezolid, our patient’s symptoms worsened again with increased vomiting, head deviation, ataxia and tremor. While cerebrospinal fluid exams turned normal, imaging revealed new lesions (Figure 1A): multiple cerebellar tuberculomas/abcesses compromising the brain stem. After starting steroids, our patient recovered as expected in case of PR. Weaning however was not successful, with worsening of symptoms and increase of brain lesions one month later (Figure 1B). Our patient received 3 doses of infliximab over a period of 6 weeks, in this period steroids could be weaned while the patient showed clinical improvement.
Learning Points/Discussion: Paradoxical reaction during tuberculosis treatment should be considered when there is clinical deterioration after the start of treatment but also after starting a new treatment regimen for treatment failure. Corticosteroids are the first treatment choice. Historically, thalidomide has been used for central nervous system tuberculomas inadequately responding to steroids. This case report supports the use of infliximab in this context. Special thanks to doctors Solomons, van Thoorn, Schaaf, Marais and all ptbnet members.
SPHINGOMONAS PAUCIMOBILIS MENINGITIS IN A NEWBORN: A CASE REPORT

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Title of Case(s): Sphingomonas Paucimobilis Meningitis in a Newborn: A Case Report

Background: Sphingomonas paucimobilis (SP) is gram negative aerobic bacteria with a single polar flagellum. It is ubiquitous, found in water, soil, and plants. It is increasingly being recognized as a cause of health care associated infections in immune compromised. Infections reported with this microorganism are pneumonia, sepsis, arthritis, peritonitis, and endophthalmitis. Only 3 cases of meningitis only in adults have been reported.

Case Presentation Summary: A preterm (25+3/7 weeks), 820 grams male baby was born to a primigravida booked mother. Mother had history of leaking PV for 10 days. Baby was admitted in view of prematurity, respiratory distress and risk of sepsis. Initial sepsis screens were negative. On Day three baby developed frequent apneas and feed intolerance, and was started on piperacillin tazobactam and amikcin for suspected sepsis. As part of sepsis work up CSF examination revealed no cells, protein 157mg/dl, sugar 65mg/dl, but it grew SP which was sensitive to ciprofloxacin and colistin (Table-1).

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Antibiotics were changed to colistin and ciprofloxacin on D7 of life. Ultrasound brain revealed Grade I caudothalamic bleed. Cultures of maternal stool, urine and high vaginal swab did not grow Sphingomonas. Environmental cultures were also negative. In spite of appropriate antibiotics the baby worsened and died because of multiorgan dysfunction and refractory shock on D15.

**Learning Points/Discussion:** SP previously known as Pseudomonas paucimobilis, is an infectious agent that is prevalent in nature but may also be isolated in hospital settings. An outbreak of sepsis affecting 13 newborn in a NICU has been described. All had sepsis and/or shock. None of the newborns had meningitis. This is probably the first case of meningitis due to SP. It may not always be possible to find the source of infection as was in our case.
CLINICAL FEATURES OF ENTEROVIRAL INFECTION IN CHILDREN WITH ONYCHOMADESIS

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Background: Enteroviral infections are commonly encountered infections, caused by group of RNA viruses, especially affect infants and children. Clinical features of enterovirus infection are very variable; from mild benign fever to life-threatening encephalitis, myocarditis, or sepsis.

Methods: We present a case report of 34 children from one kindergarten with nail changes that were observed in Ternopil region, Ukraine. Nail trauma, periungual dermatitis, significant medication intake history, systemic diseases were excluded. All patients were clinically examined, and their paediatric and dermatological records were studied to confirm precedent enteroviral infection. Faecal samples were obtained from children with onychomadesis for enterovirus testing.

Results: The median age of the examined children was 3.97±0.78 years (range, 2–5 years). All patients were presented with nail changes. Due to the history of present illnesses it was revealed that interval between onsets of enteroviral infection to nail changes varied from 4 to 12 weeks. Clinical features of enteroviral infection were very variable. Fever occurred in 64.7% of patients. The average duration of fever was 1.87±0.92 days. Gastrointestinal symptoms were presented by nausea, vomiting, diarrhea without blood and mucus. In 7 (20.6%) cases maculopapular, vesicular rash was on hands, feet and around mouth. Skin rash was followed by skin desquamation in 3 (8.8%) patients in 2-6 weeks. Nail changes were presented by Beau's lines and onychomadesis (nail shedding). The number of the affected nails varied from 1 to 16. The mean number of the affected nails was 4.88±4.09.

Conclusions: Our study proved association between onychomadesis (nail shedding) outbreak and outbreak of enteroviral infection, mainly hand-foot-mouth disease. Enteroviral infection was followed by onychomadesis in 4–12 weeks. Clinical features of enteroviral infection were very variable, with prevalence of cutaneous lesions.

Clinical Trial Registration: Clinical study. N/A
EPIDEMIOLOGICAL DATA OF ACUTE TONSILLITIS AND ITS COMPLICATIONS IN PEDIATRIC AGE GROUP IN ALBANIA.

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Background: Tonsillitis is a common infection disease in childrens. It can be acute or chronic. The most common causes are viruses and bacteria. The aim of this study was to show the epidemiological data, clinical profile and the complications of tonsillitis in the pediatric age for all the cases presented during the year 2018, in the Emergency Department of "Mother Teresa" University Hospital Tirana, Albania.

Methods: This is a retrospective study over a 12-month period from January to December 2018. In the study we have included all the children diagnosed with tonsillitis from 1 month to 14 years old, presented to our service with yellowish beads of pus on the surface of tonsils with varying degree of enlargement of them. Epidemiological data analyzed were sex, age, seasonality, origin, clinical manifestation and complications.

Results: 2757 cases were collected during this period. The average age was 9.5 years, with a range 2 to 14 years. Age group most affected was 1-5 years old (1645)59.7%, followed by 5-14 years old (1112)40.3%. Males were (1639)59.5%, females (1118)40.5%. Tonsillitis occur in all climatic seasons, with an increase in November and April (1968) 71%. Among the cases 2692(97.6%) were self-limited or improved under the use of oral antibiotics and 64(2.4%) cases were hospitalized. The most common complications is acute otitis media followed by peritonsillar abscess, parapharyngeal abscess, sepsis.

Conclusions: This study shows that we have an increased number of the cases presented as tonsillitis in our emergency department. Being a developing country, our service doesn't offer the mainly and rapidly test for etiological diagnosis as RADT for GABHS. So, in this way many cases may be misdiagnosed. We hope, in the future we can realize that as soon as possible.
EVALUATION OF THE RESISTANCE PROFILE AND RESEARCH OF BIOFILM AND FIMH GENES ASSOCIATED TO ESCHERICHIA COLI AND ENTEROBACTER SPP STRAINS UROPATHOGENS ISOLATED AT BETHESDA HOSPITAL OF COTONOU

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Background: Urinary tract infection is an attack on all or a part of the urinary shaft by one or more microorganisms that generate an inflammatory reaction and clinical manifestations. The virulence and antibiotic resistance of uropathogenic enterobacteria are increasingly a real public health problem in developing countries. The aim of this study was to improve the knowledge about the level of the pathogenicity of Escherichia coli and Enterobacter spp uropathogens strains isolated at BETHESDA hospital in Cotonou.

Methods: To achieve this, within 104 urine samples, 75 strains of Enterobacteriaceae were identified. Furthermore, we had 25% of Escherichia coli, 24% of Enterobacter cloacea and 4% of Enterobacter aerogenes. These strains were identified according to the conventional method and were the subject of the determination of the conventional antibiotic resistance profile. Then, the genomic DNAs were extracted according to the protocol of the QIAGEN® red kit (QIAGEN®, Hilden, Germany) and made the standard PCR amplification model for virulence gene research (biofilm and fimH).

Results: The results obtained shows that almost all strains of E. coli and E. spp are penicillin-resistant, 88% and 89% respectively. A low resistance of these strains to carbapenems and aztreonam. The amplification of the biofilm gene from genomic DNA have showed that 61% of the E. coli strains were positive but no strain of E. spp revealed it and the fimH gene have revealed that 89% and 42% of E. coli and E. spp had this gene.

Conclusions: In conclusion, these uropathogenic strains demonstrated total resistance to bectalactamines and average resistance to carbapenemes and monobactam. In addition, Virulence of E coli strains is related to biofilm formation and adhesins, but Enterobacter spp is only related to adhesives with respect to virulence genes.

Clinical Trial Registration: Clinical trial.govB104
RECURRENT PLASMODIUM VIVAX MALARIA: A CASE REPORT

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Title of Case(s): Recurrent Plasmodium Vivax Malaria: a case report

Background: Currently the majority of malaria cases in Europe are imported by international travelers and immigrants. About 50 cases of malaria are reported annually in Ukraine. The prevalence of abdominal pain in the cases of malaria ranges from 21.4% to 29.5%. The peculiarity of the presented case is the dominance of fever without characteristic cyclicity and pronounced abdominal pain in the onset of the disease, which led to the delayed of the correct diagnosis.

Case Presentation Summary: A 17-year-old Indian citizen was admitted to the surgical department of Regional Children's Hospital with fever and severe abdominal pain. General weakness, vomiting, fever, severe headache, muscle pain, chills, red urine were also reported. First symptoms were noted 8 days before the admission, and include fever and moderate abdominal pain. The clinical examination revealed fever, mild jaundice, tachycardia, painful abdomen, especially in the right iliac region. Symptoms of peritoneal irritation were doubtful. The liver was slightly enlarged, and the edge of the spleen was palpated. Acute appendicitis was suspected. The epidemiological history established that two years ago the patient was treated for malaria in India, and did not receive antirecurrent therapy. Investigation of a drop of blood for malaria plasmodium detected P. vivax. Progression of the disease showed splenomegaly and the signs of hemolytic anemia: We also detected thrombocytopenia, leukopenia, high level of lactate dehydrogenase.

Learning Points/Discussion: Severe abdominal pain may be a sign of malaria. A careful, thorough case history is one of the key points in the path to the correct diagnosis. In patients with fever who came from endemic countries, malaria should be excluded. Abdominal pain in combination with other clinical signs (fever, jaundice, splenomegaly, anemia, hepatomegaly) in patients at risk requires differential diagnosis with malaria.
VENTILATOR-ASSOCIATED PNEUMONIA IN NEONATAL INTENSIVE CARE UNIT PATIENTS IN LIBYA

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**Background:** Ventilator-associated pneumonia (VAP) is pneumonia that develops at or after 48 hours in patients placed on mechanical ventilation. VAP is considered one of the most common hospital-acquired infection among patients in the intensive care unit. Diagnosing VAP accurately and appropriate treatment is crucial to decrease the risk of mortality. We aim to identify risk factors associated with ventilator-associated pneumonia in the neonatal intensive care unit.

**Methods:** All patients who were admitted to the pediatric intensive care unit from January 2018 to January 2019 and who received mechanical ventilation for 48 hours or more were enrolled in the study. Patients’ baseline characteristics, disease, duration of mechanical ventilation, and length of stay in the pediatric intensive care were recorded retrospectively. We used Microsoft Excel to record the data and statistical analysis was done by SPSS 25.

**Results:** Two hundred fifty-three patients were eligible for inclusion in the study. Of those included, mean age was 30.8±15.2 months. The mean duration of mechanical ventilation for patients with VAP was 15±3 days among patients with VAP. The mean PICU stay was 26±10 days. The most prevalent organisms isolated were Pseudomonas, E. coli and Staphylococcus aureus. History of aspiration, enteral feeding, bronchoscopy, and prolonged mechanical-ventilation was associated significantly with VAP. Prior antibiotic use was not associated with an increased risk of VAP. The mortality rate was 45.3% in patients with VAP.

**Conclusions:** This study has established the baseline for further studies of VAP in Libya. Additional studies are needed to determine other risk factors and develop prevent measure to decrease the VAP in the intensive care unit. The antibiotic use in the pediatric intensive care units is being revied and restriction policy and guidelines are being revised to ensure that VAP can be reduced.
RECURRENT INFECTIONS IN PATIENTS WITH PRIMARY IMMUNODEFICIENCIES

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Background: Primary immunodeficiencies (PID) include more than 430 different genetic disorders characterized by immune system abnormalities. A large number of diseases causes variability of clinical symptoms. Recurrent infections are often a leading clinical sign of these diseases. The aim of our study was to define the frequency and features of recurrent infections in patients with primary immunodeficiency, in order to improve early detection of these diseases.

Methods: This retrospective and prospective study involved 36 patients with PIDs, whose clinical symptoms were followed up from the disease onset. A prospective analysis was performed for 26 patients still being under medical supervision by an immunology specialist. Retrospective analysis was based on a review of medical (clinical) records, and includes 10 patients. We paid special attention to the clinical manifestations of PID.

Results: In this study, the majority of diagnoses were within the category of combined immunodeficiencies (CID) with associated or syndromic features (55.6%) followed by antibody deficiencies (30.6%). Recurrent infections occurred in 29 (80.6%) patients. Recurrent bacterial respiratory tract infections were evidenced in 22 (61.1%) patients, recurrent viral respiratory infections – in 16 (44.4%) patients. Recurrent pneumonia was present more often in patients with antibody deficiencies (63.6%). Skin infections were reported in 25.0% of patients, most frequent in patients with phagocyte defects. Mycoses and unusual infections took place in patients with CID.

Conclusions: Recurrent infections dominated among the clinical signs (80.6%) in patients with primary immunodeficiencies. Infections were present primarily as recurrent bacterial respiratory tract infection, commonly pneumonia, especially in children with antibody deficiencies. Types of infections can be a clue to the diagnosis of certain groups of primary immunodeficiency diseases. Other clinical signs of PID (autoimmune disorders, allergies, malignancies) occurred less often.
THE KNOWLEDGE, ATTITUDES AND PRACTICES OF PEDIATRIC DOCTORS REGARDING ANTIBIOTIC RESISTANCE IN LIBYAN HOSPITALS

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**Background:** Antibiotic resistance has emerged as one of the dangerous threats to the quality of health. It was estimated that more than half of the antibiotics prescribed by physicians were inappropriate. The recent reports of the emergence of multidrug-resistant bacteria pathogens in Libya is a serious concern with observed high antibiotic prescription to pediatric patients specifically. This study aimed to assess knowledge of pediatric doctors regarding the use of antibiotics in teaching hospitals in Tripoli.

**Methods:** This cross-sectional descriptive study was conducted through a survey in university hospitals in Tripoli, Libya. Eligible participants were pediatric doctors working in university hospitals. A total of 120 paediatricians were approached using a survey based on a questionnaire from the alliance for the prudent use of antibiotics. The questionnaire included primary characteristic data, knowledge, and physician attitude toward antibiotic prescription.

**Results:** Out of 120 paediatricians approached, 72 (58.9%) accept and responded to the survey. Year of experience was associated with less likely to prescribe antibiotics for uncomplicated cases (p < 0.05). About 85 (80.5%) of participants believed that over-prescription of antibiotic is routine in clinical practice. Participant thought that the problem is globally (60%), and the majority thought it was nationally (90.2%). The majority of physicians have adequate knowledge of resistance factors (86.1%). All participants reported that the hospitals did not have guideline or policy for an antibiotic prescription.

**Conclusions:** This study has established and identify the knowledge gaps and provide a baseline for future interventions that could lead to the appropriate use of antibiotics in Libya. However, the limitation of a local resource in terms of bacterial culture and laboratory analysis remains a challenge for Libyan hospitals. Policy changes are needed from local authorities strategies against emerging antibiotic resistance.
THE CONTRIBUTION OF SYNDROMIC DIAGNOSTIC TESTS TO PERTUSSIS EPIDEMIOLOGY

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Background: Pertussis is a highly contagious acute respiratory illness caused by the bacterial pathogen Bordetella pertussis. Although it may affect all susceptible age groups, it can lead to severe clinical manifestations in infants who have not yet been vaccinated. In this study, increase in diagnostic rate of pertussis with the introduction of syndromic polymerase chain reaction has been shown and the clinical features were examined.

Methods: Nasopharyngeal swabs of patients who were admitted to our hospital with pertussis-like clinical manifestation between April and December 2017 were evaluated at the Microbiology Reference Laboratory of Public Health for culture and PCR testing for B. pertussis. Nasopharyngeal swabs of patients who were admitted to our hospital with pertussis-like clinical manifestations between April and December 2017 were tested for B. pertussis using FilmArray® Multiplex PCR.

Results: Nasopharyngeal swab specimens of 7 patients presented with pertussis-like illness between April - December 2017 were sent to Public Health Microbiology Reference Laboratory. Bordetella pertussis culture and PCR positivity were detected in two patients at this period. Between April and December 2018, nasopharyngeal swab specimens of 17 patients who presented with pertussis-like illness were found to be positive for Bordetella pertussis with FilmArray Multiplex PCR. In 2017, there were two definite pertussis cases. With the introduction of the syndromic PCR in 2018, all 17 patients were recorded as definite pertussis cases.

Conclusions: Pertussis continues to be a public health issue even in developed countries, where high vaccination rates. Although culture has been considered to be the most specific method to diagnose B. pertussis infection, it has low sensitivity and does not provide rapid results. Rapid diagnosis of pertussis with syndromic PCR makes a significant contribution to pertussis epidemiology. It also improves the timely diagnosis, postexposure prophylaxis and management.
Background: As a result of therapeutic failures and the rising costs of treating enteric pathogen infections, scientists are trying to find alternative care. Hence, the resort to plants of the traditional pharmacopoeia for their many pharmacological activities of K. pneumoniae, K. rhinocleromatis, K. oxytoca, P. oryzihabtans, P. aeruginosa, E. coli, C. freundii, S. cholerasius and S. flexner. The present study was initiated in the general objective, to evaluate the chemical composition of the aqueous and ethanolic extracts of some plants of Southern Benin namely Cajanus cajan (leaves), Vernonia amygdalina (leaves) and Psidium guayava (leaves and roots) and their activities on multi-resistant bacterial strains.

Methods: The content of the total polyphenol and flavonoid extracts was measured by the method of Basli and al. and Kim and al. The toxicity of the extracts was assessed by the larval toxicity test using Artemia salina larvae. The agar and liquid diffusion methods were used for the sensitivity test and the determination of the minimal inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) of plant extracts on enteropathogenic strains.

Results: Selected plants all had high levels of flavonoids and polyphenols. All these plants are nontoxic at the concentration of 100 mg / ml. The MICs and MBCs of the active extracts varied according to the extracts and bacterial strains studied. The ethanolic extract of Psidium guayava leaves showed bactericidal activity on the strains of Pseudomonas aeruginosa, Salmonella cholerasius and Shigella flexneri. The ethanolic extracts of the leaves of Cajanus cajan and Vernonia amygdalina showed bactericidal activity on the strain of Shigella flexneri.

Conclusions: The extracts of plants showed bactericidal activities against the various enteropathogenic strains tested and can therefore constitute substituents for antibiotics following transformations into improved traditional nedecines.

Clinical Trial Registration: In order to be considered for the ESPID Annual Meeting Travel Award you are required to upload a copy of your photo ID.
THE DYNAMICS OF CYTOKINE SERUM LEVELS IN CHILDREN WITH ACUTE EBV INFECTION.

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Background: Acute EBV infection remains a major medical and socio-economic burden in many countries worldwide. The aim was to evaluate the dynamics of cytokine serum levels of pro-inflammatory IL-6 and TNF-α, anti-inflammatory human IL-10 (hIL-10) cytokines and interferon IFN-α in hospitalized children in an infectious diseases department 1 at Saint-Petersburg Pediatric Medical University.

Methods: We collected venous blood samples twice from 49 pediatric patients aged 1-17 years old: immediately after admission in hospital and one more time in the early stage of recovery. Children were divided into two groups: group 1 (1-7 years) comprised 20 children, group 2 (8-17 years)-29. An even distribution by sex was established in all groups. In all cases, acute infectious mononucleosis was determined by ELISA and/or PCR diagnostic methods. Cytokine levels were quantified using ELISA (Vector-Best, Russia). Data were analyzed in Stat Soft Statistica 12.0. for windows 10.

Results: There was a strong statistical evidence of Cytokine levels decrease in group 1 in the early recovery stage: IL-6 (20,7 (S.D 18.29) vs 6,25 (S.D 6,4) pg/ml ;P=0.01), IL-10 ( 31,9(S.D 16,6)vs 10,6(S.D 6,4) pg/ml; P<0.001); TNF-α (11,4(S.D 3,6 ) vs 8,9(S.D 2,7)pg/ml; P<0.001). In group 2 we also observed significant differences comparing the means of the first collected samples to those obtained before patients discharge for pro-inflammatory (IL-6 P<0.001, TNF-α P=0.02) and anti-inflammatory (hIL-10 P=0.03) cytokines including interferon (IFN-α P<0.001).

Conclusions: A decrease in the studied cytokine serum levels was observed in all groups independently of the patients' age.

Clinical Trial Registration: Not applicable
AN UNUSUAL CASE OF INFECTION INDUCED RAPID PROGRESSIVE NEUROPATHOLOGY: A DIAGNOSTIC AND MANAGEMENT CHALLENGE

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Title of Case(s): An unusual case of infection induced rapid progressive neuropathology: a diagnostic and management challenge

Background: Leptospirosis is often unrecognized due to the broad spectrum of symptoms. Neuroleptospirosis, mostly related to the immune-phase of the disease, is found in 10-15% of the patients and varies in severity from minimal symptomatology to fatal brain involvement. Here we report, an extremely rare case of an adolescent affected by extensive neuroleptospirosis and illuminate the disease-related diagnostic and management challenges.

Case Presentation Summary: A 17-year-old woman with no past medical history presented with 4 days of fever, abdominal pain, nausea, icterus and rash. Initial laboratory work-up demonstrated signs of inflammation, hyperbilirubinemia, autoimmune hemolytic anemia and nephritis. A broad differential diagnosis was generated. Accordingly, radiography and numerous laboratory tests were conducted. Empirical treatment with intravenous amoxicillin/clavulanic-acid and gentamycin was started. After a brief apparent improvement, the clinical picture deteriorated dramatically as the patient developed severe headaches, vomiting and impaired consciousness. Neuroimaging revealed cerebellar edema with multifocal lesions. On suspicion of meningoencephalitis antibiotics were switched to ceftriaxone and amoxicillin, and high-dose corticosteroids were added to reduce an inflammatory response. Nevertheless, the neurological condition of the patient deteriorated further, necessitating intubation and ventilation, placement of an extra-ventricular drain and fossa posterior decompression surgery. The list of differential diagnoses was narrowed down daily and eventually the diagnosis of leptospirosis was confirmed. Despite appropriate initial antibiotic therapy, follow-up MRI cerebrum showed significant increase of destructive neuropathology(Figure).
Learning Points/Discussion: This case report shows the diagnostic challenges of leptospirosis complicated by neurological involvement. Additionally, it illustrates the poor therapeutic options, with a dramatic outcome in our case, and necessity for new insights in the treatment of the disease-related immune-phase. Hopefully, public awareness of leptospirosis reduces disease-related damage in other cases, due to rapid diagnosis and start of appropriate treatment in early-disease-stage.
RASH AND MUCOSITIS: WHAT NOT TO FORGET?

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Title of Case(s): Rash and mucositis: what not to forget?

Background: Rash and mucositis are common symptoms of a range of diseases in paediatric population, from mild ones such hand-foot-mouth disease to more severe ones, as Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN). Some of these diseases have similar clinical presentation in the beginning, therefore detailed anamnesis and physical examination are crucial for an accurate diagnosis. We report a case of mucocutaneous eruptions associated with respiratory symptoms, leading to the diagnosis of Mycoplasma pneumoniae-induced rash and mucositis.

Case Presentation Summary: A previously healthy 9-year-old boy presented to our service with cough and coryza for fifteen days. Along the last five days, skin and mucosal lesions had appeared: conjunctival hyperaemia and palpebral edema, crusting of lips and erosions on tongue and buccal mucosa, and papular, vesiculobullous and targetetoid lesions over trunk and extremities (picture).
He had fever only in the day before consultation. Apart from the lesions described, there were rales in pulmonary auscultation at admission. He was evaluated by paediatric infectious diseases, dermatology and ophthalmology consultants, and hypothesis of *Mycoplasma pneumoniae*-induced rash and mucositis was made. Positive results of investigation done: chest x-ray with diffuse infiltrate; positive *Mycoplasma pneumoniae* IgM and IgG; skin biopsy of one lesion resulting in epidermal erythema multiform. Azythromycin was given along with supportive care - pain management, intravenous hydration and mucosal care -, with a good outcome without sequelae.

**Learning Points/Discussion:** Although mucocutaneous lesions are a common extrapulmonary manifestation of *Mycoplasma pneumoniae* infection, only in 2015 the term *Mycoplasma pneumoniae*-induced rash and mucositis was described, distinguishing it from SJC/TEN and erythema multiform. This distinction, sometimes difficult in the beginning of clinical presentation, is fundamental and should be pursue through anamnesis, physical examination and laboratory tests, as these diseases have different pathophysiology and outcomes.
LYME BORRELIOSIS IN CHILDREN IN PRISTINA REGION-REPUBLIC OF KOSOVO

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Background: Lyme borreliosis is a tick-borne multi-systemic disease caused by the spirochete Borrelia burgdorferi. The existence of Ixodes ricinus the main vector for Lyme borreliosis had been already confirmed in Kosovo environment. This fact encouraged us to investigate disease development in pediatric patients after a tick bite. Research was done at the Outpatient Department of Infectious Diseases Clinic at University Clinical Center of Kosovo in Pristina.

Methods: Twenty-four children seen after a tick bite at our clinic during 2015 were included in the study. During the first visit the embedded tick was removed and stored for identification. The serum for enzyme-linked immunnosorbent assay was taken during the first week after a tick bite, and children were followed up for next two months for development of any clinical manifestation. In children in which second blood sample was taken after two months of follow-up, seroconversion was analyzed as well.

Results:
The mean age of patients was 10 years (4 to 15), with predominance of male sex 16/24. Seven ticks removed completely were available for identification and all were *Ixodes ricinus*. Three children were lost for further follow up. In seven (7/21) children clinical manifestation of Erythema migrans was developed during two month period of follow up. All were treated with amoxicillin or erythromycin for 14 to 21 days.
with prompt regression of the skin lesion.

**Conclusions:** There are no previous data about Lyme borreliosis in children in Kosovo. Erythema migrans (EM) is the most common early clinical manifestation of the disease. Recognizing and prompt treatment of early stage of the disease is important for preventing early disseminated manifestation as neurological or musculoskeletal symptoms and late serious manifestations as chronic neuroborreliosis, lyme arthritis and acrodermatitis chronica atrophicans.
Background: Data on infections associated with cerebrospinal fluid (CSF) shunts among children are limited, particularly data about epidemiology, clinical presentation, microbiological aetiology and best treatment options. Current recommendations are supported mainly by case series or relay on expert opinion. Aim of this study is to describe the epidemiological, clinical, laboratory, and microbiological characteristics (including antibiotic susceptibility) of shunt-associated infections and treatment outcome.

Methods: Retrospective study of shunt-associated infections in children. Patients aged < 17 years with infections associated with CSF shunts and admitted to our institution in the last 10 years were included. The following definition of shunt infections was used: (1) growth of a pathogen in the CSF, on the shunt tip, or in wounds overlying the implanted shunt material (if the pathogen was interpreted as relevant), or (2) fever (temperature 138°C), headache, neck stiffness, cranial nerve signs, or irritability without another recognized cause.

Results: 107 episodes of shunt-associated infections were included. 67.3% of the patients were men. Most infections manifested within 1 month after shunt surgery. Fever was present in 78% of cases. C-Reactive protein was normal in 20% of cases. Similarly, CSF leucocyte count was normal in 20% cases. CSF cultures were positive in 70% of. The most prevalent organisms were coagulase-negative staphylococci. A surgical procedure was performed to treat infection in 70% of the episodes. No deaths described.

Conclusions: Shunt-associated infections among children often present with non specific clinical signs, and affected patients can have normal blood and CSF tests; therefore, a high index of suspicion and improved diagnostics are required for diagnosing shunt-associated infections, also in the absence of neurological signs and symptoms. Shunt-associated infections were caused predominantly by gram-positive skin flora. It is mandatory to obtain microbiological confirmation.
Title of Case(s): BCG (Bacillus Calmette- Guerin) vaccine site chemical skin burn after brilliant green application

Background: Tuberculosis is re-emerging infection, many of the countries do not have recent experience with BCG vaccines. Vaccination against tuberculosis plays significant role in prevention of severe tuberculosis. BCG vaccine is included in Latvian National Immunization Program. Typical local reactions following vaccination are observed and gradually disappear within next few months. It is highly recommended not to make any applications on vaccine site during ongoing local reactions. In the case, chemical skin burn was observed after brilliant green application.

Case Presentation Summary: Six month old girl was brought by mother to the outpatient consultation in Children Clinical University hospital, Children Vaccination centre with complains about local skin changes at BCG vaccine site. Examination showed local 6 cm diameter hyper-pigmentation with central crust on left hand deltoid region where BCG vaccination was performed. Vaccine was received at the age of four months. Approximately four weeks later typical local site reaction was observed – a pustule with redness. Despite well known recommendations do not apply any substances on BCG vaccine site, GP recommended applications with brilliant green. Lately mother has noticed skin changes with redness and bullous lesions. Brilliant green solution application was stopped and skin gradually healed. Child was consulted by tuberculosis specialist, who concludes chemical skin damage after brilliant green application.

Learning Points/Discussion: Local site reactions after tuberculosis vaccine are typical and are observed in 80 to 90% of vaccine recipients. There are no specific vaccine site care recommendation like disinfection or any applications. Brilliant green is well known skin irritant and can cause skin burns. Problem showcased here is that inadequate postvaccination local skin reaction care leading to visible skin damage can influence parents attitude to vaccine safety and vaccination in the future.
Background: In recent years movements across borders are becoming more frequent and numerous migrants are travelling to Europe searching for better opportunities. As a consequence, there has been an important increase in the number of unaccompanied minors (UMs) arriving to our countries. Access to health care is challenging for this population due to cultural and language barriers. We describe our experience in the medical care of UMs.

Methods: Descriptive retrospective study. We reviewed the medical charts of all the UMs referred from reception centers of Madrid area and attended in a reference Unit for Pediatric Tropical Diseases from January 2018 to October 2019. Data regarding demographic (age, sex, country of origin) and clinical variables (including infectious diseases and other disorders) were included, as well as treatments received, adherence to care and follow-up.

Results: 140 minors from 14 different countries had been screened. Mean age was 16.7 ± 0.8 years, 94.3% male. Main infectious diseases diagnosed were: 101 (72%) latent tuberculosis infection, 4 pulmonary tuberculosis, 17 hepatitis B infection, 1 HIV infection, 19 schistosomiasis, 3 toxocariasis and 2 strongyloidiasis. Other diagnosis: 35 cavities/periodontitis, 27 substance abuse, 10 recent traumatic injuries, 6 anaemia, 4 psychiatric disorders, 3 sexual abuse and 1 undesired pregnancy. 118 (85%) required treatment; adherence to care was good in 74 (62.7%) but loss of follow-up was frequent (27.9%)

Conclusions: UMs are a very vulnerable population with a high prevalence of medical, social and psychiatric problems. Their medical care is a challenge due to language and cultural barriers. Latent tuberculosis infection was the most common diagnosis, therefore screening of tuberculosis in this population is a Public Health priority. Specific protocols and multidisciplinary teams are needed to ensure adherence to care.
THE EFFECTS OF 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE ON INVASIVE PNEUMOCOCCAL DISEASE BURDEN AND THE SEROTYPE DISTRIBUTION OF STREPTOCOCCUS PNEUMONIAE IN TURKEY

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Background: In 2008, Turkey introduced the 7-valent pneumococcal conjugate vaccine (PCV7) in the national immunization programme. In 2011, PCV7 replaced by the 13-valent pneumococcal conjugate vaccine (PCV13). The aim of this retrospective single-center study was to determine the changings in incidence of invasive pneumococcal disease (IPD), serotype distribution and the antimicrobial resistance patterns of S. pneumoniae in children with IPD after the implementation PCV7 and PCV13.

Methods: The study was conducted on 50 Turkish children with meningitis and sepsis/bacteremia between October 2009 and October 2019 in Ankara, Turkey. Only immunocompetent children with meningitis and sepsis/bacteremia and S. pneumoniae isolated from blood and cerebrospinal fluids were included in the study criteria. The serotype analysis of the isolates and the antimicrobial (penicillin and ceftriaxone) susceptibility were performed by Quellung reaction and E-test, respectively.

Results: The median age of the patients was 40.7 months. The overall annual incidence rate of IPD among the healthy children aged <5 years decreased significantly from 9.35/100,000 to 0.83/100,000 (p<0.001). The PCV13-serotypes represented 44.7% of isolates. The most frequently isolated serotypes were 19F, 23F, 7F, 31 and 24B. The percentage of non-vaccine serotypes increased over the years as 54.5% in PCV7 period and 70.3% in PCV13 period. According to the minimum inhibitory concentration values (for meningitis) of the isolates penicillin and ceftriaxone resistance rates were 43.9% and 9.75%, respectively.
Conclusions: In conclusion, this is the first study about the changings of incidence of meningitis and sepsis/bacteremia in healthy children aged under 5 years after the implementation of PCV13 in Turkey. Our study showed that the incidence of IPD decreased significantly in healthy children aged under 5 years after the implementation of PCV13. It was determined that the percentage of non-vaccine serotypes causing serotypes increased.
UNIMICROBIAL PNEUMOCOCCAL APPENDICITIS: A RARE PRESENTATION OF INVASIVE PNEUMOCOCCAL DISEASE IN A CHILD

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Title of Case(s): Lo and behold ! Its the wolf in sheep’s clothing
Background: Appendicitis is the most common cause of acute abdomen. Appendix inflammation triggered by an infection is usually polymicrobial in aetiology, frequently involving anaerobic and aerobic gram-negative bacilli. We report a rare manifestation of unimicrobial pneumococcal appendicitis in a 6-year-old boy. Six similar pneumococcal appendicitis has been described in literature. This unique presentation is thought to occur in only 0.3% of all appendicitis.

Case Presentation Summary: A 6-year-old immunocompetent boy presented with one day history of cough and fever with progressive localised right lower quadrant pain. Physical examination on admission revealed a relatively well child. There was localised abdominal tenderness in the right lower quadrant with no obvious signs of peritoneal irritation. The psoas sign was present along with normal bowel sounds. The remaining systemic examination was unremarkable. Prior to surgery he developed one spike of temperature, which subsided after initiation of intravenous antibiotics. Laboratory investigations revealed haemoglobin 12 g/dL, white blood cell count 9.3 × 10⁹/L with normal differential, platelet 353 × 10⁹/L and normal urinalysis. He underwent appendectomy and his appendix was found to be inflamed with no perforation noted. The cultures of the inflamed appendix yielded pure growth of penicillin-susceptible Streptococcus pneumoniae and his blood cultures were negative. He completed a seven day course of intravenous ceftriaxone and was allowed home.

Learning Points/Discussion: S. pneumoniae causes a remarkable array of clinical manifestation. As this organism is usually known as a respiratory tract isolate, gastrointestinal presentation is very intriguing. This case presented with a rare gastrointestinal manifestation of IPD. Classically appendicitis presents with a polymicrobial aetiology, however this case reported a pure growth of S. pneumoniae from the inflamed appendix. To date, only 6 cases of pneumococcal appendicitis have been reported in children throughout the world.
Background: Diarrhea is the most common cause of hospitalization in the pediatric population. Bacterial diarrhea usually occurs in poor hygiene and in poor sanitation but they are responsible for 80-85% of all travelers' diarrhea. The aim of the study was the analyze of the prevalence and clinical picture of the bacterial diarrhoea in children hospitalized in Department of Pediatrics in 2019 year.

Methods: The study included a group of 22 patients (12 boys and 10 girls) aged 1 month to 18 years (average age 4 years 2/12 months) hospitalized from January 1 to December 31, 2019 in the Department of Paediatrics, Medical University of Silesia in Katowice. The analysis included age, gender, diarrhea etiology, time of year, time of hospitalization, laboratory and imaging results, and other co-existing conditions.

Results: Bacterial aetiology accounted for 4.8% (22/460) of patients. The most common causes were: Salmonella (63.6%), E. coli enteropathogen (18.2%), less often Campylobacter (9.1%). 5/22 children had concomitant rotavirus and 4/22 had adenovirus. Bacterial infections were most often observed in the summer months, most often in August (18.2%). 15/22 of patients had fever, 3/22 bloody diarrhoea. In 3/22 children accompanied by respiratory tract infection, in 1/22 urinary tract infection. Increased inflammatory markers were observed in 14/22 people, leukocytosis in 5/22. The average time of hospitalization was 6 days.

Conclusions: Diarrhea of bacterial etiology is a relatively rare cause of hospitalization in Poland. More often occur in the summer months (August). The most often the etiologic factors of bacterial diarrhoea were Salmonella infection. And the most common age group is preschool children. Systemic symptoms were most commonly observed in the form of fewer with elevated inflammation parameters - mainly CRP in most patients with bacterial diarrhea.
CLINICAL IMPACT OF PERTACTIN-NEGATIVE BORDETELLA PERTUSSIS: A SINGLE CENTRE PROSPECTIVE STUDY

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Background: New genetic variants of B. pertussis (Bp), possibly related to the persistence and resurgence of the disease, were identified in the last years. The most compelling data are about the evolution of pertactin-negative Bp strains. The aim of this study was to evaluate the clinical impact of Bp genetic variants among infants admitted to a Tertiary care University Hospital in Italy.

Methods: We prospectively evaluated infants <1 year of age hospitalized for pertussis from Jan-2013 to Dec-2019. Samples of Bp were obtained by nasopharyngeal aspirates; DNA was extracted and investigated by sequence-based analysis to evaluate virulence-associated genes ptxA, ptxP and prn. Pertactin gene was entirely sequenced. Immunization status, clinical data and the Pertussis Severity Score (PSS) were compared in prn-deficient (Mut-prn) and prn-wild (Wild-prn) groups.

Results: Twenty-two cases of pertussis were documented with a mean (SD) age of 2.3(2.5) months. Recently emerged Bp variants ptxA1, ptxP3 and prn2 were detected in all samples. The Prn-deficient gene was identified in 17 samples (9 insertion IS481, 8 deletion 660). Median (IQR) range of PSS was 7.5(6.25-12.5) vs 5(4-10.5) in Mut-prn versus Wild-prn, respectively (p=.208). Among 8 vaccinated infants, Mut-prn was detected in 5 cases, one of whom received 2 doses, whereas in Wild-prn group all infants received a single-dose (p=.625).

Conclusions: Due to our small sample-size, we did not find a statistically significant relationship between a prn-negative status and severe pertussis, despite a clinically relevant difference among PSS. Our data support international evidences of a wide diffusion of the ptxA1-pxp3-prn2 profile and of the prn-deficient gene. Larger data are needed to follow the evolution of Bp in terms of virulence and impact on the effectiveness of vaccination programs.
EFFECTIVENESS OF PROBIOTICS IN ELIMINATING DURATION OF ACUTE INFECTIOUS DIARRHEA IN PEDIATRIC PATIENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS IN DEVELOPED COUNTRIES.

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Background: Acute diarrhea is one of the most frequent reasons for Pediatric Emergency Department visits. Probiotics have been reported to mitigate duration of diarrhea; however, recent methodologically enhanced randomized controlled trials (RCTs) support a non-existent benefit. The current systematic review and meta-analysis aims to clarify these ambivalent outcomes.

Methods: We included double-blind, randomized controlled trials (RTCs) from developed countries assessing the efficacy of probiotics administered in children with acute gastroenteritis. EMBASE (Ovid), MEDLINE (PubMed), the Cochrane Central Register of Controlled Trials and reference lists of included studies were searched for eligible RCTs, from inception (1991) until September 2019.

Results: Seventeen RCTs met the eligibility criteria, and access to raw data was feasible in 16 RCTs included in the meta-analysis (N = 3,199 patients). Random effects model was selected for the estimation of the overall effect. Data pooling demonstrated precedence of probiotics in reducing the duration of diarrhea (mean difference = -14.82 hr; 95% CI: -21.42 to -8.22, p<0.0001). However, upon risk of bias assessment, studies possessing low overall risk of bias showed a marginal advantage of probiotics (mean difference = -3.75 hr; 95% CI: -8.78 to 1.29, p=0.84) compared to control. Studies graded as entailing unknown/high risk of bias exhibit a positive effect of probiotics (mean difference: -20.33 hr; 95% CI: -29.35 to -11.31, p<0.00001).

Conclusions: Probiotics seem to offer benefit in eliminating diarrhea duration, though data from higher quality RCTs denote insignificant contribution. Further large scale trials in a tightly controlled environment are needed to determine the place of probiotics in the therapeutic options of acute gastroenteritis.

Systematic Review Registration: The protocol of present meta-analysis has been submitted for registration in PROSPERO (ID: 152966).
Background: Arthritis is a common sign and symptom among children and it can be related with various conditions. Also, arthritis can be a presenting symptom of a wide spectrum of diseases such as infectious, malignant or rheumatologic diseases. In this study, we aimed to describe the different types of arthritis among children who were hospitalized for the first episode of arthritis.

Methods: A total of 78 patients aged under 18 years were included in the study who were hospitalized between January 2000 and November 2018 in Ankara University Faculty of Medicine, Department of Pediatric Infectious Diseases with the diagnosis of arthritis. Demographic characteristics, first assessment symptoms and signs, joint fluid findings, affected joint sites, imaging results, acute phase reactants, microbiological and rheumatologic laboratory examination results were evaluated in the study.

Results: The mean age of the patients was 84.7±54.6 months. The male/female ratio was 1.6. The most frequent complaints at the onset were fever, pain and movement problems and the most affected joint sites were knee and hip. The 88.5% of them had single joint involvement. The most common definitive diagnosis was septic arthritis (43.5%). Brucella arthritis (21.7%) and reactive arthritis (11.5%) were the second and third common causes, respectively. In 12.8% of the patients, arthritis was associated with the first episode of rheumatologic disorders.

Conclusions: Arthritis is a common sign among children and can be related with many diseases. As a result, its diagnosis is challenging for the clinician especially on the onset of the disease. The early diagnosis and intervention in the treatment of arthritis is mandatory to avoid its complications. Finally, septic arthritis must be the first diagnosis that should be ruled out during the evaluation of the children with arthritis.
EVALUATION OF SEROLOGY TO PNEUMOCOCCAL CAPSULAR ANTIGENS FOR THE DIAGNOSIS OF PNEUMOCOCCAL INFECTION IN CHILDREN WITH COMMUNITY-ACQUIRED PNEUMONIA IN NEPAL

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Background: New diagnostic tests for the aetiology of childhood pneumonia are needed. We evaluated the accuracy of serology to pneumococcal capsular polysaccharides (PS) for the diagnosis of pneumococcal infection in children with clinically-diagnosed pneumonia admitted to Patan Hospital, Kathmandu.

Methods: Enrolled children had acute sampling within 48 h of admission, and convalescent sampling at 6-8 weeks following admission. All children had chest radiographs, full blood count, culture of blood (and pleural fluid), and nasopharyngeal (NP) specimens for pneumococcal culture, Quellung serotyping, and PCR detection of respiratory viruses. Serum concentration of IgG to pneumococcal capsular polysaccharides was measured using a fluorescence-based multiplex immunoassay for IgG to serotype-specific PS contained in the 13-valent pneumococcal conjugate vaccine.

Results: 897 children were sequentially enrolled to the cohort. Of these children, 454 (51%) returned for convalescent sampling, and 221 (49%) paired samples were analysed. 8 children were classified as pneumococcal pneumonia (positive blood or pleural fluid culture), 11 children as probable pneumococcal pneumonia (CRP concentration ≥60 mg/l and NP serotype 1 or 5), 90 children as probable bacterial (CRP ≥60 mg/l and NP other/no serotype), 68 children as RSV pneumonia (NP RSV positive and no radiographic consolidation), 5 children as other bacterial pneumonia (pathogen from blood culture) and 39 children as unknown. There were no significant differences in the concentration of IgG to pneumococcal PS by classification of pneumonia aetiology (Wilcoxon rank sum tests, p>0.1 for all). Pneumococcal serotype-specific IgG concentration was greater in children with infection by, or NP carriage of serotype 1 (Wilcoxon rank sum test, p=0.04), but not other serotypes.

Conclusions: Paired serology to pneumococcal PS did not accurately discriminate between pneumococcal pneumonia and other pneumonia aetiologies in children in Nepal.

Clinical Trial Registration: Not applicable.
TRANSITION OF THE NATIONWIDE EPIDEMIOLOGY OF PEDIATRIC BACTEREMIA IN JAPAN

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²Aichi Children’s Health and Medicine Hospital, Department Of General Pediatrics, Aichi, Japan,
³Kyushu University Graduate School of Medical Sciences, Department Of Health Care Administration And
Management, Fukuoka, Japan

Background: The burden of pediatric bacteremia is considerable even in developed countries. Since the
bacteria’s ecological distribution differs by countries, domestic epidemiology in bacteremia is significant. 
*Haemophilus influenzae* type b and 7-valent and 13-valent pneumococcal vaccines were introduced in
December 2008, February 2010, and November 2013, respectively, in Japan. Nevertheless, the impact of
these vaccines was not evaluated by nationwide surveillance.

Methods: We extracted blood culture results between 2010 and 2016 from the Japan Nosocomial
Infections Surveillance (JANIS) database. To eliminate the effect of participating facilities, we only
included data that were obtained from facilities that participated in the JANIS throughout the study period.
Trends of the number of blood culture and causes of bacteremia were analyzed. Bacteria that cause
blood stream infections in immunocompromised patients or are regarded as contaminants (e.g.
Coagulase-negative staphylococci) were excluded from the analysis.

Results: From the 592 hospitals, we obtained 827,780 and 3,512,524 blood culture samples from
children and adults, respectively. Overall, the number of positive samples was 47,125 (5.7%) in children
and 959,522 (27.3%) in adults. *Staphylococcus aureus* bacteremia was observed in the majority of
children. *Streptococcus pneumoniae* and *H. influenzae* bacteremia both showed decreasing trends from
2010 to 2013 in children; however, *S. pneumoniae* bacteremia became steady 2013 onwards. On the
other hand, *H. influenzae* bacteremia continued to decrease.
Conclusions: In Japan, the current major causative organism for pediatric bacteremia is *S. aureus*. *S. pneumoniae* and *H. influenzae* bacteremia may be decreased due to the prevalence of 7-valent pneumococcal and Hib vaccinations. However, the pneumococcal bacteremia incidence did not show an obvious change after the 13-valent pneumococcal vaccine introduction; serotype replacement may occur. Improved awareness regarding obtaining blood culture possibly biased these results.
CLINICAL COMPARISON OF CHILDREN INFECTED BY MACROLIDE-RESISTANT OR MACROLIDE-SENSITIVE BORDETELLA PERTUSSIS

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**Background:** According to the government of China, reported cases of pertussis have increased remarkably and are still increasing in recent years. Macrolide-resistant Bordetella pertussis is very common in north and east of China, the situation of macrolide-resistant Bordetella pertussis in South of China is not know, particularly the differences in clinical characteristics between macrolide-resistant and sensitive Bordetella pertussis in children are unclear.

**Methods:** The strains and clinical data of pertussis children diagnosed by culture in ID department of SZCH from December 2015 to December 2017 were collected. The antibiotic susceptibility of retained strains was evaluated using E-Test for erythromycin, azithromycin, clarithromycin, SMZ-TMP, amoxicillin and levofloxacin. Children were divided into macrolide-resistant(MR) group and macrolide-sensitive(MS) group, and the clinical characteristics were compared retrospectively between these two groups.

**Results:**
<table>
<thead>
<tr>
<th>clinical characteristic</th>
<th>MR group (n=78)</th>
<th>MS group (n=76)</th>
<th>$\chi^2$</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>age/month</td>
<td>4(3,6)</td>
<td>3(1.46,4)</td>
<td>-3.85</td>
<td>0.00</td>
</tr>
<tr>
<td>male</td>
<td>49(62.82)</td>
<td>41(53.95)</td>
<td>1.25</td>
<td>0.26</td>
</tr>
<tr>
<td>contact history</td>
<td>39(72.2)</td>
<td>41(64.06)</td>
<td>0.89</td>
<td>0.34</td>
</tr>
<tr>
<td>DTP vaccination</td>
<td>38(48.71)</td>
<td>21(27.63)</td>
<td>7.24</td>
<td>0.00</td>
</tr>
<tr>
<td>flush complexion after coughing</td>
<td>75(96.15)</td>
<td>71(93.4)</td>
<td>0.16</td>
<td>0.69</td>
</tr>
<tr>
<td>spastic cough</td>
<td>66(84.61)</td>
<td>63(82.89)</td>
<td>0.08</td>
<td>0.77</td>
</tr>
<tr>
<td>chicken-like echo</td>
<td>43(55.12)</td>
<td>38(50)</td>
<td>0.41</td>
<td>0.52</td>
</tr>
<tr>
<td>stuffy nose, running nose and sneezing</td>
<td>35(44.87)</td>
<td>37(48.68)</td>
<td>0.22</td>
<td>0.64</td>
</tr>
<tr>
<td>vomiting after coughing</td>
<td>49(62.82)</td>
<td>41(53.95)</td>
<td>1.25</td>
<td>0.26</td>
</tr>
<tr>
<td>coughing at night</td>
<td>67(85.90)</td>
<td>59(77.63)</td>
<td>1.77</td>
<td>0.18</td>
</tr>
<tr>
<td>coughing after eating</td>
<td>4(5.13)</td>
<td>10(13.16)</td>
<td>3.00</td>
<td>0.08</td>
</tr>
<tr>
<td>cyanosis</td>
<td>26(33.33)</td>
<td>30(39.47)</td>
<td>0.63</td>
<td>0.43</td>
</tr>
<tr>
<td>wheezing</td>
<td>25(32.05)</td>
<td>12(15.79)</td>
<td>5.58</td>
<td>0.02</td>
</tr>
<tr>
<td>shortness of breath</td>
<td>12(15.38)</td>
<td>15(19.74)</td>
<td>0.50</td>
<td>0.48</td>
</tr>
<tr>
<td>apnea/hold breath</td>
<td>2(2.56)</td>
<td>5(6.6)</td>
<td>0.65</td>
<td>0.42</td>
</tr>
<tr>
<td>fever</td>
<td>17(21.79)</td>
<td>14(18.42)</td>
<td>0.27</td>
<td>0.60</td>
</tr>
<tr>
<td>pneumonia</td>
<td>35(48.61)</td>
<td>33(47.83)</td>
<td>0.00</td>
<td>0.93</td>
</tr>
<tr>
<td>WBC/×10^9/L-1</td>
<td>19.17(14.57,25.97)</td>
<td>18.55(14.29,27.23)</td>
<td>-0.21</td>
<td>0.83</td>
</tr>
<tr>
<td>WBC/ (≥20×10^9/L-1)</td>
<td>36(46.15)</td>
<td>35(46.05)</td>
<td>0.00</td>
<td>0.99</td>
</tr>
<tr>
<td>L/%</td>
<td>74.55(67.83,78.70)</td>
<td>76.1(71.28,79.43)</td>
<td>-1.09</td>
<td>0.28</td>
</tr>
<tr>
<td>the logarithmic value of PCR copy number of pertussis</td>
<td>5.86±1.07</td>
<td>4.97(4.08,5.84)</td>
<td>-5.01</td>
<td>0.00</td>
</tr>
<tr>
<td>IgG antibody of pertussis</td>
<td>3.1(0.29.6)</td>
<td>1.9(0,14.8)</td>
<td>-0.81</td>
<td>0.42</td>
</tr>
<tr>
<td>glucocorticoid</td>
<td>16(20.51)</td>
<td>8(10.53)</td>
<td>2.92</td>
<td>0.09</td>
</tr>
<tr>
<td>intravenous</td>
<td>24(30.77)</td>
<td>12(15.79)</td>
<td>4.82</td>
<td>0.03</td>
</tr>
<tr>
<td>immunoglobulin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SMZ-TMP</td>
<td>13(16.67)</td>
<td>0(0)</td>
<td>13.8</td>
<td>0.00</td>
</tr>
<tr>
<td>readmission</td>
<td>13(16.67)</td>
<td>9(11.84)</td>
<td>0.73</td>
<td>0.39</td>
</tr>
<tr>
<td>hospitalization days</td>
<td>8(7.11)</td>
<td>8(7,10)</td>
<td>-1.08</td>
<td>0.28</td>
</tr>
</tbody>
</table>
(1) 154 children with culture-confirmed pertussis were analyzed, of whom 117 (75.97%) were younger than 6 months, 95 (61.69%) were unvaccinated with DTaP and 80 (51.95%) were clearly exposed to their household members or nannies who coughed at that time. (2) Among the 154 strains of Bordetella pertussis, 76 (49.35%) were sensitive to macrolides, 78 (50.65%) were resistant to them and all (100%) were sensitive to SMZ-TMP, amoxicillin and levofloxacin. Except for one patient who was discharged automatically, all the children in the two groups were discharged after improvement.

**Conclusions:** MR Bordetella pertussis was common in Shenzhen. Except wheezing, there was no significant difference in other clinical manifestations of children infected with MR or MS Bordetella pertussis. The vaccinated children were more frequently in MR group. Most of children who infected with macrolide-resistant strains could be cured effectively with erythromycin, only a small fraction of them need to be treated with SMZ-TMP.
Background: Hepatitis A & E virus is transmitted mainly through contaminated drinking water. These outbreaks frequently occur in resource-limited countries with limited access to essential water, sanitation, hygiene and health services. An estimated 20 million infections and 3.3 million acute cases occur annually worldwide with an estimated 56 600 deaths. Objective of the study was to investigate and control the outbreak of hepatitis in Biratnagar.

Methods: Qualitative and quantitative mix-method was used to collect data during the study period. The risk behavior, sanitation/ hand washing practices were also assessed. Verbal autopsy was done for conformation the mortality due to hepatitis. Indepth interview was done Jaundice developed cases followed by family members who were residing in Biratnagar. Those identified case were clinically examined and further conformed serologically & biochemical laboratory test.

Results: A total of 2469 symptomatic jaundice cases were reported in Biratnagar during study period. In initial phase there were 90 blood sample collected from different place, out of that 45 (50%) were reactive for hepatitis E IgM, Nine(8.1%) were reactive for Hepatitis A IgM. Three samples (2.7%) among these were reactive for both Hepatitis A & E. Ten drinking water sample, reservoir and end users tap were also collected and accessed. Out of that five test result was found to be bacteriological contaminated which was unsatisfactory for drinking purpose.

Conclusions: A large hepatitis outbreak involving around 2500 people in differnd age group majjour young productive age & 15 deaths conformed including female. Outbreak of hepatitis E was gradually subsided after initiating the preventing and control measure like water purification and safe drinking behavior practice education in community level huge amount continually long period. Authority of the Minuspality should awair of such outbreake management.
USE OF ANTIBIOTICS AMONG PEDIATRIC PATIENTS HOSPITALIZED FOR ASTHMA EXACERBATION: EXPERIENCE FROM THE UNITED ARAB EMIRATES

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¹SEHA, Pediatrics/west yas /Abu Dhabi, United Arab Emirates, ²SEHA, Pediatrics, ABU DHABI, United Arab Emirates

Background: Acute asthma exacerbation is a common pediatric health problem, primarily attributed to viral and atypical bacterial infections. Although current guidelines discourage routine administration of antibiotics during exacerbations of asthma, little is known in literature about the use of antibiotics in clinical practice. This study aims to evaluate the antibiotics use in children admitted to a hospital due to an asthma exacerbation.

Methods: A retrospective study was conducted for all hospitalizations in our facility due to acute asthma exacerbation in patients (range 2-15 years) over 10 years’ period (range 2008-2018), Patients were recruited using electronic medical records (EMR) search for admissions with principle diagnosis of asthma exacerbation in Tawam hospital, Al Ain, United Arab Emirates. Clinical and laboratory data were explored and analyzed.

Results: 760 patients identified (range 2 – 16), 718 (94%) admitted in the general ward and 42 (6%) in the ICU. 129 (17%) patients had fever and 144 (19%) experienced hypoxia. 557 (73%) tested for viral infections, 89 (16%) tested positive (influenza (24, 27%), RSV (20, 22%)). 17 patients had positive blood culture and (n=14/17) were contaminants. 530 (70%) patients treated with antibiotics with higher prescriptions in patients with fever (r=0.139) and previous ICU admission (r=0.179). Prescribed antibiotics were amoxicillin (24%), amoxicillin/clavulanate (12%), ceftriaxone (11%), piperacillin/tazobactam (2%), clindamycin (0.5%) and antibiotics combinations in 268 (51%).

Conclusions: We found a high rate of potentially inappropriate antibiotic prescriptions in pediatric patients admitted with asthma exacerbations in our institute with a positive correlation of antibiotic prescriptions associated with fever and previous ICU admissions highlights the clinical challenge of differentiating bacterial from non-bacterial infections. These findings provide a significant opportunity to promote antimicrobial stewardship program interventions and clinical practice guidelines.
INFLUENZA VACCINATION STATUS OF CAREGIVERS OF CHILDREN WITH ASTHMA

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University Hospital of Patras, Paediatrics, Patras, Greece

Background: Annual immunization against influenza is universally recommended for caregivers of children with asthma to provide indirect protection against the disease. Data on the vaccination rates of this particular population are lacking. We therefore performed a questionnaire based survey in caregivers of asthmatic children. Our aim was to assess the vaccination status of this group and the parameters that may determine it.

Methods: We distributed anonymous self-administered questionnaires to parents of children with mild-moderate asthma (under controller therapy) attending the Paediatric Respiratory Unit of the University Hospital of Patras, Greece, from March to August 2019. We collected data on demographics and general attitudes towards influenza vaccination, and we performed factor analysis to explore the presence of groups of non-vaccinated caregivers with common characteristics.

Results: Out of 178 participants, 16.9% of mothers and 9% of fathers were vaccinated during the 2018-2019 season. Factor analysis revealed three groups with common characteristics: a) those who believe in flu vaccine but were unaware that they should have been vaccinated or they were too old to (31% of variance), b) parents of older children and lower educational level who were concerned about side effects (did not vaccinate their child) (25.8% of variance) c) older parents of high educational level who do not believe in flu vaccine (19.8% of variance).

Conclusions: Influenza vaccination status among caregivers of asthmatic children is poor in our region and urgent action is required in the field. To improve vaccine uptake among household contacts of children with asthma, appropriate information and educational programs should take into account the specific characteristics of this group such as beliefs about vaccine efficacy and safety, age and educational level of caregivers.
TIME TO POSITIVITY OF BLOOD CULTURES IN NEONATAL EARLY ONSET SEPSIS – 24 HOURS OF INCUBATION MIGHT NOT BE LONG ENOUGH***WTDN BY THE AUTHOR***

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**Background:** Early onset sepsis, an invasive bacterial infection in neonates in the first days after birth, has high mortality if treatment is not initiated promptly. Since signs and symptoms can be very subtle and non-specific, treatment is started in many children. We hypothesized that after 24 hours, if clinical suspicion is low, C-reactive protein (CRP) is low and the culture does not show growth, it would have been safe to stop the antibiotics.

**Methods:** We retrospectively reviewed data from 2007 until 2018 of all neonates admitted with a blood culture taken in the first two days of life because of suspicion of an infection, either based on risk-factors or clinical signs. We collected the blood culture results, CRP and, in patients where time to positivity (TTP) of the blood culture was exceeding 24 hours, clinical parameters.

**Results:** 3591 patients were included, in 41 (1.1%) patients the blood culture showed growth of a pathogenic microorganism. TTP (time between ordering the blood culture and the positive signal in the laboratory information system) had a median of 17.1 hours (range 8.5-44). Seven patients (17%) had a TTP more than 24 hours (range 24.01-44), of which six patients had a CRP >10mg/L and/or were clinically ill. One patient (TTP 29.7 hours) was not clinically ill nor had a raised CRP.

**Conclusions:** Early prediction of the absence of a culture proven sepsis in neonates would significantly reduce the time of hospitalization and antibiotic treatment. A small proportion of patients has blood culture proven sepsis with TTP >24 hours without clinical signs of infection and a normal CRP. Further research is needed to avoid missing blood culture proven sepsis at 24 hours in these children.
Background: We aimed to determine the prevalence of pneumococcal nasopharyngeal colonisation (PNC) and to identify the pneumococcal serotypes circulating among Bhutanese children hospitalised with WHO-defined pneumonia, before the introduction of the pneumococcal conjugate vaccine (PCV13) in the country. We also aimed to contribute to the understanding of the interplay between PNC and viral co-infection among this population.

Methods: During 12 consecutive months, we prospectively enrolled children between two and 59 months of age who were admitted with WHO-defined clinical pneumonia to the National Referral Hospital in Bhutan. We collected blood for bacterial culture and molecular identification of *Streptococcus pneumoniae* in dried blood spot, and nasopharyngeal washing for detection of respiratory viruses and for detection, quantification and capsular typing of *S. pneumoniae* by real-time polymerase chain reaction.

Results: We enrolled 189 children. Of the nasopharyngeal samples so far analysed, PNC was found in 64/104 children (61.5%). *S. pneumoniae* was identified in blood in one child (both by culture and molecular methods). Respiratory viruses were detected in a similar proportion among children with (52/60; 86.7%) and without PNC (31/35; 88.6%), but rhinovirus detection was less common among children with PNC (26.7% versus 51.4%; p=0.015). Capsular typing identified 31 different serotypes. Over half of the children (35/64; 54.7%) were colonised with two to five serotypes, and a third (20/64; 31.3%) presented with highly invasive serotypes. Half of the children (33/64; 51.6%) presented with at least one serotype included in PCV13. Infants, high C-reactive protein, high erythrocyte sedimentation rate, and poor prognosis showed a trend towards association with higher nasopharyngeal pneumococcal load.

Conclusions: PCV13 covers at least one serotype of half of the children in this study, suggesting a role for the vaccine to reduce the burden associated with *S. pneumoniae*.

Clinical Trial Registration: Clinical trial registration: N/A
Background: The Coalition for Epidemic Preparedness Innovations (CEPI) is funding multiple candidate vaccine platforms against Lassa Fever, MERS, Chikungunya, Nipah and Rift Valley Fever, nCoV-2019 and Disease X. Harmonized assessment of adverse events across the CEPI portfolio will facilitate identification of relevant safety issues, as safety signals may be missed in individual small trials. CEPI funded the SPEAC project through the Brighton Collaboration to monitor safety of CEPI funded vaccines.

Methods: SPEAC’s work is divided in 4 areas: (1) providing vaccine safety experts for individual study Data Safety Monitoring Boards (DSMB) and implementing a meta-DSMB to oversee safety across studies; (2) providing tools and guidance documents for safety assessment; (3) evaluating use and applicability of SPEAC outputs; and (4) scientific coordination and review of protocols, and communicating with CEPI, vaccine developers, and other stakeholders.

Results: SPEAC is operational and created a meta-DSMB with 12 members; a charter for the meta-DSMB and a pool of 30 potential members for study DSMBs. In the area of tools and guidance lists of AESI for Lassa Fever and MERS were created, existing BC tools were put online; and a new BC definition was created for sensorineural hearing loss. In the area of evaluation a systematic review of use of BC definitions was conducted. In the fourth area relationships and collaboration were built with the different CEPI funded vaccine developers for Lassa Fever and MERS.

Conclusions: Through the SPEAC project the Brighton Collaboration has the unique opportunity to harmonize safety assessment for CEPI funded vaccines. The processes which were developed around Lassa Fever and MERS vaccines will be extended and scaled up to include Nipah virus, Chikungunya, Rift Valley Fever, nCoV-2019 and other CEPI priority pathogens in the future.

Clinical Trial Registration: ClinicalTRials.gov 0000000
NON-SPECIFIC EFFECTS OF MMR VACCINATION ON GP CONSULTATIONS FOR INFECTION

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Background: Non-specific effects of vaccines are effects of a vaccine beyond their intended target pathogen or disease. We investigated the risk of infection-related general practitioner (GP) consultations following receipt of the live-attenuated MMR vaccine versus an inactivated DTP-containing vaccine as most recent vaccine in the Netherlands, where a DTP-containing vaccine is given at 2-3-4-11 months and MMR at 14 months of age. We linked vaccination data of children born between 2005 and 2011 to the NIVEL-primary-care-database, covering 4-10% of the Dutch population.

Methods: We followed children from their third DTP-containing vaccine until two years of age for GP consultations for infections or for injuries or poisoning (negative control outcome). Andersen-Gill Cox regression was performed with age as timescale and the 'most recent vaccine received' as time-varying exposure. Adjustment was made for sex, chronic diseases before baseline, birth weight, gestational age, maternal age and parity, parental country of birth and analyses were stratified by date of birth.

Results: Among 18763 children, having had MMR (+MenC) as the most recent vaccination compared with the fourth DTP-containing vaccine (+PCV) was associated with a lower rate of infection-related GP consultations (HazardRatio:0.86;95%CI:0.81-0.92)). The fourth compared with the third DTP-containing vaccine as most recent vaccination was also associated with a lower rate of infection-related GP consultations (HR:0.90;0.84-0.96)). The HRs for GP consultations for injuries or poisoning were 1.13 (0.90-1.42) and 0.92 (0.70-1.21), respectively.

Conclusions: Lower rates of infection-related GP consultations were found after the last-received vaccine, both for MMR and DTP-containing vaccine. Although less pronounced, these results are in line with our earlier study on non-specific effects of MMR in relation to hospital admissions for infections. Like in our earlier study, healthy vaccinee bias may partly explain these lower rates.
PREVALENCE OF ACUTE BACTERIAL MENINGITIS IN NEONATES WITH URINARY TRACT INFECTION. A MULTICENTER RETROSPECTIVE DESCRIPTIVE STUDY.

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¹Hospital Sant Joan de Reus, Paediatrics, Reus, Spain, ²Hospital Joan XXIII, Paediatrics, Tarragona, Spain

**Background:** Urinary tract infection (UTI) is the most common bacterial infection in neonates and infants. Neonates have a higher risk of developing acute bacterial meningitis (ABM) due to their immunological immaturity. Despite this, there is controversy about the need to perform lumbar puncture (LP) in infants with suspected UTI and there are important differences in usual practice. The primary objective is to describe the frequency of concomitant bacterial meningitis in neonates with UTI, diagnosed in 2 hospitals in southern Catalonia (Spain) in the last ten years.

**Methods:** Retrospective descriptive study with data obtained from 2 reference hospitals in the province of Tarragona (Spain) of neonates (< 30 days) diagnosed of UTI between 2010 and 2018 in the emergency departments of both hospitals. Confirmed ABM was defined as bacterial growth in cerebrospinal fluid (CSF) and probable in case of pleocytosis (> 25 leukocytes/mm3) without culture positivity.

**Results:** A total of 61 infants with UTI were included. The average age was 18.8 days (SD 7.3); 77% males. Fever was the most frequent reason for consultation (75.4%). *E.coli* was the microorganism predominantly found in urine culture (77%). 7 of the cases developed bacteremia (11.4%). No neonate (0%, 95% CI: 0-0.26%) met criteria for confirmed ABM and 1 (1.9%; 95% CI: 0-5.3%) for probable ABM.

**Conclusions:** The results obtained are consistent with previous studies. The frequency of ABM in neonates with UTI is low but, at the moment, it cannot be considered insignificant. The realization of LP would be the safest strategy, but it is a procedure that is not without complications. Prospective studies should be carried out with larger samples that allow limiting their performance to those cases with significant risk of presenting ABM.
THE UNUSUAL CASE OF COMORBIDITY OF BRUCELLOSIS, ANKYLOSING SPONDYLITIS AND FAMILIAL MEDITERRANEAN FEVER

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Title of Case(s): THE UNUSUAL CASE OF COMORBIDITY OF BRUCELLOSIS, ANKYLOSING SPONDYLITIS AND FAMILIAL MEDITERRANEAN FEVER

Background: Comorbidity is the presence of one or more additional diseases or disorders co-occurring with (that is, concomitant or concurrent with) a primary disease or disorder. There are several diseases that produce strikingly similar symptoms. Thus, confirmation of one disease cannot exclude others with the similar symptoms. This report describes a rare case of comorbidity of Brucellosis, Ankylosing Spondylitis(AS) and Familiar Mediterranean Fever(FMF).

Case Presentation Summary: A 30-years old man presented to the infectious hospital with the following complaints: cervical and lumbar pain, fever, myalgia, arthralgia, chills and shivering for the last month. Past medical history relieved periodic episodes of fever and pain in joints and muscles since 17. At 27 he was diagnosed with AS(HLA-B27- positive and Sacroiliitis in MRI) and received appropriate treatment. The reaction of the Wright-Hedelson - 1:800, Brucellosis IgM - positive, IgG – negative. Ultrasound showed splenomegaly(spleen-14.1cm)and MRI of cervical and lumbar part of spine – spondylitis and bilateral sacroiliitis. The diagnosis of acute brucellosis was confirmed and treatment including Doxycycline and Rifampicin was started. Three months later patient still had periodically repeating episodes of arthralgia and fever despite the ongoing treatment. Considering aforementioned complaints, MEFV-gene analysis for FMF was performed. Diagnosis was confirmed and Colchicine was initiated. The follow-up period was 6 months, which showed improvement of general condition. Wright-Hedelson 1:100 and Brucellosis IgM - negative, IgG – positive.

Learning Points/Discussion: This case is a remarkable example of a missed diagnosis of FMF, which could have been diagnosed since the age of 17. We should take into account that the disease can rarely occur beyond the age of 20 years. Existence of one disorder/disease does not rule out others. This case report demonstrated that different diseases can be masked under the similar symptoms.
A CASE OF BRUCELLOSIS IN A 1.5-YEAR-OLD GIRL

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Title of Case(s): A CASE OF BRUCELLOSIS IN A 1.5-YEAR-OLD GIRL

Background: Despite being long recognized and controllable disease brucellosis remains one of the most common bacterial zoonotic infection in many countries worldwide, including Armenia. All age groups are susceptible to human brucellosis, which can cause severely debilitating and disabling illness. Brucellosis may be more common in children in developing countries due to lack of pasteurization of milk. Breastfeeding is the best choice for a newborn.

Case Presentation Summary: A 1.5-years-old child presented to “Nork” Infectious Hospital with febrile temperature and difficulties to walk. During last 1.5 moth child had 4 episodes of febrile temperature lasting 5-10 days. During the last episode of temperature parents noticed difficulties to walk. From 7 months old the child started to consume unpasteurized milk. Family history: mother is on a treatment for Familial Mediterranean Fever (FMF). Physical examination: hepatosplenomegaly, enlargement of cervical lymph nodes, painful and swollen right knee. Laboratory findings: WBC ` normal, ESR ` 30mm/hr, CRP 14.7 mg/L, RF, TB, EBV` negative. Testing for FMF showed single heterozygote mutation in recessive MEFV gene. Agglutination test and IgM, IgG for Brucellosis were positive. Ultrasound: hepatosplenomegaly, enlargement of cervical, inguinal, axillary and supraclavicular lymph nodes up to 1.5cm. Chest X-Ray: normal. Diagnosis of Brucellosis was confirmed and the treatment with Gentamicin, Trimethoprim-Sulphamethoxazole, Ibuprofen was initiated. Child was recovered after 14 days of the treatment.

Learning Points/Discussion: Breastfeeding is the cornerstone for healthy growth and development of infants. Infants younger than 1 year old should be breastfed or use the formula if breastfeeding is impossible. Unpasteurized milk and milk products must be excluded from use not only for infants. The best way to prevent brucellosis infection in elderly population is do not consume undercooked meat or unpasteurized dairy products.
MENINGOENCEPHALITIS ASSOCIATED WITH MYCOPLASMA PNEUMONIAE INFECTION

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Title of Case(s): MENINGOENCEPHALITIS ASSOCIATED WITH MYCOPLASMA PNEUMONIAE INFECTION

Background: Mycoplasma Pneumoniae is a frequent cause of respiratory tract disease mainly in school-age children. Less commonly, it can be the cause of extrapulmonary disease with respiratory symptoms or independently. Central nervous system (CNS) disease affects approximately 0.1% of all patients and approximately 6% of hospitalizations associated with M. pneumoniae infections. We present a rare case of M. pneumoniae meningoencephalitis in a child.

Case Presentation Summary: A 6-year-old previously healthy boy was referred to our hospital with a 10-days history of headache, accompanied by vomiting and low grade fever. He also had an transient episode of paresis (left extremities and right facial nerve). An MRI/ MRA/ MRV turned out to be normal. A Lumbar puncture (LP) revealed 27 WBCs/μl with normal glucose. The electroencephalogram revealed focal slowing over the Rt occipital parietal area. The patient was initiated on intravenous Cefotaxime and acyclovir. Culture, serology and molecular studies did not detect usual bacteria or viruses in the CSF or blood. Autoantibodies were negative. Because of the persistence of symptoms, a second LP was performed which continued to have increased WBCs 90/μl. On the 13th day of hospitalization the IgG and IgM antibodies in the blood were strongly positive against Mycoplasma pneumoniae. Therefore intravenous doxycycline was started and the patient became completely free of symptoms within 48 hours. He was discharged after 14 days of doxycycline.

Learning Points/Discussion: M. pneumoniae should be considered in the differential diagnosis of persistent fever and findings compatible with CNS infection especially if no other pathogens can be detected. Treatment should include antimicrobials active against Mycoplasmas which can penetrate the Blood Brain Barrier and also achieve therapeutic levels within the brain parenchyma, such as the doxycycline and the newer quinolones such as levofloxacin.
Background: In this era of antimicrobial-resistance it has become essential quickly identify a serious bacterial infection (SBI) for early initiation of therapy as well as to prevent unnecessary use of antibiotics. The high cost added to its poor yield limits its use in resource limited settings. We investigated the role of four clinical and lab parameters in diagnosing SBI early in its course.

Methods: A prospective study, enrolled children who presented with history of acute fever. The general appearance and grade of fever were noted. All children were investigated for C-reactive protein (CRP), absolute neutrophil count (ANC) and investigations specific to the suspected infection. A SBI was identified if the child had a positive blood/urine/CSF culture, a CSF routine suggestive of bacterial meningitis, X-ray findings of pneumonia, osteomyelitis or deep seated pus.

Results: Of 95 children enrolled in the study 37 (38%) had SBI. Grade of fever (OR=7.7, 95% CI=3.3-19, p<0.001) had the strongest association with the presence of a SBI. Other parameters which were strong predictors of SBI included CRP >60 (OR=5.52, 95% CI=1.3-22.0, p=0.01) and high ANC (OR=2.7, 95% CI=1.1-6.3, p=0.02). The assessment of general appearance correlated poorly (OR=1.5, 95% CI=0.6-3.6, p=0.2) with the presence of a SBI. Three or more of the above parameters being positive had a negative predictive value of 80% (95% CI=69%-87%) and a positive predictive value of 56% (95% CI=46.2%-66.4%).

Conclusions: Grade of fever and CRP>60 seem to be the strongest predictors of SBI. Combining three or more of routinely performed clinical and lab parameters may help in effectively ruling out a bacterial infection and thus avoid unnecessary antibiotics. However, considering the poor yield of a culture it is essential to have a rapid, affordable test that can help rule in serious bacterial infections to prevent delay in appropriate therapy.
OPTIMISING ANTIMICROBIAL DOSING AT THE POINT OF CARE: A PROOF OF CONCEPT STUDY USING MID-INFRARED SPECTROSCOPY

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Background: To optimise antimicrobial dosing, there is a need to develop minimally invasive bioanalytical techniques for drug level detection in children. Antimicrobials are some of the most commonly prescribed medications in children yet there is limited data on optimal dosing. Suboptimal dosing may lead to under-treatment and the development of AMR. One promising method is Mid-Infrared Absorption Spectroscopy (MAS). This technique allows for label-free detection of medications in biological fluids through the characterisation of molecular bond vibrations. Rapid analysis can be performed directly in urine or whole blood without any further processing and requires sub-millilitre volumes. This could facilitate gathering accurate dosing data using micro-sampling methods at the point of care.

Methods: Amoxicillin was serially diluted in urine for clinically relevant concentrations of 50 – 5000 µg/ml, and in whole blood for concentrations of 5 – 500 µg/ml. MAS was performed using 600 µl of each sample with an Agilent FTIR spectrometer and ATR attachment in the range 400 – 6000 cm⁻¹.

Results: The lower limit of detection (LLOD) for amoxicillin in urine was 50 µg/ml, which is below the expected range of 84 – 3900 µg/ml in the 6 hours following a dose in paediatric patients. The LLOD in whole blood was 10 µg/ml. This is below the mean peak plasma concentration of 12 µg/ml in adults given 1000 mg doses orally and 10.5 µg/ml in children given 25 mg/kg doses orally. The concentration response was linear for blood and urine.

Conclusions: MAS can be used to detect medications in biological fluids at clinically useful levels. Further bioanalytical work will analyse the validity of the technique against international guidelines and parallel engineering work will investigate microfluidic extraction methods for improving the LLOD and sample volume requirements.

Clinical Trial Registration: Not applicable
A CASE OF MONOARTHRITIS WITH VZV

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Title of Case(s): A case of monoarthritis with VZV

Background: Nonbacterial acute arthritis, usually monoarthritis of the knee, is a rare complication of varicella (chicken pox) in children, which occurs in the early days of the exanthem. The age range of aseptic varicella arthritis in immunocompetent healthy children with no risk factors is between 1.5 to 10 years. VZV can be isolated from synovial fluid performing PCR, which will identify viral DNA in synovial fluid of individuals with suspected varicella arthritis.

Case Presentation Summary: We describe a case of an 8 years old girl who developed acute monoarthritis of the left knee on the second day after the onset of the VZV rash. She presented with a 48 hour history of mild popular-vesicular eruption on the trunk and subfebrile temperature. She had difficult and quite uncomfortable walk due to a painful, tender, hot and swollen left knee. There was no history of previous injury or arthritis. US and R-graphia showed enlargement of the left knee synovial space due to a large amount of fluid. The ERS and WBC were normal, CRP’ 48mg/L. Treatment was included: Acyclovir, Ceftriaxone and Metronidazole. The vesicular rash resolved over seven days and the knee joint swelling resolved during ten days.

Learning Points/Discussion: VZV PCR testing of joint synovial fluid can be beneficial in distinguishing viral from bacterial associated arthritis, which can be valuable in determining appropriate patient management. Differential diagnosis of aseptic arthritis from septic arthritis will minimize unnecessary usage of antibacterial therapy. Besides, early diagnosis of VZV would raise the question of using acyclovir to shorten the duration of the arthritis.
Title of Case(s): Case Series of Acute Respiratory Viral Infections in Pediatric Cancer Patients in Armenia

Background: Immunocompromised patients remain vulnerable to respiratory infections. Diagnosis of respiratory illness in resource-limited settings is deemed important to the physician even though treatment might not be available for a specific pathogen. Molecular testing has considerably improved the diagnosis of respiratory pathogens and is being considered as the new “gold standard”. Approximately 80% of these respiratory infection cases are caused by viral pathogens. It is pivotal to obtain nasopharyngeal swabs with further PCR to identify them.

Case Presentation Summary: This case series describes four patients with upper respiratory viral infections which were developed during cancer treatment. The age range of patients varied 5.5-16 years old (1 female and 3 male patients). All four patients were undergoing chemotherapy and developed the same complaints of prolonged fever, cough and malaise. The following laboratory and imaging investigations were performed: CBC, biochemical analysis of blood, blood culture, swabs from nasopharynx and throat, rapid diagnostic tests for Influenza A, B, ultrasound, chest X-ray. Parainfluenza was positive in two cases. One of which additionally was co-infected with bacterial infection and adenovirus. Rhinovirus was identified in other two cases. One of the patients with rhinovirus also had febrile neutropenia. Therefore, antibacterial therapy was prescribed for aforementioned cases. The remaining two patients did not receive antibacterial therapy. All four patients were recovered eventually.

Learning Points/Discussion: Immunocompromised patients remain vulnerable to respiratory viral infections. In case of prolonged fever and non-specific clinical presentation of respiratory infection, especially in cancer patients, it is pivotal to timely obtain nasopharyngeal swabs for PCR. The results will facilitate the further management of these patients, and in perspective of antibacterial therapy, early results can help to avoid unneeded prescription and/or switching of antibiotics.
CAPTURE-RECAPTURE INCIDENCE OF INVASIVE PNEUMOCOCCAL DISEASE IN CHILDREN IN GERMANY, 2018-2019

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Background: Surveillance of invasive pneumococcal disease (IPD) began in Germany in 1997. There are two independent surveillance systems for IPD, one by the German Nation Reference Center for Streptococci (GNRCS) collecting cases reported by diagnostic laboratories, and one by the German Pediatric Surveillance Unit (ESPED) reporting cases from pediatric wards in hospitals. IPD will become a mandatorily reportable disease in 2020, so an incidence calculation now will provide a useful comparison point to test the impact of this surveillance system change.

Methods: We used the Lincoln-Peterson mark and recapture to calculate the incidence of IPD in German children for July 2018- June 2019. Matching of cases was based on date of culture collection, and the patients’ birth date, sex, and postal code.

Results: 178 IPD cases were identified by GNRCS; 95 by ESPED. 41 cases were matches. The resultant IPD incidence for children 0-15 years old was 3.42 per 100,000. For meningitis cases, 62 cases of IPD were identified by the GNRCS and 46 were identified by ESPED. 26 were matches, which resulted in an incidence of 0.91 cases per 100,000. For children under 2 years of age overall IPD incidence was 14.03 per 100,000 (meningitis: 3.95). For the age groups 2-4 years and 5-15 years incidences were 5.44 (1.22) and 0.81 (0.24) respectively.

Conclusions: Capture-recapture surveillance is a useful tool in health systems that do not include IPD as a reportable condition.

Clinical Trial Registration: 0123456789
INVASIVE PNEUMOCOCCAL DISEASE AMONG CHILDREN IN GERMANY, TEN YEARS AFTER PCV13 INTRODUCTION

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Background: Childhood PCV vaccination was generally recommended in Germany in 2006. In 2009, two higher-valent PCVs (PCV10, PCV13) were licensed. Here, we present data on invasive pneumococcal disease (IPD) cases following PCV introduction.

Methods: IPD in children in Germany has been monitored since 1997. Isolates were serotyped using the Neufeld Quellung reaction.

Results: In 2018-2019, the GNRCS received 102 IPD isolates from children <2 years, of which 14 had PCV13 serotypes. Two of these were from unvaccinated children, four from incompletely vaccinated children. This represents a 34% reduction compared to 2005/2006 (n=154), but an increase since 2011-2012 (n=75). However, the PCV13 proportion has decreased from 88% prior to vaccine introduction (2005-2006), to 69% at the introduction of higher-valent vaccines (2009-2010), to 14% in 2018-2019. Future vaccines PCV15 (25%) and PCV20 (46%) would increase coverage considerably. Residual PCV13 serotypes in 2018/2019 were 3 (n=5), 19F (n=4), 19A (n=2) and 6A, 14, 23F (n=1, each). Among all three age groups (0-1y, 2-4y, 5-15y), serotypes 3, 19F and 19A persist. Among non-vaccine serotypes, 10A (n=17) and 23B (n=12) were most prevalent.

Conclusions: Ten years after the introduction of higher-valent vaccines, PCV13 serotypes have been reduced among children, but serotypes 3, 19F and 19A persist. Future vaccine formulation would considerably increase serotype coverage.

Clinical Trial Registration: 0123456789
KNOWLEDGE AND PRACTICE OF PEDIATRIC NURSES IN LOW-RESOURCE SETTINGS TO ADMINISTER INTRAVENOUS MEDICATION FOR CHILDREN

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Background: Clinicians and global health leaders seem more interested than before in enhancing the capacity of nurses as an intervention to improve the quality of health care. While medication is an important element of patient care requiring adequate knowledge, skills, and judgment, administering medicines to children poses additional challenges in comparison to the adult population. We evaluated the knowledge and practice of pediatric nurses, in low-resource settings, regarding intravenous (IV) medication administration to pediatric patients.

Methods: A cross-sectional study was conducted among pediatric nurses of four hospitals. Based on the recall of definition, indication, dosage, preparation technique, and complications of IV medication, nurses' 'Knowledge Level' was categorized into inadequate(<50% of total score), moderately adequate(51-75%), adequate(>75%). Similarly, based on their performance during prescription-transcription, drug preparation, dispensing-administration, and monitoring-evaluation, 'Practice Level' was categorized into poor(<59% of total score), fair(59-79%), and good(>80%). Data were analyzed using descriptive and inferential statistics.

Results: Of 115 pediatric nurses studied, only 14(12.2%) had adequate knowledge, whereas none of them had good level and only 20(17.4%) had fair level of practice regarding IV medication administration to children. Nurses working in critical care units were more knowledgeable than those in wards and nurseries. There was a statistically significant relationship between working hours and practice level of nurses—those on >6-hour shift had a fair level whereas those working 6-hour shifts had poor practice. There was a weak negative correlation (r= -0.202) between knowledge and practice scores.

Conclusions: We report inadequate knowledge and poor practice of pediatric nurses in relation to IV medication administration to children. A high level of knowledge regarding IV medication did not guarantee good practice. As the world celebrates 2020 as the Year of Nurses, there is an urgent need to upgrade the capacity of nurses, particularly in low-resource settings, in order to improve the quality of nursing care in pediatrics.
E-POSTER VIEWING
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10-28-2020 8:00 AM - 7:00 PM

A CASE OF CAT SCRATCH DISEASE WITH EBV INFECTION IN 11 YEARS OLD GIRL

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Title of Case(s): A case of Cat Scratch Disease with EBV infection in 11 years old girl

Background: Cat scratch disease (felinosis), caused by Bartonella henselae, typically presents with a local papule, a localized lymphadenopathy and a brief period of fever. The domestic cats are a major reservoir for this gram negative bacteria. Diagnosis of the disease is clinical and confirmed by biopsy or serologic tests. DDx includes diseases with lymphadenopathy, such as tularemia, mycobacterial infection, brucellosis, Epstein-Barr virus (EBV) etc. Treatment includes analgesics and antibiotics.

Case Presentation Summary: A 11 years old girl admitted to “Arabkir” MC complaining to painful, enlarged right axillary lymph nodes, which occurred during the ten days and sub-febrile temperature for last two days. The girl has a cat, and she has many scratches on her hands. Physical examination showed enlarged and painful right axillary lymph node ~3.0 cm, cervical lymph nodes up to 1-1.5 cm. Laboratory findings: atypical lymphocytes (Downey cells) in peripheral blood smears’ 8%, EBV IgM positive, TB and Tularemia’ negative, ESR’ 22 mm/hr, CRP’ 14.5 mg/dL. Ultrasound verified enlarged right axillary lymph nodes (32*24mm and 11*9mm), splenomegaly (103*32mm). Diagnosis: EBV, Cat scratch disease? Treatment: azithromycin (7 days), ibuprofen. The patient was recovered and discharged on seventh day of the treatment.

Learning Points/Discussion: Although, EBV usually is associated with lymphadenitis, other infections should also be considered for differential diagnosis in patients with lymphadenopathy. Cat scratch disease is one of those infections that should be taken into account in these patients. The essential role for diagnosis of felinosis is detailed history, which includes contact with cats, especially scratches or bites. We should keep in mind, that confirmation of one infection does not exclude others.
CHILDREN IN INTERNALLY DISPLACED PEOPLES' CAMPS: EXPERIENCE OF PEDIATRICIANS IN MAIDUGURI, BORNO STATE, NORTH-EAST NIGERIA.

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Background: The North East zone of Nigeria has suffered severe humanitarian crisis due to Boko Haram insurgency. This has led to many deaths, and displacement of persons, exposing them to various socioeconomic and health challenges. The most vulnerable groups, being women and children. Borno state being the most affected has 1,606,406. Out of this, 1,100,000 (54%) are Children. The study attempts to identify the problems of children living in the internally displaced persons' (IDP) camps, in Maiduguri, Borno state capital.

Methods: Three of the 11 IDP camps in Maiduguri, the Borno State capital were visited twice weekly over a period of four months. We supported the existing health services by providing medical expertise and essential drugs. The socio-demographic characteristics, nutritional status and the pattern of illnesses among the children were assessed. Psychosocial problems and the living conditions of the children were noted.

Results: A total of 380 children were assessed. There were 226 males and 154 females (M: F ratio of 1:1.5). 202 (53.2%) were <5 years old. Fourteen (7.2 %) of the under five children had severe acute malnutrition (WHZ <-3SD) and 22 (5.8 %) had severe wasting (WAZ <-3SD), while 8 (2%) were stunted (HAZ<-3SD). Other problems identified were infections (ARI, skin infections, Malaria, Diarrheal disease, Helminthic infestations, poor living conditions, poor state of health facilities, psychosocial problems including child abuse, and poverty.

Conclusions: Insurgency has had and is still having devastating effects on children. Displaced children are facing serious health, psychosocial and economic challenges. Malnutrition and associated infections especially respiratory and gastrointestinal were commonly observed among the children. Gastrointestinal and urinary Helminthic infections were also observed, resulting in routine deworming of all the children with albendazole. Child abuse and other negative social behaviours were also observed.
CAN RESPIRATORY Syncytial VIRUS (RSV) PROPHYLAXIS BE COST-EFFECTIVE? A LITERATURE REVIEW

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Background and Objective: Respiratory syncytial virus (RSV) results in a substantial economic burden worldwide. The cost-effectiveness of existing and expected RSV-interventions is important for policy-making. This review aims to identify the key parameters in the economic evaluations of RSV-interventions among <5-year-old children.

Methods: A search was conducted in PubMed for the time period 2010 to 2019. Search terms included: RSV, orthopneumovirus, cost-utility, cost-effective, cost-benefit, economic evaluation and budget impact analysis. Case reports, trials, reviews and studies without reporting input parameters were excluded. Two independent reviewers performed screening and extraction.

Learning Points/Discussion: The searches yielded 121 citations, of which 26 were retained, geographically from Europe(n=12), North America(n=12), Israel(n=1) and Turkey(n=1). Most(23/26) analyses focused on palivizumab in various high-risk populations; only 3 assessed the cost-effectiveness of hypothetical RSV interventions in a general birth cohort. Our review shows: 1. Hospitalisation rate, the interventions’ cost and efficacy, and the discount rate were generally the most influential parameters. 2. Seven studies included RSV-associated ambulatory and/or emergency visits. Twenty-four studies reported hospitalisation rates showing differences between countries and risk-groups, but ICU admission and mortality rates were reported in only 8 and 14 studies, respectively. 3. Most studies ignored RSV-related wheezing and asthma (included in 5 and 6 studies, respectively). 4. Among palivizumab studies, one used Disability-Adjusted-Life-Years and 6 used a baseline Quality-Adjusted-Life-Year (QALY) value of 0.95 for high-risk children versus 0.88 for hospitalised children. Disutility value (QALY) of 0.01 (outpatients) and 0.4 (hospitalisation) were applied in 2 studies using birth cohort. Only one study considered a QALY impact on caregivers (disutility 0.07), although 14 studies accounted for productivity loss. RSV-associated ambulatory visits and ICU admissions for both high-risk and general populations are crucial to obtain. Further research on quality-of-life is also important.
PORTUGAL DISTINCT FROM MOST EUROPEAN COUNTRIES: INFLUENZA B DOMINANCE IN THE 2019/2020 FLU SEASON

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Background: According to the joint ECDC-WHO/Europe weekly influenza update regarding 2019/2020 flu season, type A viruses have dominated across the European Region (67% of all positive-tests). On the contrary, in Portugal, type B viruses accounted for 66% of all influenza-positive tests reported (INSA). In the last 5 flu seasons (2014/15-2018/19) there was a clear type A dominance in our paediatric hospital, with type B representing <30% of the positive-tests.

Methods: Description of the 2019/20 flu season in a tertiary pediatric hospital in central Portugal. This is a retrospective analysis of all confirmed influenza cases, detected by PCR in nasopharyngeal swabs from symptomatic children, from October 1st 2019 to January 16th 2020. The analysis included 114 positive tests, 99 (87%) with influenza B. The results were compared to the previous 5 flu seasons in the same hospital: 70% type A, median age 3.4Y, 38% admitted (median length of stay 5D).

Results: The median age of the all group was 6.7Y (1M-17Y), for B cases was 7.3Y and for A was 3.4Y. The highest number of cases occurred between weeks 47-51/2019. Influenza A cases started in week 52. 20% were admitted to the hospital, of whom 74% had no risk factors, with a median duration of stay of 2D (1-8D). There were complications 21%, with myositis being the most common (9, highest CPK=14716U/L), followed by pneumonia (6), acute otitis media and encephalitis (3 each). 19% had a suspected bacterial co-infection. There were no deaths.

Conclusions: Despite the dominance of type A viruses across the European Region in the 2019/2020 season, in our county and in our hospital there was a clear dominance of influenza virus type B, a different pattern from the previous 5 flu seasons. Influenza B started early in the season, affected mostly older healthy children and is currently being replaced by type A.
SINGLE CENTER EXPERIENCE WITH VISCERAL LEISHMANIASIS IN A NON ENDEMIC AREA IN BRAZIL

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Title of Case(s): Single center experience with visceral leishmaniasis in a non endemic area in Brazil

Background: Visceral Leishmaniasis (VL) is a severe and disseminated protozoan infection considered endemic in Brazil. It is heterogeneously distributed in the territory and the city of São Paulo is a non-endemic area, where all cases come from other regions. This case series describes a single center experience with VL in a pediatric tertiary hospital in São Paulo from December 1999 to September 2017.

Case Presentation Summary: We found 33 children with VL in our hospital. Median age was 3 years-old. Median time to diagnosis was 21 days and average length of stay was 36.7 days. Main symptoms were fever (97%), splenomegaly (96%) and hepatomegaly (91%). Other manifestations were abdominal pain, cough, jaundice, diarrhea and vomiting. All patients performed a complete blood count. Anemia was present in 97%, thrombocytopenia in 79% and leukocyte count below 5,000 in 79%. Regarding the diagnosis, 58% of cases were confirmed with direct microscopy in bone marrow aspirates, 21% with antigen-test rK39 and 21% with other serologic tests. The drug choice for treatment was amphotericin-B in 60% of cases and pentavalent-antimonial in 36.3%. Data on treatment was missing for one patient. Complications were present in most cases: bacterial infections in 87% and acute kidney injury in 12%. Two infants younger than 1-year-old died from acute hepatic and kidney failure and one patient developed stage 1 chronic kidney disease.

Learning Points/Discussion: VL should always be considered in the differential diagnosis of patients presenting with fever, hepatosplenomegaly and peripheral blood cytopenias. The use of the rK39 test can improve diagnosis as it is a less invasive method than bone marrow aspirate. Our cases confirm the literature observation that mortality in leishmaniasis is related to age younger than 1-year-old and acute renal injury.
MULTIPLE PULMONARY CAVITARY LESIONS IN AN ADOLESCENT BOY IS NOT ALWAYS RELATED WITH INFECTION

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Title of Case(s): Multiple pulmonary cavitary lesions in an adolescent boy is not always related with infection

Background: Cavitary lesions in the lung often suggest infectious diseases such as necrotizing pneumonia, tuberculosis, hydatid cyst disease or invasive fungal infections in immunocompromised patients. However, primary pulmonary malignancies or metastasis can be rarely presented with multiple cavitary lung lesions in childhood. Herein we reported a rare case with dyskeratosis congenita who had squamous cell carcinoma both in mandibula and presented multiple metastatic cavitary lesions in lungs.

Case Presentation Summary: A 17-year-old boy was diagnosed with squamous cell carcinoma originating from the left mandible and operated 1 year ago. He admitted to hospital for complaints of acute chest pain and cough. His general condition was good but he had hyperkeratosis of palms and soles, nail dystrophy and mild dyspnea. Laboratory findings were normal instead of anemia and elevated acute phase reactants. Bilateral pneumothorax was seen on the chest X-ray. Thorax CT showed multiple pulmonary cavitary lesions (Figure 1). Antibiotic therapy was started. Acid-fast stain and tuberculosis PCR were negative in sputums and pleural fluid. Lung biopsy from the cavitary lesion resulted in squamous cell carcinoma. The patient died 2 weeks after admission to the intensive care unit. In the genetic analysis of the case, homozygous mutations were detected in Grainyhead-Like 2 (GRHL2) and endothelin receptor type B (EDNRB) genes which may cause ectodermal dysplasia and squamous cancer in the mandibula and lungs.
Learning Points/Discussion: We firstly reported an adolescent boy with both homozygous mutation with GRHL2 and EDNRB presented with multiple pulmonary cavitary lesions and multifocal squamous cell carcinoma. The history, the physical examination and radiological findings of the case should be carefully evaluated and it should be kept in mind that, pulmonary malignancies may appear with a similar clinical picture rarely seen in pediatric ages.
A SUSPECTED CASE OF MENINGOCOCCAEMIA WITH GANGRENE IN A RESOURCE-POOR SETTING

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Title of Case(s): A case of an acutely ill child with gangrene of the lower limbs in a resource-poor setting

Background: Meningococcaemia is a severe form of infection with *N. meningitides*. The protean manifestation of the disease sometimes leads to delay in presentation in Sub-saharan Africa with an attendant trial of over the counter and alternative medications. This usually results in difficulties in identifying the offending organism. We report a suspected case of meningococcaemia associated with gangrene of the digit and feet.

Case Presentation Summary: A 9-year-old boy presented during the dry, harmattan period with fever and neck stiffness of 4 days’ duration, skin rash of 3 days’ duration and darkish discolouration of the feet of 2 days’ duration. The child sleeps in a poorly ventilated room with five of his sibs. Vaccination and recent travel history were absent. He was acutely ill-looking, febrile, (axillary temp 38.9°C) moderately pale with multiple non-blanching ecchymotic and purpuric skin lesions. The lower limbs were cold, tender with dry gangrene of both feet. Dorsalis paedis arterial pulsation was absent. He received multiple over the counter antibiotics and traditional medication at home with no clinical improvement. Meningococcaemiawas was suspected with gangrene of the feet. Cerebrospinal fluid(CSF) and blood cultures were negative, Low CSF glucose raised protein concentration. Grams stain - negative. Blood count showed raised granulocytes. He had ceftriaxone, daily antiseptic bath, anticoagulant and wound dressing with honey/povidone-iodine. He improved clinically with the gangrenous limb slowly demarcated awaiting amputation.

Learning Points/Discussion: - The indiscriminate use of antibiotics before sample collection leads to difficulties in the identification of the offending organism. This was the case in our patient who had multiple over the counter medications. Irrational use of antibiotics can lead to drug resistance -Educating the populace on the protean manifestation of meningococcal disease in sub-Saharan Africa can reduce delay in presentation.
SALIVA FOR MONITORING CYTOMEGALOVIRUS REACTIVATION IN HEMATOPOIETIC STEM CELL TRANSPLANTED CHILDREN

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Background: Cytomegalovirus (CMV) is the most common complication after hematopoietic stem cell transplantation (HSCT) with significant mortality. Monitoring of CMV reactivation after HSCT is based on the detection of viral DNA in blood samples. Invasiveness of blood collection and the low sensitivity of the test, make blood not adequate for routine monitoring. This study aims to evaluate the usefulness of saliva samples for the diagnosis and monitoring of Cytomegalovirus reactivation in HSCT patients attended at the National Institute of Child Health in Lima-Peru.

Methods: Saliva samples were collected twice a week after transplantation, by (i) swabbing the inside of the mouth with a synthetic swab (saliva swab) and (ii) aspirating the saliva accumulated under the tongue (liquid saliva). A total of 50 paired saliva samples were tested for CMV by qPCR targeting the UL-97 gene. Routine qPCR in blood was assessed using GeneProof Cytomegalovirus PCR Kit. Viral load on saliva and blood samples were compared using Kruskal-Wallis on STATA.

Results: A total of 18 children, candidates for HSCT, were included in the study. Eight underwent allogenic HSCT and received ganciclovir 5 mg/kg-body weight b.i.d for 10 to 14 days, previous to transplantation. All donors and recipients tested positive for anti-CMV IgG. Three children had at least one positive qPCR either in saliva or blood, out of a total of 15 paired samples (blood, saliva and swab). Among those samples, 4 showed negative results in blood, but were positive in saliva. Higher viral loads were observed in liquid saliva (19366 copies/ml) than in saliva swab (12006 copies/ml, P=0.004).

Conclusions: Saliva is easy and rapid to obtain in a non-invasive and painless way and seems to be useful for monitoring of Cytomegalovirus reactivation after HSCT.

Clinical Trial Registration: National Fund for Scientific, Technological, and Technological Innovation Development (FONDECYT), Contract N° 107-2018-FONDECYT-DE
A RARE COMPLICATION AFTER A DEEP NECK INFECTION OPERATION: MARGINAL MANDIBULAR PARALYSIS

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Title of Case(s): A rare complication after a deep neck infection operation: Marginal mandibular paralysis

Background: The marginal mandibular branch (MMB) of the facial nerve provides lower lip symmetry during a human smile or cry. The most frequent cause of paralysis of this nerve is an iatrogenic injury during operations. It is a rare complication and the number of pediatric cases reported is very low. We report a MMB paralysis in an infant after surgery for a deep neck infection.

Case Presentation Summary: One-year-old boy admitted to the clinic due to fever and neck swelling. Five days ago, fever and upper respiratory infection symptoms were started and he was referred to our center because of the persistent fever and development of swelling in the cervical region despite antibiotic therapy. On physical examination, there was a sensitive mass of 2 cm in diameter in the right submandibular cervical region. Ceftriaxone and clindamycin were started. On the contrast-enhanced cervical MR imaging, there was an abscess extending from the right submental region. The abscess was evacuated by the ear-nose-throat department. No pathogen identified from the cultures. On the second day after the operation, we saw an elevation of the lower lip of the right side results during especially crying. Isolated paralysis of the MMB was diagnosed. Steroid and B12 vitamin therapy were started and antibiotic treatment completed for 14 days. The paralysis gradually decreased within 3 months. No recurrent infection was observed during the 6-month follow-up.
Learning Points/Discussion: The marginal mandibular nerve may be injured during surgery in the neck region. An injury to this nerve during a surgical procedure can distort the expression of the smile as well as other facial expressions. It is a non-infectious complication of surgery and conservative treatment can be a choose. Some patients' paralysis can resolve completely without any additional surgical intervention.
Background: Immunization is the most cost-effective and highest-impact health intervention which reduces hospitalization, treatment costs and mortality. However, despite the success of immunization programs, many vaccine-preventable diseases have remained prevalent in developing countries. One factor is parental practice regarding vaccination since parental decisions regarding immunization are important for increasing the immunization rate and compliance and for decreasing any possible immunization errors.

Methods: This study employed a prospective cross-sectional analytical approach to determine the knowledge, attitudes, and practices of mothers regarding childhood immunization. Mothers answered a questionnaire based from validated questionnaires. Data was encoded in SPSS version 10. Descriptive statistics were generated. For nominal data, frequencies and percentages were computed. For numerical data, ± SD were generated. Analysis of the different variables were done using ANOVA and Kruskal Wallis test.

Results: 54% of the mothers had fully immunized children. The top reason for failure of immunization was fear of side effects. The mothers’ scores on knowledge were significantly higher with increasing age of parents, education status of parents, and family annual income. The mothers’ scores on attitude were significantly more positive with increasing age, education status, and family annual income. Both knowledge and attitude scores were significantly highest among those with fully immunized children, while the lowest scores were among those not immunized.

Conclusions: Many children die from vaccine preventable diseases globally, and one of the reasons for vaccine failure is parental practices. There is a significant association between the knowledge and attitudes of mothers on getting their child immunized. There are both increased knowledge and better attitude on immunization for mothers with older age, higher education status, and higher family income; which in turn leads to positive practices on getting their children immunized.
RISK FACTORS FOR ANTIBIOTIC USE AMONG HOSPITALIZED CHILDREN WITH PNEUMONIA IN JAPAN

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\textbf{Background:} Viruses are the main cause of acute respiratory tract infection, even in children hospitalized for pneumonia. Recommendations for community-acquired pneumonia suggest the use of antibiotics in all children admitted with pneumonia. However, confirmation of the causative organism of paediatric pneumonia is often difficult. There are no studies evaluating factors of antibiotics prescription for pneumonia among hospitalized children. Here, we aimed to evaluate the factors influencing antibiotic prescription for pneumonia at a tertiary children’s hospital.

\textbf{Methods:} We retrospectively assessed patients diagnosed with pneumonia at discharge between January 2017 and June 2019. We excluded patients who were transferred to other hospitals. We retrieved the following data from electronic medical records: the history of patients’ illness, physical examination findings, laboratory data, and length of hospital stay. Demographics and characteristics of patients were compared based on whether or not antibiotics were prescribed.

\textbf{Results:} Antibiotics was prescribed for 78 (56\%) of the 140 enrolled children. Multivariate analysis revealed that the co-existence of acute otitis media (AOM) (OR 7.65; 95\%CI 1.70 to 34.50) and higher C-reactive protein\textsuperscript{[A1]} (OR 1.52; 95\% CI 1.26 to 1.83) were significantly associated with antibiotics prescription, whereas wheezes on physical examination (OR 0.89; 95\% CI 0.29 to 2.71) and positive rapid antigen test (OR 0.55; 95\% CI 0.22 to 1.37) were negatively associated.

\textbf{Conclusions:} This is the first study to examine the factors influencing antibiotic prescription for hospitalized children with pneumonia. The concomitance of AOM was the most significant factor associated with antibiotic-prescription. However, the eardrum was evaluated only in 59\% of the patients in this cohort. Routine eardrum examination is critical to determine whether the prescribed antibiotic is appropriate, even when pneumonia has been diagnosed.
IMMUNOGENICITY AND SAFETY OF ONE HEXAVALENT DTaP-IPV-HB-PRP~T COMBINED VACCINE IN HIV-INFECTED AND HIV-EXPOSED UNINFECTED INFANTS IN REPUBLIC OF SOUTH AFRICA (RSA).

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Background: DTaP-IPV-HB-PRP~T Sanofi Pasteur vaccine (Hexaxim or Hexacima or Hexyon) was studied in an immunocompromised population following the European Medical Agency’s request. For the indicated age HIV-exposed infants were the most relevant population for the study. Among countries with high prevalence of HIV infection in pregnant women, RSA was chosen as Hexaxim had been implemented into National Immunization Programme in 2015.

Methods: A single center, open-label, two-arm study in HIV-exposed infected (Group A) and exposed uninfected (Group B) infants evaluated descriptively the immunogenicity and safety of DTaP-IPV-HB-PRP~T vaccine administered at 6, 10 and 14 weeks (primary series) and at 15-18 months (toddler booster) of age.

Results: Despite a screening period of 18 months during which more than 5000 infants born from HIV-infected mothers were screened, the study failed to enroll 50 HIV-infected subjects. The enrollment failure was due to high compliance to anti-HIV treatment of HIV-infected pregnant women, which decreases dramatically the antenatal and postnatal transmission of the virus. A total of 64 subjects were enrolled: 14 in Group A and 50 in Group B. DTaP-IPV-HB-PRP~T vaccine was highly immunogenic with seroprotection/seropositivity achieved in more than 95% of subjects for all antibodies after the infant primary series and in all subjects after the toddler booster. The safety profile of DTaP-IPV-HB-PRP~T vaccine in HIV-exposed infants was good in both groups.

Conclusions: DTaP-IPV-HB-PRP~T hexavalent vaccine is safe and immunogenic in a population of HIV-exposed infants regardless of their HIV status at birth. Due to low number of HIV-exposed infected subjects enrolled, the results should be read and interpreted with caution.

Clinical Trial Registration: NCT 02817451; UTN U1111-1161-2610
STAPHYLOCOCCAL SCALDED SKIN SYNDROME AS A COMPLICATION OF VARICELLA-ZOSTER VIRUS PRIMARY INFECTION – A CASE STUDY.

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Title of Case(s): Staphylococcal scalded skin syndrome as a complication of varicella-zoster virus primary infection – a case study.

Background: Varicella zoster primary infection is a common and highly contagious disease caused by the varicella-zoster virus (VZV). In healthy, immunocompetent children varicella usually have a benign course. Nevertheless a wide range of complications can be observed, including bacterial sepsis, pneumonia and central nervous system involvement. Bacterial superinfection of skin lesions is the most frequent complication of VZV primary infection in both immunodeficient patients and immunocompetent individuals.

Case Presentation Summary: A 2-year old, previously healthy girl was referred to the Department of Children’s Infectious Diseases with a bacterial superinfection of varicella lesions. Parents observed new skin lesions formed within a few hours on prior varicella vesicles. At the admission to the hospital extensive bullous impetigo and presence of mild erythema and tenderness were observed. Nikolsky’s sign was negative. Patients vital signs were in the normal range. Despite of severe and vast skin lesions, inflammatory markers were slightly elevated. Empiric ceftriaxon and vancomycin were provided until blood and skin culture results known. The cultures from the skin lesions grew methicillin-sensitive Staphylococcus aureus, blood cultures were negative. Vancomycin was discontinued after 5 days of therapy. The girl was treated with ceftriaxone to 7 days and recovered without sequelae.
Learning Points/Discussion: Regardless varicella high morbidity, underestimation of its complications is very widespread. *S.aureus* is frequently responsible for skin and soft tissue infections, including bacterial superinfections as complications of varicella. However, staphylococcal scalded skin syndrome is rarely observed as a complication of VZV infection. Providing varicella vaccination is highly effective in preventing VZV infection and its complications. Universal vaccination with a two-dose strategy has significantly reducing morbidity and mortality of this infectious disease. Not all countries have introduced varicella vaccination into the recommended routine childhood national immunization schedule.
Background: Therapeutic drug monitoring (TDM) of aminoglycosides and vancomycin is recommended in newborns due to their physiological and clinical daily changes that affect their pharmacokinetic/pharmacodynamic parameters; especially in treatments > 3 days as reflected in our local protocol. However, its implementation in clinical practice is not always easy. The objective of the study was to evaluate the adherence to our TDM protocol and its effects over the newborns’ outcome.

Methods: A descriptive, single-center and prospective study was performed between June 2017 - May 2019, including all newborns that have received at least 2 doses of amikacin, gentamycin and/or vancomycin. Demographic, clinical, microbiological and pharmacological data was analyzed, to define compliance with the protocol and to determine which factors were related with TDM request and drug levels below or above normal range.

Results: Five-hundred sixty-one antibiotic courses (201 vancomycin, 195 amikacin, 320 gentamycin) in 349 newborns (58% male, 78% preterm); 85% due to suspected; 40% confirmed infection (16% microbiologically). Mortality, renal and auditory impairment were 5%, 0.5% and 11%. TDM was performed in 153 patients (120 vancomycin, 29 amikacin, 4 gentamycin). Adherence to protocol was 47% (82% vancomycin, 30% amikacin, 6% gentamicin). Confirmed infection, underlying diseases and prematurity were related with TDM request. Drug levels were abnormal in 48% and 45% for vancomycin and amikacin, respectively. No factor was statistically related with non-therapeutic drug levels.

Conclusions: Adherence to TDM protocol depended on the antibiotic, being higher with vancomycin due to longer treatments. TDM allowed adjusting antibiotic dose in half of the cases when requested. Gentamycin TDM seems unnecessary in stable term neonates and more studies are needed in preterm newborns. Vancomycin and amikacin TDM in newborns is useful and its use should be encouraged through educational activities.
Background: Hepatitis A (HA) is a mandatory declaration disease (EDO) in Spain since 1995. Currently, our country has a low endemicity pattern of HA, which causes the appearance of outbreaks in susceptible groups. The main objectives of this study were to evaluate the underdeclaration of HA from healthcare network and analyse clinical and epidemiological characteristics of reported cases in Lorca, Murcia (Spain).

Methods: Cross-sectional study. Case definition was a symptomatic patient with elevated transaminases and IgMHA positive. For the analysis of the underdeclaration, all the serological records provided by the reference laboratory were compared, with notified cases to Surveillance Service during 2011-2018. Epidemiological characteristics were obtained from EDOSAN-database. Sociodemographic variables, risk factors and clinical aspects were analysed. Statistical analysis was performed with the SPSS 23.0 program: underdeclaration rate, descriptive and association analysis of the selected variables.

Results: 8692 serological determinations of HA were made, 1.54% positive IgM (n=134). 74 subjects fulfilled the case definition HA. Two patients were not declared to EDOSAN-database (underdeclaration rate: 2.7%). The first notification source was EDOSAN-database, 59.9% (n=41). According to the gender, men were 59.5% (n=44). The median age was 11.64 (P25:7.27-P75:39.53) years. HA affected mostly the immigrant population (55.4%), this group was associated with childhood (p<0.001) and having recently travelled to endemic countries (p<0.001). The native cases were older, men with risky sexual practices (p<0.001).

Conclusions: Underdeclaration rates of HA was very low, which indicates an adequate epidemiological surveillance system in our region about this disease. The most susceptible groups to contract HA infection were children of foreign nationality, with a recent record of trip to endemic countries, and Spanish males with risk sexual behaviours. The control measures should be focus mainly on these weak collectives.
COST-EFFECTIVENESS OF A NEW POINT-OF-CARE DIAGNOSTIC TEST FOR THE MANAGEMENT OF CHILDREN PRESENTING TO EUROPEAN EMERGENCY DEPARTMENTS WITH ACUTE INFECTION

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Background: There is a need for more reliable and timely diagnostics to improve accurate diagnosis of acute childhood infection. Recent research demonstrates the possibilities of measuring host responses to bacterial or viral infection, using RNA and protein biomarkers. We aimed to model how a new rapid test to identify bacterial infection would influence clinical management of febrile children presenting to the emergency department, and explore the value of such a test in different patient groups and health system settings.

Methods: We developed a decision-analytic model, following a patient’s clinical pathway from presentation in the emergency department, through diagnosis and treatment, to final health outcomes. Using data from 38,000 febrile children at PERFORM network hospitals (www.perform2020.org) across Europe, we evaluate the impact of a new test on clinical decision-making, including the likelihood of receiving antibiotics or being admitted. We compare health service costs and outcomes of current pathways of care with implementation of the new test, to assess the ‘value’ of such a test for different patient typologies.

Results: Given high levels of over-treatment of suspected bacterial infection, the value of such a test is primarily in providing reassurance of a negative test result and preventing unnecessary admission. Our modelling indicates that a new more accurate test may change practice where decision-making regarding treatment is closely associated with the assessed risk of bacterial infection. Hence, such a test has particular value for certain groups, including febrile infants aged <3 months and children with undifferentiated fever or suspected lower respiratory tract infection.

Conclusions: Our modelling illustrates how early-stage economic evaluations can help developers and decision-makers target appropriate patient groups, and understand how these may vary across different health system settings.
ESTIMATE THE ECONOMIC BURDEN OF VARICELLA IN EUROPE IN ABSENCE OF UNIVERSAL VARICELLA VACCINATION

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Background: The disease burden of varicella has been reported previously in Europe. However, the economic burden needs further elucidation. This study estimated the economic burden of varicella in Europe from both payer (direct costs) and societal (indirect costs) perspectives in the absence of Universal Varicella Vaccination (UVV).

Methods: A systematic literature review was conducted to obtain the country specific unit cost per varicella case and associated healthcare utilization between 1/1/1999 and 10/15/2019. Predictive modeling was used to estimate the economic burden in 2018 costs in European countries. The number of annual varicella cases, deaths, outpatient visits and hospitalizations was calculated (without UVV) based on age-specific incidence rates (Riera-Montes et al. 2017) and 2018 population data by country. Unit cost per varicella case and disease burden data were combined using stochastic simulation: 10,000 iterations were run to estimate 2018 costs stratified by country, age and healthcare resource.

Results: Overall annual total costs associated with varicella were estimated to be €662,592,061 (Range: €309,552,363 to €1,015,631,760) in Europe in absence of UVV. Direct and indirect costs were estimated at €229,076,206 (Range €144,809,557 to €313,342,856) and €433,515,855 (Range €164,742,806 to €702,288,904) respectively. Total cost per case was €121.45 (direct: €41.99; indirect: €79.46). Almost half of the costs were attributed to cases in children under 5 years, owing mainly to caregiver work loss (Figure1). The distribution of costs by healthcare resource was similar across countries. France and Germany accounted for 49.28% of total costs, potentially attributed to high minimal wage.
Conclusions: The economic burden of varicella across Europe in the absence of UVV is substantial (over 600M€). It is important to consider UVV implementation to avert direct and indirect costs, including caregiver burden.

Systematic Review Registration:
Background: Neisseria meningitidis is a common cause of meningitis. Introduction of meningococcal conjugate vaccines (MCV) has reduced meningococcal meningitis due to vaccine-type serogroups. We estimated the cases and deaths of meningococcal meningitis in children <5 years of age from 2000 to 2015 globally.

Methods: WHO country-specific meningitis deaths in children 1-59 months were estimated using country vital registration data or verbal autopsy data (Maternal and Child Epidemiology Estimation (MCEE); Liu, Lancet 2016). Countries with year-specific reports of meningitis epidemics were apportioned into endemic and excess epidemic deaths using regression (single global coefficient for epidemic effect). Endemic meningitis deaths were apportioned into pathogen-specific causes (Wahl, Lancet 2018) using pathogen-specific case fatality ratios (CFR) and pathogen distribution of cases, and meningococcal serogroup distribution which were obtained from literature review and meta-analysis for meningococcus, pneumococcus, Haemophilus influenza type B and all other (grouped) pathogens. Estimates accounted for HIV prevalence, vaccine use and access to care. Country-specific meningococcal meningitis death estimates were divided by the meningococcal meningitis CFR to estimate meningococcal meningitis cases.

Results: Global endemic meningococcal meningitis death estimates declined from 24,700 in 2000 to 11,600 in 2015; cases declined from 72,500 to 38,400, respectively. Deaths fell 32.3% from 2010 to 2015 following MCV-A introduction in the African meningitis belt, compared to 15.6% from 2005 to 2010. Africa and Asia have the most endemic meningococcal meningitis deaths (6,000 and 4,400 in 2015, respectively). Pneumococcal meningitis deaths exceed meningococcal deaths in all regions except Europe.
Conclusions: Global meningococcal meningitis disease burden has decreased, in part due to MCVs, but regional differences continue to be large. Addressing model limitations of access to care definition and incorporating epidemics will increase morbidity and mortality estimates.

Systematic Review Registration: - N/A
Title of Case(s): Got the 'hump' with dairy? Think again.. Rare case of an imported zoonosis in the UK

Background: Brucellosis is a rare zoonosis in humans, with just 5 confirmed cases in the UK in 2017. It is contracted by ingestion of unpasteurised milk, undercooked meat or from secretions from infected animals. Symptoms of brucella in children can be vague with an insidious onset, but is characterised by prolonged fever associated with anorexia, fatigue, and musculoskeletal complaints. We present a paediatric case with likely acquisition from Pakistan.

Case Presentation Summary: A healthy 2 year old child on a dairy-free diet travelled to a major urban town in Pakistan for a 2 month holiday. The family were unable to provide pasteurised milk from the UK, and was given boiled unpasteurised goat and camel milk to supplement his diet. He developed fever 6 weeks into his stay and was seen by health professionals in Pakistan and on return to the UK for suspected upper respiratory tract infections, as well as a presumed transient synovitis of the hip. His temperature remained above 38 degrees centigrade after return to the UK. He re-presented with high fevers, and was treated for possible serious bacterial infection with broad spectrum antibiotics. Blood cultures grew gram negative bacilli, identified by MALDI-TOF as Brucella melitensis (pending confirmation at APHA). The child was clinically well one week after the initial blood culture, and is completing a 6 week course of oral antibiotics.

Learning Points/Discussion: Brucellosis is a rare zoonosis with the majority of cases acquired in the Mediterranean Basin, South America, Asia and Middle East. With ever-increasing rates of travel abroad, coupled with a rising trend in non-dairy diets for clinical and lifestyle reasons, clinicians should consider brucellosis in the investigation of children with persistent fever after travel, particularly in those with an unconventional dietary intake.
CHARACTERISATION OF PROTEIN-BASED MENINGOCOCCAL VACCINE ANTIGENS AMONGST UKMENCAR4 CARRIAGE STUDY ISOLATES

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**Background:** Conjugate polysaccharide meningococcal vaccines can induce indirect protection by reducing the acquisition of carriage. This has a major impact on the efficacy of vaccine programmes and protects the unvaccinated population. Subcapsular protein-based meningococcal vaccines were developed to prevent endemic serogroup B disease. The impact of Bexsero (4CMenB) on carried meningococci in an Australian clinical trial did not demonstrate a reduction in carriage of disease-causing (B,C,W,Y) meningococci. This study aimed to characterise vaccine antigens amongst UK meningococcal carriage genomes for both vaccines 4CMenB (Bexsero) and rLP2086 (Trumanba).

**Methods:** The UKMenCar4 study comprised a collection of oropharyngeal carriage meningococci (n=1420) isolated from 19,641 adolescents from 11 UK centres, that underwent whole genome sequencing. High-throughput genomic analysis tools Bexsero Antigen Sequence Typing and Outer Membrane Vesicle peptide Typing was used to characterise the variation in protein antigens.

**Results:** Of the 1,420 carried meningococci (Table 1), all had fhbp, nhba and porA genes present, only 126 (8.9%) had a nadA gene. There were 79 (5.6%) isolates that had at least one exact 4CMenB vaccine variants (fhbp 1: NHBA 2, NadA 8: PorA VR2 4). For rLP2086 vaccine antigens, peptide 45 was found in 82 (5.8%) isolates and peptide 55 was not present. For 4CMenB, the isolates that had exact vaccine variants comprised genogroups B, C, Y, E, Z and capsule null. For rLP2086, the isolates that had exact vaccine variants comprised genogroup B only.

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<tr>
<th>Capsular group</th>
<th>Genotype (n)</th>
<th>Expression (n)</th>
<th>% expressing capsule</th>
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<tbody>
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<td>346</td>
<td>193</td>
<td>55.8</td>
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<td>C</td>
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</tr>
<tr>
<td>Other (E, H, L, X, Z)</td>
<td>287</td>
<td>Not tested</td>
<td>-</td>
</tr>
<tr>
<td>Total</td>
<td>1,420</td>
<td>532</td>
<td>37.5</td>
</tr>
</tbody>
</table>

**Conclusions:** A small proportion of carried meningococci of all genotypes and capsular groups have the potential to express proteins that are contained in Bexsero and capsular group B for Trumenba. The impact on commensal meningococci from vaccines targeting subcapsular and outer membrane proteins remains undetermined and a question for further study within the oropharyngeal microbiome.

**Clinical Trial Registration:** Not a clinical trial
**INTRACRANIAL CYSTS – WHAT COULD IT BE?**

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**Title of Case(s):** Intracranial cysts – what could it be?

**Background:** This is a rare case of a 12 year old Indonesian previously well girl who presents with the problem of multiple intracranial cysts with obstructive hydrocephalus seen on imaging.

**Case Presentation Summary:** The patient first presented with fever and headache for 2 weeks. An infectious workup during admission for dengue and typhoid returned negative. She was readmitted due to persistent symptoms and her work up suggested military TB. The Mantoux test and 3 sputum samples for AFB were negative. She was treated for presumptive pulmonary TB with RHEZ. She persisted to have fever and headaches and developed a right ptosis with convergent squint, left sided weakness and paraesthesia. An urgent brain scan showed thrombosis of the vein of Galen. She was treated with mannitol infusions, dabigatran and methylprednisolone. Streptomycin was also added for suspicion of CNS TB involvement. Although a repeat chest xray and CT thorax scan showed interval improvement in her pulmonary lesions and her symptoms improved, she again presented with an acute episode of altered mental status with urinary incontinence, slurred speech and swallowing difficulty. This time the MRI Brain scan revealed multiple intracranial cysts with obstructive hydrocephalus seen on imaging. A work up for toxoplasmosis and neurocysticercosis returned negative. The TB PCR test on a biopsy of the lesions returned positive. All other TB work up returned negative. She was given intravenous dexamethasone before tapered doses of oral prednisolone. Her anti-TB medications included a 5drug regime- rifampicin, isoniazid, pyridoxine, ethambutol, pyrazinamide, levofloxacin for 2 months before moving on to a maintenance regime for 10 months. She was given seizure prophylaxis.

**Key Learning Points:** 1) Differentials of multiple intracranial cysts on imaging and the relevant work up  
2) A complicated course of CNS tuberculosis and its management including the need for a multi systemic approach (including neurological, ophthalmological, ENT considerations)
INFECTIONS-A MAJOR CAUSE OF TREATMENT-RELATED MORTALITY IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA IN A LOW-MIDDLE INCOME COUNTRY

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**Background:** Despite noteworthy improvements in the outcome of children with Acute Lymphoblastic Leukemia (ALL), patients who are treated in low-middle income countries (LMIC) have far lower survival rates. The objectives of this study were to determine the proportion of treatment-related mortality (TRM), the incidence of infection-related mortality (IRM), the etiology of IRM and factors associated with outcome of children with ALL being treated in a LMIC.

**Methods:** An observational; retrospective, cohort study, conducted over 21 months, in Pediatric Hematology-Oncology department, The Children’s Hospital Lahore, Pakistan. All pediatric patients of ALL on chemotherapy and expired during treatment and not due to the relapse, resistant or progressive disease were included in the study. Infections were defined on the basis of clinical or lab evidence. Data was analyzed in SPSS 16.

**Results:** Total 247 patients of ALL expired during the study period. Proportion of TRM (n=144) was 58.3%. Median age was 5 years with male-to-female ratio of 1.3:1. Sepsis was found in 126 (87.5%) patients. Lower respiratory tract infection was found in 78 patients (54.2%), mucositis in 63 (43.8%), bloodstream infections in 41 (28.5%), gastrointestinal infection in 20 (13.9%), invasive fungal infection in 16 (11%), central nervous system infections in 15 (10.4%), urinary tract infection in 2 (1.4%) while mucormycosis, dental abscess and EBV infection was found in one patient each (0.7%).

**Conclusions:** Weight-for-age, immunophenotype, phase of chemotherapy and absolute neutrophil count of patients were the statistically significant factors associated with the outcome of these patients. Infections are a major cause of treatment-related mortality in patients with ALL being treated in low-middle income country. TRM though potentially avoidable is still a significant cause of treatment failure. Improvement in infection prevention and control is imperative in improving the outcome.
FACTORS AFFECTING ROUTINE VACCINATION DURING PREGNANCY IN CRETE, GREECE

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Background: In Greece, women should routinely receive pertussis vaccine between the 27th and the 36th week of every pregnancy, regardless of prior Tdap history, and influenza vaccine at any stage. The purpose of this study was to determine the vaccination rates for B. Pertussis and Influenza virus during pregnancy and detect the factors that affect routine vaccination during pregnancy in Crete, Greece.

Methods: Questionnaires were distributed to 3/4 Maternity Departments in Heraklion, Crete (January 2019 – December 2019) and mothers were interviewed soon after delivery, after receiving detailed information about the study. The questionnaire consisted of questions regarding information on family composition, sources of medical care, maternal education, maternal employment, mother and infant health during pregnancy and delivery, vaccine uptake during pregnancy and sources of information re vaccination.

Results: 987/1006 agreed to participate. Uptake of influenza and pertussis vaccination was 27.1% and 2.13%, respectively. The commonest reason for non-vaccination was the lack of recommendation by the health care practitioner (HCP) (66.0% and 89.8% for influenza and pertussis, respectively). Factors positively associated with vaccination against influenza were maternal age (p<0.011), pregnancy duration (p<0.030), vaccination during previous pregnancy (p<0.010), educational level (p<0.0007) and previous birth (p<0.024) while for pertussis were maternal age (p<0.033), vaccination during previous pregnancy (p<0.0001) and educational level (p<0.0001).

Conclusions: Vaccination uptake rates during pregnancy appear suboptimal. The issue that needs to be addressed is the reluctance of the HCPs to discuss antenatal vaccination. Increasing awareness and key strategies, would be required to optimize the uptake of routine vaccines during pregnancy, with a specific focus on informing women of high risk; namely younger women, without previous children and of lower educational level.
RESPIRATORY Syncytial Virus and Influenza Co-Infection in Children Under 2 Years of Age: A Rare Issue, But a Risk Factor for an Increased Length of Stay

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²Hôpital de la Croix-Rousse - Hospices Civils de Lyon, Service De Bactériologie, LYON, France

Background: Viral respiratory infections are a major cause of morbidity and mortality in pediatrics. In northern hemisphere, these 2 viruses are characterized by a strong winter circulation. Little data exists on the clinical impact of co-infections with Respiratory Syncytial Virus (RSV) and Influenza. The objective of our retrospective study is to determine the frequency and clinical impact of RSV and influenza co-infections.

Methods: Between January 2011 to February 2017, we carried out in a tertiary pediatric hospital, a retrospective, monocentric, case-control study in children under 2 years of age. A univariate analysis was performed to compare a group with RSV and influenza positive respiratory PCR to a group with RSV positive and Influenza negative PCR, matched on age and gender. Patients with an empty medical record were excluded.

Results: There were 4246 PCR positive for RSV, 928 were positive for Influenza, and 36 were positive for both. Thirty patients with RSV-Influenza co-infection and 60 with RSV alone were included. The length of stay was longer in the co-infection group with a mean of 8.37 days compared to 5.47 days in the RSV group alone (p = 0.02). No significant differences were found regarding the respiratory rate on admission, the presence of apnea or breathing pauses, oxygen requirement, high-flow nasal cannula oxygen therapy, non-invasive ventilation, or intubation.
Conclusions: RSV and Influenza co-infections are infrequent events in children under 2 years of age, even though both viruses circulate substantially in that population. The hypothesis of competition between the two viruses should be considered. In terms of respiratory outcome, our study does not show any difference in clinical severity. However, a longer length of stay in the RSV-Influenza group was observed.
Title of Case(s): Sydenham hemichorea in a child living in a developed country – a diagnostic challenge

Background: Acute rheumatic fever (ARF), a complication of group A streptococcus infection has a very low incidence in developed countries and usually has a latent period of two to three weeks following initial infection. Sydenham chorea is one of the major clinical manifestations of ARF and is the most common form of acquired chorea in childhood being characterized by chorea, emotional lability and hypotonia.

Case Presentation Summary: A previously healthy 7-year-old male, presented with rapid, irregular, and nonstereotypic jerking movements of the right limbs, restlessness of the trunk worsened by attempted action, and improvement with sleep. Other symptoms included restless movements of the tongue, motor impersistence and emotional lability. Physical examination had no other significant findings. He had a previous history of hospital admission for suspected ulnar osteomyelitis, treated with flucloxacillin and amoxicillin-clavulanate, during which he had odynophagia and fever, three weeks before. After discharge he was symptom free, there was no report of any other recent trips, mood disorders, sleep problems, trauma or use of medications. CT and CT angiography-head scans, brain MRI, complete blood count, CSF analysis and CRP were normal, throat culture for GAS was negative, ASO titer and ESR were increased. Cardiac echocardiography showed moderate mitral and mild aortic regurgitation without other abnormal valvular findings. He was treated with prednisolone and carbamazepine for chorea with good clinical response and started monthly prophylaxis with benzylpenicillin. Cardiac follow-up showed improvement of valvulitis.

Learning Points/Discussion: Jones’ Criteria were revised to include subclinical carditis making possible a quicker diagnosis and allowing treatment earlier in the course of the disease. Moreover, in patients with chorea, evidence of previous GAS infection is not mandatory. The low incidence of ARF in developed countries make its diagnosis a serious challenge.
Background: Viral-bacterial co-infections have been increasingly diagnosed among children with community-acquired pneumonia (CAP). We described the frequency of viral-bacterial, only viral, and only bacterial infections in children with CAP and compared their clinical characteristics upon recruitment and during follow-up.

Methods: Children aged 2-59 months with non-severe CAP (respiratory complaints plus radiographic pulmonary infiltrate/consolidation) were enrolled in a prospective cohort, in Salvador, Brazil. From 820 patients recruited in a clinical trial (ClinicalTrials.gov Identifier NCT01200706), 705 (86.0%) had nasopharyngeal aspirates (NPA) and serum collected upon admission and serum collected 2-4 weeks apart. NPAs were tested for 16 respiratory viruses by PCRs and bacterial infections were investigated by serology. Follow-up assessments occurred.

Results: Viral-bacterial (35.6%), only viral (55.6%), and only bacterial (4.1%) infections were detected. Children with viral-bacterial co-infections had higher frequency of disease length ≥5 days (68.1% vs. 59.9%;P=0.04) and decreased pulmonary expansion (11.2% vs. 6.6%;P=0.04) upon admission and of signs of consolidation on 1st day (7.6% vs. 2.3%;P=0.001), on 2nd day (5.7% vs. 2.1%;P=0.02), tachypnoea on 2nd day (37.8% vs. 28.8%;P=0.02), on 4th day (46.7% vs. 13.0%;P=0.02), and vomiting on 3rd day (8.6% vs. 2.9%;P=0.02) compared to those with virus alone. Children with only bacterial infection had higher frequency of somnolence (17.2% vs. 4.8%;P=0.02), tachypnoea (62.1% vs. 42.3%;P=0.04), and decreased pulmonary expansion (20.7% vs. 6.6%;P=0.02) upon recruitment and tachypnoea on 1st day (69.0% vs. 46.7%;P=0.02), signs of consolidation on 1st day (17.2% vs. 2.3%;P=0.001), on 2nd day (17.2% vs. 2.1%;P=0.001), on 3rd day (23.5% vs. 1.4%;P=0.001) compared with those with only viral infection.

Conclusions: Viral-bacterial co-infections occurred in one third of the cases. Patients with either bacterial or viral-bacterial infection have worse outcomes than patients with only viral infection.

Clinical Trial Registration: ClinicalTrials.gov Identifier NCT01200706
NECROTIZING FASCIITIS DUE TO EXTENSIVELY-DRUG RESISTANT PSEUDOMONAS AERUGINOSA IN A LEUKEMIC CHILD WITH FEBRILE NEUTROPENIA

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Title of Case(s): Necrotizing fasciitis due to extensively-drug resistant Pseudomonas aeruginosa in a leukemic child with febrile neutropenia

Background: Necrotizing fasciitis (NF) is a rare, rapidly progressive and life-threatening infection of the subcutaneous tissue and the superficial fascia. NF carries a high mortality rate in the immunocompromised patients, not because of co-morbidity but also because of the antibiotics frequently administered can be ineffective. Here, we reported a patient with NF due to extensively-drug resistant (XDR) Pseudomonas aeruginosa and discussed the medical and surgical approaches. Case Presentation Summary: A 3-year-old girl with refractory acute lymphoblastic leukemia (ALL) admitted for chemotherapy and developed neutropenic fever on the 17th day of hospitalization. On the second day of fever, redness and erythema appeared on the right labium majus. Despite the broad-spectrum antibiotics (vancomycin, meropenem and amphotericin B) started, and granulocyte suspension transfused started, fever persisted and the lesion on labium majus progressed. P. aeruginosa was detected in blood culture and it was only sensitive to colistin. Colistin was added to the current treatment. Despite the treatment change, necrosis appeared ten days after the first lesion appeared. The patient was evaluated as necrotizing fasciitis, meropenem was stopped and levofloxacin+colistin combination therapy continued. Debridement was performed and a flap was placed. P. aeruginosa cultured in the tissue culture too. On the third day of the debridement, the fever was resolved and levofloxacin-colistin combination therapy continued for 23 days.

Learning Points/Discussion: NF is often misdiagnosed as erysipelas or cellulitis. In the presence of unresponsiveness to antibiotic treatment in 24–48 h, NF should be suspected. Prompt diagnosis, enabling treatment with appropriate antibiotics and early surgical intervention are the key factors in NF management. For XDR P. aeruginosa, colistin and levofloxacin combination therapy can provide a time to the case until the operation.
Background: With the development of respiratory syncytial virus (RSV) vaccine candidates and new monoclonal antibodies, there is a need to better understand the burden of RSV infections among young children. The aim of this study is to develop and evaluate the feasibility of a protocol to measure the burden of RSV in children aged <5 years in primary care.

Methods: The RSV ComNet protocol covers children, aged <5 years that visited their general practitioner (Netherlands) or paediatrician (Italy), who met the WHO acute respiratory infection (ARI) case definition or influenza like illness (ILI) case definition, and had a positive test result for RSV, in a prospective cohort study. Disease burden, including health care use, duration of symptoms, and quality of life (PedsQL® questionnaire), was measured 14 and 30 days after consultation. The feasibility of the protocol will be evaluated in terms of response rates on requests for swabbing and questionnaires, data flow, application of case definitions, and the impact of enhanced surveillance on routine practice.

Results: In the Netherlands, the RSV ComNet protocol was implemented in the routine influenza surveillance system, while in Italy a new infrastructure was established for this study. Participants and data will be collected during the winter of 2019/20. Up to week 04/2020, 26 swabs were tested RSV-positive in the Netherlands and 65 in Italy. Questionnaire response rates were 42% in the Netherlands (11/26) and 98% (43/44) in Italy.

Conclusions: The evaluation of the RSV ComNet pilot in the Netherlands and Italy will be used to validate the protocol and present preliminary disease burden estimates. The validated RSV ComNet protocol will be made available to any country wishing to assess the burden of RSV in primary care.

Clinical Trial Registration: Not applicable
Background: Urinary Tract Infections is a common infection in children due to the increased prevalence of antibiotic-resistant, Extended Spectrum Beta Lactamases and non-Extended Spectrum Beta Lactamase producers. Analyzing antibiotic sensitivity data and monitoring the changes in the susceptibility profiles, has become crucial for successful management of these children. Administration of appropriate antibiotics will help in reducing the duration of illness and hospitalisation.

Methods: Objective: To analyze the antibiotic resistance trend of Urinary tract Infections in pediatric patients at a tertiary care hospital retrospectively. Method: Antibiotic sensitivity data of children with UTI were analyzed for the prevalence of Extended Spectrum Beta Lactamases and non-ESBL producers during the period 2013-2018, along with antibiotic susceptibility test (AST) pattern retrospectively. Data analysed using R version 3.0.

Results: 1417 bacterial isolates -predominant were Ecoli and Kpneumoniae. Carbapenems, Aminoglycosides effective against ESBLs. Increased resistance towards imipenem, meropenem noted against non-ESBLs. Statistically significant decrease in antibiotic sensitivity among non-ESBL producers was noted against tested antibiotics, except trimethoprim-sulfamethoxazole, ciprofloxacin, ofloxacin, and nitrofurantoin (p <0.05). A statistically insignificant trend towards antibiotic sensitivity was noticed among ESBLs (p >0.05) Aminoglycosides, carbapenems demonstrated higher bactericidal properties towards ESBLs. Among non-ESBL producers, gentamicin demonstrated higher bactericidal properties.

Conclusions: E. coli and K. pneumonia are frequent isolates in ESBL and non-ESBL UTI in children. Carbapenems, are very effective against ESBL producers along with aminoglycosides. Decreasing trend in sensitivity of antibiotics was observed among non-ESBL producers. Percentage of isolates sensitive to antibiotics is also declining among non-ESBL producers as compared to ESBL producers. It is noted that potent antibiotics- carbapenems have become significantly less active against non-ESBL producers. There is an urgent need for the practice of antibiotic stewardship and to renew our search for newer novel antibiotics.
VENTRICULITIS IN AN INFANT: A RARE COMPLICATION OF MENINGOCOCCAL MENINGITIS

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Title of Case(s): A rare complication of a meningococcal meningitis in an infant

Background: Ventriculitis is a well-known complication of neurosurgery and of primary gram-negative meningitis in neonates. Acute suppurative complications due to N. meningitides are however extremely rare and we found only one previous paediatric report of meningococcal ventriculitis. A prolonged course of antibiotics, ranging from 2 to 6 weeks, is mostly advised in treating ventriculitis. However, the optimal duration is still unknown.

Case Presentation Summary: A 4-month-old girl with type B meningococcal meningitis was referred because of deterioration (again fever, altered consciousness, ataxia and opisthotonus) after one week of proper treatment. CSF demonstrated adequate WBC’s and protein decrease. New cultures remained negative. 16S PCR confirmed N. meningitides. MRI demonstrated a ventriculitis of the posterior horns. NSAIDS were added and she defervesced after three days. After 6 weeks, cefotaxime was discontinued despite a small temporal lobe lucency on MRI. Immunological work-up demonstrated consecutively transiently absent B-cells and absent neutrophils in the presence of neutrophil antibodies. Monthly IVIG was initiated when IgG dropped to 1,99 g/l. Ten days after discontinuation of cefotaxime, she presented again with fever, neutropenia and 18 WBC’s/µl in the CSF. Meropenem was started and later switched to oral moxifloxacin. The lucency was still visible on a third MRI, but also a mastoiditis for which mastoidectomy was performed. Antibiotics were stopped after 8 weeks with a normal fourth MRI. Further immunological work-up is ongoing.

Learning Points/Discussion: This is only the second report of a child with meningococcal B ventriculitis. The unsatisfying clinical response alerted us to perform additional MRI imaging which allowed for the diagnosis. We prescribed prolonged IV antibiotics although clear evidence for this is lacking. We also performed a mastoidectomy for source control. Furthermore, an immunological work-up is recommended for unusual infectious disease complications.
GBS MATERNAL COLONISATION, RISK FACTORS, AND ANTIBIOTIC PROVISION AND RESISTANCE PATTERN OF ISOLATES IN SOUTH LONDON: A NESTED CLINICAL AUDIT

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Background: Despite having preventative measures in place, incidence of EOGBS is increasing in the UK. This audit examines the proportion of colonised women with clinical risk factors outlined by Royal College of Obstetrics and Gynaecology (RCOG) and compares IAP provision between the two hospitals. Due to the rise in antimicrobial resistance, the antibiotic resistance pattern in the bacterial isolates will also be considered.

Methods: Data for this audit is nested from a larger feasibility study which focused on the development of a sero-correlate of protection against iGBS. Extracted data and laboratory reports from 138 pregnant women colonised with GBS from two hospitals (A and B) in South London, are then collated in a spreadsheet and analysed to give quantitative measures (i.e. proportions, percentages) to fulfill the set objectives.

Results:

Figure 2. Proportion of women with clinical risk factors

Figure 5.
**Figure 1.** Proportion of women with clinical risk factors outlined by RCOG and comparison of IAP administration between two hospitals. Benzylpenicillin (51%) is the commonest IAP given to these women. There is a greater proportion of colonised women who underwent C-section with rupture of membranes (67%) that received IAP, compared to those who delivered via C-section without rupture of membranes (43%) or vaginally (43%). There is higher antibiotic resistance pattern in hospital A for both erythromycin (56.4%) and penicillin (57.7%) compared with hospital B (54.4% and 33.3%, respectively).

**Conclusions:** Current national screening for GBS should be reconsidered in the UK. Awareness of the clinical risk factors surrounding EOGBS is vital to appropriately manage GBS-colonised women. It is advisable for colonised women delivering vaginally to receive IAP due to the risks involved e.g. EOGBS. Antimicrobial stewardship, which should include testing of bacterial resistance prior to provision of antibiotics, must be actively practiced.
HEALTH STATUS OF UNACCOMPANIED MINOR MIGRANTS ARRIVING TO A BORDER EUROPEAN COUNTRY

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Background: Unaccompanied migrant minors are a high-risk group for acquiring infectious diseases and data on their vaccination status is scarce. Different approaches are used to screen newly arrived minors in Spain. The aim of this study is to describe their demographic characteristics, as well as their health status and serological protection against different vaccine preventable diseases (VPD) in order to homogenize screening protocols.

Methods: Observational retrospective study of unaccompanied migrant minors that were visited at a reference centre for International Health in Barcelona city from November 2018 to October 2019. After ethical approval, data were obtained from electronic medical records and registered in an anonymous database. SPSS v20 was used to undertake the descriptive statistical analysis expressed with measures of central tendency and frequency distribution.

Results: Among 131 minors (mean age:16), 76% were asymptomatic and 85% completed follow-up.

<table>
<thead>
<tr>
<th>Area of origin</th>
<th>Maghreb</th>
<th>Asia</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sub-Saharan Africa</td>
<td>40.0%(8/20)</td>
<td>11.1%(2/18)</td>
<td>29.3%(36/123)</td>
</tr>
<tr>
<td>LTBI TB</td>
<td>0.0%(0/20)</td>
<td>0.0%(0/18)</td>
<td>1.6%(2/123)</td>
</tr>
<tr>
<td>Intestinal Parasites</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S. mansoni</td>
<td>13.3%(2/15)</td>
<td>11.1%(2/18)</td>
<td>22.2%(26/117)</td>
</tr>
<tr>
<td>Hookworm</td>
<td>0.0%(0/15)</td>
<td>0.0%(0/18)</td>
<td>6.0%(7/117)</td>
</tr>
<tr>
<td>Others</td>
<td>13.3%(2/15)</td>
<td>5.6%(1/18)</td>
<td>16.2%(19/117)</td>
</tr>
<tr>
<td>HBsAg+</td>
<td>0.0%(0/20)</td>
<td>0.0%(0/18)</td>
<td>8.1%(10/124)</td>
</tr>
</tbody>
</table>

Conclusions: We found a high prevalence of latent tuberculosis infection (LTBI), intestinal parasites and
hepatitis B infection even in asymptomatic minors, and especially among those from Sub-Saharan Africa. Protection against hepatitis B virus (HBV), measles and varicella were low. Efforts in elaborating efficient protocols for screening and immunizing newly arrived migrants should be a Public Health priority, especially in border European countries.
CHRONIC OSTEOMYELITIS FOLLOWING AN OPEN FRACTURE IN A 12-YEAR OLD CHILD CAUSED BY A GRAM POSITIVE ANAEROBIC STRAIN: A CASE REPORT

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Title of Case(s): Consequences of an open fracture: how difficult can be managing it.
Background: Osteomyelitis in childhood are mostly secondary to hematogenous spread. Staphylococcus aureus is the most common pathogen isolated in this setting. Less frequently, osteomyelitis are related to an open trauma, and in these cases polymicrobial flora may be involved.
Case Presentation Summary: A 12 y/o child falling from a tree reported an open fracture of his arm. A X-ray showed fractures of supracondylar humerus and proximal radius, he was immobilized with K-wires in the nearby hospital. After few days, he presented early fistulation, unsuccessfully treated with only medications. After 5 months, a surgical debridement was performed. Nevertheless, a month later wound dehiscence occurred, forcing to remove K-wires. After surgery a 10 days treatment with amoxicillin/clavulanic followed by 5 days with ceftriaxone and teicoplanin was prescribed. End-treatment WBC-scintigraphy and CT-scan showed infection of distal humerus, proximal radius and ulna. Eight months after the accident, the child was centralized to our hospital. We observed persistence of the fistula so another debridement was performed and then we started empirical treatment with piperacillin/tazobactam plus teicoplanin. Intraoperative cultures yielded Clostridium clostridioforme (penicillin and piperacillin/tazobactam-R) and Clostridium sporogenes (clindamycin and penicillin-R), so therapy was switched to oral metronidazole. Five weeks later, treatment was discontinued for hypertransaminasemia. After 3 months of wellbeing, another fistulation occurred and the fourth debridement was performed, followed by antibiotic therapy with piperacillin/tazobactam and teicoplanin. Intraoperative cultures resulted negative; therapy was switched to teicoplanin alone for the next 6 weeks. After 1 y/o of follow-up, no other events occurred.
Learning Points/Discussion: Effectively eradication of chronic osteomyelitis can be difficult and even more challenging when anaerobic species are involved. Aggressive surgical debridement and use of antibiotics with good bone penetration are key aspects for a successful management.
THREE SIMILAR CHEST X-RAYS - THREE DIFFERENT DIAGNOSES

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Title of Case(s): THREE SIMILAR CHEST X-RAYS - THREE DIFFERENT DIAGNOSES

Background: Radiography is often employed when diagnosing chest pathologies in pediatric patients. Various conditions requiring different treatment tactics may manifest similarly in an x-ray, posing diagnostic difficulties. Complaints, medical history and additional testing are crucial when evaluating radiological chest imaging, diagnosing and treating patients. This is a review of three pediatric cases of chest pathology presented with similar radiological imaging findings.

Case Presentation Summary: Patient A presented with febrile fever and cough. Patients’ blood work showed neutrophilic leukocytosis and CRP of 135 mg/l, lung auscultation revealed a slight diminishing of sound on the right, chest X-ray indicated possible round pneumonia. Antibiotic therapy was started. Further testing revealed a tumor like formation of the kidney that was proven to be nephroblastoma with lung metastases. Patient B presented with no complaints, family history of parental tuberculosis, a positive Mantoux reaction and round infiltration of the right lung on chest x-ray. No AFB or M.tuberculosis DNA were obtained during the bronchoalveolar lavage fluid microscopy, culture or Xpert MTB/RIF assay. Biopsy indicated granulomas with necrosis. Patient was diagnosed and treated for tuberculosis. Patient C complained of right side chest pain, lack of appetite, irritability and subfebrile fever. Chest x-ray revealed a suspected right lung pneumonia, blood work showed neutrophilic leukocytosis and ESR of 49 mm/h. Patient was diagnosed and treated for pneumonia.

Learning Points/Discussion: Three different chest pathologies in our case study presented in similar radiological imaging findings. This perfectly exemplifies the importance of a holistic approach to patient care. Patient complaints, clinical and family history as well as additional tests must always be taken into account when evaluating radiological findings of pediatric patients. This enables the clinician to accurately diagnose and successfully treat the patient.
A RARE CAUSE OF NEONATAL MENINGITIS COMPLICATED BY POST-MENINGITIC HYDROCEPHALUS

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Title of Case(s): A rare cause of neonatal meningitis complicated by post-meningitic hydrocephalus

Background: *Listeria monocytogenes* is a rare but very important cause of neonatal sepsis and meningitis. It can cause severe infection with devastating consequences, many of which are highlighted by this case. Population based epidemiological surveillance data indicates that infection is most common in infants less than 30 days of life, and that infection is very rare after this period.

Case Presentation Summary: A woman presented with fevers >38°C at 37+4 and underwent emergency section. A boy, 2.52kg, was born floppy with poor respiratory effort. He was admitted to NICU for respiratory distress; benzylpenicillin, gentamicin and dextrose (glucose 1.1) were given. He deteriorated with a rising lactate, apnoeic episodes, tachycardia, become febrile, and from 8 hours started seizing. Baseline CRP of 100 rose to 294 at 24 hours. At 18 hours, maternal blood cultures grew Gram positive rods; amoxicillin was added. The baby's culture flagged at 22 hours and *Listeria monocytogenes* was identified. Amikacin and amoxycillin were given for 12 days, then subsequently only amoxicillin (to complete 4 weeks). Day 12 cranial ultrasound showed bilateral ventricular dilation with cystic areas. An external ventricular device was sited for hydrocephalus at 4 weeks. This was complicated by *E. Coli* and *Enterobacter cloacae* infection so was removed on day 10 and a 6-week course of meropenem initiated. A VP shunt was placed 11 days later.

Learning Points/Discussion: The UK NICE guideline for suspected early-onset neonatal infection (within 72-hours of birth) suggests an empiric regimen of benzylpenicillin and gentamicin has good coverage of *L. monocytogenes*. The NICE guideline for febrile children ≥3 months suggests using cefotaxime and amoxicillin until listeria has been ruled out. The USA, Canada and Norway recommend adding amoxicillin only for infants <1 month of age.
NON-CONGENITAL SYMPTOMATIC ZIKA VIRUS INFECTIONS IN CHILDREN AND ADOLESCENTS: A SYSTEMATIC REVIEW

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Background: Recent Zika virus (ZIKV) outbreaks in the Pacific and the Americas have highlighted clinically significant congenital neurological abnormalities resulting from ZIKV infection in pregnancy. However, little is known about ZIKV infections in children and adolescents, a group that is potentially vulnerable to ZIKV neurovirulence.

Methods: Our systematic review collated the evidence from a total of 1830 pediatric ZIKV cases representing 14 countries and territories, identified in 6 case-series and 20 case-reports.

Results: The most commonly observed signs and symptoms of ZIKV infection in children and adolescents, were mild and included fever, rash, conjunctivitis and arthralgia. Severe outcomes, including neurological complications and death, were rarely reported.

Conclusions: Non-congenital symptomatic ZIKV infection in children and adolescents appears to be primarily mild; however, reliable estimation of the risks of ZIKV complications in these age groups is limited by the scarcity of published data.

Systematic Review Registration:
DANGEROUS PLAYTIMES: MICROBIOLOGICAL HAZARD POSED BY SOAP BUBBLES AND OTHER AQUEOUS MEDIUM CONTAINING TOYS.

University of Padua, Dctvsp, Padua, Italy

Background and Objective: Child toy safety usually focuses on chemical, physical and electrical hazards. Microbiological risk is mostly neglected and only a few studies addressed this concern. Among the many toy categories, products containing an aqueous medium are especially at risk of microbial contamination, straight from their manufacturing, since polluted water was reportedly used in the process. The present study discusses the current international regulatory vagueness, provides an insight on the last 10 years alerts in Europe and suggests a core protocol for the assessment of toys microbial safety.

Methods: Considered regulations are the European Toy Safety Directive 2009/48/EC, its Relevant Standard EN 71-3 and the international standard ISO 8124 - Safety of Toys. The European Rapid Alert System (RAPEX) was searched for “microbiological risk” alerts in the “toys” product category, over the years 2009-2019.

Learning Points/Discussion: The query provided 124 alerts, all for toys containing aqueous media. Soap bubble toys accounted for 77% of them and were almost the unique toy category recorded for microbiological risk until 2013. Retrospectively, soap bubble alerts surged (25 notifications) during 2013. The year before literature reported how three kids got hospitalized after playing with a soap bubble toy contaminated with Pseudomonaceae. The number of alerts decreased in the following years. Although evidence supports microbiological risk in this kind of toys, no defined legislation measures have been implemented to address the issue. In our opinion toys should be compulsory tested before obtaining the well-known CE mark, especially if they are intended to be used in pediatric hospitals (e.g. clown therapy, distraction from pain). Minimal indicator parameters and guideline values could be: Total Mesophilic Viable Count <100 CFU/mL and absence of Pseudomonas aeruginosa.
HAND WASHING HABITS AMONG PUPILS IN FOUR PRIMARY SCHOOLS IN ITALY: AN OBSERVATIONAL STUDY

University of Padua, Dctvsp, Padua, Italy

Background: Hand hygiene is an easy and cost-effective type of primary prevention which could avoid up to 40% of respiratory and 30% of gastro-intestinal infections. Schools are one of the major hubs for the diffusion of infective diseases. Although hand hygiene is a widely discussed topic, most of the official indications are aimed at an adult target.

Methods: An observational study has been conducted in four primary schools in North-Eastern Italy, aiming to check if and how pupils wash their hands before and after playtime and lunchtime. The use of soap, the way they dry hands, the hand hygiene after toilet usage were also assessed. 622 pupils, aged between 6 and 11, have been observed. Pupils were not aware of the study, to avoid the Hawthorne effect.

Results: The adherence to hand hygiene practice at any time of the school-day varies from 37.4% to 4.9% among schools. Only 44.5% of pupils who wash their hands use soap; only 29% of pupils use the provided drying paper. The moment of greatest adherence to hand washing occurs before lunchtime, when 42.5% of pupils wash their hands. Only 33.6% of pupils wash their hands after using the toilet. Girls practice more the hand hygiene (51.5%). The youngest pupils (27.3% of 6-7 years old) wash their hands more than the oldest (16.7% of 10-11 years old). However, the correct hand hygiene is more frequent among older pupils.

Conclusions: The emerging scenario points out that hand hygiene is underused and poorly practiced among primary school students. It could be advisable and urgent to carry out tailored projects aimed at highlighting the extent to which this simple practice protects against the transmission of infectious diseases among pupils, even in European countries.

Clinical Trial Registration: Not applicable.
HEPATITIS A EPIDEMIOLOGY IN LATIN AMERICAN COUNTRIES: A SYSTEMATIC LITERATURE REVIEW

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**Background:** Due to globalization and improvement in socio-economic conditions, there have been significant changes in hepatitis A (HepA) epidemiology worldwide. In Latin America (LATAM), the average infection age is increasing, leaving a large proportion of adolescents and adults susceptible to HepA virus (HAV) infection and at increased risk of severe complications. The changing HepA epidemiology emphasizes the need for an up-to-date analysis. Here we report a current review of HepA incidence and prevalence in LATAM.

**Methods:** We conducted a systematic literature search of several databases according to PRISMA guidelines, to search for data in LATAM populations published between 01/01/2000 and 01/03/2019. Articles were screened to identify publications on HepA epidemiology (incidence, seroprevalence, morbidity, hospitalizations, sequelae, and impact of HAV vaccination on HepA incidence). The estimated age at midpoint of population immunity (AMPI) to HAV was used as an indicator of endemicity levels.

**Results:** Our review included 57 articles on HAV epidemiology, including studies presenting the positive impact of HAV pediatric vaccination programs on HepA incidence in Argentina, Brazil, Panama and Uruguay. Using AMPI and socio-economic indicators, HAV endemicity was estimated to be high-intermediate, intermediate, low-intermediate or low. While there is a high heterogeneity within each LATAM country, most countries have an intermediate endemicity, level for HepA ranging from high-intermediate to low-intermediate (Figure).
Conclusions: LATAM has a heterogeneous HepA endemicity profile extended over a broad intermediate level. Since age is a risk factor for HepA, reducing the burden in adolescents and adults is important and can be achieved with childhood immunization programs. Recent data are lacking in most of the LATAM countries, an epidemiologically transitioning region, highlighting the need for further nationwide studies and implementation of prevention strategies against HepA infections. **Funding:** GlaxoSmithKline Biologicals SA

**Systematic Review Registration:** N/A
THE EFFECT OF HYPERGLYCEMIA ON THE RESPIRATORY SYNCYTIAL VIRUS IMMUNOPATHOGENESIS IN MOUSE MODEL

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**Background:** Respiratory syncytial virus (RSV) is a leading causative agent of viral respiratory tract illnesses, resulting in considerable mortality and morbidity worldwide. The complicated pathogenesis of RSV infection is a major obstacle toward developing an effective vaccine. RSV infection is raised from immune system dysfunction and obviously might affect patients with weak immune system responses. Diabetes as a chronic metabolic disease is deeply associated with immune system impairment and malfunction. Hyperglycemic condition can affect the immune system through modification and alteration the chemotactic factors, adhesion molecules as well as by changing metabolic and immune related pathways. Accordingly, the influence of hyperglycemia on immunopathogenesis of RSV in mouse model is perused in the current study.

**Methods:** Hyperglycemia was induced by Streptozotocin (STZ) administration, and mice were infected with 6.3×10\(^6\) pfu/50 µl/ mouse dose of RSV-A2. The airway immune cell influx, T lymphocyte subtypes, cytokine/chemokine secretion, lung histopathology, and viral load were assessed at day 5 following infection.

**Results:** Following RSV infection the ratio of CD4/CD8 T lymphocyte increased while hyperglycemia caused reduction of the immune cells infiltration into the bronchoalveolar lavage fluid (BALF). Also, hyperglycemia following RSV infection resulted in IFN-γ and IL-17A cytokines decrease and IL-10 increase. In addition, Hyperglycemia induction decreased the lung pathology following RSV infection, while RSV load increased in the BALF supernatant.

**Conclusions:** The data indicated that hyperglycemic condition in short term can diminish the RSV-induced complications due to the inflammatory cells and cytokines decline. However, it seems that, because of increasing in the viral load, it can accelerate the virus spreading and act as a hidden potential source of virus for other high risk population.

**Clinical Trial Registration:** Not included in this project.
MOLECULAR EPIDEMIOLOGY OF RESPIRATORY SYNCTIAL VIRUS IN EUROPEAN COUNTRIES BETWEEN 2017 AND 2019

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Background: Respiratory syncytial virus (RSV) is classified into two subgroups, A and B, and multiple genotypes. Whole-genome phylogenetic analysis has been shown to provide optimal resolution for tracking virus evolution and epidemiology; however, the whole-genome diversity of RSV strains circulating in Europe, critical for monitoring viral diversity and public health surveillance, remains poorly understood.

Methods: Nasopharyngeal swabs were collected from participants (≤1 or ≥60 yr) with RSV infection that were enrolled in a clinical study, RESCEU, in England, Spain, and the Netherlands during the 2017–18 and 2018–19 RSV seasons. Whole-genome RSV sequences were reconstructed from Illumina sequencing, and used to infer the maximum-likelihood phylogeny using RAxML with other global strains collected during 2010–2019.

Results: 240 RSV-positive samples were collected and 169 (70%) sequenced. Among the sequenced samples, >50% of the RSV genome was reconstructed in 147 (87%), with 63 RSV-A and 84 RSV-B. All of the RSV-A and RSV-B strains had a 72-nucleotide and 60-nucleotide duplication respectively in the second hypervariable region of the G gene and were therefore classified as ON1 (RSV-A) and BA (RSV-B) genotypes, the predominant genotypes in recent years. For RSV-A, the study strains were scattered over the ON1 clade, interspersed with strains collected from across the globe, primarily after 2013, whereas the rest of the tree mainly consisted of global strains without the 72-nucleotide duplication that were collected before 2013. For RSV-B, the study strains, similar to those appearing in the global collection after 2015, were found in a BA9 subclade (Figure). The whole-genome phylogenies had sufficient power to differentiate strains that are identical in conventional partial G gene analysis.
**Conclusions**: The strains collected in multiple European countries during 2017–2019 circulated globally, dominated by ON1 and BA9 genotypes.

**Clinical Trial Registration**: ClinicalTrials.gov: NCT03627572, NCT03756766, and NCT03621930
A DIFFERENTIAL DIAGNOSIS OF A VESICULAR ERUPTION

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Title of Case(s): A differential diagnosis of a vesicular eruption

Background: Varicella-zoster virus (VZV) infection has two clinically distinct forms of disease: primary infection with VZV that causes varicella and herpes zoster (HZ) that results from reactivation of endogenous latent VZV infection within the sensory ganglia. Pediatric herpes zoster is an uncommon, well-tolerated and benign condition with 1 to 3 weeks of evolution. Varicella in early childhood is a risk factor for the disease.

Case Presentation Summary: We report the case of an 8-year-old girl, previously healthy, with no history of chickenpox, that was admitted to the emergency department of Hospital Agostinho, Santiago island in Cape Verde, following 4 days of fever and painful skin lesions. Examination revealed exuberant confluent vesicles and bullous with an erythematous base and some necrotic and hemorrhagic areas, involving the left cervicodorsal region with extension for the upper limb, corresponding to C3-C5 dermatomes. She was hospitalized and started therapy with flucloxacillin and the initial diagnosis of bullous impetigo was assumed. In D2, she was observed by a dermatology colleague that started therapy with oral acyclovir 80mg/kg/day on the suspicion of herpes zoster with secondary bacterial skin infection, with favorable clinical evolution. No serologies for varicella zoster virus were requested.
Learning Points/Discussion: Herpes Zoster clinically is characterized by a painful, unilateral vesicular eruption, which usually occurs in a restricted dermatomal distribution. The rash starts as erythematous papules, typically in a single dermatome. Within several days, grouped vesicles or bullae are the predominant manifestation. Treatment with antiviral therapy is more effective in the first 72 hours of illness. In the differential diagnosis of herpes zoster, bullous impetigo and herpes simplex, which have similar skin lesions, must be considered. The absence of previous history of varicella does not exclude the diagnosis of Herpes Zoster.
Title of Case(s): Migrant health, political advocacy and the paediatric infectious disease clinician

Background: Infectious disease clinicians are uniquely placed to provide advocacy for migrant and refugee children as they often provide the initial screening, vaccination and treatment of families with imported infections. Recent years have seen increasing barriers to health for migrant families, including restrictive health policies and hostility and scapegoating of migrant families. In this work, we aim to highlight the wider roles of paediatric infectious disease clinicians beyond treatment in the UK and EU, in advocating for and supporting their patients to access the best possible health.

Case Presentation Summary: Cases: 1) A 12 year old with tuberculosis, unable to access treatment; 2) A 9 year old with septicaemia, presenting late and charged during treatment; 3) A neonate colonised with MRSA, whose mother cannot obtain prescriptions; 4) A 7 year old with recurrent otitis media, unable to access surgery. Themes: In each case, treatment was impeded by wider barriers, including restrictions to healthcare, stigma and misunderstanding. The children were successfully treated in terms of their current infection, but only with wider advocacy to ensure treatment compliance, access to medications and follow up. This included direct liaison with management, clarification of exemptions from charging, raising awareness, and involving senior management. These highlight the scope for paediatric infectious disease clinicians to advocate for their patient to ensure timely, equitable access to healthcare and wider services.

Learning Points/Discussion: Paediatric infectious disease clinicians are uniquely placed to advocate for migrant children and families to reduce poor health outcomes associated with hostile policy. Clinicians must be familiar with advocacy tools. These cases are grounded in U.K. policy, although advocacy is required across Europe. Without effective advocacy, infectious disease clinicians will be unable to treat children or attend to their wellbeing.
A WEB-BASED PARENT-REPORTED PROSPECTIVE STUDY REGARDING THE INCIDENCE OF RESPIRATORY SYMPTOMS IN CHILDREN WITH DOWN SYNDROME.

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Background: Children with Down syndrome are known to have numerous health-related problems. Among others, they have an increased risk of having recurrent respiratory tract infections, with a decreased quality of life, increased hospitalization and sometimes even death as a consequence. We aimed to obtain more insight in the incidence of respiratory symptoms and their consequences in children with Down syndrome.

Methods: We performed a prospective parental-reported observational study. Children with Down syndrome aged 0 to 18 years of age were included between March 2012 and June 2014. Their parents or caregivers received a baseline questionnaire, a questionnaire at 1 and 2 years after inclusion, and a weekly short questionnaire regarding respiratory complaints, fever, use of antibiotics, doctors' visits and further consequences.

Results: 9011 childweeks were reported (66% response rate). 33% of parents reported their DS-child is ill more often than non-DS-children. The influence of season on the proportion of DS-children with complaints (figure 1) such as runny nose, blocked nose and cough, was limited; the complaints were also frequently present in summer. In 48% frequent use of antibiotics (>5 times) was reported, and in 18% prophylactic antibiotics were used.
**Conclusions:** Our findings support the impression of parents that their DS-children are ill more often than non-DS-children [DOI:10.1093/fampra/cmi035]. The limited seasonal influence is remarkable, compared to non-DS-children; this could indicate that respiratory symptoms in DS-children cannot be fully explained by viral infections (which generally show a clear seasonal occurrence) [DOI:10.21945/RIVM-2019-0079]. The antibiotic usage in our cohort was high, many children even used prophylactic antibiotics. It would be interesting to investigate whether respiratory symptoms in DS-children are caused by bacteria as often as they are being treated with (prophylactic) antibiotics [DOI:10.1016/j.bjid.2013.05.002, DOI:10.1111/j.1442-200X.2009.02825].
Background: In the past years, Romania has reported high numbers of measles cases and deaths, among EU countries. The vaccine coverage rates have lowered, especially regarding the Measles, Mumps and Rubella (MMR) vaccination. The aim of this study is to address local parental perception on vaccination by a new Social Media tool. Furthermore, we propose a user-friendly app to decrease vaccine hesitancy.

Methods: A questionnaire with 26 items, grouped into 3 sections (demographic characteristics of respondents, children’s immunization status and views on vaccination) was delivered through Social Media, using “Spitalul Virtual pentru Copii” platform, via a Google Forms survey. Perception was evaluated by assessing respondents’ position regarding vaccination “myths” using the Likert scale. We propose an Android app “Vaccinează (Vaccinate)” for parents as an electronic immunization record, with a built-in vaccine reminder.

Results: 9321 responses were recorded (9270 validated) during a limited 2 months survey. Formal vaccine hesitancy declared was 39% and 42.4% of the respondents had not used optional vaccines (as per NIP regulation), the main reason being lack of information from healthcare provider (22%). 27.3% believe that locally manufactured vaccines are safer, 22.2% prefer monovalent vaccines and 19.8% consider vaccine adjuvants as toxic. Other popular beliefs (e.g. link between vaccines and autism) were not endorsed by respondents. Young parents manifested highest values of vaccine hesitancy.
Conclusions: Young, technology-dependent parents need to be targeted in the national health programs on vaccination. Healthcare providers’ ability to establish a doctor-patient relationship should be improved with proper tools to meet the expectations of the millennial generation. New Social Media communication strategies in local language and smartphone apps could decrease the parental vaccine hesitancy by delivering information through their medium of choice.
PREVENTING RESISTANT INFECTIONS IN NEONATES: LITERATURE REVIEW AND APPRAISAL OF THE EVIDENCE

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Background and Objective: Resistant infections cause significant morbidity, mortality and healthcare cost with neonates at particular risk due to prolonged hospital admissions, widespread antibiotic use, and use of central line catheters. The evidence for preventative measures in neonates is rarely appraised. We aim to critically review the quality of available evidence for preventative measures against resistant infections in neonates, and suggests next steps.

Methods: A pragmatic study design: literature review in pubmed, medline and embase and googlescholar by one author; 44 articles were identified and data extraction performed. Critical appraisal of evidence quality according adopting GRADE criteria for risk of bias. Recommendations were based on data quality. Data was appraised in the neonatal setting, and where minimal data was available adult data was incorporated.

Learning Points/Discussion: The majority of the data was of poor quality with insufficient sample sizes, large heterogeneity and significant scope for confounding. The main findings are included in the table below. Handwashing, invasive catheter care and antimicrobial stewardship had the highest quality evidence, whilst other interventions require further research including randomisation, blinding and control.

<table>
<thead>
<tr>
<th>Quality of evidence</th>
<th>Recommendations</th>
</tr>
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<tbody>
<tr>
<td>Handwashing and gloves</td>
<td>Moderate (handwashing); strong (non-sterile gloves), low (resistance)</td>
</tr>
<tr>
<td>Patient isolation in an outbreak setting</td>
<td>Low (isolation in neonatal setting), low quality against isolation. Moderate (complementary data in adult settings)</td>
</tr>
<tr>
<td>Invasive catheter care</td>
<td>Moderate (preventing invasive infection), Low (preventing resistance)</td>
</tr>
<tr>
<td>Surveillance +/- decontamination</td>
<td>Low (preventing transmission of resistant bacteria); low (counterexamples); conflicting (adult data).</td>
</tr>
<tr>
<td>Stewardship</td>
<td>Moderate (preventing resistant colonisation and infection)</td>
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ANTI-STAPHYLOCOCCAL EFFICACY OF LOCAL ANAESTHETICS, ROUTINELY USED IN CLINICAL PRACTICE

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Background: Staphylococcus aureus, including its methicillin-resistant strains (MRSA), is considered to be a common cause of infectious complications and a leading agent of postoperative wound infection (ESCs) both in Ukraine and around the world. The aim of the study was to examine in vitro antimicrobial properties of local anaesthetics, at clinical doses against clinical isolates of Staphylococcus spp.

Methods: Antimicrobial activity of local anaesthetics (0.25-0.5%, bupivacaine, 2.0% lidocaine, 0.75% ropivacaine) was investigated against reference strains of S. aureus ATCC 25923, S.epidermidis ATCC 14990 and clinical isolates of S. aureus (n = 35), S.epidermidis (n = 28) isolated from patients with postoperative infectious complications, by means of the standard wells method. The results were considered after 24 hours of cultivation at t 37°C on Muller-Hinton agar diameter of zone of growth inhibition (in mm) of microorganisms around the well with anesthetics.

Results: Antimicrobial properties of 0.5% bupivacaine and 2.0% lidocaine against S. aureus, S.epidermidis were established, as evidenced by clear zones of growth inhibition of microorganisms in dense nutrient media around the wells with these analgesics. Significant benefits of delayed growth of S.aureus around wells with 0.5% bupivacaine were found to be significantly different from the effect of 2.0% lidocaine. There was found that 0.75% ropivacaine had a weak anti-staphylococcal effect. Clinical isolates of Staphylococcus spp. were proven to have sensitivity to bupivacaine 0.5%, with the advantage of its antimicrobial properties in comparison with other drugs of this group (p<0.001).

Conclusions: Particularly, the use of local anaesthetics, obtaining antimicrobial properties, is appropriate in postoperative period as simultaneous analgesic and antimicrobial management at high risk of infection with S.aureus, S.epidermidis isolates (after surgery) and the spread of multidrug-resistant isolates of the pathogens Staphylococcus spp..

Clinical Trial Registration: (Please input N/A if not registered)
IMMUNOCYTOCHEMICAL DETECTION OF HIV ANTIGEN(P24) IN THE OROPHARYNGEAL EPITHELIAL CELLS IN HIV-POSITIVE CHILDREN.

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Background: HIV/AIDS infection remains the most persistent epidemic disease of the 21st century worldwide. While still hoping for an anti-HIV vaccine to be discovered, the test and treat strategy is promising in terms of improving patients' well-being and limiting virus transmission to others. Therefore, diagnostic methods need to be affordable, rapid and efficient. The aim of our study was to determine if immunocytochemistry can detect HIV (p24) antigen in HIV-positive children.

Methods: HIV-positive paediatric patients under antiretroviral therapy were enrolled in our study. To harvest epithelial cells, swabs from the posterior pharyngeal wall and palate tonsils were collected in the morning before patients cleaned their teeth or had breakfast. The obtained swabs were spread on slides. Slides were then sent to the immunohistochemical laboratory. Anti-HIV-1 monoclonal p24 antibodies (DAKO, USA) were used to detect HIV-1 p24 antigen in the samples.

Results: Swab samples were collected from 10 children. Their ages ranged from 3 to 16 years old. All of them had been under HIV treatment for at least 2 years. The viral load was undetectable (< 20 copies/ ml) in 9 examined patients (9/10). The disease clinical stage was 4B in 4 children and 4A in the other six. HIV-1 p24 Ag was detected in five patients. The results came positive in both swab samples collected from the posterior pharyngeal wall and palate tonsils of the same paediatric patient.

Conclusions: Despite the undetectable viral load, HIV-1 p24 antigen was found in oropharyngeal epithelial cells. However, we can not state whether the low percentage of p24 detection was due to viral suppression or not. Another study before treatment should be conducted to compare immunocytochemical diagnostic efficacy to existing HIV diagnostic methods.

Clinical Trial Registration: Not applicable
HOW TUMOR NECROSIS FACTOR-RELATED APOPTOSIS-INDUCING LIGAND (TRAIL) BEHAVES AMONG CHILDREN WITH VIRAL, VIRAL-BACTERIAL OR BACTERIAL COMMUNITY-ACQUIRED PNEUMONIA

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Background: Distinguishing viral from bacterial infection among children with community-acquired pneumonia (CAP) is challenging. We compared the novel viral-induced host protein called tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) in children hospitalized with CAP with viral, viral-bacterial, or bacterial infection and in healthy controls.

Methods: Children <5-years-old hospitalized with CAP in a 21-month period were thoroughly investigated in this prospective study in Salvador, Brazil. On admission, clinical data were registered in pre-defined forms and biological samples were collected to investigate 19 aetiological agents (11 viruses, 8 bacteria). Blood sample was collected upon elective surgery anaesthesia from 31 healthy controls in the same age group. TRAIL was measured by LUMINEX in the remnant serum collected upon recruitment. For this analysis, viral infection comprised the subgroup with viral infection without bacterial infection; the subgroup with bacterial infection comprised cases with bacterial infection irrespective of also having viral one.

Results: Out of 277 enrolled patients, 214 (77.3%) had complete etiological investigation performed, out of which 201 (93.9%) had enough serum for TRAIL measurement. Viral (n=87; 43.3%), bacterial (n=32; 15.9%), viral-bacterial (n=50; 24.9%) infections, and no aetiology (n=32; 15.9%) were diagnosed. TRAIL (median [interquartile rage]) was significantly higher among patients with viral infection (29.2[19.4-40.4]) in comparison with patients with bacterial infection (n=82) (22.6[16.3-34.1];P=0.01) or with healthy controls (12.3[9.5-19.3];P<0.001). TRAIL was also significantly higher among cases with bacterial infection in regard to healthy controls (P<0.001). When children with only bacterial infection (n=32) were compared to controls, TRAIL was also higher among them (20.2[13.7-33.8];P=0.001), although to a lesser intensity.

Conclusions: TRAIL is considerably increased among children with CAP, irrespective of aetiology, being higher among cases with viral infection and lower in cases with sole bacterial infection.

Clinical Trial Registration: ClinicalTrials.gov Identifier NCT01200706
Background: Respiratory illness secondary to respiratory syncytial virus (RSV) is one of the largest causes of childhood morbidity and mortality. Determining the host genetic characteristics of childhood pneumonia secondary to RSV infection may inform the development of new clinical interventions for the disease. We performed a genome-wide association study to identify the genes associated with RSV pneumonia in childhood.

Methods: DNA collected from healthy Nepalese children and children admitted to Patan Hospital, Kathmandu with clinician diagnosed pneumonia were genotyped using Illumina Global Screening Arrays. Children with pneumonia were categorised as having RSV pneumonia if they were found to have RSV detected by PCR of their nasopharyngeal swab. DNA array data underwent QC and filtering before undergoing imputation using the HRC R1.1 2016 reference panel. Association analysis was performed using PLINK 1.9.

Results: 191 children with RSV pneumonia (cases) and 2121 healthy community based children (controls) were analysed. Following filtering of the imputed data 1565078 variants were included in the association study. One variant, within an intergenic region on chromosome 1, was found to be associated with RSV pneumonia ($p=7.4 \times 10^{-8}$, MAF cases 0.07 vs MAF controls 0.02, OR=3.8, 95% CI 2.3-6.1).

Conclusions: We identified a host genetic variant associated with RSV pneumonia. Further studies confirming this association and its biological role in RSV pneumonia are needed.

Clinical Trial Registration: ClinicalTrials.gov/N/A
Background: Tick bite is not a common reason for emergency room visit, so general pediatricians are not usually familiar with its management. Our goal was to evaluate if the implementation of an extraction protocol, possibility of immediate phone consultation with the expert, microscopic analysis of the tick and follow-up for all patients brought a significant improvement in the management of this entity.

Methods: One hundred tick bite cases who attended the emergency department of a tertiary hospital in Madrid between March 2011 and July 2018 were studied retrospectively. Later on, the referred measures were implemented and 19 cases who attended between April and December 2019 were studied prospectively. Tick bite management improvement was evaluated through three parameters: tick removal using fine forceps, microbiological confirmation of a tick-borne disease where specific antibiotics were initiated and use of antibiotics in the absence of fever.

Results: Tick removal using fine forceps was carried out in 100% (14/14) of children after the intervention, whereas, before, tick removal using scalp or needle was carried out in 26.9% (14/52, p=0.03). Suspected diagnosis justifying antibiotics was confirmed in a higher percentage of patients after the intervention (66.7% vs. 7.7%, p=0.04). Antibiotics in the absence of fever were more frequently prescribed in the pre-intervention group (27% vs. 0%, p=0.02), all non-treated patients in the post-intervention group being asymptomatic after 30 days.

Conclusions: Tick bite management at the emergency department is a possible area of improvement in which the Infectious Diseases’ specialist should be involved, being three of the most important aspects the following ones: 1) correct tick removal, 2) microbiological testing (microscopic analysis of tick to identify its genus and serologic tests) and 3) antibiotic overuse when tick-borne disease suspicion is low.
IDENTIFICATION OF ANTIRETROVIRAL MEDICATIONS: A STUDY OF ADOLESCENTS AND THEIR CAREGIVERS ATTENDING HIV CLINIC AT A TEACHING HOSPITAL IN GHANA

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Background: The ability of patients on antiretroviral therapy to correctly identify their medications is essential to medication adherence and prevention of medication related adverse effects. This is especially important in a resource limited setting where antiretroviral medications are sometimes changed due to shortage of one brand or the other. Adolescents and their caregivers's ability to identify their antiretrovirals were assessed. This study also observed medication package discarding practices of the adolescents.

Methods: We interviewed 44 adolescents perinatally infected with HIV and their caregivers who attended the HIV Clinic of Komfo Anokye Teaching Hospital (KATH) between October and December 2019 to assess their ability to identify their antiretroviral medications. We also observed the practice of discarding their antiretroviral medication secondary packaging material in the Clinic bin in order to disguise medication due to stigmatization.

Results: This study revealed that 98 % of the adolescents identify their medication by colour. Also, 21 out of 24 (88 %) caregivers who accompanied their children to the Clinic correctly identified their medication by colour. All the adolescents and their caregivers were unable to identify their medications by name. The educational level of the adolescents and their caregivers were 69 % and 75 % basic respectively. Furthermore, 64 % of the adolescents discarded the secondary packaging materials of their medications in the hospital bin.

Conclusions: Neither of the adolescents nor their caregivers were able to identify their antiretroviral medications by name. The main mode of identification of their antiretroviral medications was by colour. A majority of the adolescents discarded the secondary packaging material of their antiretroviral medication. Effort should be made to enhance medication identification through colour coding to address the challenges of medication identification.
MACROLIDE USE IN PEDIATRIC PRACTICE: A SINGLE-CENTER STUDY FROM SRI LANKA

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Background: Macrolides have shown to be clinically useful in the treatment of a wide range of infections. Macrolides play an important role in the treatment of atypical pathogens as *Mycoplasma pneumoniae*, Macrolide resistance is an emerging problem, mainly results from the misuse, particularly in pediatric practice. This study descriptively analyzes the macrolides use in children, at a Sri Lankan tertiary-care setting.

Methods: A descriptive, cross-sectional study was conducted retrospectively in three pediatric wards at a tertiary-care-hospital located in Western province, Sri Lanka. The study was conducted from January-2018 to April-2019. Clinical records of 652 patients, who were prescribed antibiotics were analyzed. The study was conducted following ethical approval from the Ethics Review Committee of Faculty of Medicine, University of Kelaniya, Sri Lanka.

Results: Beta-lactams (67.94%-443/652) were most commonly prescribed, macrolides (227/652-34.81%). 17(2.60%-443)-aminoglycosides, 12(1.84%-443)-quinolones and <1%-metronidazole, glycopeptides, nitrofurantoin and clindamycin. In 98.93%(223/227) macrolides were prescribed for respiratory tract infections, in 1.76%(4/227) for pyrexia of unknown origin. No information on microbiological tests. WBC and CRP were normal in 42.78%(86/201). A Macrolide was the first-line antibiotic in 74.44%(169/227). Clarithromycin, azithromycin and erythromycin were prescribed in 59.03%(134/134), 33.92%(77/134) and 7.05%(8/134) respectively. Macrolide overdosing and under-dosing were 41.4%(94/227) and 7.48%(17/227) respectively. In 81.49% (185/227) macrolides were prescribed for <5 days, 17.6%(40/227) for 5-10 days, 0.9%(2/227), for >10 days.

Conclusions: Macrolides were the second common antibiotic prescribed. Nearly all macrolide prescriptions were for RTIs. Microbiological study results were not available to justify therapy in any macrolide prescribed children. In about half of the children, there was hematological evidence. Macrolides were the first-line therapy in about 75% of patients. Clarithromycin was the most common macrolide prescribed. Dosage errors were very high among children receiving macrolides, where overdosing was noted in nearly half.
CLINICAL PROFILE AND OUTCOME OF ACUTE SUPPURATIVE BONE AND JOINT INFECTIONS IN CHILDREN

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Background: Acute suppurative bone and joint infections in children mainly refer to septic arthritis and osteomyelitis. The pathological invasion and inflammation of joint is known as septic arthritis. Any inflammation involving bone tissue or marrow caused by a pathogenic organism is called osteomyelitis. We conducted this retrospective study to evaluate the clinical profile and outcome of children presenting with acute suppurative bone and joint infections at our centre.

Methods: We included all children, 2 months-14 years, presenting to Pediatric emergency of a tertiary-care centre with acute suppurative bone & joint infections i.e septic arthritis and / or osteomyelitis over last 2 years. We excluded children with skin and soft tissue infections. Demographic profile, clinical presentation and treatment history along with risk factors for morbidity was noted. Descriptive statistics were used to describe various parameters.

Results: 9750 children got admitted, of which 26 children [13 males], median age 39 months (IQR-10,134), had septic arthritis ± osteomyelitis. Common symptoms were joint swelling, pain, fever and limitation of movement. 88.5% children had monoarticular and 11.5% had polyarticular involvement. Knee was the most common (38%) joint involved followed by shoulder, hip and elbow. Comorbidities included trauma, malnutrition, obesity and diabetes. Intra-articular aspirates were positive in 65% children. Salient laboratory investigations are given below.

<table>
<thead>
<tr>
<th>Investigation</th>
<th>HB(g/L)</th>
<th>CRP(mg/L)</th>
<th>ALP(IU/L)</th>
<th>TLC(x10^9/L)</th>
<th>Neutrophil (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>#Mean±SD *Median (IQR)</td>
<td>#9.9±2.2</td>
<td>101(54,263)*</td>
<td>#196±97</td>
<td>13.1(7.7,19.2)*</td>
<td>62.5(49,75)*</td>
</tr>
</tbody>
</table>

Conclusions: Acute suppurative bone and joint infections were an important cause of hospitalization in children. Their mean duration of hospital stay was 19 ± 12 days. Knee was the most common joint involved and staphylococcus aureus remained the most common aetiological organism reported. Children recovered with broad spectrum antibiotics and surgical drainage when required. There were no deaths reported in our cohort.
Background: Measles, a highly infectious disease, is still causing outbreaks world-wide despite the availability of a safe and effective vaccine for decades. During March 2018–May 2019, an epidemic of 4,300 measles cases occurred in Israel, 2150 were in the Jerusalem District, mainly unvaccinated children in Jewish ultraorthodox communities. This necessitated a rapid response of both public health agencies and health providers.

Methods: Measles is a mandatory reportable disease in Israel. Cases are defined clinically and confirmed by laboratory tests (Measles PCR/IgM) or by epidemiological linkage. The Israel routine immunization schedule includes two Measles vaccine doses at 12 months and 6 years. The first dose is provided in Maternal Child Health Clinics and the second by the School Health Service, both free-of-charge. The district health office leads the outbreak investigation and containment measures.

Results: Some 80% of cases were children younger than 15 years. Most (85%) were non-vaccinated. About 10% required hospitalization (the leading complication pneumonia/pneumonitis). Three patients died. A community oriented intervention was applied in the Jerusalem District targeting the socio economic and cultural characteristics of high incidence communities. The program included mass vaccination of children aged 1-5 years. A mobile vaccination unit rotated throughout the affected areas. The measles vaccination coverage increased from 80% to 95% within 3 months in these communities. This was followed by a significant decline in measles incidence.

Conclusions: Measles outbreaks still prevail among hard to reach communities, differing the WHO global measles elimination goal. The underlying issues and causes for under-vaccination identified during the outbreak should be acted upon and used to inform national policy makers. While mass vaccination can indeed rapidly increase the immunization coverage and contain epidemics, insuring the long standing vaccination coverage sustainability is essential.
BACKGROUND: Acute malnutrition (AM) or wasting is a serious health problem among infant and young children in Bangladesh. AM increases childhood morbidity and mortality as well. Some information on etiology for AM is still unknown as it is much more complex. Thus more information on the major risk factors of wasting in children would be useful to augment appropriate prevention programmes.

METHODS: This case-control study aimed to find the factors associated with AM in 6-59 months old children reporting to the Dhaka Hospital of icddr,b in Bangladesh conducted in 152 children with weight for-height z-score (WHZ) < -2 (cases) and 146 reference (controls) children with WHZ > -1. Variables found significantly associated with AM (wasting) in bi-variate analysis were used in logistic-regression analysis after checking multicollinearity between the independent variables.

RESULTS: There were no significant differences between the groups in age (12.1±4.5) and sex distribution. Attributes significantly associated with AM (wasting) in under-five children by logistic regression were: i) mother’s education (≤ 5 years of schooling) [adjusted odds ratio (AOR) 2.16 p=0.023]; ii) family with monthly income <12000 taka [2.3 times higher odds of having wasted children than that of the higher income family children (p=0.010)], children suffering from two or more episodes of iii) fever and/or iv) diarrhoea.

CONCLUSIONS: This is one of the extremely rare reports asserting the previous three months’ morbidities as risk factors of wasting in under-five children. These characteristics will help in preventive intervention programs. Prevention of diarrhea, pneumonia and other preventable disease by vaccination and other program can decrease the prevalence of wasting which in turn ameliorate the morbidity and mortality of under-five children in Bangladesh.
Background: Kawasaki disease is one of the most common vasculitis in children below 5 years, frequently complicated with Coronary artery abnormalities like dilation and aneurysm and increased risk of ischemic heart disease in adolescents and early adulthood. Diagnosis is based on principal clinical findings and few laboratory tests and echocardiogram. In incomplete Kawasaki disease, diagnosis is delayed and they also carry high risk of CAA.

Methods: To study clinical, laboratory and echocardiographic profile of KD, identify risk factors associated with development and compare the risk of CAA in complete and incomplete KD, in early and late diagnosed cases. Retrospective cohort study was conducted from January 2010 - April 2018. Clinical, laboratory, echocardiographic data retrieved retrospectively before May 2017, prospectively from May 2017 to April 2018. Data analyzed using Chi-square test and Student T test with SPSS package. (p<0.05 statistically significant).

Results: Delayed appearance and dispersion of principal clinical finding was associated with delayed diagnosis. Incidence of complete and incomplete KD was 42.6% and 57.4% respectively. CAA was found in 32.5% of complete KD, 50% of incomplete KD cases. 84 % cases were diagnosed early, 16% cases diagnosed late. CAA was found in 37.9% of early diagnosed cases, 66.6% of delayed diagnosed cases. CAA resolution was seen in 59.4% cases by 12 weeks, in 85% cases and partial resolution in 7.5% cases by 12 months.

Conclusions: In our study incomplete KD and delayed diagnosis were found to be associated with higher risk of CAA. Delayed resolution of fever and high initial platelet count are associated with CAA to some extent. Majority of the cases with CAA resolved during follow up and no mortality observed. Awareness among the health care providers about the illness will reduce the delay in diagnosis and also its long term complications.
KNOWLEDGE AND PREVENTIVE BEHAVIORS TOWARDS TICK-BORNE DISEASES IN BIALYSTOK, POLAND – PRELIMINARY RESULTS

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Background: Tick-borne diseases (TBD) are prevalent in Poland. The mainstay of TBD prevention is avoiding tick bites, proper tick removal, and vaccination. However, tick-borne encephalitis vaccine is the only anti-TBD vaccine available currently. It is imperative, therefore, to fight misconceptions about TBD prevention methods and to focus on developing new vaccines. We report preliminary results of a survey evaluating knowledge about TBD in Bialystok, Poland.

Methods: Parents of children hospitalized in the teaching hospital or consulted in the single outpatient clinic in Bialystok, Poland were asked in December’19 and January’20 to complete an anonymous survey. The survey consisted of 37 questions and covered the following topics: general knowledge about ticks and TBD, preventive behaviors towards TBD, and anti-TBD vaccine uptake and perceptions. We surveyed 35 adult participants (20 female and 15 male).

Results: 28/35 properly identified a tick on a picture. Consulting a healthcare professional to remove a tick is preferred by 18/35 respondents. After removing a tick 25/35 would like to test the arachnid for pathogens, and 7/35 would take an antibiotic. In the ten-point grading scale TBD were recognized as the major health problem (median 8 points), preceded by cardiovascular diseases (median 9 points), and cancer (median 10 points). Only 5/35 respondents received a vaccine to prevent TBD. 8/35 consider vaccinating themselves or their children in the future.

Conclusions: This preliminary results has shown that there are multiple shortcomings and misconceptions in public knowledge about TBD. Although TBD are considered almost equally as dangerous as cancer and cardiovascular diseases, minority of respondents considers vaccination to protect themselves or their children. Therefore there is a need to implement a wide-ranging education campaign about TBD recommend vaccination as the most effective method of prophylaxis.
Pharmacokinetic Evaluation of Micafungin Prophylaxis for Invasive Mould Disease in Childhood Acute Lymphoblastic Leukaemia: Part of the Optima Study

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Background: The Princess Máxima Center for pediatric oncology introduced a biweekly regimen of micafungin for prophylaxis of invasive mould disease, which could overcome the need of frequent hospital visits. We determined the pharmacokinetics (PK) of micafungin and defined with simulations the most optimal regimen to be deployed for mould active prophylaxis.

Methods: Micafungin was given biweekly at 9 mg/kg during the first five weeks of the induction treatment in patients with childhood ALL. A five-point curve was obtained (t=0, 2.5, 4, 5 and 24h). PK analysis was done using nonlinear mixed effects modelling, with clearance (CL) and volume of distribution (Vd) allometrically scaled to a total body weight of 70kg. Monte Carlo simulations with four dosage regimens were performed: 5 mg/kg, 7 mg/kg and 9 mg/kg (max. 300 mg) and flat dosing per weight band (0-10kg received 50mg; 10-20kg received 100mg; 20-40kg received 150 mg and >40kg received 300 mg). Simulated paediatric exposure was compared to adult exposure after 100mg daily.

Results: 62 patients were included with a total of 270 observations. Median age (range) and weight (range) were 4(1-17) years and 19.3(8.6-177.2) kg. A two-compartment model best fitted the data. Typical parameter values with relative standard error (RSE%) were for clearance (CL) 0.668(3%) L/h, central Vd 9.87(15%) L, peripheral Vd 7.15(17%) L and intercompartmental CL 2.65(35%) L/h. Simulated micafungin exposure (median area under the curve [AUC0-168] with interquartile range [IQR]) for the 5 mg/kg, 7 mg/kg, 9mg/kg and flat dosing regimens were respectively 783(245) mg·h/L, 1043(301) mg·h/L, 1251(380) mg·h/L and 951(323) mg·h/L. All simulated regimens exceeded the adult exposure of 690(244) mg·h/L.

Conclusions: Our 9mg/kg biweekly dose results in an above average micafungin exposure compared to adults receiving 100mg daily. A flat dose per weight band may be a suitable alternate.

Clinical Trial Registration: Not registered
Title of Case(s): Refractory facial fungal infection in an immunocompromised child

Background: This case describes a patient with a rare underlying immunodeficiency which resulted in an unlikely fungal infection. This is an interesting case in view of the complexity and the initial difficulty in diagnosing the offending fungal agent.

Case Presentation Summary: A 4 year old girl presented with recurrent epistaxis, malodorous nasal discharge, and a nasal lump fistulating through the nasal palate. She underwent surgical excision of affected tissue and was treated with amphotericin. She was lost to follow up and represented at 8 years old. The tissue damage had progressed with a raised galactomannan which suggested invasive aspergillosis with superimposed bacterial infection. She received treatment with voriconazole, amphotericin, vancomycin, and clindamycin and was discharged with oral voriconazole. Months later she was re-admitted and underwent fungal genomic analysis which found the infective fungus to be Corynespora cassiicola. She was treated with lysosomal amphotericin and posaconazole and was discharged on oral posaconazole with terbinafine. Extensive surgical debridement was conducted during admission. The patient was once again lost to follow up and readmitted for repeat multimodal fungal treatment, superimposed infection treatment, and was again discharged on oral posaconazole and terbinafine. During this extended hospital stay of over 6m she received comprehensive wound care and dietetic input. Despite this her fungal infection appeared to reactivate and it was decided that further surgical management would not be indicated and a decision was made for rescue therapy as needed to control rather than cure the infection. Notably, C. cassiicola typically infects plants. Therefore whole exome sequencing was undertaken which revealed heterozygous CARD9 mutations resulting in no expression in PBMCs - a poorly understood but likely reason for the susceptibility to the unlikely pathogen.

Key Learning Points: A positive galactomannan dose not necessarily mean invasive aspergillosis. Complex infections and/or underlying diseases require reliable long-term community follow-up for adequate management.
CONCURRENT OUTBREAK OF CHOLERA AND SHIGELLA IN RONIHAL VILLAGE, BIJAPUR, KARNATAKA, INDIA, 2016.

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Background: Ronihal village in Karnataka state, India, reported cluster of diarrhea cases. Two stool samples were positive for *Vibrio cholera* and one was positive for *Shigella*. We investigated to identify risk factors.

Methods: We did retrospective cohort study. We defined cholera case as occurrence of ≥3 loose stools within 24 hours, between 15th May and 21st June, 2016. We defined shigella case as occurrence of fever and diarrhoea ≥3 times within 24 hours, between 15th May and 21st June 2016. We reviewed medical records. We interviewed for water sources. We computed proportions for attack rate (AR) and relative risk (RR) with 95% confidence interval (95% CI). We cultured 6 stool samples for *Vibrio cholerae*, *Salmonella* and *Shigella*. We collected 8 water samples and tested for coliforms by H2S method. We cultured water for *Vibrio cholera*, *Shigella* and *Salmonella*.

Results: We interviewed 3746 people. Mean age was 29 years. Outbreak lasted between 25th May and 21st June, 2016. We identified 116 cholera cases (AR=3.1%). Using handpump water was associated with cholera {RR=2.1, 95% CI=1.4 – 3.2}. There were 42 shigella cases (AR=1.1%). Using overhead tank (OHT) water was associated with shigella incidence{RR=2.6, 95% CI=1.2 – 5.7}. Two stools samples were positive for *Vibrio cholerae El Tor* and one sample was positive for *Shigella*. All samples were negative for *Salmonella*. There were four water sources – handpump water, river water, well water and OHT water. OHT water was from underground borewell. All 8 water samples were unfit for consumption. There was no growth in water culture.

Conclusions: Handpump water caused cholera outbreak and OHT water caused shigella outbreak. We recommend to avoid consuming handpump water. We also recommend to regularly clean OHT and chlorinate OHT water.

Clinical Trial Registration: This is not clinical trial.
DIFFERENT RECOMMENDATIONS OF PNEUMOCOCCAL VACCINATION FOR PRETERM (3+1) AND TERM (2+1) INFANTS IN GERMANY (BIRTH COHORT 2016) – IMPACT ON VACCINATION RATES

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Background: In August 2015, the German Standing Committee on Vaccination (STIKO) changed the pneumococcal conjugate vaccination (PCV) schedule for term infants (TI) from a 3+1 scheme (2, 3, 4, and 11-14 months of age) to a 2+1 scheme (2, 4 and 11-14 months of age). For preterm infants (PI) the 3+1 schedule remained. Study aim was to assess vaccination rates and timeliness for PCV in PI after the change of recommendation based on real world data.

Methods: Retrospective claims data analysis using the InGef research database containing an age and gender representative sample of the statutory health insured population in Germany was conducted. The study population consisted of all preterm infants in the database (identified by ICD-10-GM codes P07.2 and P07.3) born in 2016 with an individual follow-up period of 24 months. Hexavalent combination vaccination (HEXA) with a consistent 3+1 recommendation for TI and PI was analysed as reference vaccination.

Results: After a follow-up period of 24 months, 68.3% of PI received the full HEXA vaccination (4 doses) according to the STIKO recommendations while only 40.5% received the full PCV vaccination, 5.4% obtained no HEXA and 5.9% no PCV vaccination at all. Of the vaccinated PI with respective PCV doses, 44.8% received the 1st dose, 25.6% the 2nd dose, 19.1% the 3rd dose, and 47.6% the 4th dose on time as recommended.

Conclusions: Although STIKO still recommends a 3+1 PCV schedule for PI in Germany, only 40.5% of all PI received the four recommended doses within 24 months of age whereas 34.3% presumably received a 2+1 schedule. Vaccinations were often delayed; more than 5% of all infants remained unvaccinated. In order to protect this vulnerable group efforts are needed to increase adherence to recommendation.
RECENT TRENDS IN THE EPIDEMIOLOGY AND RESISTANCE OF CHILDHOOD BACTERIAL ENTEROPATHOGENS IN CRETE

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Background: We have already reported on considerable changes in the epidemiology of childhood bacterial enteropathogens in Crete during the 1990s and 2000s. In the present study, we aimed to evaluate the recent trends in epidemiology and susceptibility patterns of bacterial enteropathogens among children being treated as outpatients or inpatients on the island of Crete i.e. a well-defined child population of adequate health standards.

Methods: The study included all children less than 14 years of age treated for enteritis at Heraklion University Hospital from January 2011 through December 2019. Stool specimens or rectal swabs for culture were obtained from patients either from the emergency department or upon admission to the Hospital. Stool specimens were tested for Salmonella, Shigella, Campylobacter, enteropathogenic Escherichia coli (EPEC), Yersinia, and Aeromonas species.

Results: Of 17,484 stool samples from patients of any age, 317 from children yielded a bacterial pathogen; namely Campylobacter spp. (52.4%), S. enterica (26.8%), EPEC (12.0%), Y. enterocolitica (5.36%), A. hydrophila (2.21%), and Shigella spp. (1.26%). Increasing rates were observed for Campylobacter spp (p<0.004) and decreasing for EPEC (p=0.006). As a total, enteropathogens were susceptible to imipenem, gentamicin, erythromycin, and amoxicillin in 100%, 93.7%, 91.6%, and 53.7%, respectively. Susceptibility rates increased for amoxicillin (p<0.004), gentamicin (p=0.013), co-trimoxazole (p<0.001), tetracycline (p=0.03) and decreased for erythromycin (p=0.016).

Conclusions: The present study provides updated information on enteric bacteria diversity and antibiotic resistance in the study area. The predominance of Campylobacter infections is in contrast with the previous predominance of Salmonella spp. Our findings confirm considerable changes in the epidemiology of bacterial enteropathogens and in susceptibility rates to antibacterial agents. These changing trends call for ongoing surveillance and tailored management.
ACUTE LEUKEMIA PATIENTS ADMITTED TO PEDIATRIC INTENSIVE CARE UNIT (PICU): CLINICAL CHARACTERISTICS AND PROGNOSIS OF PATIENTS ADMITTED FOR INFECTIOUS VS. NON-INFECTIOUS REASON

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Background: Pediatric hematologic patients affected by acute leukemia (AL) are a high-risk population for infection and life-threatening conditions that require PICU admission. One of the main reasons for admission is infection, which is related with higher mortality and poor prognosis according to several studies. The objective of this study is to compare clinical and microbiological characteristics, prognostic factors and outcome of patients admitted to PICU for infectious vs non-infectious reason.

Methods: Retrospective single-center analytic-observational study conducted from January 2011-December 2018 in a tertiary-care center with approximately 210 new AL diagnoses in this period. All patients from 28 days-18 years old with AL admitted to PICU were included. Patients with previous history of HSCT or CAR T-cell therapy were excluded. We collected variables related to epidemiological and clinical characteristics, laboratory and microbiology results and outcome of the patients. Data were analyzed with SPSS Statistics v.25.

Results: Sixty-four patients with AL were admitted, 33 (51.6%) had infection. Twenty-one of them (63.6%) presented with septic shock (7/21 bloodstream infection, 8/21 abdominal infection). Twelve patients had infection without sepsis, the main cause of admission was respiratory failure (8/12). 31/64 patients were admitted for non-infectious reason, mainly with hyperleukocytosis at the diagnose. Patients with infection significantly presented with severe aplasia, higher CRP and procalcitonin levels, higher PRISM score, multiorgan failure and needed more inotropics and mechanical ventilation. Three patients died during admission, all of them had infection.

Conclusions: The main cause of PICU admission in patients with AL is infection, which is associated with more severity and longer admission. It is an independent risk factor for inotropic support and mechanical ventilation, but not for death. Probably, mortality rate is low because of the early identification and PICU admission of these patients.
REAL-WORLD EFFECTIVENESS OF MEASLES-MUMPS-RUBELLA VACCINE IN CHILDREN BORN AFTER 2004 IN THE UK, ESTIMATED OVER TWELVE YEARS

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¹GSK, Vaccines, Wavre, Belgium, ²Gillian Hall Epidemiology Ltd, -, London, United Kingdom

Background: Vaccine hesitancy and/or non-compliance to vaccine schedule are major factors in the reported worldwide re-emergence and recurrent outbreaks of vaccine-preventable diseases such as measles and mumps. Data on the benefits of immunisation might encourage vaccination, yet there is limited information on the effectiveness of measles-mumps-rubella (MMR) vaccine. This is the first study evaluating simultaneously the real-world vaccine effectiveness (VE) of GSK’s MMR vaccine against measles and mumps in children, in the UK.

Methods: This observational, retrospective, matched case-control study performed in the UK Clinical Practice Research Datalink-GOLD (CPRD) and the Hospital Episodes Statistics (HES) databases included all children diagnosed with measles or mumps between January 2006–December 2018. The index date (ID) was the date of disease diagnosis for cases, recorded in CPRD, or HES linked to CPRD. Cases and controls were matched by month/year of birth and practice region. Inclusion in the study required birth after 2004 and at least one consultation recorded in the year prior to the ID. Exposure to GSK’s MMR vaccine was identified directly in CPRD by using specific vaccine batch string characters. Children who received MMR vaccines other than GSK’s were excluded from the study; only children with continuous follow-up from 10 months of age until the ID were included. VE of ≥1 vaccine dose in all children (primary objective), and VE of 1 dose and ≥2 doses in children ≥4 years of age at ID (secondary objective) was assessed.

Results: VE estimates for ≥1 dose were 78.0% against measles and 66.7% against mumps (Table).
### Table. Estimated VE of GSK's measles-mumps-rubella (MMR) vaccine stratified by dose and children's age

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Measles</th>
<th>Mumps</th>
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<tbody>
<tr>
<td></td>
<td><strong>VE (97.5% CI)</strong></td>
<td><strong>VE (97.5% CI)</strong></td>
</tr>
<tr>
<td>N</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td><strong>Overall (all children)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥1 dose</td>
<td>299 cases; 1196 controls</td>
<td>243 cases; 970 controls</td>
</tr>
<tr>
<td></td>
<td><strong>78.0 (67.2; 85.3)</strong></td>
<td><strong>66.7 (48.1; 78.6)</strong></td>
</tr>
<tr>
<td><strong>By age at index date, ≥1 dose</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1–3 years of age</td>
<td>262 cases; 1048 controls</td>
<td>180 cases; 720 controls</td>
</tr>
<tr>
<td></td>
<td><strong>73.1 (58.5; 82.6)</strong></td>
<td><strong>56.2 (26.1; 74.0)</strong></td>
</tr>
<tr>
<td>4–13 years of age</td>
<td>37 cases; 148 controls</td>
<td>63 cases; 250 controls</td>
</tr>
<tr>
<td></td>
<td><strong>92.3 (75.1; 97.6)</strong></td>
<td><strong>85.7 (63.3; 94.4)</strong></td>
</tr>
<tr>
<td><strong>Children ≥24 years of age at index date</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 dose</td>
<td>37 cases; 148 controls</td>
<td>63 cases; 250 controls</td>
</tr>
<tr>
<td></td>
<td><strong>74.6 (-21.7; 94.7)</strong></td>
<td><strong>82.3 (32.7; 95.3)</strong></td>
</tr>
<tr>
<td>≥2 doses</td>
<td>37 cases; 148 controls</td>
<td>63 cases; 250 controls</td>
</tr>
<tr>
<td></td>
<td><strong>94.4 (79.7; 98.5)</strong></td>
<td><strong>86.5 (64.0; 94.9)</strong></td>
</tr>
<tr>
<td><em><em>By disease severity (reported in HES</em> linked to CPRD)</em>*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥1 dose</td>
<td>21 cases; 84 controls</td>
<td>8 cases; 32 controls</td>
</tr>
<tr>
<td></td>
<td><strong>91.6 (52.7; 98.5)</strong></td>
<td><strong>-30.1 (-1731.0; 90.8)</strong>*</td>
</tr>
</tbody>
</table>

VE, vaccine effectiveness (derived from an adjusted conditional logistic regression); N, total number of children in each group with documentation of the corresponding data; CI, confidence interval; HES, Hospital Episodes Statistics (*available only for England); CPRD, UK Clinical Practice Research Datalink-GOLD; *insufficient subjects/children.

### Conclusions
GSK’s MMR vaccine is efficacious to prevent measles and mumps in real-world settings. Given the expected herd effect of MMR vaccination, these effectiveness data are likely underestimated.

### Funding
GlaxoSmithKline Biologicals SA

### Clinical Trial Registration
Not Applicable
SCORE TO PREDICT NON-RESPONSIVENESS TO INTRAVENOUS IMMUNOGLOBULIN IN KAWASAKI DISEASE: PROPOSAL FROM A MULTICENTRE SPANISH NETWORK

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Background: Asian scores to predict non-responsiveness to intravenous immunoglobulin (IVIG) in patients with Kawasaki disease (KD) are not useful in Western countries. We aimed to develop a score to predict failure to treatment with IVIG in Western population.

Methods: Kawa-Race network compiled retrospective data from children with KD from 84 Spanish hospitals, from May 2011-June 2016: 625 cases were collected. In order to select variables for the score, a penalized regression model was used. For continuous variables, optimal cutoffs were selected according to ROC curve. Weights of each variable were calculated with multivariate logistic regression. Score was validated with data from 98 patients collected prospectively within the Kawa-Race network, from January 2018-December 2019.

Results: Nine variables were selected with different weights for the score: masculine sex (+1.6 points), age at diagnosis <3 months (+1.6), ≥8 days of fever (+7.6), adenopathy (+1.3), inflammatory cardiologic condition (+1.3), creatinine ≥0.4 mg/dL (+3.4), C-reactive protein ≥8.7 mg/dL (+3.7), haemoglobin <10 g/dL (+2.3) and sodium <134 mEq/L (+2.4). Patients scoring ≥8 points would have a higher risk of non-response to IVIG with a sensitivity 95%, specificity 34% and area under the curve (AUC) 82.6%. Validation with the prospective cohort showed: sensitivity 78%, specificity 50% y AUC 72.7%.

Conclusions: The development of a score to predict non-responsiveness to IVIG in KD patients from Western countries would help paediatricians with initial management of these patients. Validation of this score in other cohorts will allow generalizing first therapeutic approach to children with KD, being more aggressive when necessary.

 Clinical Trial Registration: N/A (it is not a clinical trial)
EVALUATION OF SEROCONVERSION FOR THE MMR-V AND HBV VACCINES AND ITS CORRELATION WITH THE IMMUNOLOGICAL STATUS IN CHILDREN WITH HIV INFECTION.

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¹University of Naples Federico II, Department Of Translational Medical Sciences, Section Of Pediatrics, Naples, Italy, ²University of Naples Federico II, Department Of Translational Medical Sciences - Section Of Pediatrics, Naples, Italy

Background: While healthy children show a good serological response to the main vaccines little is known about the serologic response in HIV-infected children. The study evaluates the immune response towards selected vaccines in children with vertically acquired HIV infection.

Methods: All patients with vertical HIV infection, followed-up in the pediatric reference centre of Naples (Italy) were included in the study. The control group included 30 otherwise healthy children matched for age and sex. The serological response for MMR-V and HBV vaccines was tested. A booster was administered to non-responder children and serological response was checked again.

Results: 30 subjects (13 male, median age 14 years) were enrolled. 15 patients received the vaccinations as scheduled and 7 started the vaccination program before the ART. The response rate was lower for all vaccines, in HIV group compared to the control group. A significant difference was detected for Rubella (64% responders in HIV vs 89% in the control group, p= 0.0257) and HBV (38% vs 74%, p=0.0219). Nine patients did not respond and received a booster. In the booster group the seroconversion rate was 100% for Measles, 75% for mumps, 66.6% for Rubella, 85% for HBV and 66.6% for chickenpox. Children who received vaccines before being started on ART were less responsive comparing to children receiving vaccines after the beginning of ART (Measles 41% vs 72%; Mumps 29% vs 68%; Rubella 57% vs 70%, HBV 14% vs 57%)

Conclusions: The response to vaccines is lower in HIV children. The beginning of ART before vaccination allows a better response to the vaccines. The evaluation of serological response to the vaccines may be routinely checked in children with HIV infection to test the protection toward vaccine preventable diseases.

Clinical Trial Registration: Clinical trial registration: N/A
Background and Objective: MenB is a major cause of invasive meningococcal disease (IMD). For 2 MenB protein-based vaccines, 4CMenB (GSK) and rLP2086 (Pfizer), immunogenicity and safety data supported licensure, since efficacy studies are not possible due to low IMD incidence. Immunogenicity was evaluated by serum bactericidal antibody assay using human complement (hSBA) against reference strains. A high variability in antigen presence and expression level across strains/isolates precludes extrapolation of these results, and hSBA testing against all MenB strains is impossible. Therefore, alternative methods were needed to predict strain coverage by MenB vaccines.

Methods: We reviewed publications describing all methods assessing vaccine coverage across IMD-causing MenB strains, to provide a better insight as to their purpose and how predictions are obtained/derived. In addition to hSBA, 4 methods were developed: the Meningococcal Antigen Typing System (MATS), the flow cytometric MEningococcal Antigen SURface Expression (MEASURE) assay, genetic MATS (gMATS), and Bexsero Antigen Sequence Type (BAST) scheme.

Learning Points/Discussion: •MATS predicts 4CMenB strain coverage by assessing the level of antigen expression and cross-reactivity for vaccine components. MATS combines ELISA for 3 antigens (using polyclonal antibodies) with genotyping/serosubtyping for the 4th (Table). •MEASURE predicts rLP2086 strain coverage by quantifying surface expression of factor H binding protein variants in MenB strains, using a single monoclonal antibody which recognizes a region conserved among different variants or subfamilies. •gMATS uses genotyping of 4CMenB antigens and predicts strain coverage based on matching of peptide variants significantly-associated with MATS coverage. •BAST is based on the same principle as gMATS, with some differences across peptides predicted to be covered. •While not without limitations, current methods afford a robust and rapid prediction of MenB strain coverage by protein-based vaccines. Funding: GlaxoSmithKline Biologicals SA
<table>
<thead>
<tr>
<th>Vaccine</th>
<th>MATS</th>
<th>MEASURE</th>
<th>gMATS</th>
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<tbody>
<tr>
<td></td>
<td>4CMenB</td>
<td>rLP2086</td>
<td>4CMenB</td>
<td>4CMenB</td>
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**Description**
- **phenotypic method combining 3 antigen-specific sandwich ELISAs for fHbp, nadA and NHBA with genotyping/subserotyping information for PorA**
- **phenotypic method assessing fHbp surface expression and accessibility on intact bacteria**
- **genotypic method using antigen genotyping measuring coverage in alignment with MATS**
- **genotypic method evaluating association of genetic lineage (sequence type) with 4CMenB antigen components and MATS**

**Strain coverage prediction**
- **A strain is considered covered when the MATS value for ≥1 of the 4 antigens is higher than a defined threshold**
- **A strain is considered covered when fHbp expression is higher than a defined threshold**
- **By identifying peptide IDs significantly associated with MATS coverage/non-coverage for that antigen**
- **By examining antigen peptide sequences present in both the vaccine and epidemiological dataset and genotype-phenotype modelling**

ELISA, enzyme-linked immunosorbent assay; fHbp, factor H binding protein; nadA, Neisseria adhesin A; NHBA, neisserial heparin binding antigen; PorA, porin A; IDs, peptide identification numbers.
Background and Objective: Meningitis and neonatal sepsis combined are estimated to be the second largest infectious killer of children under the age of 5 years, so tackling them is integral to ending preventable child deaths. To accelerate progress, the World Health Organization have launched a global plan to defeat meningitis by 2030. Meningitis Research Foundation (MRF) created an interactive visualisation to track progress.

Methods: MRF collated meningitis and neonatal sepsis burden estimates from the Institute of Health Metrics and Evaluation (IHME), WHO, Maternal Child Epidemiology Estimation group (WHO-MCEE) and Johns Hopkins Bloomberg School of Public Health. Burden estimates, vaccine introduction dates, programme types and coverage rates, plus meningitis surveillance data and socio-demographic data were input into Tableau to gain insights into the status of meningitis prevention, surveillance, diagnosis and treatment, and support and aftercare.

Learning Points/Discussion: There is considerable variation between global meningitis and neonatal sepsis death estimates in under 5 year olds (IHME and WHO-MCEE estimated 355,770 and 479,730 respectively in 2017). Over 93% of modelled deaths came from countries with low quality or no underlying data. Nevertheless, these estimates suggest mortality is highest in countries with limited access to health care. In 2015 pneumococcal vaccines had been universally introduced in 129 countries yet 60% of all children aged 1-59 months remained unimmunised. WHO figures show that meningococcal vaccines were available routinely or to at risk groups in 68 countries in 2019. An estimated 42 million healthy years of life were lost from meningitis and neonatal sepsis in 2017 The MPT has been viewed over 27,000 times by users including epidemiologists, patient groups, ministries of health and public health bodies from 79 countries. User testing to expand content is planned in July 2020.
E. Mutsaerts¹, M. Nunes¹, S. Bhikha¹, B. Ikulinda¹, L. Jose¹, A. Koen¹, A. Moultrie¹, D. Grobbee², K. Klipstein-Grobusch², A. Weinberg³, S. Madhi¹
¹University of the Witwatersrand, Respiratory And Meningeal Pathogens Research Unit, Faculty Of Health Sciences, Johannesburg, South Africa, ²University Medical Center Utrecht, Utrecht University, Julius Global Health, Julius Center For Health Sciences And Primary Care, Utrecht, Netherlands, ³Anschutz Medical Center University of Colorado Denver, Department Of Pediatrics, Medicine And Pathology, Denver, United States of America

Background: HIV-exposed uninfected (HEU) children have increased risk of infectious morbidity during early childhood. We evaluated the immunogenicity and safety of single dose inactivated hepatitis-A virus (HAV) vaccine and live attenuated varicella zoster virus (VZV) vaccine in South African children.

Methods: 195 HIV-unexposed and 64 HEU children received either one dose of HAV or VZV vaccine at 18 months of age. Blood samples were tested for hepatitis-A or VZV antibodies before and one month after vaccination by chemiluminescent microparticle immunoassay and enzyme-linked immunosorbent assay, respectively. All children were evaluated for solicited adverse events (AEs).

Results: One-month post-vaccination, a similar percentage of HIV-unexposed (91.8%) and HEU (82.9%) children were seropositive for hepatitis-A (p=0.144). VZV antibody geometric mean fold-rise was also similar in HIV-unexposed (5.6; 95%CI: 4.6-6.7) and HEU children (5.1; 95%CI: 3.7-7.2); however, only 44% HIV-unexposed and HEU seroconverted (titers >50 mIU/ml). AEs occurred with similar frequency and severity between groups.

Conclusions: Single dose HAV and VZV vaccine was similarly safe and immunogenic in HIV-unexposed and HEU children. We did not identify differences in humoral immunity after administration of either a live attenuated or inactivated vaccine. Seroconversion rates after a single dose of VZV vaccine were, however, lower compared to reports from previous studies (85%-89%).

Clinical Trial Registration: ClinicalTrials.gov NCT03330171
Title of Case(s): Epidemiological evaluation of complex bone and joint infections in children in four French hospitals

Background: Paediatric bone and joint infection (BJI) exhibit epidemiological, microbiological and pathophysiological differences in comparison with BJI affecting adults. Guidelines from european or french pediatric societies have been published but focus on hematogenous infections. In contrast, data are lacking concerning complex BJI such as comorbidities/immunodeficiency or postoperative infections. Better understanding will allow us to improve our diagnostic and therapeutic practices that determine their prognosis.

Case Presentation Summary: Complex BJI are defined by comorbidities, recurrence of infection, microbiology or surgery. This retrospective observational study was carried out between January 2009 and December 2016 in four French hospitals. Patients from 0 to 17 years old hospitalized for complex BJI were included. We assessed the presentation at a multidisciplinary staff (main objective) and the treatment's adequacy with the recommendations and its quality. We included 111 patients. 69 % of the infections were osteitis, the preferential location was the lower limb (59 %) and the predominant bacterial agent was Staphylococcus aureus (42 %). 66 % were postoperative infections and 51 % occurred on orthopedic device. 47 % of patients had a complex microbiological criterion. 45 % had comorbidities, half of which was neuromuscular deficiency and one quarter immune deficiency. 23 % had a recurrence of infection. 37 % benefited a multidisciplinary staff meeting. 31% had at least one sequel at 6 months. 5 % stays were revalorized.

Learning Points/Discussion: Our multicenter study showed that complex bone and joint infections represent a significant proportion of bone and joint infections. Their less formal management, with adaptation to the comobidities and the bacteriological samples of the patient, is complex. Hence the importance of multidisciplinary management in experienced centres. The impact in terms of sequelae, hospitalizations and costs is substantial and remains little revalorization.
Background: Children who breastfeed have a stronger immune system, which is a factor that can prevent them from infectious and viral diseases. Therefore, they can easily recover after being treated for severe illness.

Methods: Material & Methods: This study reviewed the effect of breastfeeding on the prevention of infectious disease on children. For this reason, we searched the scientific sites and search engines and reviewed related articles.

Results: Many research pointed out that breast milk not only prevents and protects infections in infancy but also reduces the risk of some diseases at an older of age. Researchers believe that breast milk contains immunogenic substances that are not found in any milk and have no such nutrients. Breastfeeding can work well because of the immunogenic properties of a newborn infant whose immune system is defective. Studies have shown that in the country where most infants are breastfed especially exclusive breastfed, the incidence of fatal diseases, including respiratory, gastrointestinal, and lung infections, has been significantly reduced. Besides, some mothers may deprive the baby of breastfeeding when supplemental foods started at the age of six months, the baby exposed to diarrhea and infectious diseases and the rate of infectious disease raised.

Conclusions: Breastfeeding is one of the most important preventive factors for children's diseases, especially infectious diseases. Thus, we recommended that health care providers during pregnancy and after birth persuaded and trained parents to commence breastfeeding at birth and continue after 6-month combined with supplementary food for two years. As a result, child health increases and infant mortality declines.
Background: The ongoing measles outbreak in Ukraine has already involved over 115000 people since 2017. Measles usual care involves vitamin A administration, and supportive treatment. Ribavirin has previously been found to effectively block rubeola virus replication in vitro, and some data confirming its efficacy in adults with measles are available. The interventional clinical study aimed to investigate safety and clinical efficacy of ribavirin in treatment of measles in immunocompetent children.

Methods: After obtaining local ethics committee approval and patients’ informed consent we enrolled 28 immunocompetent patients aged 3 to 18 years no later than 48 hours since the onset of exanthema. Rubeola infection was confirmed with serum IgM detection. None of the participants had received any post-exposure prophylaxis prior to enrollment. Eighteen patients were randomly assigned to the main group to receive oral ribavirin plus usual care; ten children getting conventional therapy only were the controls. We performed clinical efficacy assessment and safety monitoring. Mann-Whitney U-test and Pearson Chi-squared test were used to evaluate statistical significance.

Results: We found no differences between the groups regarding the duration of exanthema or hospital stay. However, the duration and expression of fever, malaise, cough and conjunctivitis were reduced in patients receiving ribavirin compared to controls. No cases of rubeola complications were documented in the main group. We registered no signs of drug-related toxicity of ribavirin. Basing on the subgroup analysis we suggest that earlier administration of ribavirin may influence the disease duration more significantly.

Conclusions: Ribavirin administration in immunocompetent children with measles in the first 48 hours of exanthema is well-tolerated and alleviates a set of clinical manifestations of the disease. Further studies are required to address the efficacy and indications for ribavirin use in pediatric patients.

Clinical Trial Registration: Not applicable
ANTIBIOTIC PRESCRIPTION FOR RESPIRATORY TRACT INFECTIONS IN THREE LEVELS OF HEALTHCARE: WHERE AND HOW CAN WE DO BETTER?

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Background: Respiratory tract infections (RTIs) are common in children with febrile illness visiting the general practitioner or emergency department. In this retrospective observational study we will zoom in to the management of, and more specifically antibiotic prescription for children with fever and a RTI visiting three different levels of healthcare in Nijmegen area, the Netherlands. We will analyse the differences between these levels of care.

Methods: This retrospective observational study is part of the MOFICHE (Management and Outcome of Fever In Children) study as part of the PERFORM (Personalised Risk Assessment in Febrile illness to Optimise Real-life Management across the European union) study. MOFICHE aims to assess the management and outcome of children with fever presenting to emergency departments across Europe. Data are used from face-to-face patient contacts in three different healthcare settings in the Nijmegen area, the Netherlands during the year 2017.

Results: Antibiotic prescription rate for RTIs irrespective of focus was around 30% in all three levels of healthcare. Otitis has the highest prescription rate being around 60% in all levels. In primary care, mostly narrow spectrum betalactams were prescribed whereas in secondary or tertiary care a more mixed picture was seen including also broad spectrum betalactams, macrolides and cefalosporins. Modelling antibiotic prescription to absolute numbers per 100.000 children shows that the vast majority of antibiotics are prescribed in primary care.

Conclusions: Antibiotic prescription rate for RTIs in children is around 30% in all three levels of healthcare in Nijmegen area, the Netherlands and comparable with earlier studies. A higher prescription rate in cases of otitis and the use of broad spectrum antibiotics is worrying and probably not according to national guidelines. Absolute numbers of antibiotic prescriptions are highest in primary care.
REDUCTION OF ANTIVIRAL ADMINISTRATION AND HOSPITALIZATION WITH THE USE OF RAPID SENSITIVE MOLECULAR TESTING FOR INFLUENZA

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¹Attikon University Hospital of Athens, Pediatrics, Athens, Greece, ²Attikon University Hospital of Athens, Clinical Microbiology, Athens, Greece, ³National and Kapodistrian University of Athens, Third Department Of Pediatrics, Athens, Greece

Background: Influenza is associated with significant morbidity, health care costs, hospitalization rates and mortality in children. Rapid immunofluorescence assay (IFA), a test with low sensitivity, is often used as point of care (POC) test. Recently, a rapid molecular test (FilmArray Respiratory Panel, FA RP; BioFire Diagnostics, Salt Lake City, UT) became available. This study aims to evaluate whether the use of FA RP would decrease the use of antivirals and hospitalization rates among children presenting to ER with influenza-like symptoms (ILI).

Methods: Nasopharyngeal swabs were prospectively collected from all children (0–16 years old) presenting with ILI at the ER of a tertiary hospital during the peak endemic period. Patients were randomized to be tested by either FA RP or IFA according to the day examined (odd versus even days). Use of antivirals and hospitalization rates were noted and the results were analyzed.

Results: Overall, 155 children were included (mean age: 5 years). Administration of oseltamivir in both outpatients and hospitalized children with negative influenza test was significantly decreased in the FA RP group when compared to the IFA group (0% vs 46.4%, p=0.00013 and 12.5% vs 66.6%, p=0.007, respectively). Hospitalization rate was lower among children with FA RP(+) compared to those with IFA(+) (12.5% vs 45.4%, p=0.04). The implementation of rapid molecular test had no impact on complementary diagnostic testing or antimicrobial prescription.

Conclusions: The use of FA RP significantly reduced oseltamivir administration in children, since pediatricians felt more confident. Of note, 12.5% of hospitalized children with FA RP(−) received oseltamivir. Children with IFA(+) had higher hospitalization rates, indicating need for further education on the use of POC tests. Improving the reliability of rapid influenza diagnosis may improve current management of children presenting with ILI and decrease associated health care costs.
IMPORTANCE OF AN EARLY IDENTIFICATION OF A FORGOTTEN CONGENITAL INFECTION IN A SETTING WITH NATIONAL PREGNANCY SCREENING

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Title of Case(s): Importance of an early identification of a forgotten congenital infection in a setting with national pregnancy screening

Background: Congenital syphilis (CS) may have severe and long term outcomes. Signs and symptoms may appear several weeks after birth, making it difficult to get an early diagnosis. Prevention and detection of CS depend on an adequate screening in pregnant women. Italian guidelines for the management of physiological pregnancy recommend a treponemal screening test in the first and third trimester of pregnancy.

Case Presentation Summary: We describe 4 children (2 males, mean age 9.5±13.6 months) who received a diagnosis of CS (Nov 2018-Sept 2019) based on evocative signs or symptoms and lack of third trimester treponemal screening in the mother. Three child (75%) had macular rash and shedding on palms and soles. Two of them (50%) had severe anaemia, needing blood transfusion. The onset of the disease was marked by pneumonia in Case#1 and by periostitis in Case#2. The fourth case, a two-years old boy with a mild developmental delay and language disorder, was investigated for late congenital syphilis because of positive maternal screening during a new pregnancy. He had microcrania at birth and presented with peg-shaped upper central incisors and saber shins. Clinical suspicion of congenital syphilis was confirmed by treponemal and nontreponemal tests that were also positive in the cerebrospinal fluid in 3 children (75%). Appropriate treatment with intravenous penicillin G was administered to all children.

Learning Points/Discussion: Even in countries where treponema screening is mandatory in the first and third trimester of pregnancy, some women may skip controls. The rarity of the CS may increase misdiagnosis, resulting in a delay in appropriate treatment. This case series renew the importance of an early identification of signs and symptoms of infection to avoid late diagnosis and severe long term outcomes.
INFECTIOUS COMPlications FOLLOWING SURGERY FOR ACUTE APPENDICITIS IN CHILDREN: IS LAPAROSCOPY THE BEST APPROACH?

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**Background:** Laparoscopic approach is currently the gold standard for appendectomy in children but may be associated with a high rate of infectious complications of both surgical site and deep tissue.

**Methods:** A single centre prospective study was performed at Regina Margherita Children's Hospital in Turin, involving all patients aged 0-14 years with acute appendicitis, treated by laparoscopic (LA) or laparotomic (OA) surgery between 22/06/18 and 21/11/19, describing the incidence of post-appendectomy infectious complications.

**Results:** 150 patients were recruited, 90 males and 60 females, mean age was 8.8 years. LA intervention was performed in 66% of cases, OA intervention in 34%; 61 patients showed an uncomplicated acute appendicitis (40.7%), 47 patients (31.3%) a complicated appendicitis and 42 cases (28%) a generalized peritonitis. All patients underwent pre-intervention antibiotic therapy. No differences in the mean length of hospital stay between LA- or OA-treated patients were founded (LA: 6.8 days; OA: 6.9 days), nor comparing post-LA and post-OA duration of antibiotic therapy or considering home treatment after discharge. The overall rate of postoperative infectious complications was 12%, significantly higher in the LA-group (16.2% vs 2% post-OA, p=0.012): 14 cases of organ/space surgical site infection (14 post-LA vs 0 post-OA, p=0.003), 3 cases of deep tissue infection (2 post-LA vs 1 post-OA).

Relative risk for infective complications post-LA versus OA was 8 (95% CI: 1.1-58.6).

**Conclusions:** Incidence of postoperative infections in acute appendicitis is significantly greater post-LA, which furthermore did not even demonstrate advantages in terms of reduction of hospitalization time and procedure costs. However, patient postoperative well-being is greater, in terms of resumption of daily activities and less painful symptoms linked to smaller skin incision. A better balance between the two techniques is therefore desirable.

**Clinical Trial Registration:** No clinical trial registration
Necrotizing Osteomyelitis of the Femur Due to Fusobacterium Nucleatum in a 15-Year-Old Adolescent

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Title of Case(s): Severe infection due to Fusobacterium spp.

Background: Fusobacterium infections present a broad clinical spectrum from benign pharyngitis to thrombophlebitis or bacteremia. Few cases of Fusobacterium osteomyelitis have been reported, mainly of the head and neck secondary to dental or ear infections. Hematogenous osteomyelitis have exceptionally been described. We report a case of monomicrobial severe necrotizing pyomyositis leading to chronic osteomyelitis of the leg due to Fusobacterium nucleatum.

Case Presentation Summary: A previously healthy 15-year-old boy presented a month after minor trauma with a painful left thigh swelling, weight loss and 2-days of pyrexia and shivering. Blood tests showed important inflammatory syndrome (CRP>300mg/L). MRI and CT-scan revealed diffuse pyomyositis with moderate femoral cortical osteolysis. The patient underwent an emergent curettage and drainage surgery followed by intravenous treatment with Clindamycin and Amoxicillin/Clavulanic acid. Anaerobic cultures from surgical samples yielded massive growth of Fusobacterium nucleatum, further confirmed by 16S DNA-sequencing (Fusobacterium spp.). After 7 days, he was discharged home with oral Clindamycin. MRI follow-up at 8 weeks revealed extensive chronic osteomyelitis of the femoral diaphysis with bony sequestrum. A second surgery was conducted for extensive bone curettage and external fixation. Pathology demonstrated extensive necrotic bone tissue with lymphoplasmacytic infiltrates. After another 2 weeks of intravenous Clindamycin and Metronidazole, oral Clindamycin was continued for 4 months. After 5 months external fixation was removed but femur remains non-vascularized and patient is under close orthopedic follow-up.

Learning Points/Discussion: We report an unusual case of necrotic muscle and bone infection due to Fusobacterium nucleatum leading to extensive bone loss in a young patient. Our case emphasizes the importance of maintaining a high index of suspicion for anaerobic osteomyelitis, given its atypical presentation and unique growth requirements of anaerobic bacteria, and the value of multidisciplinary collaboration when treating osteoarticular infections.
WHOOPING COUGH: THE EXPERIENCE OF A PEDIATRIC DEPARTMENT OVER THE LAST 7 YEARS

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Title of Case(s): Whooping cough: The experience of a pediatric department over the last 7 years

Background: Whooping cough is a respiratory infection caused by Bordetella pertussis. With introduction of pertussis vaccine there was a decrease in the number of cases worldwide, however, over the past decades, pertussis incidence has been increasing. We report a series of cases of hospitalized patients with Bordetella pertussis infection in a level II hospital pediatric department for the last 7 years.

Case Presentation Summary: There were 23 patients diagnosed with whooping cough: 4 in 2013, 2 in 2014, 4 in 2015, 11 in 2016 and 1 in 2017 and 2019. Median age was 2 months (16 patients ≤ 2 months) and 12 patients were male. Symptoms were presented in a median of 7 days before admission and the majority had cough (n=22) and/or episodes of cyanosis (n=17). Apnea, rhinorrhea, whooping and fever were seen in a minority of patients (n=4; n=10; n=4; n=3 respectively). Fourteen patients had a relative with cough. Laboratory tests showed leukocytosis in 11 patients, lymphocytosis in 8 and thrombocytosis in 13. Three patients were co-infected with other agents (2 metapneumovirus, 1 E. coli). Almost all patients were treated with azithromycin (n=22) and only 8 needed oxygen supplementation. The median days of hospitalization was 6. One patient had to be transferred to intermediate unit care and 2 patients were re-hospitalized after discharge. There were no other complications.

Learning Points/Discussion: Infants below 2 months are at higher risk of having this disease because of their incomplete immunization, and we also reported a higher prevalence in this age group. There was a reduction of hospitalized patients with B. Pertussis infections in our hospital after 2016. Although Pertussis has cyclic epidemics, we relate this result to the introduction of maternal immunization in 2016 in our country.
Background: Pertussis is a severe respiratory infection of global distribution caused by Bordetella pertussis. Vaccination play an important role to reduce the number of cases. However, the disease has reemerged in the last decade in several countries, including Brazil. We describe the clinical and epidemiological aspects of pertussis in Salvador in order to evaluate factors associated with the occurrence of the disease.

Methods: This is a descriptive and retrospective cross-sectional study conducted in five hospitals in Salvador that reported the highest number of pertussis cases during 2011-2016. For each patient, basic demographic information and clinical data were recorded. Prevalence ratios and difference between groups (confirmed vs unconfirmed cases) were analyzed using Poisson Regression with robust variance and Pearson's Chi-square or Fisher's exact test, respectively.

Results: The most affected age groups was <2 months (PR=2.82; CI=2.03-3.94; p<0.001) and ≥ 2 months to <4 months (PR=2.44; CI=2.01-2.97; p<0.001). Occurrence of pertussis was associated with non-vaccinated individuals (PR=1.51; CI=1.34-1.72; p<0.001) and individuals with incomplete immunization (PR=1.23; CI=1.03-1.47; p=0.022). All investigated cases presented cough in association with one or more symptoms especially paroxysmal cough (p=0.001) and cyanosis (p<0.001). Most of cases were confirmed by clinical criteria.

Conclusions: The outcomes were consistent with other studies, occurring mostly in infants and unvaccinated individuals. The predominance of clinical criteria to confirm the cases indicates the necessity of improvement of the laboratory tools for rapid diagnosis of pertussis. This study highlights the importance of vaccination strategies to reduce the burden of severe disease, particularly in susceptible young infants, and the epidemiological surveillance to better understand reemerging pertussis.
ROSEOLOVIRUSES-INDUCED INFECTIOUS MONONUCLEOSIS IN CHILDREN OF BELARUS

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Background: Roseoloviruses (Human herpesviruses types 6A (HHV-6A), 6B (HHV-6B) and 7 (HHV-7)) can induce infectious mononucleosis (IM) during primary infection or reactivation in immunocompetent hosts. Although three distinct viruses exist, most primary infections in children are caused by HHV-6B. The aim of the study was to determine the frequency of detection of roseoloviruses in patients with IM Epstein Barr virus (EBV) and cytomegalovirus (CMV) negative.

Methods: Roseoloviruses were detected in serum from 35 patients aged 0 to 10 years who were hospitalized with suspected roseolovirus infection at City Children’s Clinical infectious Disease Hospital. Quantitative detection of HHV-6, EBV and CMV DNA was carried out by real-time PCR with a commercial kit, and HHV-7 primers and probe (Wada et al., 2009) were used for detection of HHV-7 DNA. EBV and CMV infections were also excluded by ELISA.

Results: Most patients were 3 years of age (57.1%). HHV-6B DNA was found in 7 (20.0%) patients. Both HHV-6B and HHV-7 DNA were detected in 1 (2.9%) patient. The patients admitted on 2.9±1.1 day of disease. Mild cervical lymphadenopathy and fever were the most common presentation (about 4.7±1.5 days long). 3 (42.9%) children had exanthema; 5 (71.4%) - tonsillitis; 2 (28.6%) - adenoiditis; 5 (71.4%) – hepatomegaly; 1 (14.3%) splenomegaly. The highest quantity of HHV-6 in serum was in patients with exanthema >10³ copies/ml.

Conclusions: Our results show that IM induced by HHV-6B proceeded in a moderate and mild form in children of out of ages. IM should be suspected in young children with fever, mild cervical lymphadenopathy, tonsillitis and hepatomegaly. Children under 3 years old had an exanthema. Etiotropic therapy was not performed. In one child with mononucleosis, cHHV-6 was detected in the absence of other viruses.
Background: Familial Mediterranean Fever (FMF) is a rare inherited autoinflammatory disease and information about it would be helpful.

Methods: The search was carried out using the electronic database PubMed attempting to find reviews, clinical trials, case reports from the recent bibliography.

Results: FMF is considered an autosomal recessive disease associated with mutations of MEFV gene, which encodes pyrin (a regulator of the production of interleukin-1). However, heterozygotes may also present FMF. FMF is prevalent among Arabic, Turkish, Jewish and Armenian communities. Its onset is usually, before the age of 20. Incidence between males and females is almost equal (M/F:1,2/1). FMF is characterized by recurrent, self-limiting episodes of fever, serosal, synovial or cutaneous inflammation that last from 12 to 72 hours. The duration of interval periods varies from weeks to years. Although between the episodes patients are free of symptoms, there is a sub-clinical state characterized by increased inflammation markers such as CRP or ESR, however, autoantibodies are not detected. Major complication of FMF is amyloidosis which is related with male gender, presence of arthritis and some gene mutations (e.g. MEV694V). It mainly affects kidneys even leading to renal injury. It may involve gastrointestinal duct, spleen, liver, heart, and lungs. There is also a higher risk of ischemic heart disease among patients with FMF. The main treatment of FMF is colchicine which also plays a preventive role in the development and advance of amyloidosis. In colchicine-resistant cases, anti-IL-1 agents are used such as canakinumab, with less side effects and recession of the disease.

Conclusions: FMF is a crucial disease because of the danger of amyloidosis. Diagnosis is mainly clinical, relying on clinical manifestations, assessment of inflammatory markers, response to colchicine and genetic testing.

Systematic Review Registration:
BONE SCINTIGRAPHY FOR OSTEOARTICULAR PAIN OR FUNCTIONAL DISABILITY IN CHILDREN: A RETROSPECTIVE STUDY

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**Background:** Osteoarticular pain or functional disability in children are common reasons to visit pediatric emergency department. Osteoarticular infections are potential causes and their early diagnosis is a major concern since risk of complications may be avoid by a prompt treatment. Bone scintigraphy can help physicians when the children's examination is non focal. The objective of this retrospective study is to determine the benefit of bone scintigraphy according to the age of children consulting for osteoarticular pain or functional disability.

**Methods:** In this retrospective study, we included all children having a bone scintigraphy prescribed by an emergency physician from January 2017 to December 2017. Our main outcome was the rate of osteoarticular infections diagnosed by bone scintigraphy in the children under and above 3 years. We also compared the rate of traumatic diseases, inflammatory diseases, and normal results of bone scintigraphy.

**Results:** During the study period, 104 children performed a bone scintigraphy. 16/49 (33%, 95% CI[21% - 47%]) children < 3 years and 3/55 (5%, 95% CI[2% - 15%]) children >3 years were diagnosed by bone scintigraphy as osteoarticular infection. **Table : Scintigraphy results**

<table>
<thead>
<tr>
<th>Normal</th>
<th>Infectious</th>
<th>Inflammatory</th>
<th>Traumatic</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3 years N=49 (%)</td>
<td>11 (22%)</td>
<td>16 (33%)</td>
<td>1 (2%)</td>
<td>18 (37%)</td>
</tr>
<tr>
<td>&gt;3 years N=55 (%)</td>
<td>27 (49%)</td>
<td>3 (5%)</td>
<td>6 (11%)</td>
<td>9 (16%)</td>
</tr>
</tbody>
</table>

**Conclusions:** In our study, bone scintigraphy was more often helpful to diagnose osteoarticular infection in children under 3 years than in older one. Despite ionizing radiation and the lack of soft tissue detail or abscess detection, the physician should consider bone scintigraphy particularly when history, physical examination, radiograph, and ultrasound findings fail to localize the pathologic area and when Magnetic Resonance Imaging examination is not possible.
SAFETY OF 9-VALENT HUMAN PAPILLOMAVIRUS VACCINE ROUTINELY ADMINISTERED TO 216,000 INDIVIDUALS

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Background: The nine-valent human papillomavirus (HPV) vaccine (9vHPV, Gardasil®9) was licensed in the United States in December 2014 and targets HPV 6, 11, 16, 18, 31, 33, 45, 52 and 58. Using a self-controlled risk interval design, we conducted a post-licensure retrospective cohort study within Kaiser Permanente in Northern California (KPNC) to assess 9vHPV safety following routine administration.

Methods: We included KPNC members 9-years or older who vaccinated with 9vHPV between Oct-2015 and Sep-2017 regardless of prior 4vHPV (Gardasil®) administration. Post-vaccination emergency room and hospitalization were compared by diagnoses during risk intervals (days 1-60 and 0-14) with later self-comparison intervals across all doses using conditional logistic regression. We investigated significant findings by assessing post-vaccination timing and medical record reviews. We evaluated and reviewed medical records for all day 0 allergic reaction and syncope events, as well as all deaths during the study. An independent Safety Review Committee reviewed potential safety signals.

Results: The study included 215,965 9vHPV-vaccinated individuals, including 84,908 (39%) who received 2 doses and 29,901 (14%) 3 doses, totaling 330,774 doses. Comparing risk and self-comparison intervals, only delirium (OR 8.93 95%CI [1.13, 70.53]), digestive disorders (OR 2.06 [1.04, 4.09]) and skin disorders (OR 2.83 [1.02, 7.66]) were significantly increased. Some vaccination day allergic reactions and syncope were potentially related to vaccination. None of the 37 deaths were related to 9vHPV administration.

Conclusions: This study of individuals vaccinated with 9vHPV, regardless of prior 4vHPV, did not identify any new safety events related to 9vHPV administration. Most findings were previously known, preceded vaccination, or were better explained by other medical history. This large study of individuals vaccinated with 9vHPV during routine medical care provides reassuring evidence of the favorable safety profile of the 9vHPV.

Clinical Trial Registration: ClinicalTrials.gov N/A
Background: Parapneumonic effusions in children are usually associated with pneumococcal infections. In Greece, the 7-valent pneumococcal conjugate vaccine was replaced by higher-valent pneumococcal conjugate vaccines; 10-valent was introduced in May 2009 and 13-valent in June 2010.

Methods: We studied all pneumococcal pediatric community-acquired pneumonia (CAP) cases with empyema hospitalized at the University General Hospital of Larissa, Central Greece, from January 2008 to December 2019.

Results:

There were 24 cases of empyema due to *Streptococcus pneumoniae* aged 1.8-9.7 years (median 4 years). The identifiable serotypes were: 3, 19A, 7F, and 9N/L. After September 2011, no more cases caused by serotypes 7F and 19A were observed, whereas serotype 3 emerged as the predominant pathogen (16 of 24 cases, $\chi^2$ for trend; $p<0.005$). Among the 16 cases of empyema caused by serotype 3, eight children were vaccinated with PCV13 either fully in a 3+1 schedule (n=7) or with one booster dose at the age of 21 months (n=1).

Conclusions: In Central Greece after the implementation of PCV13, serotype 3 was the only PCV13 serotype that persisted in children with empyema. We did not observe any significant increase of cases of CAP complicated with empyema due to non-PCV13 serotypes.
CONFIRMED HOSPITALIZED MEASLES CASES IN A PEDIATRIC DEPARTMENT OF A TERTIARY HOSPITAL IN PIRAEUS, GREECE; A DESCRIPTIVE STUDY.

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Background: Measles is a highly infectious vaccine-preventable disease of the respiratory system, leading to significant childhood morbidity and mortality. The disease has alarmingly reemerged in the recent few years in several geographic regions around the world, including Greece. The aim of the present study was to describe demographic and clinical characteristics of children hospitalized for measles in the city area of Piraeus in Greece.

Methods: Epidemiological characteristics of children with measles admitted to our hospital during a 7-month period (10/2017-4/2018) were evaluated retrospectively. Laboratory diagnosis of measles cases was based on positive serologic testing (IgM/IgG). Statistical analysis was performed with the statistical software IBM SPSS Statistics V25. Individual patient data was anonymized, while all stages of this study were in full compliance with bioethical principles.

Results: Fourteen episodes requiring hospitalization were analyzed. Median patients’ age was 3 years (28.6% < 1 year of age). Greek Roma children living in crowded conditions were mainly affected (78.6%). The majority of cases (92.9%) was recorded in totally unvaccinated children, while 7.1% of patients had received a single vaccine dose. No case was reported among fully vaccinated children. In 64.3% of episodes, prior close contact with other patients was recorded. No underlying disease was identified. Clinical characteristics of hospitalized children are illustrated in Table 1. Complications were present in 35.7% of cases; Subsequent pneumonia (40%), acute otitis media (20%), croup (20%), bronchitis (20%). No death was documented.

Table 1. Clinical features of children hospitalized for measles.

<table>
<thead>
<tr>
<th>Clinical feature</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Clinical signs of dehydration</td>
<td>71.4%</td>
</tr>
<tr>
<td>Rhinitis</td>
<td>92.9%</td>
</tr>
<tr>
<td>Koplik spots</td>
<td>78.6%</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>50%</td>
</tr>
</tbody>
</table>

Conclusions: In this retrospective study, measles was mainly reported in otherwise healthy Roma children. The majority of patients was totally unvaccinated and previously exposed to other close contacts diagnosed with measles. The aforementioned findings are in line with literature, indicating the need for full 2-dose vaccination course as well as the high epidemic potential of measles leading to significant disease burden.
MOLECULAR EPIDEMIOLOGY OF STAPHYLOCOCCUS AUREUS INFECTIONS IN CHILDREN IN CRETE: A CHANGING LANDSCAPE.

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Background: Infections caused by Staphylococcus aureus (S. aureus) are common in childhood including skin and soft tissue infection (SSTI), toxin-mediated disease (TMD) and invasive disease (INV). Aim of this prospective cohort study was to investigate the clinical, microbiological and molecular characteristics of methicillin-resistant (MRSA) or methicillin-susceptible (MSSA) S. aureus strains causing infections in children admitted in a referral centre.

Methods: We performed a four-year cohort study with culture-proven invasive and non-invasive, community-associated (CA), community-onset healthcare associated (COHA) and hospital-associated (HA), MRSA or MSSA S. aureus infections in children from January 2015 to December 2018. EUCAST standardised antimicrobial susceptibility testing was applied and genes encoding Panton–Valentine leukocidin (lukS/lukF-PV), toxic shock syndrome toxin-I (tst), exfoliative toxins (eta, etb), fibronectin binding protein A and B (fnbA, fnbB) were investigated by polymerase chain reaction.

Results: In total, 140 isolates were recorded (107 CA, 16 HA, 17 COHA). SSTI predominated (95.67.8%), followed by INV (22,15.7%) and TMD (23,16.4%). Thirty-one (22.1%) isolates were MRSA. Thirteen isolates (9.4%) were lukS/lukF-positive, 27(19.4%) eta positive, six (4.3%) etb positive, 125(89.9%) fnbA positive and 21(15.1%) fnbB positive. tst was more common among MRSA and eta among TMD strains. MSSA rates increased from 2015-2016 to 2017-2018 (OR 3.13; 95%CI 1.36-7.21;p 0.007) along with a rise in FA resistance (OR 2.93; 95%CI 1.08-7.92;p 0.03) and in TMD frequency (OR 3.46; 95%CI 1.06-11.21;p 0.04).

Conclusions: In this cohort, we found rising trends of MSSA S. aureus isolates causing primarily skin and soft tissue infections and toxin mediated disease in children. A predominance of CA strains with no significant differences among CA, COHA and HA strains was also noted. Over the four-year study period, increasing rates of fusidic acid resistance and toxin-mediated disease were identified.
CASE REPORT: ENTEROBACTER ASBURIAE ASSOCIATED OSTEOMYELITIS AND BACTERAEMIA

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Title of Case(s): Case report: Enterobacter asburiae associated osteomyelitis and bacteraemia

Background: Enterobacter asburiae is a member of Enterobacteriaceae family. Enterobacter asburiae is gram negative, facultative anaerobic bacteria. Invasive infections due to E. asburiae are very rare. It may proliferate on blood, urine, fecal and wound site cultures. Herein, we present a case of a 4 year old girl with 3M syndrome and osteomyelitis caused by E. asburiae in calvarium after corrective surgery for craniosynostosis.

Case Presentation Summary: A 4 year and 7 month old girl, who had a corrective surgery for craniosynostosis, presented with fever, four days after discharge. On 3rd day of admission, blood culture was yielded gram negative bacilli. Meropenem and amikacin combination was started in pediatric intensive care unit. On the 4th day of admission, purulent drainage was observed at the wound site. Wound swab cultures and blood cultures yielded E. asburiae. Seizures were observed and cranial CT was consistent with collections on the left cerebellar hemisphere and the falx cerebri region. Surgical debridement was repeated due to persistent purulent discharge from the wound site. E. asburiae was reported in bone tissue culture and bone abscess cultures. After four weeks of meropenem therapy, CRP and erythrocyte sedimentation rate returned to normal values, wound site drainage was stopped and the local inflammation findings relieved. Causative microorganism was known to be susceptible to ciprofloxacin and the patient was discharged with consecutive oral ciprofloxacin treatment.

Learning Points/Discussion: E. asburiae is an uncommon human pathogen. It is often used in agriculture and pharmaceutical industry. E. asburiae act as a biocontrol agent for nematode control on plants. Invasive infections related to E. asburiae is reported very rare in the literature. It can cause healthcare-associated infections and cross-transmission can occur. Their antibiotic resistance features are well known based on overproduction of AmpC β-lactamases.
EVALUATION OF DEEP NECK SPACE INFECTIONS IN CHILDREN: A SINGLE-CENTER EXPERIENCE

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**Background:** Deep neck space infections (DNSIs) are serious clinical conditions that involve potential spaces of the fascial planes of the neck. Complications in DNSIs can occur due to delay in treatment and can result in sepsis, death or prolonged hospitalization. The aim of this study is to evaluate the clinical findings, predisposing factors, causative agents, outcomes and management of DNSIs in children.

**Methods:** The data of patients with deep neck space infections were examined retrospectively for demographic characteristics, clinical presentation, microbiological and radiological findings, complications, and outcomes. Subjects included children under 18 years old admitted for DNSIs in our hospital. The study conducted at Marmara University Pendik Training and Research Hospital, Department of Pediatric Infectious Diseases in Turkey between October 2017 and December 2019.

**Results:** A total of 42 patients presented with DNSIs during the study period, there were 15 (36%) females and 27 (64%) males. The mean age was 7 years. The most common symptoms at presentation were neck swelling (87.5%) and fever (52.5%). The submandibular space was the most affected region (80%). Two patients (5%) had peritonsillar, two (5%) had parapharyngeal and four (10%) had retropharyngeal infection. The most common etiology was odontogenic infection (40%). *Streptococcus viridans* was the most common organism isolated in 8 (36%) patients. All patients were discharged without complication.

**Conclusions:** Deep neck space infections are severe infections occurring in the potential cervical fascial planes of the head and neck and continue to cause morbidity and lethal complications. Rapid diagnosis and treatment of DNSIs may improve prognosis in children. Educating the population about orodental health and the early removal of an affected tooth or teeth is essential to reduce these challenging infections.
VITAMIN A SUPPLEMENTATION IN CHILDREN HOSPITALIZED FOR MEASLES IN A HIGH-INCOME COUNTRY

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**Background:** Medical authorities recommend vitamin A supplementation for severe measles infections requiring hospitalization. However, evidence supporting its use in high-income countries is very limited and outdated. A nationwide vitamin A shortage reported in concomitance with a recent measles outbreak in Italy provided the opportunity to test the effectiveness of vitamin A in a high-income setting, simulating a random allocation to treatment.

**Methods:** This prospective controlled cohort study enrolled children admitted for measles to a tertiary-care hospital in Southern Italy (Nov-2015 to May-2019). Based on the local availability, only some children received two doses of oil-based vitamin A. Matched children receiving standard care served as controls. The primary outcome was the duration of fever, secondary outcomes included the length of hospitalization, rate of complications, need for antibiotics, and body temperature.

**Results:** Overall 108 children (median age 16.3 months) were enrolled: 36 receiving vitamin A and 72 controls. There were no significant differences between groups in the duration of fever (7.03±2.67 vs. 6.82±3.27, p=0.74), length of hospitalization (median, 5.5 vs. 5.0 days, p=0.36), maximum body temperature (median, 39°C in both groups, p=0.90), rate of organ (69.4% vs. 63.9%, p=0.56) and hematological complications (41.7% vs. 59.7%, p=0.07), or the need for antibiotics (66.7% vs. 61.1%, p=0.57). Overall, vitamin A supplementation did not reduce the risk of any complications (Relative risk 1.33, 95%CI 0.59-2.96).

**Conclusions:** According to the results of this prospective cohort study, vitamin A does not change the clinical course of measles or the rate of complications in children hospitalized in a high-income country. Sub-group analysis in children with chronic conditions, weight-for-age <2 SD, known measles contact, or receiving care within 48h of fever did not demonstrate effectiveness of vitamin A over standard care.
Background: Respiratory syncytial virus (RSV) is a major worldwide cause of morbidity and mortality in young children and the leading cause of hospitalization for acute respiratory infection in infants. However, recent studies have indicated that the burden of RSV is great also among outpatient children. There are few data on the clinical features and management of RSV in young children treated as outpatients.

Methods: We compiled data from three prospective cohort studies of respiratory infections in outpatient children performed in Turku, Finland, between 2000-2018. In all studies, the children were examined at a study clinic at any signs or symptoms of respiratory infection, and nasopharyngeal swabs were obtained for viral detection during each illness. Clinical data were recorded on standardized medical records, and the parents filled out daily symptom diaries.

Results: In total, 430 children 0-3 years of age had a laboratory-confirmed RSV infection. Acute otitis media was diagnosed in 279 (64.9%) children with RSV; the frequency was highest in children <1 year of age (78.5%) and lowest in children 3 years of age (48.8%). Pneumonia was diagnosed in 11 (2.6%) children. Altogether, 284 (66.0%) children with RSV received antibiotic treatment, 21 (4.9%) were referred to the hospital emergency department, and 10 (2.3%) were hospitalized.

Conclusions: This study demonstrates that although some children with RSV are hospitalized, most of them are managed completely in the outpatient setting. Acute otitis media was the most frequent complication of RSV illness, and two-thirds of children 0-3 years of age received antibiotics. The results emphasize the medical need to develop effective ways of preventing and treating RSV infections in children.
Communal Acquired UTI in the Rural Area. New Times, New Resistance Patterns

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Background: Community-acquired Urine Tract Infections (CA-UTI) is one of the most common infections in childhood. The increasing rates of resistance in healthy kids entails a challenging issue. Hitherto, our centre (located in a rural area), had have low taxes of resistance to Amoxiciline-Clavulanate (A/C). The objective of this report is to study the clinical and microbiological evolution of the CA-UTI at our area.

Methods: Observational retrospective study. We included all the patients under 14 years with UTI or acute pyelonephritis (defined as positive urine culture and symptomatology), diagnosed at our hospital and primary care area from 2014 to 2018, and Hospital patients in 2019. We studied their clinical features, urine culture results, antibiograms (EUCAST), and received treatment. Study of statistical significance through chi-square test

Results: 344 patients included (F76%). Age average: 12 months. Sample origin: 50% Hospital. Nephropathy in 14.5%. Admission in 27.3%. Causative bacteria: 73% E.Coli, 10.7% K.Pneumoniae, 7% P.Mirabilis. Focusing on E.Coli, we found an stable resistance pattern: Ampiciline 53%(46%-65%), Cotrimoxazole 26.6%(19%-29.7%), Quinolones 8.1%(3.8%-10.2%). However, an increasing trend was observed in A/C (table). Non statistical relationship between admission and higher resistance rates.

The 21% received oral antibiotics 6 months previously (55.3%A/C, 12.5%Cefuroxime, 10%Fosfomicine). On this subgroup, the resistance rates were: 80% Ampiciline, 22% A/C, 33.3% Cotrimoxazole. The main treatment was A/C(59%), followed by Cefalosporines(14%), Gentamicine(6%), Fosfomicine(1.5%).

![R A/C rate in E.Coli](image-url)
**Conclusions:** In our area, the main responsible of CA-UTI was *E.Coli*. It has a high stable resistance rates to Ampicilnine and Cotrimoxazole over the years. A global increasing trend on the resistance to A/C has been observed, with a large rise the last year on the hospital samples. These results leads to perform an adequacy of our antibiotic stewardship to the current data and hold a prospective surveillance to reduce resistances.
PROSPECTIVE STUDY OF HEARING LOSS IN PATIENTS WITH KAWASAKI DISEASE

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Background: Hearing loss is a common complication observed in patients with Kawasaki disease. Some studies have shown an incidence of up to 36%, even higher than the presence of coronary aneurisms (21%), but more prevalence studies and better understanding about the pathophysiology is needed. We have monitored the hearing function in patients with Kawasaki Disease in our Hospital in a prospective study.

Methods: Children diagnosed with Kawasaki disease in a Tertiary Hospital between November 2018 and January 2020 were included in this study. Gender, age, presence of coronary aneurism, complete or incomplete disease, and IVIG resistance were described. Hearing tests were performed depending on the age of the patient during the acute period (first month after the diagnosis) and six months after the diagnosis.

Results: Ten patients were diagnosed with Kawasaki disease, with a mean age of 33.1 months. Three of them (30%) presented coronary aneurisms. One of them needed a second IVIG dose. Three of them (30%) had criteria of complete Kawasaki disease. Only one of them (10%) presented abnormal audiometry and in this patient testing was performed during a suspected serous otitis media and confirmatory hearing tests are pending.

Conclusions: We did not find hearing loss as a common complication in Kawasaki disease patients in our study despite the presence of aneurisms in 30% of the patients, contrary to the results observed previously in another studies. More research and a higher number of patients is needed in future to test the real magnitude of this problem and to clarify the risk factors involved.
Title of Case(s): Congenital syphilis presenting with severe metabolic acidosis and shock: A case report.

Background: Congenital syphilis (CS) caused by *T. pallidum* remains a public health issue despite universal prenatal screening. Recently, a rise in the incidence of CS has been observed parallel to the rise of primary and secondary syphilis in adults. Here, we report a case of CS in a 21-day-old infant who presented with severe metabolic acidosis, poor feeding and skin eruption.

Case Presentation Summary: A 21-day-old girl was admitted with poor feeding, diarrhea and desquamating skin rash. She was born to a 32-year-old mother at 38 weeks by caesarean section with a birth weight of 3,160gr. On examination, she was pale, poorly perfused with sunken fontanel and palmoplantar desquamation weighing 2,730gr. Laboratory studies showed severe metabolic acidosis (pH=6.84, pO2=139, pCO2=18.3, HCO3=4.3 mM/l, BE=-28mM/l), raised WBC, anemia and leukocytosis on CSF examination with elevated protein concentration (WBC: 65/mm^3, red blood cells: 12/mm^3, protein: 294mg/dL). CSF and serum rapid plasma reagin (RPR) were positive at titers of 1:8 and 1:256 respectively (prozone phenomenon) and syphilis serology test showed positive immunoglobulin M and G. Review of maternal records revealed that syphilis testing had not been performed until then. Both parents tested positive for RPR and were referred to the STI clinic while siblings were found negative. The infant was treated with penicillin G for 14 days. Ophthalmic examination including fundoscopy was normal and skeletal survey revealed no radiological evidence.

Learning Points/Discussion: Early diagnosis of CS can be challenging. This case emphasizes the importance of universal antenatal screening even in low-risk pregnancies. All pregnant women should be screened for syphilis at least once during pregnancy and should be treated promptly to prevent mother-to-child transmission. Syphilis screening should be reviewed at delivery or prior to home discharge to avoid life-threatening manifestations.
SACROILIITIS BY CORYNEBACTERIUM DIPHTHERIAE

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Title of Case(s): Sacroiliitis by an unexpected agent

Background: Although potentially fatal, infection by Corynebacterium diphtheriae became rare in the developed world since the introduction of effective immunization. The burden of disease lies mainly in developing countries. Nevertheless, systemic infections have recently been increasing, mostly from emerging nontoxigenic strains with potential to cause invasive disease. These infections are often associated with travel to prevalent endemic areas of C. diphtheriae.

Case Presentation Summary: An incompletely immunized 10-year-old girl with corrected tetralogy of Fallot presented to the emergency department with limping due to right upper thigh pain, fever, vomiting and diarrhea. She had returned from rural Cape Verde where she contacted with livestock and unsafe water. Blood tests revealed microcytic, hypochromic anemia, leukocytosis (17350/uL), thrombocytopenia, elevated C-reactive protein (355.8 mg/L), procalcitonin (5.05 ng/ml) and erythrocyte sedimentation rate (76 mm/h). Hip and pelvic radiography and ultrasonography were normal. MRI confirmed sacroiliitis. Blood and fecal cultures were obtained and she started ceftriaxone and clindamycin. A nontoxigenic strain of Corynebacterium diphtheriae was isolated from 2 blood cultures and treatment was changed to penicillin. Cutaneous, otolaryngologic and cardiac involvement were excluded. On day 4, she developed signs of arthritis on her right ankle and underwent arthrocentesis, whose culture was negative. She completed 4 weeks of amoxicillin with favorable outcome. Remaining cultures were sterile. On discharge, she received a sixth dose of diphtheria toxoid. She stayed asymptomatic on reevaluation.

Learning Points/Discussion: Corynebacterium diphtheriae remains a major human pathogen worldwide. Infection by nontoxigenic clones in Europe has been rising, although osteoarticular infection has rarely been reported. Despite lacking diphtheria vaccine booster, toxoid immunization still would not have protected our patient against nontoxigenic strains. These strains are known to cause atypical course of disease especially in predisposed individuals such as congenital heart disease.
"EFFECT OF INTERVENTIONS ON COMPLIANCE OF FIVE MOVEMENTS OF HAND HYGIENE, IN PICU AND PHDU OF TERTIARY CARE HOSPITALS IN PAKISTAN"

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Background: Hand hygiene (HH) is the single most effective measure to prevent health care associated infections. Germs are a source of severe infections in healthcare and are spread by hands. Hand hygiene is therefore the most simple and effective approach to prevent infections. Poor hand hygiene compliance increases the risk of obtaining hospital acquired infections (HAIs) especially in Pediatric oncology through direct contamination of patients Prevention of health care associated infections in pediatric oncology which results decrease in morbidity and mortality in developed and developing countries.

Methods: Observational study was conducted at peds department from July 2018 to July 2019. Nurses and doctors were the target population for study from The Indus Hospital. There are a total of 74 nurses and 14 doctors. Intervention provided in the form of lectures through PowerPoint presentations and videos. Pre and post observation was collected by the Trained Infection Control Practitioners (ICP).

Results: Total 2649 events of HH recorded. Out of these events, the nurses exhibited greater adherence (65%) to the HH recommendations than did the doctors (46%). The nurses' compliance rate was significantly increase (65% vs. 86%) and the doctors also increase (46% vs.73%). There was also reduction in the total rates of HAIs, calculated as the healthcare-associated infection (HCAI)/1000 patient-days, from 23.58% to 5% in the pre- and post-intervention periods, respectively.

Conclusions: Many studies have been conducted to assess the overall compliance of hand hygiene. Although it is very difficult to achieve the five moment of hand hygiene in hospitals. core competency by WHO is focusing on educational intervention for increase the hand hygiene compliances, that can helps to decrease the HAI's, and our study showed better results of HH compliances in resulting decreases in HAIs.
Background: Central line blood stream infections in cancer children are high risk for hospital Acquire infections and leading causes of death. The prevention of healthcare associated infections is the key of safe and high quality care that can decrease morbidity, mortality and cost burden, purpose of this study is to access the impact of education of care bundle and reduction in infection rates at pediatric oncology unit.

Methods: Core competency model by WHO of education were followed. education about prevention of central line associated cblood stream infection care bundle were given to 145 pedeatric oncology nurses, check list were used. data were collected between Jan 2018 to December 2019, All cancer children admitted in PICU and PHDU and aged between 1 year to 12 year were part of study.

Results: Before education Central Line Associated Blood Stream Infection rate was 43.47 and after education rate was decreased to 24.39 The common organisms causing Central Line associated BSI were Vancomycin Resistant Enteroccus (VRE) 17.6%, Klebsiella spp 11.76% ,Burkholderia cepacia 11.76% ,Acinetobacter 11.76%,E.coli 11.76% where as Stenotrophomonas maltophilia 9% ,Candida 9% and contamination of enviornmental organisms also found and that was Coagulase negative staph were 9%.

Conclusions: There is a need regular education in reduction in devisees associated infections in critical care area of hospitals, this is expected to significantly reduction in infection related morbidity and mortalities. As studies have proven that if Healthcare workers have frequent educational activities can improve the practices. However, with more awareness and better guidelines, both sepsis and central line infections appear to be declining.
INFLUENCE OF SCHOOL CLOSURES AND SOCIAL DISTANCING CAUSED BY HEAVY SNOWFALL ON THE SEASONAL INFLUENZA EPIDEMIC IN FUKUI PREFECTURE

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Background: School closures and social distancing are important mitigation strategies during influenza pandemics. In early February 2018, the heaviest snowfall in the last 37 years struck the northern area of Fukui prefecture. Traffic paralysis prevented people from going out, and most schools were closed for about a week in the northern area. We analysed the effects of snowfall on an influenza epidemic.

Methods: A nationwide influenza epidemic began in late November 2017. The number of influenza patients across Japan reached a peak in the 5th week of 2018. Thus, we investigated the change in the frequency of absenteeism in elementary and junior high school children due to influenza in Fukui prefecture before and after the heavy snowfall that occurred in the 5th week of 2018.

Results: In the northern area, the school absenteeism rate due to influenza reached a peak in the 4th week, dramatically dropped shortly after the heavy snow, and showed a second peak in the 9th week. In other areas of Fukui without serious snowfall-related damage, a second peak was not observed. During the heavy snowfall and the following 2 weeks, the absenteeism rate was significantly lower in the northern area than in the southern area (0.07–0.13% vs 0.28–0.22%, p < 0.05).
Conclusions: The cumulative incidence rate of influenza did not differ significantly between the northern and southern areas at the end of the season, suggesting that simultaneous school closure could not control the epidemic in children susceptible to seasonal influenza. However, simultaneous school closure and social distancing might be useful to prevent the overconcentration of influenza patients in clinics and hospitals for a short period.
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INFLUENZA VIRUS LARYNGOTRACHEITIS COMPLICATED BY BACTERIAL SUPERINFECTION

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Title of Case(s): A Rare Respiratory Complication of Influenza A Virus

Background: Influenza infection is a self-limited disease. However, it is a year-round burden worldwide. The spectrum of clinical finding and severity of disease may vary according to type or subtype of influenza. Factors associated with increased mortality is underlying medical problems, age <5 years old (particularly <2 years old), bacterial coinfection, and increase circulation of influenza A H3N2 strains. This is a case report of an 18 month-old child with a rare respiratory complication of Influenza virus Laryngotraceitis complicated by Bacterial Superinfection.

Case Presentation Summary: A previously healthy 18 month-old boy presented with a one day history of high fever, chill, cough, and runny nose. Influenza screening of nasal swab was positive for influenza A. Hospital admission was suggested but parents refused due to personal problem. Tamiflu was prescribed. Next day, he visited emergency room due to stridor at rest, dyspnea, cyanosis, and high fever. He had a sign of respiratory distress caused by upper airway obstruction. In addition, his white cell count was high with neutrophil predominance. His neck x-ray revealed steeple sign. He was given IV Dexamethasone and Adrenaline nebulizer every 1 hour with oxygen support, Ceftriaxone, and Tamiflu. The definitive diagnosis was Influenza A infection with complication of Bacterial Tracheitis. He was admitted to ICU. Fortunately, he didn’t need artificial airway support. He then got better gradually.

Learning Points/Discussion: Laryngotraceitis can be a severe complication of influenza A infection, particularly if having bacterial superinfection. Hospital admission is crucial for influenza infection in high risk population because they are at increased risk of severe or complicated disease. Influenza vaccination should be given to anyone, from 6 months of age, as it is the best tool to prevent influenza and reduce its complication and death.
A RARE BUG, WHAT IS THE DRUG?

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Title of Case(s): A rare bug, what is the drug?

Background: Trichosporonosis is a common cause of fungemia in immunocompromised patients after Candida spp. The mortality rate is between 50-80% and outcomes depend on host's immune status and extent of infection. Trichosporon species are rare agents of CNS infections. Its diagnosis is likely to be missed, because of lack of awareness. This is a rare case of Trichosporon Asahii infection in a 4 year old involving the brain.

Case Presentation Summary: A 4 year 7 month old well grown, developmentally normal male child presented with fever and altered sensorium for 30 days. Vitals were stable with left sided facial nerve palsy and hemiparesis. The child was managed as HLH for a month with steroids elsewhere. There was no contact with tuberculosis and the child was completely immunised for age. The complete hemogram revealed leucocytosis with neutrophilic predominance, high CRP. CT and MRI brain was suggestive of meningitis and multiple brain abscess. CSF analysis showed neutrophilic predominance with elevated protein and reduced glucose and gram positive yeast was identified. Blood culture showed Trichosporon Asahii. Managed with IV Meropenem and Vancomycin initially and was initiated on IV Voriconazole and Liposomal Amphotericin B but expired in 20 days despite therapy.

Learning Points/Discussion: Main clinical features are fever with fungemia, tissue invasion involving multiple abscess formation. Trichosporon spp. has displayed variable resistance to the most common antifungals. A recent ESCMI/ ECMM joint guidelines for the diagnosis and management of rare invasive yeast infections recommends Voriconazole. The poor outcome in the present case may be attributed to the widespread involvement of the CNS. Some T. asahii isolates belonging to genotype 3 have shown reduced susceptibility to voriconazole. This fatal case will alert the medical fraternity regarding the rare and emerging infections with minimal options for management.
PERFORMANCE OF A PAEDIATRIC EARLY WARNING SCORE FOR CHILDREN WITH INFECTIOUS SYMPTOMS IN THE EMERGENCY DEPARTMENT

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Background: Paediatric Early Warning Scores (PEWS) are simple scoring systems, traditionally used to detect clinical deterioration in hospitalized children. We developed a novel PEWS designed for emergency departments (EDs). The score consists of age and six physiological parameters: consciousness, work of breathing, oxygen saturation, respiratory rate, heart rate, and capillary refill time. We assessed the performance of the ED-PEWS for children attending the ED with infectious symptoms.

Methods: This study is part of the TriAGE project, a prospective observational study conducted in five European EDs (2012-2014). Included were all consecutive ED-visits of children <16 years, presenting with infectious symptoms. The main outcome measure was a previously developed 3-category reference standard (high, intermediate, low urgency; a composite outcome based on management during and disposition after the ED visit) as proxy for true patient urgency. Secondary outcomes were ICU and hospital admission. Performance was assessed with the area under the curve (AUC), and sensitivity and specificity.

Results: In total, 35,918 children were included: 1140 (3%) of high and 13,555 (38%) of intermediate urgency. The ED-PEWS demonstrated an AUC of 0.85 (95% confidence interval 0.84 to 0.86) for identifying high urgency and 0.73 (0.73 to 0.74) for both high and intermediate urgency patients. Regarding the secondary outcome measures, the AUC was 0.81 (0.78 to 0.83) for ICU and 0.68 (0.68 to 0.69) for hospital admission. A score ≥16 was useful for identifying high urgency patients with a specificity of 0.75 (0.73 to 0.77), while a score <6 identified low urgency patients with a sensitivity of 0.91 (0.90 to 0.91).

Conclusions: The ED-PEWS can aid healthcare workers with the prioritization of children presenting with infectious symptoms at the ED. Further validation is needed for specific populations and repeated measurements.

Clinical Trial Registration: Not Applicable
Title of Case(s): COULD THE POTTY HELP REVISIT SPINAL ARTHRITIS IN CHILDREN?

Background: Septic Arthritis of Facet Joint (SAFJ) in children have historically been scarce, though severe cases are known. Its features are poorly described in the literature and there is no consensus as to its management. To address these important gaps, we carried out the first systematic review of children's cases of SAFJ. Bringing together cases from the literature and from our hospital database, we aimed to estimate incidence of SAFJ in the general paediatric population, specify clinical, imaging and biological diagnostic criteria, and identify avenues for appropriate management.

Case Presentation Summary: A total of 16 cases are identified, including nine published case-reports and seven unpublished cases found in our hospital (One denied use of personal information). This represents the largest case series ever described in children. Incidence rate was estimated to be 0·23 per 100 000 children-years. Diagnostic criteria are painful sitting or (in toddlers) potty refusal combined with local inflammation. Associated symptoms include a febrile limp, spinal stiffness, lower back pain, and root pain. Confirmation of the diagnosis and assessment of the extent of the infection is achieved by MRI. Bacteria involved in SAFJ do not differ from those encountered in other BJI in children. SAFJ treatment is based around targeted antibiotherapy derived from blood cultures or local aspiration, and could strongly benefit from an antibiotic stewardship approach.

Learning Points/Discussion: When refusal of the potty from young toddlers—equivalent to painful sitting in children—is associated to paraspinal back infiltration, early suspicion of SAFJ is possible as early as the bedside. As the availability of spinal MRIs increases, detection of SAFJ will increase. Further work is necessary to develop awareness of this previously unrecognised disease and draw robust guidelines for its paediatric management.
DEPTHS OF TROUBLE: DIGGING DEEPER IN RELAPSING SYMPTOMS FOLLOWING OSTEOMYELITIS

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Title of Case(s): Depths of trouble: digging deeper in relapsing symptoms following osteomyelitis

**Background:** Osteomyelitis caused by Staphylococcus aureus is a common infection in childhood. The usual management of debridement and appropriate antibiotics resolves the majority of cases without complication. This case illustrates the need for further investigation when relapse occurs despite adequate treatment.

**Case Presentation Summary:** A 7 year old presented to the local general hospital with right knee pain and fever. CRP was 173 mg/L and a femoral subperiosteal collection was identified on MRI. This was drained and Staph aureus sensitive to flucloxacillin was grown from pus and blood culture. IV flucloxacillin was commenced but symptoms recurred 10 days later and there was a recollection requiring further drainage at the same site; Staph aureus grew again. Echocardiography was normal. Antibiotics were given for 3 months, with repeat thigh MRI and CRP normalised, after which they were stopped. One week later she represented with fever, CRP 147 mg/L, and was referred to Bristol. On detailed questioning, parents reported she had complained of back pain. Spinal MRI with contrast showed abnormal high signal of T8 and T9 vertebrae and adjacent left 8th and 9th ribs with extension paravertebrally up to T3 paravertebral level partly encasing the descending aorta (figure 1). Echocardiography showed no valve involvement, she was managed using a 24 hour flucloxacillin infusion via an elastomer device with the outpatient antibiotic therapy service. Repeat imaging showed reduction in size of the peri-aortic collection.

**Learning Points/Discussion:** With osteomyelitis with bacteraemia careful history of potential other sites should be sought and imaging direct to symptoms or whole body MRI used to identify other sites. If relapse of symptoms occurs despite local control and appropriate treatment further imaging and investigation is necessary.
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VIRAL LOWER RESPIRATORY TRACT INFECTIONS - STRICT ADMISSION GUIDELINES FOR YOUNG CHILDREN CAN SAFELY REDUCE ADMISSIONS

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Background: Guidelines to identify children in need of admission for viral lower respiratory tract infection (VLRTI) are lacking in the literature. In December 2012 our hospital introduced strict guidelines for admission. In particular, children 3-24 months old with SpO2 > 92%, respiratory rate < 70, pediatric early warning score < 3, Lowell's retraction score < 6/9, adequate fluid balance and intake, and without apnea or comorbidity were considered safe for discharge without admission. This study aims to retrospectively validate the safety and efficacy of the guidelines.

Methods: Single-center retrospective database search and medical record review. ICD-10 codes identified children < 24 months assessed at the emergency department (ED) for VLRTI for a 10 year period. To identify adverse events related to admission guidelines implementation, we reviewed patient records for all discharged patients who were readmitted within 14 days. Admission rates from the ED were calculated before and after the intervention.

Results: 2139 children 3-24 months old were assessed on the ED for VLRTI, 876 before and 1263 after guidelines implementation. 72.3% had a diagnosis of bronchiolitis. Hospital admission rates from the ED were 68.6% before and 53.3% after the intervention (P<0.001). 4 children not admitted on initial assessment were admitted with dehydration or severe respiratory distress within 48 hours of their primary contact to the ED, 2 before and 2 after guidelines implementation.

Conclusions: The implementation of admission guidelines for VLRTI significantly reduced the proportion of children admitted to the hospital from the emergency department. There were few adverse events among readmitted children, both before and after guideline implementation. We found the use of our strict and precise admission guidelines to be a safe and helpful tool in the assessment of children with VLRTI.
BUDESONIDE NEBULIZATION IN ACUTE WHEEZING IN PRESCHOOL CHILDREN

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Background: Recurrent wheezing is a common symptom in preschool children. Treatment with inhaled steroids may be considered for the treatment of acute symptoms and for the prevention of progression of symptoms.

Methods: A prospective randomized controlled trial was done in hospitalized children (1-5 years) with at least two episodes of wheezing in the past. Group A (57) received salbutamol and budesonide and group B (51) only salbutamol nebulization. Comparison of improvement in Pediatric Respiratory Assessment Measure (PRAM Score) was done. For normally distributed data, means of two groups were compared using T-Test. For skewed continuous variables Mann-Whitney U test was applied. Qualitative variables were described as frequencies or proportions and were compared by using Chi square or Fisher's Exact test.

Results: Baseline PRAM SCORE was comparable between two groups (P = 0.057). PRAM SCORE in group A was significantly lesser as compared to group B at 2, 6, 12, 24 and 36 hours of admission (P <0.05). However two groups was comparable at 48 hours and 60 hours of treatment. Baseline respiratory rate was comparable between two groups (P = 0.333). Respiratory rate in group A was significantly lesser in comparison to group B at 6 and 24 hours of admission (P <0.05). Spo2 in group A was more as compared to group B at 24 hours (P = 0.004). The mean (SD) duration of hospital stay of group A and B was 35.16 ± 12.18, 44.00 ± 17.58 hours respectively. Hospital stay was significantly lesser in group A as compare to group B (P = 0.003).

Conclusions: Nebulization with budesonide plus salbutamol is more effective than salbutamol alone in the initial response from acute wheezing in preschool children

Clinical Trial Registration: Not available
SEVERE POST-ARTESUNATE DELAYED HAEMOLYSIS WITH POSITIVE DIRECT ANTIGLOBULIN TEST IN A CHILD WITH PLASMODIUM FALCIPARUM HYPERPARASITAEMIA

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Title of Case(s): Severe post-artesunate delayed haemolysis with positive direct antiglobulin test in a child with Plasmodium falciparum hyperparasitaemia

Background: Delayed haemolytic anaemia has been recognised as a frequent adverse event after treatment with intravenous artesunate. Although pathophysiologically not yet fully understood, splenic "pitting" and removal of once infected erythrocytes is the most accepted mechanism. Recently, an increasing number of patients with post-artesunate delayed haemolysis (PADH) with positive direct antiglobulin test (DAT) have been reported. Thus, drug-induced autoimmune mechanisms might contribute to the development of PADH in some cases.

Case Presentation Summary: We describe the clinical, parasitological and laboratory data of an 11-year-old female patient with severe Plasmodium falciparum malaria, contracted during a family visit in Togo, who developed PADH with a positive DAT 10 days after initiation of intravenous artesunate treatment. On admission to PICU, the patient presented in a reduced general condition with fever, jaundice, dyspnoea, headache, myalgia, abdominal pain, diarrhoea and vomiting. Thick blood film showed P. falciparum hyperparasitaemia >10 %, and mild haemolysis (haemoglobin (Hb) 11g/dL, bilirubin 12 mg/dL, LDH 696 IU/L) was found. DAT was negative. After 4 doses of intravenous artesunate and a consecutive course of oral arthemeter-lumefantrine, she recovered and was discharged on day 4. On day 10, she was readmitted with severe haemolytic anaemia (Hb 6.1 g/dL, LDH 1800 IU/L, haptoglobin not detectable). DAT was now positive for complement C3d and IgG, no anti-artesunate antibodies were detected. Erythrocyte transfusion was initiated without any effect on Hb levels. After additional corticosteroid therapy for 3 days, Hb levels subsequently normalised.

Learning Points/Discussion: We describe a child with DAT positive severe PADH after hyperparasitaemic P. falciparum malaria treated successfully with erythrocyte transfusion and prednisolone. Corticosteroid treatment might be considered as therapy option in children with DAT positive severe PADH.
PARVOVIRUS B19 IN ACUTE PEDIATRIC MYOCARDITIS

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Background: Myocarditis is an important cause of acquired heart disease associated with morbidity and mortality. Various infective etiologies have been postulated for the same. Enterovirus and adenovirus were once considered as the most common etiological viruses but recent reports from the west have pointed towards Parvovirus B19 being the major cause. However, there is no information on this subject from north India.

Methods: Data was collected on all pediatric patients admitted with acute onset low cardiac output syndrome, echocardiographically diagnosed as acute viral myocarditis. The clinical presentation, course and outcome during the study period (September 2016 to September 2019) was reviewed retrospectively. Aetiological information on various cardiotropic viruses: Parvovirus, Enterovirus, HHV-6 and Adenovirus viral genome, detected by PCR from whole blood was collected and analysed.

Results: 48 patients (mean age of 4.5 years, range: 1 month–16 years) presented in cardiac failure (mean ejection fraction of 30 %, range 10-44 %). Respiratory distress and refusal to feed were the most common symptom while tachypnea, tachycardia and features of shock constituted the major signs. Viral etiology was identified in 39.5% (19/48) with Parvo virus itself in 33.3%(16/48). Mean hospital stay was 14 days (range 3-45). All patients received standard supportive care. Inotropes were required in 41.6% cases. There were 5 (10.4%) in-hospital death. No correlation was found between severity of myocarditis and inhospital deaths.

Conclusions: Acute Viral Myocarditis should be considered in all pediatric patients presenting with low cardiac output and echocardiography should be performed to confirm the diagnosis. The most common symptoms consisted of tachycardia, tachypnea and signs of shock. Parvovirus B19 was seen to be the most common cause of myocarditis in children in our study. Follow-up studies may be required towards ascertaining the outcome in these patients.
RESPIRATORY VIRUSES IN ACUTE LOWER RESPIRATORY INFECTIONS IN A TERTIARY HOSPITAL IN MALAYSIA

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Background: Acute lower respiratory tract infections (ALRTIs) continue to be the most important cause of mortality in children worldwide, especially in developing countries. The aim of the study was to determine the viral aetiology of ALRTIs in children less than five-years of age using molecular assay. The findings were further correlated with the clinical picture in terms of clinico-demographic data and outcome of patients.

Methods: Nasopharyngeal aspirates (NPA) were collected within 24 hours of admission from 165 children from Hospital Serdang, a tertiary hospital, with ALRTI’s. The final diagnosis of the study population was either pneumonia, bronchiolitis or viral-induced wheeze. Samples were subjected for hemi-nested multiplex RT-PCR in the detection of a panel of thirteen respiratory viruses. The hospital chart was reviewed to collect demographic, clinical, laboratory and radiological data using standardized study protocol.

Results: Of 165 samples tested, at least one respiratory virus was detected in 158 of the 165 children, implying a detection rate of 95.8%. Ninety percent of the cases occurred in children less than 2 years. RSV was the commonest virus causing ALRTI, followed by rhinovirus and adenovirus. Patients with IFV-A seem to have more prominent symptoms of vomiting, diarrhea, poor feeding and reduced activity. The commonest discharge diagnosis was pneumonia followed by bronchiolitis and viral-induced-wheeze.

Conclusions: The results of the study suggested that respiratory viral agents significantly contributed to the aetiology of ALRTIs among hospitalised children. The most common respiratory virus isolated was RSV, followed by rhinovirus. The study further emphasized the burden of the infection in children less than 2-year old. However, this study could not be generalised as only small numbers and in-patients was involved.
SEROPREVALENCE OF ANTIBODIES AGAINST PERTUSSIS TOXIN AMONG SCHOOL-AGE CHILDREN IN POLAND – A COMPARISON OF ACELLULAR AND WHOLE-CELL PERTUSSIS VACCINE PRIMING EFFECT

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Background: Whole-cell (wP) and acellular (aP) pertussis vaccines have been used for primary immunization in 3+1 schedule in comparable proportions of recent birth cohorts in Poland. This provided an opportunity to test the effect of primo-vaccination on protection duration. Based on the approach published by Grimprel et al. we used the distribution of age-specific anti-pertussis toxin antibody levels as a proxy for duration of protection.

Methods: From 2017 to 2019, 2,734 children 5-15 years-old were enrolled after consent and verification they received 4-dose primary series and 5-6-year booster of pertussis vaccine but no adolescent booster. Serum concentrations of pertussis toxin IgG and IgA antibodies were measured by ELISA. Recent infection was qualified according to the algorithm published by Riffelmann et al.

Results: Among a total of 22 meeting the criteria for recent B. pertussis infections detected in the study population, 9 cases in 5-year-olds were likely confounded by the recent school-entry booster. While low numbers reduced precision, the proportion of recent infections was lower among 7-12-year-olds compared to 13- and 14-year-olds. Linear regression analysis of anti-PT IgG GMCs confirmed that anti-PT response waned over time but showed that anti-PT antibody concentrations increased from 10 to 14 years of age indication these children were increasingly susceptible to B. pertussis infection. The inflection point and slope of these increasing trends were comparable between the wP-primed and aP-primed groups. (Fig. 1)
Conclusions: The distribution of anti-PT GMCs by age demonstrated an increased susceptibility to *B. pertussis* among children ≥ 10 years-old. Our results suggest the waning of protection after the school-entry booster is comparable between aP- and wP-primed children, and leaves children susceptible to *B. pertussis* infection at the same age.

Clinical Trial Registration: Not registered
THE INFLUENCE OF PRENATAL MATERNALLY ADMINISTERED ANTIBIOTICS ON INTESTINAL MICROBIOTA COLONISATION IN INFANTS: A SYSTEMATIC REVIEW

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Background: The intestinal microbiota develops in early infancy. Microbial colonisation is essential for the imprinting of the immune system and health status later in life. In this review we focus on the effect of prenatal maternally administered antibiotics on the infant intestinal microbiota.

Methods: A systematic literature search was conducted in PubMed and EMBASE on studies addressing effects of prenatal maternal administration of antibiotics on infant gut microbiota colonisation. Studies reporting on diversity or microbiota profiles using culture-independent molecular techniques were included. Evaluation of risk-of-bias was performed using the ROBINS-I tool.

Results: A total of 4030 records were encountered. After full text screening of 109 articles a total of 24 articles were included in the final analysis. Studies included a total of 3583 infants of whom 1178 mothers were exposed to antibiotics antenatally. Stool samples were collected with a range from the first day up to twelve months postpartum. Studies were characterised by substantial methodological and clinical heterogeneity. Infants from mothers exposed to antibiotics during pregnancy or delivery showed a decreased microbial diversity compared to non-exposed infants. Furthermore, the microbiota of infants exposed to antibiotics was characterised by a decreased abundance of Bacteroidetes and Bifidobacteria, with a concurrent increase of Proteobacteria. These effects were most pronounced in term vaginally born infants.
Conclusions: Maternal administration of antibiotics seems to have profound effects on the infant gut microbiota colonisation. Interpretation of microbiota aberrations in specific populations, such as preterm and caesarean born infants is complicated by multiple confounding factors, like postnatal antibiotic administration, and by lack of high quality studies, characterised by high heterogeneity in study design. Further research is needed to investigate the potential short- and long-term adverse clinical consequences of described microbial alterations.

Systematic Review Registration: N/A
SUSTAINED DECREASE IN ROTAVIRUS-RELATED HOSPITALISATIONS AND NOSOCOMIAL ROTAVIRUS INFECTIONS IN BELGIUM THIRTEEN YEARS AFTER THE VACCINE INTRODUCTION

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Background: Rotavirus vaccination has been reimbursed in Belgium since November 2006. The average vaccine coverage rate is above 85%. The objective of the study is to assess the impact of rotavirus mass vaccination on rotavirus-specific hospitalisations and nosocomial infections in children ≤2 years old in 10 paediatric wards, up to 13 years after vaccine introduction.

Methods: All rotavirus tests collected from hospitalised children ≤2 years old were analysed (ClinicalTrials.gov#: NCT01563146). The total number of positive rotavirus tests in the pre-vaccine introduction period (01/06/2004-31/05/2006) were compared with the post-vaccine introduction period (01/06/2006-31/05/2019). Annual data are presented as a percentage reduction (95% Confidence Interval [CI]) using the annual average results of the pre-vaccination period as a reference.

Results: Between June 2004 and May 2019, 5,018 (13.48%) out of 37,214 tests conducted in children ≤2 years old were positive for rotavirus. A significant drop (76% [95% CI:73%-79%]) in rotavirus-positive tests is observed over time, from an average of 931 positive tests pre-vaccine introduction to 223 during the 13th year post-vaccine introduction. A 92% (CI:90%-94%) reduction in nosocomial rotavirus infections occurred in parallel, from 139 cases pre-vaccine introduction to 11 during the 13th year post-vaccine introduction. Finally, a 48% (CI:45%-52%) reduction in acute gastroenteritis-driven hospitalisation days is observed during the 13th year post-vaccine introduction, from 11,752 days to 6,070 days pre- and post-vaccine introduction, respectively. Interestingly, 6 years after the vaccine uptake period with annual decrease in numbers, we now observe biennial small peaks of the disease.

Conclusions: Sustained and continued decline in rotavirus hospitalisations and nosocomial infections is seen in young children 13 years after the vaccine introduction in Belgium. Acknowledgements: Amandine Radziejwoski (Business&Decision Life Sciences platform) for publication coordination.

Clinical Trial Registration: NCT01563146
ATYPICAL BACTERIAL PATHOGEN IN CONGENITAL PNEUMONIA

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\textbf{Background:} Congenital pneumonia is one of the common causes of respiratory distress at birth with significant morbidity and mortality in infants. Aetiological pathogens for this condition are many and vary but atypical bacterial causes are few. The aim of this study was to detect the causes of atypical bacteria in newborns with congenital pneumonia, using molecular assay. The perinatal risk factors and clinical course were also evaluated.

\textbf{Methods:} The study population included 77 newborns, who were admitted to the neonatal intensive unit in a tertiary hospital in Malaysia and diagnosed with congenital pneumonia. Nasopharyngeal samples were collected soon after birth, within the first 8 hours of life, in order to exclude nosocomial infections. The samples were tested for atypical bacteria using multiplex real-time PCR (RT-PCR). Serological diagnosis for \textit{Chlamydia trachomatis} and \textit{Chlamydophila pneumoniae} was also performed.

\textbf{Results:} Of the 77 samples analysed, 14 (18.2\%) were found positive. The detection rate was highest for \textit{Ureaplasma parvum} (8/77, 10.4\%), followed by \textit{Ureaplasma urealyticum} (5/77, 6.5\%) and \textit{Mycoplasma hominis} (1/77, 1.3\%). However, \textit{Mycoplasma pneumoniae}, \textit{C. trachomatis} and \textit{C. pneumoniae} were not detected. No double infection was recorded. The serology for the above two pathogens was negative. Of the maternal risk factors, prolonged rupture of membranes longer than 24 hours before delivery was a significant feature of atypical bacterial pneumonia (p=0.042), particularly for \textit{U. parvum} infection.

\textbf{Conclusions:} In conclusion, our finding confirms that atypical bacteria are not common causes of congenital pneumonia. Our study highlighted that infants whose mothers had prolonged rupture of membranes of more than 24 hours were likely to be infected with \textit{U. parvum}. The development of a more sensitive molecular assay has dramatically altered the microbiological diagnosis, especially for atypical bacteria in congenital pneumonia.
IMPLEMENTATION OF THE GREEK NATIONAL IMMUNIZATION PROGRAM AMONG NURSERY ATTENDEES IN THE URBAN AREA OF THESSALONIKI

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Background: The growing phenomenon of vaccine hesitancy and the severe economic crisis may have affected compliance to the National Immunization Program (NIP) in Greece over the last years. We investigated compliance to the NIP among children attending nurseries in the area of Thessaloniki.

Methods: A prospective cross-sectional study was conducted including nursery attendees born between 01/01/2014-01/10/2015 in each of the municipalities of greater Thessaloniki urban area. Public or private nurseries were randomly selected. Immunization data were anonymously collected from the child’s health booklet. Both coverage and timeliness of immunization were recorded for all recommended vaccines according to the NIP as well as for rotavirus vaccine.

Results: 423 children with a median age of 2.9 years were studied; 57% were attending private nurseries. Full coverage was >90% for most of the recommended vaccines with the exception of pneumococcal (81%), meningococcal serogroup C (68.3%/82% for 2011/2015 schedule respectively), hepatitis A (38.7%) and rotavirus (25.9%) vaccine. Delay rates for ≥1 dose ranged between 26.1%-91.8% for all vaccines; median delay ranged between 3.8-6.7 months. Significantly lower coverage and higher delays were observed for Roma children.

Conclusions: While high coverage appears to be sustained for most of recommended vaccines, delay of scheduled shots may compromise age-appropriate protection. Suboptimal immunization against pneumococcal, meningococcal serogroup C, hepatitis A and rotavirus infections may increase morbidity in this age group and needs to be addressed.

Clinical Trial Registration: This is not a controlled clinical trial
CASE SERIES OF HAEMOLYTIC URAEMIC SYNDROME ASSOCIATED WITH ESCHERICHIA COLI O157:H7 AMONG THREE CHILDREN THAT WERE HOSPITALISED IN A GENERAL HOSPITAL OF CENTRAL GREECE (2018-19)

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Title of Case(s): CASE SERIES OF HAEMOLYTIC URAEMIC SYNDROME AMONG THREE CHILDREN THAT WERE HOSPITALISED IN A GENERAL HOSPITAL OF CENTRAL GREECE (2018-19)

Background: Haemolytic uraemic syndrome (HUS) is defined by the simultaneous occurrence of nonimmune haemolytic anaemia, thrombocytopenia and acute renal failure. Two classical types for HUS are still used in literature. Typical HUS associated with Shiga toxin producing Escherichia coli (STEC) also known as enterohaemorrhagic E. coli (EHEC), in which patients usually develop gastrointestinal symptomatology. On the other hand atypical-HUS (a-HUS) is considered to be complement related and not diarrhea associated although there are still controversies in literature concerning this entity.

Case Presentation Summary: We report three cases of HUS that were identified and supported in our paediatric clinic in a secondary hospital of central Greece, during a nine-month period. The children were two male 9 months and 2 years old respectively and one female 4 years old. All three children were at first diagnosed by our paediatric team, stabilized and transferred in a tertiary hospital with a child nephrology section for further evaluation. The presenting symptoms of the infant were acute abdominal pain, with bloody diarrhea. The second male child was admitted for bloody diarrhea, while in the third case CNS involvement was observed with tonic-clonic seizures, but without gastrointestinal involvement. Two of the children eventually needed peritoneal dialysis. We were able to identify Escherichia coli O157:H7, in the stool cultures, of all three cases using PCR molecular methods to identify specific genes.

Learning Points/Discussion: Although the incidence of HUS is considered to be 0.2-3.4 cases per 100,000 children per year, our secondary general hospital faced a significant increase in this time period. This show us that paediatricians should always be alert to recognize possible complications of gastroenteritis as every year thousands of children will get sick with gastroenteritis, but only few will eventually face severe complications.
EMERGENCE OF RARE G2P[8] ROTAVIRUS GENOTYPE AMONG CHILDREN

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Background: Recent reports from several regions identified the circulation of rare G2P[8] strains in <1%. In the Philippines, G2P[8] genotype has emerged as the third most common type of group A rotavirus in 2017 and 2018. The increasing case of G2P[8] strain in the country highlights the need to characterize the whole genomic RNA constellation of rotavirus G2P[8] strain in the Philippines.

Methods: Whole genome sequencing of specimens with G2P[8] genotype from the rotavirus surveillance were included in the analysis. Nucleotide sequences of the 11-segments of rotavirus G2P[8] strains were determined using dideoxynucleotide chain termination method. Multiple sequence alignments were constructed and edited using lasergene software. Phylogenetic and molecular analyses were also conducted. Genotypes of each of the 11-genome segments for all the specimens were determined using the RotaC 2.0 rotavirus genotyping tool.

Results: G2P[8] strains from the stool specimens exhibited a complete unique DS1-like genotype constellation of G2-P[8]-I2-R2-C2-M2-A2-N2-T2-E2-H2. This novel genotype constellation revealed a close relationship between the sample and Bangladesh strain for each segment. Based on sequence similarities, the Philippines G2P[8] strains were closely related with 88.9% to 99.5% identity in all gene segments. Phylogenetic tree constructed from the nucleotide sequences of the VP7 (1st image) and VP4 (2nd image) genes of stool specimens of rotavirus strains.
Conclusions: To date, this is the first report on whole-genome based characterization of G2P[8] strain in the Philippines. Findings provide evidence that the circulating DS-1 like G2P[8] strain in the Philippines and the DS-1 like G2P[8] strains that have emerged in other Asian countries originated from a common ancestor. Study results can provide important insights on the evolutionary dynamics of novel DS-1 like G2P[8] rotaviruses and provide essential information for vaccine development and implementation.

Clinical Trial Registration: IRB protocol no. 2016-50
HEPATIC CYST ECHINOCOCCOSIS (HYDATID CYST) ; FIRST CASE REPORTED IN AN IRISH CHILD

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Title of Case(s): Hepatic Cyst Echinococcosis (Hydatid Cyst) ; First case reported in an Irish Child

Background: Human Echinococcosis is a parasitic disease caused by tapeworms of the genus Echinococcus. Cystic Echinococcosis (CE) occurs in humans incidentally infected with the larval form of the dog tapeworm E. granulosus. Sheep/cattle are the typical intermediate host. E. granulosus strains associated with CE have not been reported in Ireland. A related strain (E. granulosus equinus) has been reported previously in Irish dogs but is apathogenic to humans. We present the first reported case of echinococcosis in a paediatric patient in Ireland.

Case Presentation Summary: A six year old Irish girl from west Ireland was found incidentally on ultrasound to have a cystic lesion in the right lobe of her liver. She was asymptomatic. A travel history revealed trips to Portugal, Spain and France over the previous 5 years. Her physical examination was normal. Suspecting CE, serology for echinococcus was undertaken and was positive. After CT scan, an MRI demonstrated features typical for CE. She was pre-treated with albendazole and praziquantel before undergoing a liver segmentectomy, and received three months of albendazole post-operatively. Histology of the hepatic cyst confirmed CE due to E. granulosus. The patient has remained well since. A faecal sample from the family dog subsequently showed no evidence of echinococcal infection.

Learning Points/Discussion: Management, as in this case, includes anti-helminthic chemotherapy and surgery, often undertaken to prevent complications that can occur with cyst rupture. Paediatricians should always consider CE in the differential of cystic liver and lung lesions, and take a careful travel history, even in children without typical risk factors. We believe that this infection was acquired from travel to mainland Europe, where CE is endemic.
PREVALENCE AND GENETIC CHARACTERIZATION OF RESPIRATORY Syncytial Viruses (RSV) CIRCULATING IN BULGARIA DURING THE THREE CONSECUTIVE WINTER SEASONS (2016-2019)

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Background: The objectives of this study were to investigate the circulation and clinical significance of RSV among children aged < 5 years in Bulgaria and to identify the RSV-A and RSV-B genotypes.

Methods: Clinical, epidemiological data and nasopharyngeal swabs were prospectively collected from children aged < 5 years presenting with acute respiratory infections during the 2016/2017, 2017/2018 and 2018/2019 seasons. Detection of 11 respiratory viruses and RSV genotyping were performed using Real Time PCR.

Results: Of the 1332 children examined, 983 (73.8%) were positive for at least one respiratory virus. Co-infections with two and three viruses were found in 150 and 14 of infected children, respectively (16.7%). Overall, RSV was the most commonly detected virus (25.2%), followed by rhinoviruses (11.5%), influenza A(H1N1)pdm09 (10.5%), influenza A(H3N2) (9.8%); adenoviruses (7.4%); bocaviruses (6.9%); human metapneumovirus (5.2%); parainfluenza viruses 1/2/3 (4.4%) and influenza type B (3.4%). Detection rate for RSV was highest (36%) during the 2016/2017 season and lowest during the 2017/2018 season (20.3%). RSV subgroup B outnumbered those of the subgroup A throughout the study period. RSV was the most common virus detected in patients with bronchiolitis (48%) and pneumonia (38%). The phylogenetic analysis based on the G gene indicated that all sequenced RSV-A strains belonged to the ON1 genotype; the RSV-B strains were classified into BA9 genotype.

Conclusions: This study showed the leading role of RSV as a causative agent of serious respiratory illnesses in early childhood, year-on-year fluctuations in RSV incidence, a RSV-B subgroup dominance and relatively low genetic divergence in the circulating strains. Diagnostic testing for RSV and other respiratory viruses using molecular methods may lead to the reduced use of antibiotics and may assist in measures to control infection.

Clinical Trial Registration: ClinicalTrials.gov 2017 – DH 13/15
DESIGN THINKING AS A PROCESS TO IMPROVE THE COMMUNICATION OF INFORMATION TO CHILDREN

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Background: Research and medical documents designed to inform children are often difficult to understand or don't include all the information relevant to them. In the framework of the project i-CONSENT (H2020 - GA.741856), 2 design thinking (DT) sessions were done to improve the understanding and acceptance of an assent for clinical research (CR), by placing the potential participants in the center of the design process.

Methods: Two consecutive DT sessions with 2 groups of 5 minors each (12-13 years) were performed in Valencian Community. During these sessions, participants co-created innovative and easy to understand assent information for CR to meet their needs and interests. Sessions included: an introductory Clinical trials video; adapted assent document reading and feedback; role play; preferences format mapping; brain storming; prototyping of specific assent parts; designing prototype of an assent website and illustration of difficult terms.

Results: Difficult terms in assent information were identified, explained and illustrated by the minors. A website with video content was identified as the preferred format for the assent. Video script was created contextualizing an entertaining story in 3rd person. Technical details and concepts weren't included, maybe because they didn't consider them a priority or they had difficulty understanding them. Based on these findings, digital assent (presented in a website format including video content) was developed.

Conclusions: To adapt the content of assent to individual needs, the i-CONSENT consortium considers DT, that includes empathizing with the problem; defining it; develop ideas; prototyping and testing solutions, to be a useful method. By introducing visual aids and placing the participant in the center of the assent process, we were better able to meet the needs and preferences of the target population when developing information materials for assent.
Background: The 1999 American Academy of Pediatrics (AAP) guidelines for children with febrile urinary tract infection (UTI) suggested renal/bladder ultrasonography (RBUS) and voiding cystourethrography (VCUG) in all patients, with continuous antimicrobial prophylaxis (CAP) if vesicoureteral reflux (VUR) was detected. The 2011 revision suggested initial evaluation only with RBUS, reserving VCUG and CAP for selected patients. We assessed the impact of implementation of the revised guidelines on the outcome of children with UTI, antimicrobial utilization and use of healthcare services.

Methods: We retrospectively studied children who were hospitalized for their first febrile UTI episode between October 2002-April 2011 (old guidelines) or between July 2014-November 2017 (revised approach) and followed-up in the UTI outpatient clinic. We compared rates of UTI recurrences, VCUGs performed, presence of VUR, CAP utilization, time-to-first recurrence and patient visits/month. Data became available via medical records or telephone communication.

Results: Eighty-one children were included (47% female, median age 5.3 months), of which 52 were managed according to the old and 29 according to the revised guidelines. We found no difference in rates of UTI recurrence (8/52 vs 5/29, P=1) or patients positive for VUR (19/52 vs 4/14, P=0.75), while VCUGs decreased by 51.7% (P<0.001) and CAP by 86.2% (P<0.001). Most recurrences occurred within a 6-month period from the first episode; patient outpatient visits decreased from a mean of 11.5 to 4/month.

Conclusions: The above findings suggest that the simplified UTI evaluation and management strategy did not compromise the long-term outcome of Greek children hospitalized for a first febrile UTI, in accordance with evidence from other healthcare settings. The 2011 AAP revision effectively tackles antimicrobial utilization, exposure to radiation, healthcare system overload and patient discomfort, without posing a detrimental impact on children’s health.
HOSPITALIZATION FOR PNEUMOCOCCAL AND UNSPECIFIED PNEUMONIA IN CHILDREN

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Background: Community-acquired pneumonia cause significant morbidity and mortality in children. Streptococcus pneumoniae is among the leading agents. In 2003, a large-scale PCV7 programme began in Liguria, reaching a coverage >80% and >90% in all districts since 2004 and 2007. We investigated pneumococcal and unspecified pneumonia-related hospitalization rates and trends from 2012 to 2018 following the introduction of PCV13 in 2010 in children <2 years.

Methods: A retrospective observational analysis was conducted to identify pneumococcal pneumonia and unspecified pneumonia cases in the Ligurian Regional Administrative Databases in children <15 years using ICD9 codes. Pneumonia cases associated with pneumococcal-specific ICD codes and bacterial pneumonia unspecified, bronchopneumonia unspecified and pneumonia unspecified ICD codes were identified. Annual incidence of pneumonia hospital admissions was annual number of inpatient admissions/1000 person-years.

Results:

Annual incidence of hospital admissions in children <15 years decreased by 63% from 0.35 in 2012 to 0.13/1,000 person-years in 2018 (p<0.001) for pneumococcal pneumonia and by 20% from 2.2 to 1.8/1,000 (p<0.001) for unspecified pneumonia. The incidence of pneumococcal pneumonia decreased in
children <5 years (from 0.7 to 0.3/1,000 person-years, p=0.003) and 5-14 years (0.21 to 0.08/1,000 person-years, p<0.001) during the analysis period. The incidence of unspecified pneumonia was stable in both <5 years (range=4.15-5.82/1,000 person-years), and 5-14 years children (range=0.94 and 1.55/1,000 person-years).

**Conclusions:** The results of this study based on administrative data show that the annual incidence of hospital admissions for pneumococcal and unspecified pneumonia in children <15 years decreased following PCV13 introduction in Liguria region, North-West Italy. This evidence contributes to the growing body of knowledge of disease epidemiology that supports the beneficial effect of the PCV13 vaccination on pneumonia hospitalisations in children.
Title of Case(s): A CASE OF ADOLESCENT BRUCELLOSIS WITH FEVER AND SCROTAL INVOLVEMENT

Background: Brucella, a zoonosis that can cause various clinical findings with multisystemic involvement. Also known as Mediterranean fever, this disease most commonly involves the bone-joint system, as well as causing cardiovascular, pulmonary, neurological, intraabdominal and genitourinary complications. It is known that it causes an epididymo-orchitis in a rate of 2-20% in adult age group. Here, an adolescent case with scrotal involvement is presented.

Case Presentation Summary: A 17 years old male patient applied to a health center with weakness for two months, weight loss and ongoing fever that started a week ago. In the scrotal imaging performed with suspicion of malignancy, millimeter multifocal hypoechoic nodular infiltrations were detected. The patient was guided by the diagnosis of lymphoma due to the thoracic and abdominal imaging. Hepatosplenomegaly and pancytopenia detected on physical examination and complete blood count, respectively. Serum samples were also sent for Brucella along with viral serologies from the patient who lives in the Eastern Anatolia Region, in Turkey and is ranching. Also, Brucella culture was sent from bone marrow aspiration sample for malignancy exclusion. While other viral serologies of the patient were negative, both Rose-Bengal test, Wright's test and Brucella culture were positive. After the appropriate antimicrobial treatment started, full response was obtained clinically, laboratory and radiologically.

Learning Points/Discussion: Although the place of brucellosis in epididymo-orchitis is more common in adults, it is very rare in the child age group even endemic regions like our country. It is possible to treat this disease, which can result in severe morbidity and mortality due to multiple organ involvement. It should definitely come to mind in the presence of fever, pancytopenia and organomegaly with scrotal involvement.
CLOSURE OF WARDS DURING NOSOCOMIAL OUTBREAKS IN PEDIATRICS AND NEONATOLOGY

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Background and Objective: Especially pediatrics and neonatology are affected by a total closure of wards which represents one of the most expensive infection control measures during nosocomial outbreaks (NO). In order to apply such a high impact measures only if necessary, knowledge of NO characteristics with a high probability of the need of ward closure is important. Unfortunately, this kind of data is not yet available. This study closes this gap of information.

Methods: A systematic search of the medical literature for NO with an eventual closure was carried out on 10/22/2019 using the Outbreak Database (www.outbreak-database.com) and PubMed. The following data were obtained: country, type of medical department, duration of NO, number of cases, types of pathogens and sources, routes of transmission, duration of closure (if applicable), other infection control measures, and costs.

Learning Points/Discussion: There were 198 NO in pediatrics and 444 NO in neonatology, thereof closure in 25 (pediatrics) and 52 (neonatology). The mean duration of closure was 22 days (median: 25) in pediatrics and 37 days (median: 14) in neonatology. Predominant pathogens requiring closure in pediatrics were serratia (3), klebsiella (2), staphylococci (2), salmonella (2), and rota virus (2) compare to serratia (8), klebsiella (6), and enterobacter (6) in neonatology. See table for further data. This data should be of interest for medical staff working in the field of pediatric patient care as well as in infection control. It might be helpful during an ongoing NO investigation when forced with the decision on whether or not to apply total closure of the unit. It also shows that sources of NO may not be determined quite often. Finally, it demonstrates the importance of proper hand hygiene to interrupt inter-patient-spread of pathogens via contact.
<table>
<thead>
<tr>
<th>Setting</th>
<th>Outbreaks in Pediatrics</th>
<th>Outbreaks in Neonatology</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>closure (n=25)</td>
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<td>duration of NO: range, mean, median (days)</td>
<td>5–730, 158, 30</td>
<td>7–210, 108, 150</td>
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<td>patients, thereof infected, thereof deceased (%)</td>
<td>717, 504, 72</td>
<td>5,006, 586, 509</td>
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<tr>
<td>rate of infections (# infected / # total; %)</td>
<td>70.3%</td>
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<tr>
<td>mortality (# deceased / # infected; %)</td>
<td>14.3%</td>
<td>86.9%</td>
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<tr>
<td>intensive care unit involved (n, %)</td>
<td>9 (36.0%)</td>
<td>68 (39.3%)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>medical devices (n, %)</td>
<td>2 (8.0%)</td>
<td>15 (8.7%)</td>
</tr>
<tr>
<td>drugs (n, %)</td>
<td>1 (4.0%)</td>
<td>11 (6.4%)</td>
</tr>
<tr>
<td>environment (n, %)</td>
<td>2 (8.0%)</td>
<td>15 (8.7%)</td>
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<tr>
<td>food (n, %)</td>
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<td>5 (2.9%)</td>
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<td>0 (0.0%)</td>
<td>2 (1.2%)</td>
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<tr>
<td>index patient (n, %)</td>
<td>9 (36.0%)</td>
<td>50 (28.9%)</td>
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<td>1 (4.0%)</td>
<td>8 (4.6%)</td>
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<td>source remained unknown (n, %)</td>
<td>11 (44.0%)</td>
<td>70 (40.5%)</td>
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<td>Route of Transmission</td>
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<td>contact (n, %)</td>
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<td>87 (50.3%)</td>
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<tr>
<td>inhalation (n, %)</td>
<td>8 (32.0%)</td>
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<td>invasive procedures (n, %)</td>
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<td>28 (16.2%)</td>
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<tr>
<td>source of transmission remained unknown (n, %)</td>
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<td>56 (32.4%)</td>
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<td>Infection Control Measures</td>
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<tr>
<td>isolation in single rooms or cohorting (n, %)</td>
<td>13 (52.0%)</td>
<td>50 (28.9%)</td>
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<tr>
<td>use of protective clothing (n, %)</td>
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<td>37 (21.4%)</td>
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<td>decolonization measures (n, %)</td>
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<td>22 (12.7%)</td>
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<td>improvement of hand hygiene (n, %)</td>
<td>17 (68.0%)</td>
<td>50 (28.9%)</td>
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<td>36 (20.8%)</td>
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<td>9 (36.0%)</td>
<td>9 (5.2%)</td>
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<td>exchange of medical devices (n, %)</td>
<td>5 (12.0%)</td>
<td>61 (35.3%)</td>
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<td>vaccinations (n, %)</td>
<td>1 (4.0%)</td>
<td>6 (3.5%)</td>
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<td>changes in antimicrobial chemotherapy (n, %)</td>
<td>4 (16.0%)</td>
<td>57 (32.9%)</td>
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<td>no measures applied (n, %)</td>
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<tr>
<td>no data on infection control measures (n, %)</td>
<td>1 (4.0%)</td>
<td>22 (12.7%)</td>
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Title of Case(s): Fungemia due to *Saccharomyces Cerevisiae* in a Immunocompetent Child

**Background:** BACKGROUND One of the most commonly used fungi in probiotics is *S. Boulardi* which is a *S. cerevisiae* strain. It is considered to be non-pathogenic, safe and widely used for the prevention and treatment of gastrointestinal diseases. As a probiotic component, this fungus may cause systemic infection in the immunocompromised adults and children. In immunocompetent individuals, probiotics are considered generally safe, yet cases of bloodstream infections following the administration of them have rarely been reported.

**Case Presentation Summary:** CASE PRESENTATION SUMMARY A 3-year-old boy was admitted to our paediatric clinic because of high fever and profound diarrhoea. He was prescribed antibiotics for presumed bacterial dysentery and probiotics containing *S. boulardi*. Two days later due to persistent fever and diarrhoea, blood tests including blood cultures were taken. The blood cultures grew *S. cerevisiae* resistant to fluconazole. The child was then admitted to the tertiary referral hospital for further detailed evaluation and started antifungal treatment. Inpatient investigations, included abdominal ultrasound (liver, spleen, kidneys) and cardiac echocardiogram, did not reveal any evidence of fungal dissemination. Extensive evaluations yielded no evidence of immunodeficiency. He completed a two week course of micafungin based on the antifungigram of the isolated agent, with good clinical response.

**Learning Points/Discussion:** LEARNING POINTS/DISCUSSION Our case illustrates the possibility of *S. Boulardi* fungemia in patients who receive broad spectrum antimicrobials. We conclude that the general paediatrician should be aware of the possibility of fungemia due to *S. cerevisiae* following probiotic administration, since fungi in probiotics can rarely cause bloodstream infection in immunocompetent children via intestinal translocation which although rare, can lead to severe complications.
13 YEAR OLD BOY RETURNING FROM THE EAST WITH FEVER: WHAT COULD POSSIBLY BE THE CAUSE?

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Title of Case(s): 13 YEAR OLD BOY RETURNING FROM THE EAST WITH FEVER: WHAT COULD POSSIBLY BE THE CAUSE?

Background: Typhoid fever is a disease caused by Salmonella enteric, typhi and paratyphi A,B,C, which are spread via contaminated food or water. S. typhi has been a major human pathogen for thousands of years and has a variety of presentations, from multisystemic severe illness to relatively minor cases. This case is particularly interesting because the patient on admission had high temperature without a source.

Case Presentation Summary: I am about to present the case of a 13 year-old boy that presented in ED with symptoms of 5 day fever up to 39.5 degrees and malaise. The boy returned from Pakistan 2 weeks prior to ED attendance, where he spent one week, tasting local food and drinks. He had two episodes of loose stool while he was there, but none after returning to UK. No vomit and no rash were present. The boy was screened for sepsis and started on iv ceftriaxone. Blood, urine and stool culture were taken. Blood culture was positive for Salmonella paratyphi A, sensitive to ceftriaxone and stool PCR came back positive for enterovirus and cambylobacter. Initial CRP was 257, with normal values up to 5. The boy remained febrile for 5 days after admission. Mild upper abdominal pain was present while eating the first days of admission. He was treated with IV ceftriaxone for 14 days. No complications occurred and he was discharged clinically well. Malaria test was negative, as well as the rest tropical infection screening (hepatitis A,B,C, rickettsioses, leptospeira, Japanese encephalitis virus, west nile virus, dengue).

Learning Points/Discussion: Typhoid fever should always be on our differential diagnosis list for travellers returning from endemic countries and present with fever. Early onset of treatment is a key to prevention of life-threatening complications. Moreover, it is important to notice that more than one pathogens can be present at the same time.
EARLY ONSET NEONATAL SEPSIS: POSITIVE BLOOD CULTURES IN 2019 IN A LEVEL 1 HOSPITAL IN LONDON

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Title of Case(s): EARLY ONSET NEONATAL SEPSIS: POSITIVE BLOOD CULTURES IN 2019 IN A LEVEL 2 HOSPITAL IN LONDON

Background: Early Onset Neonatal sepsis is infection that occurs within the first 72 hours of life. It is a very crucial pathology because it consists a significant cause of mortality and morbidity in newborns. Overall mortality is about 10%, but is even higher in premature babies. Group B Streptococcus (GBS) and Escherichia coli are the most common pathogens identified and up to 7% of newborns that survive GBS infection have a consequent disability.

Case Presentation Summary: In West Middlesex University Hospital, London, UK, during 2019, only 5 newborns of those that underwent septic screen for suspected early onset neonatal sepsis were found to have positive blood or CSF cultures. Four out of five newborns had GBS positive blood culture and no growth in CSF culture, and one newborn had negative blood culture and GBS detected in CSF. All the GBS detected were sensitive to penicillin. All of the babies were initially screened due to maternal suspected sepsis, and they were all term. Initial CRP was <5 (normal) for all 5 babies, but the repeat one revealed slight to profound rise in 4 of 5 newborns (13.5, 41, 61.3, 71.9). All of the babies were discharged after completing 7/10-14 days of IVABx when blood culture positive, and 14 days of IVABx when CSF culture positive.

Learning Points/Discussion: Early onset neonatal sepsis (EONS) is very crucial and treatment should not delay if risk factors or clinical indicators are present. In our hospital, only 5 cultures out of many sent were positive, which shows that although EONS can be life-threatening, positivity of cultures is not very common.
Title of Case(s): Recurrent pneumonia in a HIV-infected infant

Background: It is important to increase HIV awareness in settings like Vietnam where HIV infection rates are not very high. Given the vulnerability of young children to develop TB, a meticulous TB exposure history is essential in all children with pneumonia not responding to first-line treatment, especially those with HIV infection.

Case Presentation Summary: We reported on 6-month-old infant admitted to ICU with recurrent severe pneumonia. She was discharged from the same hospital 2 days ago, but developed a fever and heavy breathing at home. The mother was HIV infected, but initially failed to disclose this to doctors. Neither did she report chronic coughing of the child’s grandmother; likely due to TB. The child was given intravenous antibiotics and oxygen supplementation. Laboratory investigations revealed an abnormal full blood count (hemoglobin: 8.7 g/dl; white blood cells: 10.5 x10^9/L; neutrophils: 8.1 x10^9/L; lymphocytes: 1.4 x10^9/L), increased CRP: 144 mg/L. The CXR showed peri-hilar streakiness with diffuse patchy infiltration and visible opacification of the right upper lobe, which was worse than the CXR taken during the previous admission. The infant was diagnosed with X-pert MTB/RIF® confirmed TB and tested positive for HIV infection. Since the baby was found to be HIV-infected with severe immune compromise, triple ART was initiated, together with first-line TB drugs, including isoniazid, rifampicin, pyrazinamide, ethambutol. The child tolerated the treatment well, showed steady improvement and was discharged home after 4 weeks, without any signs suggestive of immune reconstitution inflammatory syndrome (IRIS). In follow-up at the HIV clinic she showed good improvement, without new signs or symptoms, with good weight gain.
Key Learning Points: The case demonstrates the importance of including TB in the differential diagnosis of young children not responding to first-line pneumonia treatment, especially in TB endemic areas. Taking a meticulous TB and HIV exposure history, with careful consideration of potential social stigma, is essential.
ASSESSING THE ROLE OF HOST EPIGENETIC CHANGES AFTER RSV INFECTION IN RESPIRATORY MORBIDITY DEFINED AS WHEEZING AND/OR ASTHMA

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**Background:** Respiratory syncytial virus (RSV) is a common pathogen that infects virtually all children by two years of age and is the leading global cause of hospitalization of infants as well as the principal cause of acute lower respiratory infections (ALRI) in young children. RSV infection in infants has been associated with the subsequent development of recurrent wheezing and asthma, although the mechanisms involved are not well established. The objective of the present study is to assess whether there are differences in the methylation pattern after an RSV infection among children who have recurrent wheezing, children with subsequent asthma and children with complete recovery.

**Methods:** We perform a prospective, observational study of 77 infants hospitalized for a respiratory infection due to RSV. Patients were selected according to their clinical course and after 3 years of follow-up, were classified into three different subgroups: recurrent wheezing RSV cases (n=36); asthma RSV cases (n=9); not-wheezing/asthma RSV cases (n= 32; here onwards, the control group). The genome-wide methylation pattern was measured in whole blood, using the Illumina Infinium MethylationEPIC array BeadChip (850K).

**Results:** We identified a consistent number of significant differentially methylated positions (DMPs) comparing the control group with the wheezing group, and the control group vs the asthma group. The functional analysis of the results obtained by comparing the three groups together showed significant enrichment in signaling pathways related to immune response processes and cellular processes such as the TGF-β receptor pathway, considered a key mediator of the asthmatic phenotype.

**Conclusions:** Our study demonstrates that epigenetic mechanisms can play a fundamental role in the development of asthma after RSV infection, contributing to explain the different phenotypes that children can develop after infection.

**Clinical Trial Registration:** Clinical trial registration: N/A
RELATIVE EFFICACY OF VARICELLA VACCINES: A SYSTEMATIC LITERATURE REVIEW AND NETWORK META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Background: Network meta-analyses (NMAs) provide indirect comparisons of relative treatment effects of medical interventions in the absence of head-to-head trials. This study used NMA to assess relative varicella vaccine efficacy (VE) from randomized controlled trials (RCTs).

Methods: Systematic literature review of published studies was performed from database initiation to November 2019. Eligible RCTs reported VE against all-cause and moderate-to-severe varicella in children >9 months. A contrast-based Bayesian NMA model was used to estimate relative VE. Segregated efficacy analyses were performed for vaccine doses (dose 1 vs 2), storage method (refrigerated vs frozen), and time since vaccination (TSV) (<1, 1-2, 2-5, and >=5 years) to account for heterogeneity across studies.

Results: Efficacy data were reported for four varicella (V) containing vaccines versus no vaccination in 6 different RCTs: V-MSD (dose 1 and 2), V-GSK (dose 1), MMRV-GSK (dose 2), and V-Sinovac (dose 1). Two of these RCTs also compared efficacy between doses (V-MSD dose 1 vs V-MSD dose 2; V-GSK dose 1 vs MMRV-GSK dose 2). Patient age (14.2-144 months) and study follow-up (6-120 months) varied across trials. In base-case NMA, VE versus no vaccination was highest for V-MSD dose 2 and lowest for V-GSK dose 1 (Figure). VE was higher for dose 2 (95.2-98.3%) than dose 1 (66.4-93.8%). V-MSD dose 1 had higher VE than V-GSK dose 1. Comparison of frozen vaccines (3 studies) provided similar VE results. TSV analysis showed protection against varicella was sustained (10 years), without waning effect.

Conclusions: All varicella-containing vaccines were efficacious versus no vaccination. Two doses were more efficacious in preventing varicella than one dose, although V-MSD dose 1 was also highly efficacious. V-MSD dose 2 showed highest VE compared to other varicella-containing vaccine strategies.

Systematic Review Registration: N/A
IMMUNOGENICITY AND SAFETY OF M-M-R® II BY AGE GROUPS - A SYSTEMATIC LITERATURE REVIEW OF RANDOMIZED CONTROLLED TRIALS

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**Background:** M-M-R® II is routinely recommended at 12-15 months for 1st dose and 15 months-6 years for 2nd dose, if used. However, the vaccine may need to be administered at other ages due to delays in completing the immunization schedule or during outbreaks. A systematic literature review was conducted to evaluate immunogenicity and safety of M-M-R®II by age groups (6-11 months, ≥12 months to 6 years, ≥7 years) in randomized controlled trials (RCTs).

**Methods:** The search was conducted in Medline, Embase and Cochrane CENTRAL, complemented by a search for grey literature (e.g. conferences, trial registries) until July 2019, without time restriction. Two independent reviewers screened abstracts and full-text publications against predefined eligibility criteria.

**Results:** A total of 75 open, single- or double-blind RCTs were identified. Mean age in studies varied from 9.6 (SD 0.54) months to 25.6 (SD 13.8) years. Most studies (n=68) evaluated M-M-R® II administered between 12 months and 6 years of age. The immune responses to measles, mumps or rubella regardless of dose, post-vaccination timeframe or assay were all ≥90% except in 7 studies. Seven studies reported data for M-M-R® II at ≥7 years of age. Immune response rates ranged from 96%-100% (measles), 65%-100% (mumps), and 91%- 100% (rubella). Only one study reported seroconversion rates in infants aged 6-11 months: 87.4% (measles), 92.3% (mumps), and 91.2% (rubella). The duration and method of safety follow-up varied from study to study. Across all studies, the rates of selected adverse events were 0-61% for fever (≥38 or 38.1°C), 0-52.1% for injection site reactions, and 0-12.5% for measles/rubella-like rash.

**Conclusions:** M-M-R® II was found to be immunogenic and well tolerated in all age groups, allowing administration beyond routine schedule, if needed.

**Systematic Review Registration:**
THE EFFECT OF MRP8/14 (S100A8/A9) COMPLEX ON HUMAN NEUTROPHIL FUNCTION

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¹Sanquin Research, Amsterdam University Medical Center (AUMC), University of Amsterdam, Department Of Immunopathology, Amsterdam, Netherlands, ²Sanquin Research, Amsterdam University Medical Center (AUMC), University of Amsterdam, Department Of Blood Cell Research, Amsterdam, Netherlands, ³Emma Children’s Hospital, AUMC, University of Amsterdam, Department Of Pediatric Immunology, Rheumatology And Infectious Diseases, Amsterdam, Netherlands, ⁴Imperial College London, Paediatric Infectious Diseases, London, United Kingdom

Background: Myeloid-related protein-8 (MRP8; encoded by S100A8) and MRP14 (encoded by S100A9) are two proteins comprising over 50% of the protein content of these cells. These proteins form heterodimers, MRP8/14, which are known as calprotectin in plasma or stool samples. These complexes can be released extracellularly during certain infections and inflammation where they can act as DAMPs and may indicate disease activity in patients. Apart from its calcium-binding properties, not much is known about the MRP8/14 on neutrophil activity. We isolated MRP8/14 from human neutrophils and investigated the effect of this protein complex on neutrophil function itself.

Methods: Neutrophils were isolated from healthy donor blood and the cytosolic fraction was collected. Purification of MRP8/14 from the cytosol was performed by size exclusion chromatography. The collected fractions were analysed by western blot, ELISA and mass spectrometry and confirmed the abundant presence of MRP8, MRP14, and MRP8/14.

Results: Neutrophils release of MRP8/14 coincided with NETosis instead of release through degranulation by intact neutrophils. The abundance in neutrophils enabled purification of the protein complex. The enriched fractions of neutrophil cytosol were used to test the effect on human neutrophil adhesion and priming capacity. Upon addition of the enriched fraction, an increased adhesion capacity was observed by primary neutrophils. Furthermore, upon pre-incubation of the fraction, neutrophils showed an enhanced respiratory burst when stimulated with fMLF, indicating active priming capacity.

Conclusions: We have isolated the MRP8/14 complex from human neutrophilic cytosol by size exclusion chromatography. MRP8/14-containing fractions were capable of activating neutrophils, as demonstrated by the increased adhesion- and priming capacity of these cells upon incubation. These results indicate an active and potentially inflammation-propagating role of MRP8/14.

Clinical Trial Registration: Study is no clinical trial
Background: Upper respiratory tract viral infections including rhinovirus and influenza affect Streptococcus pneumoniae (Sp) nasal carriage density. The impact of carriage density on transmission is unknown. Interrupting vaccine serotype transmission underlies the effectiveness of pneumococcal conjugate vaccines (PCV) at population level. In a multi-centre prospective randomised stepped-wedge trial, we are using the Live Attenuated Influenza Vaccine (LAIV) to modulate Sp carriage density in 2-year-olds and assess the impact on household transmission.

Methods: 410 families were recruited across 10 UK sites. Families were randomised 1:1 for early or late (4 weeks later) index-child LAIV; 5 serial saliva and nasopharyngeal samples (NPS) were collected 2-weekly within 2 months during October-December 2017 and 2018. Samples are analysed for Sp by real-time quantitative PCR, culture amplification and microarray.

Results: In the nasopharynx, Sp carriage rate, densities and density range are highest in our index children (Table 1 for baseline (visit 1) and Figure 1 for visits 1-5). Microarray analysis found 30/83 lytA-positive index children at baseline were carrying multiple strains, which include vaccine and non-vaccine serotype Sp, non-typable Sp and non-Sp alpha-haemolytic streptococci. The three serotypes most commonly detected were 11A (10 participants), 15B (8) and 35F (8). 4/83 were carrying vaccine-serotypes (3, 23F, 19). Of our 266 lytA-positive NPS analysed by microarray to date, 82 (31%) contained antibiotic-resistant strains.
Conclusions: Our Sp rates and densities are in keeping with the literature. Sp carriage density varies widely from 10s to $10^6$ bacteria/ml. The impact of density on Sp transmission will be analysed when full results are available, June 2020. Multiple strain carriage was common and is likely to effect the propagation of antibiotic resistance and general Sp evolution.

Clinical Trial Registration: International Standard Randomised Controlled Trial Number ISRCTN10720581

**Table 1.** Baseline (visit 1) nasopharyngeal Sp carriage rates and densities

<table>
<thead>
<tr>
<th>Participant Group</th>
<th>N</th>
<th>Carriers</th>
<th>Rate</th>
<th>Mean gene copies/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult (16+)</td>
<td>618</td>
<td>71</td>
<td>11.5</td>
<td>1708.25</td>
</tr>
<tr>
<td>Index Child (~2yo)</td>
<td>396</td>
<td>270</td>
<td>68.2</td>
<td>18732.96</td>
</tr>
<tr>
<td>Sibling (age&lt;16)</td>
<td>289</td>
<td>159</td>
<td>55.0</td>
<td>11037.20</td>
</tr>
</tbody>
</table>

**Figure 1. Density boxplot by age group**
Background: Postoperative wound infection (SSI) is the most common type of nosocomial infection worldwide. It incidence is are associated with increased morbidity and mortality, prolonged hospital stay of patients and significant economic costs. The aim was to study the antimicrobial activity of the local anesthetic bupivacaine 0.5% with local treatment of SSI in children.

Methods: The study involved 30 children with surgical pathology who underwent surgical interventions on the abdominal organs, average age (11±3 years). The children were randomized into two study groups. In the first group (n = 15), a continuous infusion of local anesthetic into the postoperative wound (bupivacaine 0.5% solution of 2 mg/kg) was used at the end of the operation. In the second group (n = 15), the edges of the wound weren’t infiltrated by local anesthetics. Exudate from the wounds was isolated and microbiological examination of the wound content in both groups was performed.

Results: The results of the culturing fluid revealed the most common the organisms, causing surgical infections. Among them: S.aureus (22,0%), E.coli (19,0%), S.epidermidis (13.0 %), E. faecalis (15%),P. aeruginosa (10,0%), A. baumannii (11.3 %). The in microbiological research there has been quantified the minimum inhibitory concentrations (MIC) of 0.5% bupivacaine on isolates of these opportunistic microorganisms by the method of successive two-fold serial dilutions. Clinical isolates of S. aureus, E. coli, A.baumannii, B.cepatica have been found to be sensitive to anesthetics. The advantages of bacteriostatic properties of 0.5% bupivacaine against S. aureus, E. coli, A.baumannii, B. cepatica (p <0.001) were established and a weak inhibitory effect on P. aeruginosa.

Conclusions: Local anesthetics not only provide an analgesic effect, but also have antimicrobial action. This justifies their use in the complex of prevention and treatment of SSI.

Clinical Trial Registration: (Please input N/A if not registered)
IMPLEMENTING A HOSPITAL-BASED ROTAVIRUS VACCINATION PROGRAM FOR MEDICAL RISK INFANT: AN EVALUATION

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Background: In thirteen hospitals a pilot was conducted in which rotavirus vaccination was implemented in routine care for medical risk infants. The objective was to evaluate the feasibility of rotavirus vaccination via this implementation route, prior to the introduction of a national selective rotavirus vaccination program in the Netherlands (expected start-date June 2020).

Methods: Implementation was evaluated (see fig1) based on: 1) rotavirus vaccine coverage among eligible infants, 2) perceived appropriateness and acceptance of this program among involved healthcare providers (HCP) and parents of vaccine eligible children, and 3) HCPs perceived barriers to effective execution of the program.

Results: Between May 2016 and October 2019, 4424 infants were eligible for receiving rotavirus vaccine. Of these, 1974 (56%) infants were immunized against rotavirus. 60.7% of HCP and 93.6% of parents indicated that selective vaccination was preferred, whereas 38.5% and 54.9%, respectively were also in favor of universal rotavirus vaccination. Among parents who decided against immunization for their child, 69.3% indicated they would have vaccinated if it was national policy. Only 52.8% of HCP stated that rotavirus vaccine was routinely offered to all eligible infants in their hospital. Barriers, mentioned by HCP, were lack of awareness, perceived clinical importance of rotavirus vaccine and absence of standardized outpatient follow-up, and therefore vaccination opportunity.
Conclusions: A selective hospital-based rotavirus vaccine program implementation results in sub-optimal vaccine coverage. Half of eligible infants were offered the vaccine, while with adequate parent counseling and vaccine administration support, higher coverage can be achieved (see submitted abstract by EJM Smit). Increasing awareness among HCP and expanding vaccination opportunities, by involvement of well-baby clinics, where routine immunizations are provided, will be key to improve coverage. RIVAR-project is funded by UMCUtrecht, InnovatiefondsZorgverzekeraars, ZonMw and GlaxoSmithKline(ID:203108)

Clinical Trial Registration: Clinical trial registration: trialregister.nl NTR5361
SAFETY AND EFFICACY OF SYSTEMIC BEVACIZUMAB FOR RECURRENT RESPIRATORY PAPILLOMATOSIS IN CHILDREN: A SINGLE CENTER EXPERIENCE

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Title of Case(s): SAFETY AND EFFICACY OF SYSTEMIC BEVACIZUMAB FOR RECURRENT RESPIRATORY PAPILLOMATOSIS IN CHILDREN: A SINGLE CENTER EXPERIENCE

Background: Recurrent respiratory papillomatosis (RRP) is a rare disease caused by human papillomavirus (HPV) and represents the most common benign neoplasm of the larynx and central airways. The disease is characterized by recurrent exophytic papillomas of the epithelial mucosa in the respiratory tract and has a significant impact on quality life. We describe our experience with bevacizumab (Avastin®), a humanized anti-VEGF monoclonal antibody, has shown promise in the management of aggressive RRP.

Case Presentation Summary: Case 1: A 5-year-old female patient with RRP diagnosed at six months of age received intralesional cidofovir and recombinant interferon, without clinical response. More than 20 bronchoscopies were performed for papillomas removal. In April 2018, bevacizumab was administered in 6 doses. After the 3rd dose, an improvement of 70% was achieved, which rose to 95% after the 6th dose. Almost two years after treatment with bevacizumab, she has no new lesions. No adverse events occurred. Case 2: A 4-year-old male patient with a RRP diagnosed at 3-year-old presented with papillomatous lesions affecting the laryngeal surface of the epiglottis, arytenoids, ventricular bands, and vocal cords, and a large lesion extending to the trachea, with limitation of movement of the vocal cords and obstruction of the airflow. In August 2019, systemic bevacizumab was administered after bronchoscopy for the removal of papillomas. The lesions disappeared after the 2nd dose and he received 5 doses so far. No adverse events occurred.

Learning Points/Discussion: Currently, there is no cure for RRP, so surgical excision and debulking of the lesions to preserve airway patency are the main treatment to control the disease. Systemic bevacizumab is effective, well-tolerated, and a promising treatment for RRP in children. It is effective and well tolerated. Further studies are important to define the optimal dosing frequency and duration of therapy.
EPIDEMIOLOGICAL STUDY ABOUT THE CAUSES OF HOSPITALISATION CONCERNING ROMA POPULATION

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General Hospital of Volos, Paediatrics, Volos, Greece

**Background:** The epidemiological studies concerning the health of Roma population are very few in Greece, as well as, in the rest of Europe. Our aim was to record and analyze the hospitalisation causes of Roma children in our paediatric clinic. Furthermore we wanted to compare the frequency of hospitalisations due to urinary tract infections (UTI) and pneumonia between Roma and non Roma children.

**Methods:** We studied all records of Roma children hospitalisations (1 month -14 years), in our hospital. We also analyzed all the records of non roma children concerning UTI and pneumonia. According to demographic data the Roma population in Volos is approximately 2400 and the total population 145.500. According to our electronic archive 125 out of 1059 total hospitalizations concerned Roma children

**Results:** Viral Lower Respiratory Tract Infections 31(24,8%), Upper Respiratory Tract Infections 24(19,2%), Gastroenteritis 23(17,4%), Other Viral Infections 18(14,4%) including 7 measles cases, UTI 3(2,27%), Pneumonia 3(2,27%), Skin-Soft Tissues infections 2(1,5%), Bacteremia 1(0,75%). Other: Febrile/Non-Febrile seizures 3(2,27/1,5%), Post-streptococcal arthritis 2(1,5%), Poisoning 3(2,27%), Insect bites 3(2,27%). Asthma, abdominal-pain, myositis, electrocution, choking, urticaria and Henoch-Schonlein purpura:1 each. 74,5% of the children were under 2 years old. (35,8% for Non-Roma) In the non-Roma children the percentage of UTI was 5% while of pneumonia 3,7%. 12.5% of total hospitalisations concerned Roma children.

**Conclusions:** The percentage of Roma hospitalizations to their population was 5,5%, while of non-Roma 0,53%. Thus, Roma children needed hospitalisation ten times more often. The frequency of UTI and pneumonia was lower in Roma population. As the vast majority concerned children under 2-years, we may assume that increased morbidity with 'light' infections during infant/toddler period, combined with other characteristics of their lifestyle, strengthen their immune system and protect them from infections during late childhood.
INDIVIDUAL PARENT COUNSELING RESULTS IN HIGH ROTAVIRUS VACCINATION COVERAGE AMONG INFANTS WITH SEVERE MEDICAL CONDITIONS

E. Smit¹, J. Van Dongen¹, C. Band², E. Rouers³, M. Bonten¹, P. Bruijing-Verhagen¹
¹UMC Utrecht, Julius Center, Utrecht, Netherlands, ²Spaarnse Gasthuis, Wetenschapsbureau, Hoofddorp, Netherlands, ³RIVM, Infectious Diseases, Bilthoven, Netherlands

Background: Infants with medical risk conditions (MRC), like prematurity or congenital disorders, often do not receive rotavirus vaccine despite an increased risk of severe rotavirus gastroenteritis. The tight age restrictions for rotavirus vaccination are a suggested obstacle, but it is uncertain whether this is due to medical contra-indications impairing timely vaccination, or a lack of awareness and sense of priority.

Methods: In 13 Dutch hospitals, rotavirus vaccination was implemented for MRC infants (gestational age <36 weeks, birthweight <2500 grams or severe congenital disorder). Implementation was supported by on-site dedicated nurses. From one year prior to implementation until 12-15 months post-implementation, infants were recruited for a prospective cohort study on rotavirus gastroenteritis. Parents of cohort-participants were informed by a nurse, on the study and rotavirus vaccination, at 6 weeks of age. Pre-implementation, parents were asked if they would choose rotavirus vaccination for their child, had it been available. Whereas infants recruited post-implementation were subsequently offered the vaccine, and the nurse assisted in scheduling vaccination.

Results: Of 1481 cohort participants, 625 infants were recruited pre-implementation and 856 post-implementation (Table 1). Pre-implementation, 91.5% of parents would choose rotavirus vaccination had it been available. Post-implementation actual coverage with at least one dose was 86.7% and timeliness (6-14 weeks of age) of first dose was 94.1%. Vaccination was withheld because of reported medical contra-indications in 3 infants (0.35%).
Conclusions: With individual parent counselling in the neonatal period and assisted planning of on-site rotavirus vaccination, high vaccine coverage rates and timely vaccination are feasible for MRC infants. Given their increased risk of severe rotavirus gastroenteritis, these supportive interventions should be considered to improve rotavirus vaccine coverage among MRC infants. Funded by: GlaxoSmithKline(ID:203108), InnovatiefondsZorgverzekeraars, ZonMw en UMCUtrecht. Clinical Trial Registration: Clinical trial registration: trialregister.nl NTR5361.
Title of Case(s): Diagnostic management and treatment of a 3.5 year old girl initially presenting with septicemia, and acute abdomen about a month later

Background: Immune compromise in pediatric patients may initially present with severe infection, demanding careful diagnostic and therapeutic approach. The following case pertains to a 3.5 year old girl that was ultimately diagnosed with b/myeloid leukemia after being transferred to a third grade hospital twice in the span of one month, for Salmonella septicemia secondary to soft tissue infection and acute abdomen respectively.

Case Presentation Summary: Upon her first visit to our hospital, the girl was referred for a 3-day-fever while on antibiotic medication, pallor, and tenderness of the sternum area. Laboratory evaluation revealed low blood counts, CRP elevation, while CT indicated soft tissue effusion around the sternum area. The girl rapidly became septic, was put on a triple antibiotic scheme, then transferred to a tertiary hospital for malignancy screening. Salmonella was isolated from blood cultures. Although myelogram results were unreliable due to prior cortisone administration in the context of supplementary imaging, malignancy was indicated by immunophenotyping. 20 days after her discharge, she sought care in our hospital for abdominal pain of sudden onset. Despite being afebrile at first, with moderately elevated inflammation markers and normal hematocrit due to recent transfusion, she presented with fever, acute abdomen, and immature lymphoid cells (5%) in peripheral blood smear. She was further diagnosed with acute B lymphoblastic leukemia at a tertiary hospital.

Learning Points/Discussion: A serious infection (especially of an unusual site) and/or septicemia in pediatric patients with no history of immune deficiency should always raise the clinical suspicion of malignancy. General paediatricians must be highly aware and refer such cases for thorough screening. Furthermore, cortisone administration may complicate or even delay diagnosis, affecting the patient’s outcome. For that reason, myelogram should precede in order to grant a reliable result.
IMpact of Bronchiolitis Guidelines Publication on Primary Care Prescriptions in Italian Pediatric Population

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Background: In the Italian context, two clinical practice guidelines for the diagnosis and treatment of bronchiolitis were published in October 2014 and in December 2015, the first endorsed by numerous scientific societies and the second by Italian NHS. In primary care setting both recommended supportive care instead of beta2-agonists bronchodilators, inhaled corticosteroids and antibiotics. We aimed to determine guidelines impact on prescriptions.

Methods: This retrospective interrupted time series (ITS) analysis assessed the changes in quarterly prescriptions prevalence for bronchiolitis in children (0-14) in Italy before (pre-period: December 2012-December 2014), in-between (in-between period: December 2014-December 2015) and after (post-period: December 2015-December 2018) the two guidelines publication. Bronchiolitis diagnosis were retrieved from Pediatric Database searching ICD9-CM codes (466.1x) and free text fields and manually validated.

Results: In total, 1528 non-premature children (median age= 8.13 months) received 3766 prescriptions for 1661 bronchiolitis episodes (3.3 prescriptions/episode-treated). Children received antibiotics in more than 30% of cases reaching a peak of 45% and 52% in children <3 and >12 months. Beta2-agonists-bronchodilators prescriptions decreased from 45% (pre-period) to 33% (post-period) with the highest decrease in younger children (from 36% to 19%). Inhaled corticosteroids prescriptions had the highest decrease after 2015-guidelines publication. ITS did not show any significant variation caused by either of the two guidelines publication in all age groups (Figure1).
Conclusions: Our results based on real world data confirmed unnecessary prescribing in primary care setting with no changes after both guidelines publication. In order increase guidelines compliance reducing inappropriate prescriptions and healthcare utilization and costs, stewardship interventions, such as audit and feedback, clinical decision support tools or prescriptions pre-authorization, could be implemented. The impossibility to validate the clinical diagnosis might represent a limitation.
Background: Nonpolio enteroviruses are the predominant cause of serous meningitis in children. The majority of people infected with enteroviruses remain asymptomatic. Meningitis occurs in only 5% of symptomatic cases and tends to have a subclinical course, which leads to poor recognition of enterovirus meningitis (EVM) cases. The retrospective study addressed clinical and epidemiological features of EVM in Ukrainian children aiming to improve diagnostics of pediatric EVM in the medical settings.

Methods: We performed a retrospective assessment of medical documentation in Dnipro City Children Hospital 6 (Ukraine) for the period of 2015-2018 years. A total of 116 children aged 1 to 17 years with EVM clinically suspected on admission were included in the analysis. We evaluated the prevalence of clinical manifestations as well as their correlation with the laboratory confirmation of EVM.

Results: Positive CSF PCR for enteroviral RNA confirmed EVM in 68% of cases; severe headache and enanthema combination was the most predictive for the confirmation. Among the confirmed cases 59.5% were 6 to 10 year old; EVM occurred predominantly from August to October; 97.5% reported prior exposure to enteroviral infection. Clinical presentation most commonly included fever, headache and herpangina. Despite severe headache, meningeal signs were often unclear, particularly, in those with the late admission (>24 hours after the onset). Inflammatory changes in CBC were detected only in 35.4% of patients.

Conclusions: Pediatric EVM has a clear summer-autumn seasonality. A history of a prior exposure to enteroviral infection and younger school age are supportive for the diagnosis. Clinical presentation is most typically associated with fever, headache, vomiting and enanthema; on the contrary, evaluation of meningeal signs is not a reliable diagnostic tool; CSF PCR confirmation is required. CBC in EVM demonstrates non-specific changes.
IS CSF SYNAPSE-RELATED PROTEINS PROFILE DIFFERENT IN NEONATES EXPOSED TO ZIKA VIRUS DURING FETAL LIFE?

E. Nascimento Carvalho¹, G. Nascimento Carvalho¹, C. Ramos¹, A.-L. Vilas-Boas², O. Moreno-Carvalho², L. Zeneyedpour³, R. De Groot⁴, T. Luider⁴, C. Nascimento Carvalho²
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Background: Zika virus (ZIKV) efficiently infects astrocytes which are ZIKV early targets. ZIKV infection is involved in the disruption of formation, maturation, and plasticity of synapses. We sought to compare the concentration of cerebrospinal fluid (CSF) synapse-related proteins from neonates exposed to ZIKV infection during foetal life with the concentration of the same proteins from age-matched controls.

Methods: We identified 16 neonates who underwent lumbar puncture (LP) in the CSF Laboratory in Salvador, Brazil, whose mothers reported ZIKV clinical symptoms during gestation. Then we identified neonates who underwent LP in the same Lab and fulfilled criteria to be controls: age ≤4 days, CSF White Blood Cell count ≤8/mm³, CSF protein ≤132mg/dL, CSF Red Blood Cell count ≤1,000/mm³, no Central Nervous System illness, nor congenital infection, nor microcephaly. CSF proteins were measured by Lumos Fusion Orbitrap by shot gun mass spectrometry in Rotterdam, The Netherlands and compared as medians (p25th-p75th).

Results: Fourteen controls were included and tapped due to sepsis (n=6), maternal syphilis (n=5), seizure, fever without source, and maternal acute cytomegalovirus infection (n=1 each). Congenital syphilis and cytomegalovirus infection were safely ruled out. The median (p25th-p75th) age (days) was 2 (1-3) and 3 (1-4) among cases and controls, respectively. Up to this moment, we identified 28 synapse-related proteins which median (p25th-p75th) was significantly decreased among cases in regard to controls. Moreover, 6 proteins had median (p25th-p75th) equal to 0 (0-0) among cases.

Conclusions: Our preliminary data suggests that the CSF synapse-related protein profile is different among cases and controls.

Clinical Trial Registration: ClinicalTrials.gov Identifier NCT01200706
MANAGEMENT OF BRONCHIOLITIS IN CHILDREN HOSPITALS

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Background: Bronchiolitis is the most important cause of viral lower respiratory tract illness in young children and a major cause of hospital admission worldwide. Nevertheless, bronchiolitis management in pediatric hospitals is variable with poor evidence for international existing guidance. European and American guidelines, both suggest supportive management therapy. Routine imaging and treatment with steroids are not suggested. Bronchodilators have just little benefit. Aim of the study is to evaluate the management of bronchiolitis in children hospitals in different countries.

Methods: Children aged 1-12 months were eligible for inclusion if they were hospitalized for bronchiolitis at Bambino Gesù Children Hospital (OPBG), Italy, Europe comparing them with the Institution Members of the Children’s Hospital Association (CHA), USA. Exclusion criteria included: comorbidities complicating the course or treatment of these conditions, hospitalization longer than 10 days, intensive care services and extreme severity of illness (level 4) from the All Patient Refined Diagnosis Related Group (3M Corp, Wallingford, CT). Data regarding bronchodilators use and Chest X-rays (CXR) were analyzed.

Results: CXR’s were prescribed in 51,4% of OPBG infants and in 34,4% of CHA respectively. Bronchodilators were prescribed in 89% of OPBG and in 17,9% of CHA respectively.

Conclusions: Routine use of CXR’s and bronchodilators is variable but a common practice in the management of infants with bronchiolitis admitted in pediatric hospitals regardless of geographic location. We speculate that physicians, under parental pressure tend to overuse CXR’s and to over medicate. Improving the care of hospitalized pediatric patients should include a more strictly application of the current evidence. These findings represent a roadmap for improvement.

Clinical Trial Registration: no clinical trial
ENTERIC FEVER IN INDIA-A RETROSPECTIVE STUDY

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Background: Enteric fever is an important public health challenge in children in a resource limited setting like India. Knowing the local antibiogram of the infection is essential to make rational antimicrobial decisions and prevent antibiotic misuse. To understand the current clinical and microbiological profile, we conducted a retrospective chart review of all children diagnosed with enteric fever in a tertiary care hospital in India.

Methods: A retrospective chart review of ambulatory and hospitalized pediatric patients between 0 and 18 years of age with either blood culture positive for Salmonella typhi/paratyphi or a positive serology was done. An automated blood culture system was used and antimicrobial susceptibilities were assessed by the Kirby-Bauer method. As per protocol children were treated with a third generation cephalosporin for 14 days.

Results: The records of 62 children were included. Blood culture was positive for S in 75% (N= 47/62) of the study population. S.Paratyphi was isolated in one case (1.6%). All the isolates of S.Typhi and S.Paratyphi were sensitive to third generation cephalosporins(n=46/46,100%). Only 6.5% (3/46) of the isolates tested for Ciprofloxacin/Nalidixic acid were sensitive. 97.7% (43/44) of the isolates tested for co-trimoxazole were sensitive. The median time for defervescence after initiation of treatment was 5 days (IQR 3-11 days).

Conclusions: High rates of fluoroquinolone resistance in children is surprising considering its scarce use in this age. Though use of third-generation cephalosporin has been effective in children, these drugs are essential first-line empiric therapy in other serious conditions like meningitis and their use should be conserved. There is increasing risk of resistance emerging in Salmonella isolates as evidenced by the increasing time for defervescence in enteric fever. The high sensitivity of the isolates to co-trimoxazole should encourage greater use of this inexpensive alternative in children.
MEDICINES FOR PAEDIATRIC POPULATION: OLD BUT NOT FOR ALL?

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**Background and Objective:** The 7th WHO Essential Medicines List for Children (EMLc) presents efficacious, safe and cost-effective medicines for priority conditions. However, countries may not be able to procure them because appropriate formulations are lacking, too costly, or not registered. To illustrate this, we studied availability of amoxicillin, amoxicillin-clavulanate and clindamycin formulations in Italy, UK and USA listed in the EMLc Access antibiotic group.

**Methods:** Summary of product characteristics of all available paediatric formulations were retrieved from "Banca data farmaci" of AIFA for Italy, from Datapharm Ltd Database for UK and from FDALabel Database for USA in December 2019. Information regarding pharmaceutical formulations, strength, ingredients, age/kg restriction, medicine preparation and packaging specification were manually searched and included in an Excel database and described in infographic tables.

**Learning Points/Discussion:** Country and age bands stratified formulation of 1296 SMPCs are presented in Figure 1.

Amoxicillin sugar-free oral suspension (OS) is available only in UK and packaging including a dosing-tool are marketed in Italy and UK. OS is prepared by pharmacist only in UK and USA, with differences in instructions within countries. Also amoxicillin OS conservation varies, from 7 days at 2-8°C to 14 days.
without refrigeration. Amoxicillin-clavulanate ratio is 1:16 in USA, 1:7 in Italy and 1:2 in UK. Differently from Italy and UK, in USA, clindamycin is marketed also as OS (75mg/ml) and the injectable solution paediatric dosage is expressed also as mg/m²/day. In Italy there are no clindamycin formulations for children < 2 years. Our results highlighted wide differences in medicine availability, age restrictions and formulations specifics of three first-/second- choice antibiotics for the most common paediatric infectious syndromes. A critical appraisal of the EMLc from a therapeutic guidance, market/distribution, pharmaceutical industry, and end-users viewpoints is needed.
RAPID DETECTION OF ENTEROVIRUS AND PARECHOVIRUS MENINGITIS IN CHILDREN

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Background: Enteroviruses (EV) and parechoviruses (HPeV) may cause pediatric meningitis. Screening for HPeV on cerebrospinal fluid isn’t a common practice and may require 12-24 hours. Commercially PCR testing platforms with fully automated processes may test turnaround in as little as one hour.

Methods: We retrospectively evaluated diagnosed EV/HPeV meningitis in children aged 1 month-18 years who presented to first AID in Nicklaus Children Hospital Miami, Florida, USA from May 2016 till July 2018. FilmArray ME Panel test which consists of automated nucleic acid extraction, reverse transcription, nucleic acid amplification, and results analysis in approximately 1 h per run (i.e., per specimen), is used to simultaneously test for 14 targets on a single CSF sample (Escherichia coli, Haemophilus influenzae, Listeria monocytogenes, Neisseria meningitidis, Streptococcus agalactiae, Streptococcus pneumoniae, Cryptococcus neoformans/gattii, Cytomegalovirus, Enterovirus, Herpes simplex virus 1 and 2, Human herpes virus 6, Human parechovirus, Varicella zoster virus)

Results: Out of 88 cases of confirmed meningitis, 54 were caused by enterovirus (61.4%) and 13 (14.8%) by parechovirus. Of note, 22% of EV and 77% of HPeV cases presented with normal WBC count in CSF.

Conclusions: Viral meningitis is still the most common form of infectious meningitis. In the pre-PCR era, viral meningitis was a diagnosis of exclusion. In this series not only did we confirm that EV is the most common cause of viral meningitis but also that HPeV is a common cause of viral meningitis as well and that the absence of CSF pleocytosis and protein elevation does not exclude the diagnosis of viral meningitis. Therefore, routine multiplex PCR should be part of the routine studies of CSF when patient meningitis is considered in the differential diagnosis.

Clinical Trial Registration: no trial registration
Clinical Manifestation and Evaluation CD4 Count Response to Anti-Retrovirus Treatment of HIV Children in Soetomo Hospital

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Background: Antiretroviral treatment gives good impact to clinical improvement in HIV patient children. Baseline clinical presentation and CD4 count can be used to evaluate the response of the treatment where viral load was not available in limited resources country. We analyze CD4 evaluation and its association with several clinical presentation of pediatric HIV infection after six month of antiretroviral (ARV) therapy.

Methods: This cross sectional study from pediatric HIV medical record in outpatient clinic since 2014-2018. HIV confirmation was based on serology test for children > 18 month old. Virology test and presumptive HIV was used for children < 18 month old. Nutritional status, opportunistic infection as clinical manifestation and CD4 evaluation were analyzed using chi square with p < 0.05 considered significant.

Results: Fifty consecutive patients receive first line ARV from 2014-2018. Ninety percent patients came on AIDS. Severe malnutrition (50%), pulmonary TB (44%), chronic diarrhea (31%), oral candidiasis (31%), anemia (29%) and pruritic papular eruption (13%) were most opportunistic infection at admitted. Weight loss was observed in 26% children and CD4 count evaluation showed increasing level in 59% patient after 6 month ARV. Several factors associate increasing of CD4 count were improvement of opportunistic infection (PR 5.9; 95%CI 1.4 to 25.2; P=0.013) and nutritional status (PR 0.1; 95%CI 0.2 to 0.5; P= 0.002).

Conclusions: The most clinical manifestation in pediatric HIV are severe malnutrition and present of opportunistic infection. CD4 count evaluation after 6 month first line ARV initiation had association with initial nutritional status and improvement of opportunistic infection. It is important to start treatment earlier after diagnosis confirmed regardless CD4 count level. Reasons for not increasing CD4 count may be non adherence, baseline CD4 very low, and lack of support family. It needs further investigation.
HERPETIC ENCEPHALITIS IN INFANCY-THE IMPORTANCE OF EARLY TREATMENT FOR A GOOD OUTCOME

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Title of Case(s): Viral encephalitis in infancy-the importance of early treatment

Background: Herpes simplex encephalitis is the most common single cause of viral encephalitis in infants and children. Herpes simplex virus causes serious disease in neonatal period and early infancy with very high mortality and neurologic sequelae. HSV infection in the neonates may have either a localised, disseminated or encephalitic pattern of presentation. The encephalitic form often remains undiagnosed as 40-60% of neonates with central nervous system infection have no skin lesions at the time of presentation. Without prompt treatment it has high rates of mortality and significant long-term morbidity.

Case Presentation Summary: A 9 month old girl known previously healthy was admitted to a regional hospital for low fever followed by febrile seizures. After 3 days of admission she developed multiple tonic-clonic seizures, altered consciousness and neurologic impairment. She was transferred on day 5 to our hospital. CT scan revealed temporal lobe abnormalities. A lumbar puncture was performed and Aciclovir therapy was started on day 5. The analysis of cerebrospinal fluid showed pleocytosis, normal protein and glucose, negative culture but the presence of Herpes simplex virus type 1 DNA. On day 10 a MRI was performed which detected cystic frontal and temporal lobe lesions. Motor and cognitive function were altered, with upper and lower limbs hypertonicity and swallowing reflex was lost and a gastrostoma was insterted.

Learning Points/Discussion: HSE remains a serious illness with high mortality and morbidity despite appropriate antiviral therapy. Adequate intravenous acyclovir therapy should be started as soon as possible even in suspicious cases before confirmation of the infection. Brain imaging techniques are characteristic though not pathognomonic of neonatal herpes simplex encephalitis. On computed tomography the temporal lobes are most commonly involved with multicystic haemorrhagic encephalomalacia as was seen in our case.
HOSPITALIZATION FOR ACUTE CEREBELLITIS IN CHILDREN AFFECTED BY VARICELLA: HOW MUCH DOES IT COST?

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Background: Chickenpox is a highly contagious airborne disease caused by the varicella zoster virus. It is generally benign and self-limiting, but it may be responsible of Acute cerebellitis (AC) that is the most common neurological complication and is associated with prolonged hospitalization in the acute phase (HAP). Aim of the study is to estimate the costs of AC HAP in children affected by varicella.

Methods: We retrospectively reviewed the medical records of a pediatric cohort hospitalized for chickenpox AC over a period of fifteen years (October 2003-October 2018) and we analyzed acute care costs. We performed a MEDLINE search concerning scientific publications of the last ten years referring to patients younger than 18 years hospitalized for AC in varicella.

Results: The median cost of HAP was of 5366 euro. We evaluated the cost of laboratory exams (mean cost of € 192,75); instrumental tests (mean cost of € 154,21), medical and paramedical examinations (mean cost of € 45,45) and therapeutic treatment (mean cost of € 42,42). Drugs, such as antiviral or steroid treatment, contribute to higher HAP (mean cost of 2757 euro, higher than those without therapy). The most significant part of HAP is represented by the cost of hospital accommodation and management at the Pediatric Infectious Diseases Unit, which is about € 537.78 for a single day.

Conclusions: Although AC post-varicella is rare, its HAP cost is not negligible resulting in substantial economic burden. Financial studies are important for evaluate the cost saving in order to influence public funding decisions. Further studies are necessary to investigate the economic burden of the disease.

Systematic Review Registration: no registration
SOME CLINICOLABORATORY FEATURES OF CHRONIC DUAL HBV/HCV INFECTION

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Background: In the last decade the frequency of mixed viral hepatites among all viral hepatites was rising. The most frequent type is HBV and HCV dual infection and detection of this viruses is associated with the evolution of laboratory techniques. Dual HBV/HCV infection has been associated to a severe course of the liver disease and to a high risk of developing hepatocellular carcinoma.

Methods: We studied 49 patients with HBV/HCV dual infections, among which 2 were female (4%) and 47 were male (96%). More than 1/3 of patients were in 26-35 year-old group. The diagnosis of dual HBV/HCV infection was made based on the data from physical examination, history (24.5% of patients mentioned about intravenous drug abuse), course of illness and laboratory analysis of HBV and HCV markers (HBsAg, anti-HBc IgM and anti-HBc IgG; total anti-HCV IgG and also PCR). All patients underwent to ultrasonography, esophagogastroduodenoscopy (EGD) and computed tomography (CT).

Results: In the 95% of patients was diagnosed chronic HBV/HCV infection and in 5% it was in the stage of cirrhosis. Patients complained of dyspeptic symptoms(48.9%), fatigue(79.5%) and arthralgias(46.9%), which was accompanied by jaundice(93.8%), abdominal pain(38.7%) and pruritus(33.6%). Ascites was detected in 4(8.1%) patients. Total bilirubin levels were 3.5-7mg/dL; ALT was 152-630mmol/L, AST was 81-967mmol/L. PCR detected HBV DNA in 7(14%) patients and actively-replicating HCV genome in 30(81%) patients.

Conclusions: In conclusion, HBV/HCV dual infection is a complex clinical/virological entity. This co-infection appears to be associated with the most severe forms of chronic liver disease. Chronic dual HBV/HCV hepatitis with cirrhosis mainly occur in young adults, which is due to intravenous drug abuse. The activity of pathologic process is mainly associated with actively-replicating HCV genome, which we can detect with PCR.
"CAT SCRATCH DISEASE AS A RARE CAUSE OF ERYTHEMA NODOSUM IN IMMUNOCOMPETENT CHILDREN: A CASE REPORT SERIES."

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Title of Case(s): Cat scratch disease as a rare cause of erythema nodosum in immunocompetent children: a case report series

Background: Erythema nodosum (EN) typically manifests as the appearance of tender nodular lesions usually located on anterior surface of the lower extremities. The pathogenesis of EN is poorly elucidated. It results from a hypersensitivity reaction caused by many agents, including infections (in children it is most commonly associated with group A streptococcal infections). In many cases, the cause can be unknown.

Case Presentation Summary: Case 1. A seven-year-old girl was admitted to our Department due to fever associated with tender nodular lesions on the anterior surface of the lower extremities and the forearms. In addition, a vesicular lesion on the fifth finger of the right hand and enlarged axillary lymph nodes were found. In the past history, the girl had been scratched by her cat a few weeks before the symptoms appeared. EN was diagnosed. Due to the presence of the lymphadenopathy, characteristic skin lesions, serology testing for Bartonella henselae was performed, which was positive, confirming the cat scratch disease. Azithromycin was administrated. Case 2. In the same month, another seven-year-old girl was admitted to the Department due to fever, similar erythematous nodules located on the lower extremities, and unilateral axillary lymphadenopathy. In this case, the primary lesion was located on chest. The girl had a young cat at home. Serological testing also confirmed B. henselae infection. The patient was treated accordingly.

Learning Points/Discussion: In both cases the patients improved clinically after antibiotic therapy and the skin lesions and unilateral axillary lymphadenopathy disappeared. Despite of frequent difficulties in finding the causes of EN among pediatric population, EN may be caused by an immunologic reaction to antigenic stimuli during B. henselae infection. Thus, cat scratch disease should be considered while diagnosing causes of the EN.
SECOND-YEAR INFANT MANDATORY VACCINATIONS IN FRANCE: CONFIRMATION OF A POSITIVE COVERAGE IMPACT

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Background: All children born from first of January 2018 are subject to mandatory vaccination against 11 diseases in France. Also in 2017, a new dose of MenC was introduced in the French calendar at 5 months of age in addition to the dose at 12 months. Through Vaccinoscopie survey, we measured for the second year the impact of this new policy on vaccine coverage rates (VCRs) and mothers’ perception regarding vaccination.

Methods: Vaccinoscopie is a French annual survey conducted by IDM Families on behalf of GSK since 2008. It is an online standardized questionnaire survey realised in France on a representative sample of mothers of different age ranges. We focused here on the mothers of 0 to 17-month-old infants, all born after the extension of mandatory vaccination (1,500 mothers interviewed in 2019).

Results: From 2017 to 2019, VCRs increased from 86 to 93% for hepatitis B and from 1 to 70% for Meningococcus C for a complete schedule at 15 months of age. Measles and pneumococcus VCRs non significantly increased. After a progressive decrease between 2012 and 2017, the rate of favorable mothers’ opinion towards vaccination increased in 2018 and 2019. Perception of vaccine usefulness and of being well informed also progressed over the same period. Mothers’ rate against mandatory vaccination decreased from 17% in 2017 to 8% in 2019 (p<0.001).

Conclusions: These first results confirmed for the second year that the extension of mandatory vaccination associated with the strong communication strategy implemented by the French Authorities had a positive impact on both mothers’ opinion regarding vaccination and on infant VCRs. The 2020 survey will allow to have a complete view of VCRs in 24-month-old children, especially on the two doses measles vaccination.
ADOPTION IN CANADA OF INTERNATIONAL RISK SCORING TOOL (IRST) TO PREDICT RESPIRATORY SYNCYTIAL VIRUS HOSPITALISATION (RSVH) IN MODERATE-LATE PRETERM INFANTS (32-35 WEEKS’ GESTATIONAL AGE [WGA])

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Background: The advisory board to the Ontario Ministry of Health is considering adoption of the new 3-variable IRST, which used data pooled from six observational studies (including PICNIC from Canada) to predict RSVH in 32-35wGA infants [Blanken. Pediatr Pulmonol 2018;53:605-12]. Canada is currently using a 7-variable RST developed solely from PICNIC focussed on 33-35wGA infants [Sampalis. Med Decis Making 2008;28:471-80]. We explored the potential implications of switching from the Canadian to the IRST.

Methods: The two RSTs were compared for included risk factors and predictive accuracy (area under the receiver operating characteristic curve [AUROC]). Correlations (Spearman rank) between cut-off scores for low-, moderate-, and high-risk subjects were assessed against the pooled dataset using infants born 33-35wGA with complete data for all risk factors in both RSTs.

Results: The two RSTs contain many of the same risk factors (birth proximity to the RSV season, smoking, siblings, day care), with the Canadian RST also including sex, small for GA, and familial eczema. Predictive accuracy of the two RSTs is similar (AUROC, IRST: 0.773 [sensitivity: 68.9%; specificity: 73.0%] vs. Canadian: 0.762 [68.2%; 71.9%]). Significant correlations between cut-off scores (p<0.001) and risk categories (p<0.001) were apparent, although the correlation coefficients were weak for both (scores: 0.217; categories: 0.055). While the proportion of high-risk infants was similar for the two RSTs (IRST: 0.6% vs. Canadian: 0.7%), a far greater number of infants were assigned moderate-risk by the IRST (19.9% vs. Canadian: 9.8%).

Conclusions: The IRST can be considered a simpler model (few risk factors) than the Canadian RST, but assigns more infants as moderate-risk. Combined with including 32wGA infants, adoption of the IRST in Canada has cost-effective implications for RSV prophylaxis which warrants further investigation.

Systematic Review Registration: N/A
HEMATOLOGICAL PROFILE OF HOSPITALISED CHILDREN OF ACUTE VIRAL HEPATITIS A

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Background: A change in the hematological profile is a common in systemic and infectious diseases. The knowledge of the frequency of the haematological abnormalities in children hospitalised with acute viral hepatitis A will support the need for this indispensable tool in investigation of infectious diseases. The objective of this study is to describe the haematological profile of patients with acute viral hepatitis A.

Methods: All the consecutive children who were hospitalised for acute viral hepatitis A were prospectively studied. In all these children Packed cell volume (PCV), white blood cell count (WBC), platelet count, prothrombin Time (PT) and partial thromboplastin time in kaolin (PTTK) were analysed in all of these children at dayanad medical college and hospital of baba farid university of health sciences. Final outcome was also studied.

Results: A total of 82 cases of acute viral hepatitis got admitted between the months of June 2019-december 2019. Out of these cases 71 had serology positive for hepatitis A. Majority of children were more than 10 years age. Male to female ratio was 1.4:1. In 12.6 % cases history of contact was present. Abnormal prothrombin index and ratio was seen in 48 (67.6%) patients whereas abnormal activated partial thromboplastin time was seen in 24 (33.8%) of patients. 8 (11.2%) patients had thrombocytopenia, 21 (29.5%) had anemia, 18 (25.3%) showed leucocytosis. All 71 children were discharged.

Conclusions: Acute viral hepatitis A in children has a benign course in majority. Only minority of such children develop fulminant hepatitis. Other studies done earlier have also reached a similar conclusion. There is a paucity of studies of hematological parameters in children with viral hepatitis A from northern India. Derranged hematological parameters increase the morbidity in these children. Hence it is important to monitor hematological parameters in children with acute viral hepatitis A.
Background: The clinical course of intensive care unit (ICU) patients may be complicated by a large spectrum of infections, defined by specific epidemiological, clinical and microbiological aspects. ICU acquired infections increase mortality, hospital stay and cost. However, a substantial number of ICU-acquired infections are preventable. The aim of this study is to determine more frequent diseases among pediatric population admitted to ICU in Muratsan University Hospital, Yerevan, Armenia.

Methods: The study was conducted in tertiary level university teaching hospital of Yerevan State Medical University. We have investigated retrospectively medical records of 121 patients of who were admitted to ICU during the period from December 2016 to August 2017. Inclusion criteria were the age between 1 month and 5 years. We selected to research diagnoses and complications of that patients.

Results: Of 121 cases 35.5%(n=43) of patients were diagnosed with community-acquired pneumonia, among which 1 caused by aspiration. Bronchiolitis were in 27.3%(n=33) of patients. Other infections were laryngotracheitis(n=1), purulent tonsillitis(n=1) and urinary tract infections(n=3). The most common complications were respiratory failure (76.9%,n=93), pediatric COPD (19.9%,n=24), hypovolemic shock (13.2%,n=16), burn shock (n=2), necrotizing enterocolitis with sepsis (n=2), ARDS (n=1) and polyserositis (n=1).

Throat culture were taken in 70 patients and among them 59 were found positive with different bacteria and fungi, such as St. aureus, E. coli, K. pneumonia, Candida spp, etc.

Conclusions: The results show that the most common group of diseases were respiratory tract infections. Those infections occasionally were accompanied with severe complications, such as necrotizing enterocolitis and sepsis with shock. Throat culture can indicate the presence of important pathogens and early detection of that agents can be essential for prevention of diseases, therefore, we recommend to use this assay routinely, following to guidelines.
"NONINVASIVE EVALUATION OF LIVER FIBROSIS IN TEENAGERS WITH CHRONIC HEPATITIS C"

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Background: There is a need for validation of noninvasive alternatives to liver biopsy for the evaluation of fibrosis in children with chronic hepatitis C (CHC). The aim of this prospective study was to analyze liver fibrosis in teenagers with CHC using transient elastography (TE, Fibroscan) and to compare the results with serum biomarkers: aspartate transaminase-to-platelet ratio index (APRI) and Fibrosis-4 index (FIB-4).

Methods: Thirty-three patients aged 12-17 years were qualified for the real-life therapeutic program ‘Treatment of Polish Adolescents with Chronic Hepatitis C Using Direct Acting Antivirals (POLAC PROJECT)’. Most of the patients were male (20/33, 61%), 28/33 (85%) were infected vertically, 21/33 (64%) were treatment-naïve, 28/33 (85%) with genotype 1, and 5/33 (15%) with genotype 4 HCV. Evaluation of liver fibrosis was performed using TE and serum biomarkers. Using TE results as a reference, diagnostic performance of APRI and FIB-4 was assessed by calculating AUROC.

Results: TE results revealed no or mild fibrosis (F0/1 in METAVIR scale) in 30/33 (91%) patients. In 3/33 (9%) patients significant fibrosis was observed (F≥2), including 2/33 (6%) with cirrhosis (F4). Mean APRI was 0.38±0.13, and mean FIB-4 0.34±0.11. A correlation between TE score and APRI was found (r=0.36, 95%CI 0.02-0.63, p=0.04), and a trend towards a correlation between TE and FIB-4 was observed (r=0.32, 95%CI -0.02-0.60, p=0.06).

Conclusions: For the diagnosis of significant fibrosis, AUROC (95%CI) for both APRI and FIB-4 was 0.800 (0.625-0.918) suggesting their good diagnostic performance. APRI, with the cut-off >0.347, predicted significant fibrosis with 100% sensitivity and 66.7% specificity, whereas FIB-4, with the cut-off >0.402, predicted significant fibrosis with 66.7% sensitivity and 90% specificity. Significant fibrosis, including cirrhosis, is possible in teenagers with CHC. Serum biomarkers (APRI, FIB-4) correlate positively with TE results.
Background: Neonatal impetigo is a highly contagious skin infection, usually caused by *Staphylococcus aureus* (SA), that can be transmitted by a colonized family member. In our hospital we start to search for carrier status of patient and relatives, when it is positive, we decolonize them. The aim of our study was to describe hospitalized cases of neonatal impetigo and the carrier status of the patients and their relatives.

Methods: A retrospective analytical descriptive study of hospitalized patients with neonatal impetigo was conducted between January 2010 and December 2019. Inclusion criteria: newborns (up to 28 days of life) with clinical diagnosis of impetigo. No patient was excluded. Descriptive and bivariate statistical analysis was performed (Fisher’s Exact Test) using SPSS 22® (α = 0.05). Variables analyzed: demographic, clinical, laboratory and therapeutic.

Results: Total of 44 patients hospitalized, 57% male, median age 10 days. In 93% of cases a culture from the lesions was performed with SA identification in 98%. Patient carrier status was searched in 55% (positive in 96%) and relatives carrier status in 50% (positive in 64%). We had 7 newborns hospitalized at the same time, in this group 86% of familiar members were colonized versus 53% of familiar members colonized on the other group (p=0.193). Two newborns had complications, they were both colonized, one with a multi drug resistance microorganism.

Conclusions: Patient colonization was very high, so maybe we could assume that patient carrier status is an important risk factor for impetigo neonatal, and search for it when we have suspected lesions, in order to treat, take isolation precautions and investigate familiar members. If familiar members are colonized, we consider that we should treat them. Just a minority (<5%) had complications.
Title of Case(s): KAWASAKI DISEASE SHOCK SYNDROME - A CASE REPORT

Background: Kawasaki Disease Shock Syndrome (KDSS) diagnosis is challenging. Its early recognition is essential for assertive treatment, thus improving prognosis.

Case Presentation Summary: A 12-year-old adolescent presented with a 5-day history of fever, abdominal pain, vomiting and jaundice. Physical examination: poor appearance, hypotension, pallor, painful abdomen, erythematous oropharynx, conjunctival hyperemia and nuchal rigidity. Laboratory evaluation (LE): hemoglobin 14g/dL, WBC count 6320/uL, platelets 97000/uL, creatinine/urea 1.3/45mg/dL, TGO/TGP 171/220UI/L, LDH 961UI/L, CRP 240.7mg/L, ESR 32mm/1st hour. Abdominal CT: mild hepatosplenomegaly. Septic or toxic shock were suspected and ceftriaxone/clindamycin/doxycycline and volemization started. He was admitted to PICU, requiring mechanical ventilation and vasopressors. On D3, due to refractory shock and sustained fever, intravenous immunoglobulin (IVIG) was administered. On D5, a morbilliform rash, hand edema, cheilitis, and supraclavicular adenomegaly became apparent. LE: sterile CSF pleocytosis, worsening thrombocytopenia, mild anemia, no leukocytosis, CRP 268mg/L. Cultural exams and extensive infectious workup were negative. Normal brain CT. Due to fever >5 days, conjunctivitis, mucous membranes and extremities changes, KDSS was diagnosed. Ferritin 544.6ng/mL, normal fibrinogen and triglycerides, lymphadenopathy biopsy and myelogram without signs of hemophagocytosis or malignancy. Echocardiogram: mild pericardial effusion. He started methylprednisolone pulses, aspirin and repeated IVIG, with rapid improvement. Extensive desquamation appeared later. He was discharged, completed 4 weeks of prednisolone and aspirin. Serial echocardiograms were normal.

Learning Points/Discussion: This case highlights the diagnostic difficulties of KDSS and the high index of suspicion required. The unusual initial manifestations and age, laboratorial criteria of poor prognosis (eg.hepatitis, thrombocytopenia) hindered the diagnosis. Splenomegaly, elevated liver enzymes and ferritin, and thrombocytopenia indicated subclinical macrophage activation syndrome. Whenever a patient with suspected toxic or septic shock is refractory to conventional treatment and microbiological investigations are negative, one must always remember KDSS.
INCIDENCE OF PNEUMONIA IN CHILDREN IN GERMANY FROM 2012-2017

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Background: Pneumonia is a common infectious disease that leads to substantial healthcare utilization in children. Streptococcus pneumoniae is the most common bacterial pathogen. The 7-valent pneumococcal conjugate vaccine (PCV) was introduced in Germany in 2001, followed by PCV10 and PCV13 in April and December 2009. This study estimated pneumonia incidence rates (IR) in children <16 years old after the introduction of PCV13 from 2012-2017.

Methods: Pneumonia episodes were identified in the InGef database from 2012-2017 for children aged <16 years using ICD-10-GM (German modification) codes. Pneumonia episodes were classified as pneumococcal (associated with pneumococcal-specific ICD-10 codes) or unspecified (associated with ICD codes for bacterial pneumonia unspecified, bronchopneumonia unspecified and pneumonia unspecified). IRs were numbers of episodes/100,000 person-years (p-y) and stratified by age-group (<2, 2-4 and 5-15 years).

Results: Pneumococcal pneumonia IRs declined 2012-2017; from 124 to 86/100,000 p-y in children <2, from 153 to 95/100,000 p-y in children 2-4 years, and from 58 to 32/100,000 p-y in children 5-15 years. Mann-Kendall test showed a significant downward trend (p=0.024) only in children 5-15 years. Unspecified pneumonia IRs declined 2012-2017; from 3,833 to 2,785/100,000 p-y in children <2, from 4,798 to 3,139/100,000 p-y in children 2-4 years, and from 1,315 to 884/100,000 p-y in children 5-15 years. Mann-Kendall test showed a significant downward trend (p=0.024) only in children 2-4 years.

Conclusions: Across the study period, the incidence of pneumococcal pneumonia and unspecified pneumonia was highest in children 2-4 years. Following the introduction of PCV13 in late 2009, the incidence declined between 2012 and 2017 in all age-groups. However, a significant continuous downward trend was only observed in older children. Despite the decline, there remains a burden of pneumonia in children in Germany.
SEPTIC ARTHRITIS IN TWO MONTH OLD BABY

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Title of Case(s): Septic Arthritis in Two Month Old Baby

Background: Septic arthritis in infant is uncommon, even it is more frequent in children than adult. It continues to be one of major causes of orthopedic disability in pediatric population. Diagnosis was defined based on clinical signs, laboratory, and imaging confirmed by synovial fluid culture results. Timely diagnosis and optimal management play the role to prevent irreversible joint damage and sequel. It also needs multidiscipline approach of surgical and antibiotic treatment to lead better outcomes. We report a septic arthritis case in infant emphasize to how to diagnose and management.

Case Presentation Summary: A well-nourished two month old baby was referred with chief complaint of upper right arm swollen and limited movements since last 2 weeks. There was no history of trauma. She got BCG immunization in the same arm a month ago but no suppurated wound was found. Laboratory examination revealed leukocytosis, high CRP and ESR. Imaging study showed soft tissue swelling with irregularity of caput right humerus from x-ray and chronic septic arthritis of glenohumeral joint from ultrasound. Joint synovial fluid culture revealed Staphylococcus aureus bacteria and gen expert result was negative. She underwent debridement surgery and antibiotic therapy. Ampicillin and Cloxacillin were given based on antibiotic sensitivity test. The baby was improved with good laboratory result and discharged after 10 days of treatment. Cloxacillin antibiotic was continued for 3 week.

Learning Points/Discussion: Joint swelling and movement limited should be considered as septic arthritis even it was rare in infant. Septic arthritis in infant need multidiscipline approach management. Laboratory examination, imaging and culture were needed to confirm diagnosis. It needs surgery debridement and pus drainage. Adequate antibiotic based on sensitivity should be prescribed for 3 weeks. Timely diagnosis can prevent permanent joint disability and deformity.
CLINICAL AND ECONOMIC BURDEN OF RECURRENT AOM IN CHILDREN IN GERMANY FROM 2012-2017

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Background: Acute otitis media (AOM) leads to substantial healthcare resource utilization (HCRU) in children. Streptococcus pneumoniae is an important cause of AOM. The 7-valent pneumococcal conjugate vaccine (PCV) was introduced in Germany in 2001, followed by PCV10 and PCV13 in 2009. This study estimated recurrent AOM incidence rates (IRs), HCRU and medical expenditure in children <16 years in Germany after the introduction of PCV13 from 2012-2017.

Methods: Recurrent AOM episodes were identified using ICD-10-GM (German Modification) codes in the InGef database from 2012-2017. Recurrent AOM was defined as ≥3 episodes in 6 months, or ≥4 episodes in 12 months. IRs were numbers of episodes/1000 person-years (p-y) and stratified by age group (<2, 2-4 and 5-15 years). Annual medical expenditures (hospitalizations, outpatient visits and prescriptions) were calculated by multiplying average cost/episode in 2017 by number of episodes in each year.

Results: Between 2012-2017, recurrent AOM IRs declined in children <2 years (35 to 27/1000 p-y), 2-4 years (41 to 34/1000 p-y) and 5-15 years (3.7 to 3.5 /1000 p-y). The Mann-Kendall test did not show significant continuous downward trends for any age group. Over the study period, outpatient antibiotic prescriptions declined from 8,594 to 7,772. Annual medical expenditures declined from €547,000 to €502,000.

Conclusions: Across the study period, recurrent AOM incidence was highest in children 2-4 years. Following the introduction of PCV13 in late 2009, recurrent AOM incidence declined between 2012 and 2017 in all age-groups. However, a significant continuous downward trend was not observed. Antibiotic prescriptions and medical expenditures declined in children <16 years. Despite the decline, recurrent AOM-associated disease and economic burden remain considerable.
VENTRICULOPERITONEAL SHUNT INFECTION IN PEDIATRIC PATIENTS: A SINGLE CENTRE STUDY

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Background: Shunt infections in children with hydrocephalus have been a major cause of morbidity and mortality. Disorders of cerebrospinal fluid (CSF) circulation as hydrocephalus in children occur mostly as congenital conditions, the consequence of intracranial hemorrhage or post-meningitis sequelae. Implantation of the ventriculoperitoneal shunt (VP) has improved the outcome in children with hydrocephalus but at the same time increased the risk of infectious complications.

Methods: A retrospective study was conducted by reviewing children who had the first-time shunt placement and later developed ventriculoperitoneal shunt meningitis. Information on demographic characteristics of the patients, epidemiology, treatment, developed complications, and outcome were collected from medical documentation. Data were collected for children treated at University Hospital for Infectious Diseases “Dr. Fran Mihaljević”, Zagreb from January 2004 to January 2019.

Results: Forty-seven children were enrolled in the study. The most common reason for shunt insertion was congenital hydrocephalus (43.2%). Acute bacterial meningitis was the most common complication (81%). Twenty-six of the patients acquired infection within 30 days after shunt insertion. The most common microorganism cultured from CSF was Staphylococcus epidermidis (61%). Peritonitis occurs in 14 of patients with significantly elevated CRP levels (p = 0.002) compared with patients without peritonitis. Along with antibiotics, in 46 patients shunt was removed immediately after confirmation followed by second VP conversion, after infection has been resolved.

Conclusions: Because of their high incidence and developed complications, infection of CSF remain a significant problem in children with VP shunting. Congenital hydrocephalus remains the main reason for VP shunting. Early detection and management reduce morbidity and mortality. Removal of the shunt along with antibiotics and placement of the new shunt after the sterilization of CSF seems to be optimal therapy.
Background: Respiratory diseases are one of the leading causes of children’s visit in the Emergency Department (ED) and hospitalisation in Paediatric Hospital Clinics internationally respectively. The aim of this prospective observational study is, after including several factors, to record children with respiratory tract diseases (RTD) who came to the ED and were hospitalised in our Paediatric Clinic, from March to September 2019.

Methods: A prospective seven month study carried out, including all children with respiratory diseases, in this period with the assistance of electronic archive (Asklepios), clinic’s and ED’s patients record. The study focused only on Volos City habitants. Factors that have been taken into account include nationality, most common mentioned symptom, peak arrival hours, age-group, gender, seasonal distribution, duration of hospitalisation and discharge diagnosis.

Results: In a 7 month period the children arrived with RTD in ED were 2039. Only 5% was hospitalized, 65% being Volos City habitants. The Greek/Roma population was 78% to 22% respectively. The most common symptom for children to seek care at the ED was fever. The peak arrival hours were at “16.00-00.00”. The highest arrival rate was observed at spring with 1/1 female/male ratio, and was represented mostly by children 1-6 years old. The mean hospitalization time was ≥2-5 days and the main discharge diagnosis was lower respiratory infection.

Conclusions: A significant proportion of children (in study area) with RTD arrived in ED with a notable low percentage been hospitalised. The findings are consistent with Greek and international bibliography and are correlated with seasonal variation, climatic, socio-economical conditions and so on. However, safer conclusions expected to be extracted upon completion of our study data that are still being recorded.
Background: Acute otitis media (AOM) leads to substantial healthcare resource utilization (HCRU) in children. Streptococcus pneumoniae is an important cause of AOM. The 7-valent pneumococcal conjugate vaccine (PCV) was introduced in Germany in 2001, followed by PCV10 and PCV13 in 2009. This study estimated AOM incidence rates (IRs), HCRU and medical expenditures in children <16 years old in Germany after the introduction of PCV13 from 2012-2017.

Methods: AOM episodes were identified using ICD-10 GM (German modification) codes in the InGef database from 2012-2017 in children <16 years. IRs were numbers of episodes/1000 person-years, and stratified by age group (<2, 2-4 and 5-15 years). Annual total medical expenditures (hospitalizations, outpatient visits and prescriptions) were calculated by multiplying average cost/episode in 2017 by number of episodes in each year.

Results: IRs declined between 2012 and 2017 across all age groups; in children <2 from 218 to 160/1000 person-years, 2-4 years from 264 to 192/1000 person-years, and 5-15 years from 54 to 42/1000 person-years. Mann-Kendall test indicated significant negative trends in IRs for children <2 (p=0.024) and 2-4 years (p=0.024). AOM-associated outpatient antibiotic prescriptions declined from 69,501 in 2012 to 54,516 in 2017 in children <16 years. Annual medical expenditure declined from €3.9 million in 2012 to €3.1 million in 2017 in children <16 years in the InGef population.

Conclusions: Across the study period, AOM incidence was highest in children 2-4 years. Following the introduction of PCV13 in late 2009, AOM incidence declined between 2012 and 2017 in all age-groups. However, a significant continuous downward trend was only observed in children aged <2 and 2-4 years. AOM-associated antibiotic prescriptions and medical expenditures declined in children <16 years. Despite the decline, AOM clinical and economic burden remains substantial.
BACTERIAL COINFECTIONS IN DENGUE FEVER - A NEW CHALLENGE

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Background: Dengue fever is the most common arboviral disease in the world. Dengue infection presents in a wide spectrum of severity. Bacterial coinfection has been reported in adult patients. Does it increase the incidence of bacterial sepsis in children is not known but the presence of bacterial infection can adversely affect the outcome. This retrospective study analyses the clinical, imaging and laboratory profile of children suffering from Dengue fever with coexisting bacterial sepsis.

Methods: One hundred and twenty four patients aged between 3 months to 18 years admitted in two private hospitals in Kanpur, India between 1st September and 15th December 2019 who had Dengue fever confirmed by Elisa Testing were retrospectively studied. They were divided in two groups those that had only Dengue Fever and those who had coexisting Bacterial sepsis. Their clinical profile, imaging, laboratory data, and final outcome was compared and subjected to statistical analysis.

Results: Thirteen children had concurrent sepsis (13/124, 10.4%). Children between 0 to 5 years (7/13, 53.8%, p = 0.019), having a longer duration of illness before hospitalization (8/13, 61.5%, p = 0.002), longer hospital stay (7/13, 53.8%, p = 0.0029), presence of jaundice (2/13, 15.3%, p = 0.0013), low platelet counts (9/13, 69.2%, p = 0.0033), shock (10/13, 76.9%, p = 0.0001), and increased PCT were some indicators of sepsis in these patients. Blood cultures were positive in five children with sepsis. E. coli in three and Staphylococcus aureus in two.

Conclusions: It’s a matter of speculation as to why these patients of Dengue are more susceptible to sepsis. Till now no large studies have been done in children, only stray reports of coexisting infection have been published. One postulation is that Increased vascular permeability may increase the chances of bacterial contamination. Antibiotics should not be used routinely in Dengue fever. However young children presenting with severe symptoms especially shock should be screened for sepsis and appropriate antibiotics should be started early.
Title of Case(s): Transaminasemia Combined With Anemia In an Immunocompetent Child with an Adenovirus Infection

Background: Human adenoviruses are an important cause of infections in both immunocompetent and immunocompromised individuals and a leading cause of acute gastroenteritis in children. In healthy children, adenovirus infection causes a benign, self-limited illness but can also cause symptoms that extend beyond the gastrointestinal tract. In this article, we present a case where adenovirus gastroenteritis was accompanied by transaminasemia and anemia in an immunocompetent child.

Case Presentation Summary: A previously healthy 6-year-old male presented with a 1-day history of decreased energy and fever, 2 episodes of nonbilious emesis and several episodes of diarrhea. He was prescribed antibiotics for presumed bacterial dysentery. Labs revealed elevated transaminase AST of 75 IU/L and ALT of 203 IU/L, with an INR of 1.2, serum total bilirubin 1.4mg/dL and abnormal electrolytes. Initial CBC showed anemia Hgb of 9 g/dL. Ferritin and LDH were high, as expected for inflammatory process. Abdominal ultrasonography didn't show hepatomegaly. EBV and CMV panels were also negative as well as results of a hepatitis panel. The immunochromatography test for adenoviral antigen was positive. During follow-up symptoms of gastroenteritis completely resolved on day 8 of hospitalization, as the hepatic transaminase levels dropped (AST: 46 IU L⁻¹ and ALT: 98 IU L⁻¹). On day 15 of the follow-up, the patient's AST and ALT levels returned almost to normal (AST: 28 IU L⁻¹ and ALT: 42 IU L⁻¹), and anemia had resolved.

Learning Points/Discussion: Adenovirus infection should be included in the differential diagnosis in an immunocompetent patient with acute gastroenteritis and elevated liver enzymes combined with hematologic abnormalities. Our case report highlights to clinicians the importance of including adenovirus infection in the differential diagnosis of transaminasemia combined with anemia, even in healthy immunocompetent patients, when other common causes are excluded.
COMPARISON OF SERUM CYTOKINE PROFILES IN CHILDREN WITH TICK-BORNE ENCEPHALITIS AND NON-POLIO ENTEROVIRAL MENINGITIS

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Background: Severe clinical course and long-lasting complications in tick-borne encephalitis (TBE) are frequently described in adults and in children. Growing evidence suggests that clinical presentation of TBE is shaped by the host immune responses to the virus. Unfortunately, data about underlying immunopathological reactions is limited. The aim of our study was to describe the profile of serum cytokines in children with TBE in comparison with meningitis caused by non-polio enteroviruses.

Methods: In the analysis we used Proteome Profiler Cytokine Array Kit (R&D). The kit is based on a multiplex antibody array that allows for the parallel determination of the relative levels of 102 human cytokines. We analyzed pooled serum samples collected from children consulted or hospitalized in the teaching hospital in Bialystok, Poland in 2018-2019. We included 10 children with TBE, 10 children with enteroviral meningitis (EV), and 10 children without signs of an acute infection. The difference in relative cytokine concentration greater than 50% was considered significant.

Results: In TBE concentration of multiple pro-inflammatory cytokines (including YKL-40, EMMPRIN, CXCL5, CXCL10, IL-17, IL-18) was lower than in EV. Comparison between TBE and controls did not reveal any specific pattern of inflammatory cytokines (5 were higher, 6 lower than in EV). Interestingly, proteins related to growth (GH, GDF-15, IGFBP-2, IGFBP-3) and insulin resistance (RBP4, leptin, resistin) were higher in TBE than in controls.

Conclusions: The study shows that in comparison with EV, TBE is associated with lower serum concentration of multiple pro-inflammatory cytokines. We hypothesize that in TBE the main site of infection is the central nervous system, with milder peripheral response. However, to better understand the host immune responses in TBE, qualitative studies assessing cytokine levels in serum and cerebrospinal fluid samples are necessary.
A SERVICE EVALUATION OF THE ANTENATAL VACCINATION CLINIC AT A UK TERTIARY HOSPITAL

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Background: Pregnant women in England are recommended to receive pertussis and seasonal influenza vaccines to protect the mother and infant from severe infection, however uptake remains suboptimal. In 2017, a new clinic was set up at Princess Anne Hospital (PAH) in Southampton, offering vaccines alongside antenatal appointments, with the aim of improving uptake. We aimed to assess factors influencing pregnant women’s vaccine-related decision-making within the antenatal vaccination clinic at PAH and identify how the service could be improved.

Methods: We analysed the Vaccine Referral Database, which contains records of intention and receipt of pertussis and influenza vaccines for all pregnant women referred to PAH for antenatal care between 01-Jan-2019 and 02-Oct-2019. Healthy pregnant women were approached to participate in a semi-structured interview exploring their experiences and decision-making regarding the vaccination service at PAH. Transcripts were thematically analysed using NVivo.

Results: Uptake of vaccines amongst 4,420 women on the database was 90.6% for pertussis and 78.8% for influenza vaccines. Acceptance and receipt of vaccines were significantly improved after contact by the vaccination team. The most important factors in vaccine-related decision-making amongst 20 women interviewed were healthcare professional recommendation, perceived susceptibility and risk of infection, and previous experience of vaccination. Most women interviewed described the service as efficient and convenient. Suggestions for improvement focused on greater information provision regarding antenatal vaccinations, particularly for influenza.

Conclusions: The vaccination service at PAH has achieved high uptake of antenatal vaccines, exceeding national averages, and a high satisfaction rate amongst women interviewed. Consistent information provision could further increase uptake. This research indicates the effectiveness of delivering antenatal vaccinations in secondary care. Vaccine-hesitant women should be targeted in future interview studies to gain a greater understanding of factors discouraging vaccination.
PRE-POST TREATMENT DIFFERENCES IN CEREBROSPINAL FLUID RESULTS IN TICK-BORNE ENCEPHALITIS, LYME NEUROBORRELIOSIS, AND NON-POLIO ENTEROVIRAL MENINGITIS

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Background: Tick-borne encephalitis (TBE) and Lyme neuroborreliosis (LNB) are important infections of the central nervous system (CNS). Previous studies have already reported that CNS involvement in TBE and in LNB continues for weeks after the acute phase of infection. Here we report on changes in cerebrospinal fluid (CSF) results from admission to discharge in children with TBE, LNB, and non-polio enteroviral meningitis (EV).

Methods: Children involved in the study were hospitalized in the teaching hospital in Bialystok, Poland. We included 28 children with TBE, 14 children with EV, and 13 with LNB. All children had CSF collected twice: on admission and after resolution of symptoms. The analysis involved CSF cell count, protein concentration, and the time between the first (LP1) and the second lumbar puncture (LP2). The results are compared to the TBE group.

Results: Average time between LPs was 14±2.4 days in TBE, 10.9±4.9 days in EV (p<0.001), and 19.0±3.1 days in LNB (p<0.001). In LP1 abnormal CSF protein was noted in 14/28 TBE, 9/14 EV (p=0.38), and 10/13 LNB (p=0.11) patients. CSF cell count normalized in none of TBE, 14/14 EV (p<0.001), and 2/13 LNB (p=0.12) patients. CSF protein concentration normalized in 2/28 TBE, 7/14 EV (p<0.01), and 4/13 LNB (p=0.31) patients. Increase in CSF protein was observed in 16/28 TBE, none of the EV (p=0.01), and in 1 LNB patient (p=0.01).

Conclusions: An every child with TBE and a vast majority of children with LNB had abnormal CSF results on discharge. These findings confirm that CNS inflammation in TBE and in LNB is long-lasting. Although not clinically apparent, prolonged low-grade brain inflammation might be the cause of neurological sequelae. Therefore, patients with TBE and LNB should be monitored closely for neurological complications.
CYTOMEGALOVIRUS RETINITIS AS A PRESENTING FEATURE OF MULTISYSTEM DISEASE

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Title of Case(s): Cytomegalovirus retinitis as a presenting feature of multisystem disease

Background: Cytomegalovirus (CMV) is the leading cause of congenital infection in developed countries. Up to 10% of intrauterine CMV infection results in symptomatic disease at birth. Isolated CMV retinitis is not common and other differential diagnoses should be considered. Also CMV is an opportunistic pathogen causing disease mainly in immunocompromised patients. We report a CMV congenital retinitis case in a preterm baby.

Case Presentation Summary: A very-low-birth-weight boy (1,320 g) was born at 34 weeks’ gestational age. His parents were consanguineous. At birth he had microcephaly and active chorioretinitis but not hearing loss. Lab tests showed CMV in urine (240,000 copies/ml) but not in blood or cerebrospinal-fluid. Valganciclovir was started. Two months later, there were no signs of chorioretinitis. At four-month-old, he was admitted because of VRS bronchiolitis, and transferred to PICU due to severe impairment of his respiratory condition with bronchopneumonia requiring mechanic ventilation. He developed pancytopenia so valganciclovir was stopped. Twenty days later, he presented fever and hepatitis. Simultaneously, there was a CMV reactivation in blood (up to 283,000 copies/ml), so foscarnet was started and CMV hyperimmune globulin was further added with good response. Lab tests showed hypogammaglobulinemia and a lack of B-cells. Whole-exome sequencing identified an autosomal recessive mutation in TERT gen, suggestive of Congenital Dyskeratosis. Finally, owing to irreversible and severe lung damage, adequacy of therapeutic effort was performed.

Learning Points/Discussion: Although most of cytomegalovirus congenital infections are asymptomatic, life-threatening disease can occur and clinicians should be aware of the possibility of recurrence, especially in premature infants or immunodeficiency. The occurrence of CMV retinitis should be thoroughly investigated since it is a strong indicator of the underlying poor immune status. Congenital Dyskeratosis spectrum ranges from intrauterine growth retardation and death to asymptomatic mutation carriers.
VACCINATION RATES IN CHILDREN WITH SICKLE-CELL DISEASE: HOW FAR FROM THE TARGET?

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Background: Children with sickle-cell disease (SCD) are more susceptible to severe respiratory viral and bacterial infection. In an era of decreasing vaccination coverage, no data regarding vaccine uptake in pediatric patients with sickle-cell disease is available in Brazil. This ongoing survey will address the vaccination rates in outpatient children in a reference tertiary hospital in the city of Sao Paulo, Brazil.

Methods: From August-December 2019, all children under 17 yrs. with SCD had their vaccination cards evaluated by a PID specialist during routine hematology consultations. Immunization status was classified in adequate, delayed (vaccines given with a delay >1 month) and inadequate (if any dose was missing), according to the Brazilian recommendations at the time of each dose. The influenza vaccine uptake was evaluated in the last five seasons.

Results: A total of 100 children were screened, of which 85% had the vaccination card for evaluation. Sickle cell anemia/disease (HbSS) was seen in 66%, followed by HbSC disease in 28%. The image annexed resumes the vaccination rates for routine vaccines and those also recommended for individuals with SCD. Influenza vaccine uptake fluctuated from 62% to 74%. We have not identified any case of anti-vaccines behavior among parents whose child’s vaccination was considered inadequate.

Conclusions: Despite considered as critical vaccines for SCD, we’ve found high rates of dose delays and missing pneumococcal, Hib, HAV and varicella vaccine doses, as well as low influenza vaccine uptake during the recent seasons. No anti-vaccine behavior was identified. We believe that the health professional’s unfamiliarity with vaccine recommendations was the main cause of such low rates since vaccines not comprised in the Brazilian vaccination program are given to individuals with SCD in special vaccination clinics after referral by specialists.
LONG TERM HOSPITAL-BASED SURVEILLANCE ON INVASIVE PNEUMOCOCCAL DISEASE: PEDIATRIC OR ADULT DISEASE?

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Background: Pneumococcal conjugated vaccine (PCV10) was introduced in the Brazilian National Vaccination Program in 2010 to all children under 2 years. PCV10 effect on hospitalized individuals is lacking in many Latin American countries, including Brazil. This retrospective study describes the effect of PCV10 vaccination on IPD in all ages over the last 20 years in a single tertiary center in Brazil.

Methods: In our prospective and ongoing hospital-based surveillance study, all cases of IPD (S. pneumoniae isolated in sterile fluids) in all ages were evaluated from January 1st, 2000, through December 31st, 2019. Incidence rates per 1000 hospitalizations in children (under 17 yrs.) and adults (over 17 yrs.) were analyzed according to the pre-vaccination period (2000-2009), early post-vaccination period (2011-2013) and late post-vaccination period (2014-2019).

Results: A total of 643 IPD episodes were evaluated. Incidence rates per 1000 hospitalizations dropped among children under 2 (3.0 to 0.65), 2-4 yrs. (1.15 to 0.06), and 5-16 yrs. (0.92 to 0.64), while increases occurred in adults (0.24 to 0.43) and those over 65 yrs. (0.11 to 0.32). Seven years after PCV10 use, the incidence of adult IPD exceeded the pediatric. Only 9.3% of IPD episodes occurred in children when compared with the pre-vaccine era when more than 50% of the infections occurred in children.

Conclusions: During this 20-years surveillance on IPD, we’ve identified an IPD incidence shift towards an evident adult predominance after the use of PCV10 – especially during the late post-vaccination period. Such data, when confronted with serotype distribution by age groups, might reveal useful information regarding indirect vaccine protection. Vaccination policies should also target older individuals and broader vaccines might be necessary in the future.
DIFFERENTIAL DIAGNOSIS IN PRESUMED BACTERIAL PNEUMONIA UNRESPONSIVE TO ANTIBIOTICS

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Title of Case(s): Differential diagnosis in presumed bacterial pneumonia unresponsive to antibiotics

Background: Broad spectrum antibiotics are used empirically to treat presumed bacterial pneumonia when complications or no response to initial treatment appear. Differential diagnosis must be carried out, as many alternative etiologies and underlying local or systemic diseases may be responsible. These two cases served in our center, of suspected bacterial pneumonia (right upper and lower lobe, respectively) illustrate this difficult scenario.

Case Presentation Summary: An infant hospitalised at 2months of age, presenting with fever and failure to thrive. No response was observed with ampicillin, azitrhromycin and cefotaxime. Extended-microbial (including tuberculosis) and immunological-testing were carried out, with no findings. Computed-tomography showed persistent pneumonia. Switch to linezolid achieved remission. Three weeks after discharge, same site uncomplicated infiltrate was confirmed by echography. Bronchoscopy showed endobronchial granuloma with positive tuberculosis PCR in chirurgical sample. Adolescent hospitalised at 14years. No improvement was observed despite intravenous amoxicillin-clavulanate and posterior switch to linezolid and levofloxacin. A rash appeared, along with bilateral pleural effusion and increased ferritin, with no microbial isolation, including tuberculosis, other than positive Mycoplasma and tularemia serology. Immunological and bone-marrow studies, as well as bronchoscopy showed no abnormalities. No microbial isolation was obtained in neither bronchoalveolar lavage. Autoimmune/autoinflammatory process suspected, methylprednisolone bolus were administered, with transitory response but no maintained improvement until anakinra treatment was started. Restart of corticotherapy was needed due to macrophage activation syndrome.

Learning Points/Discussion: The differential diagnosis of persistent pneumonia is broad and should include autoinflammatory etiologies. Tuberculosis remains one of the most frequent causes. Fibrobronchoscopy is a fundamental test to clarify the diagnosis. In order to optimize microbiological identification, samples as direct as possible from the site of presumed infection must be taken (bronchoalveolar lavage, pleural fluid). A multidisciplinary approach is necessary to fulfil this differential diagnosis.
THE PROBABILITY OF HIV TRANSMISSION FROM HIV POSITIVE PREGNANT WOMEN DEPENDING ON THE VIRAL LOAD IN UZBEKISTAN, MONOCENTRAL STUDY

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Background: The monocentral prospective cohort study was conducted in 2007-2017 at the National Specialized Scientific-Practical Center of Pediatrics. The purpose of the study was to determine the probability of giving birth to the HIV positive child from the HIV positive pregnant woman depending on the viral load. This was crucially important in terms of strategies to prevent mother-to-child HIV transmission, e.g. antiretroviral therapy.

Methods: Among 148 consecutive pregnant women, 50(33.8%) gave birth to an HIV-infected child, in 98(66.2%) cases, babies were HIV-negative. HIV infection was detected by ELISA, Western Blot, PCR (viral load). In 36(24.3%) women with undetectable viral load and in 14(9.5%) with<1000 copies/ml HIV-transmission was not observed. 38(25.7%) mothers with 1,000-10,000 copies/ml delivered 8(21.1%) HIV-positive babies, in 11/23 mothers with 10,000-50,000 copies/ml, in 16 out of 19(12.8%) women with 50,000-100,000 and 15 out of 18(12.2%) with>100,000 copies/ml, the vertical transmission happened.

Results: A linear regression analysis was conducted to evaluate the association between the viral load of the HIV positive mothers and the outcome of the HIV positive children. $F(1, 146) = 117.97, p < .001$, $t(146) = 36.1, p < .001$. The 95% confidence interval for the slope was 2.14 to 2.39, which did not include the value of zero. The correlation between the viral load severity and HIV-positive babies was 0.67, indicating a strong positive relationship (approximately 44.7% of the total variance).

Conclusions: The result shows that the severity of HIV viral load in pregnant women predicts the HIV prenatal transmission of the infection to the child. This suggests that the factors which influence the viral load such as early HIV detection, early antiretroviral therapy initiation and medication adherence as prevention activities may significantly increase the incidence of birth with HIV-negative children from HIV-positive mothers.
Background: Respiratory Syncytial Virus (RSV) is the most common cause of acute viral respiratory tract infections in infants and young children. While many clinical trials of anti-RSV vaccines and monoclonal antibodies are being carried out, the aim of this study was to evaluate the distribution of RSV infection in children with or without any comorbidity, including prematurity, to suggest new prevention strategies. 

Methods: This observational study retrospectively evaluated a population of hospitalized children in Tuscany, Italy, between 0-6 years of age with a laboratory confirmed diagnosis of RSV infection through Quantitative Reverse Transcription Polymerase Chain Reaction (RT-qPCR) on nasopharyngeal swabs, on bronchoalveolar lavage fluid or on both. We analyzed comorbidities, seasonality, distribution according to age and cases needing Intensive Care Unit in the last five years.

Results: Hospitalizations due to RSV were 664. In 32.8% of the patients at least one underlying condition was detected; prematurity was present in 23.2%. In 67.2% of cases no risk factor was present. Almost all the cases (99.5%) were found between November and April; 77.7% of cases were found in children under one year of age, 59.0% in children under three months and 38.7% in the first month of age. The need for intensive care was associated with younger age, with 69.5% of cases in children below three months of age.

Conclusions: As expected, most cases were found in the first three months of life. Underlying clinical conditions were found in almost 1/3 of patients and prematurity was present in almost 1/4 of cases. However, over 2/3 of hospitalizations occurred in previously healthy children. In the evaluation of prevention strategies (including incoming vaccines and monoclonal antibodies) detailed Health Technology Assessment should consider early prevention in all newborns.
THE DEMOGRAPHIC CHARACTERISTICS OF NEONATAL INTENSIVE CARE UNIT OF MURATSAN UNIVERSITY HOSPITAL, ARMENIA, DURING 2018.

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Background: Intensive Care Unit (ICU) provides the critical care and life support for acutely ill and injured patients. The NICU of Muratsan University Hospital is a republican center and a vital component of Armenian healthcare system, has 46 beds and 30 of them are for neonates. The current study was conducted to determine epidemiological structure of hospitalized patients in January to December, 2018.

Methods: We have done a retrospective review of three hundred and thirty medical charts of 2018 year in Neonatal Intensive Care Unit of Muratsan University Hospital. Exclusion criteria was age up to twenty eight days. We extracted demographic data of ICU patients, not including patients with intoxication who are treating in Department of Toxicology. The data were analyzed and presented on figure.

Results: The vast majority (84.2%) of 330 patients (mean age 13.2 months) were in age group of 1-month to 1-year-old. Sex: 61.2% males, average length of stay: 8 days (max 96 days), area: Yerevan 162 (49.1%), neighboring provinces 114 (34.5%) and 54 (16.4%) - farther regions, admissions by months (see the chart below).

Conclusions: As we expected half of patients were admitted during colder months (from November to March) due to Influenza and other ARI. There is a necessity to organize seminars in provinces about
management of respiratory infections to lower the flow of patients during this period. To take actions against respiratory infections by raising awareness among population for doing vaccinations (Influenza vaccine).
PREVALENCE OF VIREMIA IN PEDIATRIC HERPES ZOSTER

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Background: Herpes zoster (HZ) is caused by the reactivation of the latent varicella zoster virus (VZV). HZ often occurs in adult and is less common in pediatric patients. Although VZV viremia sometimes occurs in HZ patients, their prevalence in pediatric HZ patients is unclear. This study aimed to investigate the prevalence of viremia and its characteristics in pediatric patients with HZ.

Methods: The present retrospective study was conducted between January 2012 and December 2019 at Tokyo Metropolitan Children's Medical Center, a tertiary children's hospital in Tokyo, Japan. HZ diagnosis was based on polymerase chain reaction (PCR) assays of skin swab samples, and disseminated HZ was defined as a rash affecting three or more dermatomes. VZV viremia was diagnosed on the basis of positive serum samples in the acute phase. Demographic data, underlying diseases, prevalence of viremia, and viral loads were investigated.

Results: Laboratory tests confirmed 44 cases of HZ, and the serum samples were analyzed in 24 cases (55%). VZV viremia was detected in 20 cases (83%). Of the viremic patients, median age was 12 years. Underlying diseases were found in 18 patients (90%), all of whom were immunocompromised. Disseminated HZ were found in 15 (75%). Non-viremic disseminated HZ were found in 3 cases (75%). The viral loads in the viremic HZ cases and the days from onset are shown in Figure 1.
Conclusions: VZV viremia commonly occurred in pediatric patients with HZ, and most of whom were immunocompromised hosts. Most of the viremic patients were disseminated HZ, and some cases in the disseminated HZ were not accompanied with viremia. No significant variation in the viral load was detected during the period of infection regardless of the number of days after the symptom onset.
CHALLENGES IN OPTIMIZING MANAGEMENT OF PEDIATRIC AND ADOLESCENT HIV TREATMENT FAILURE IN KENYA

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Background: The New Horizons (NH) Advancing Pediatric HIV Care Collaborative is a multi-sectoral partnership designed to strengthen healthcare systems, improve access to the antiretroviral drugs (ARV) darunavir and etravirine, and to improve HIV outcomes for treatment-experienced children, adolescents, and young people living with HIV (CAYLHIV). Currently members of NH collaborative include nine sub-Saharan African countries (including Kenya) and other organizational partners

Methods: During the 2019 NH workshop, Kenya presented its national approach for identifying and managing treatment failure among CAYLHIV. National team of experts presented existing gaps and barriers in identification of treatment failure and management of 2nd and 3rd line antiretroviral treatment (ART). We conducted qualitative and quantitative in country data analysis to determine level of optimization of treatment failure management among CAYLHIV in Kenya.

Results: As of June 2019, Kenya had 75,020 children 0-19 years receiving ART. Of these, 92% were on 1st line, 11% on 2nd line and 0.05% on 3rd line. VL coverage ranged from <50% among children <5 years to100% among 15-19 years. Virologic suppression was lowest among children <1 years and 15-19 years. Challenges in management of treatment failure included delayed VL results, limited capacity to translate results into action, centralized decision making on switching ART, Insufficient expertise to switch ART and regular stock-outs of ARVs for 2nd and 3rd line.

Conclusions: Despite significant rates of virologic failure, disproportionally low number of CAYLHIV are switched to 2nd and 3rd line ART. There is an urgent need to improve the identification and management of virologic treatment failure including improving access to expanded ARV and addressing constraints within the health system in Kenya in order to maximize virologic suppression rates and improve outcomes of HIV among CAYLHIV in Kenya.
TRANSMISSION OF ENTEROBACTERIACEAE IN NEONATAL INTENSIVE CARE UNIT (NICU) PRACTISING FAMILY ORIENTED CARE

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Background: Early skin-to-skin contact and feeding with maternal breast milk (MOBM) can be beneficial to infants’ development but may be source of colonizing bacteria. Furthermore, studies have shown that extended-spectrum β-lactamase (ESBL) producing bacteria may originate from mothers. We aimed to describe colonisation of premature neonates with Enterobacteriaceae and determine the relationship between strains isolated from neonatal gut to those from MOBM.

Methods: From March to December 2018 stool and MOBM were collected at birth, at the age of one and four weeks from mother-neonatal pairs with gestation age (GA) of <34w, receiving MOBM in first hours of life and exposed to parental skin-to-skin contact within first 4 days of life. Samples were plated onto MacConkey agar and identified by MALDI-TOF. The presence of ESBL was detected by Chromatic™ ESBL media and cefpodoxime disks (10µg). PFGE was used to define genetic relatedness of strains. NICU strains were defined if similar PFGE pattern was seen in >2 subjects.

Results: We recruited 32 mother-neonatal pairs with mean (SD) GA; birth weight, and NICU stay of 29.6 (2.9) weeks, 1497 (477) g and 17.1 (4.2) days, respectively. None, 56% and 100% of neonates were colonized on admission, weeks one and four, respectively. There were 83 enterobacterial isolates [2 (2.4%) were ESBL] detected; 24 (30%) were NICU strains (Table). In the first 16% and 4th week 47% of neonates and only 3% and 9% of MOBM, respectively were colonised with NICU-strains. 5 of 8 strains with similar PFGE pattern first appeared in neonatal gut and then in MOBM.

<table>
<thead>
<tr>
<th>Enterobacterial strains/NICU strains in neonatal gut and MOBM in 1st and 4th week of life</th>
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<tbody>
<tr>
<td><strong>Gut</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>E. cloacae</td>
</tr>
<tr>
<td>E. coli</td>
</tr>
<tr>
<td>Klebsiella spp</td>
</tr>
<tr>
<td>Other enterobacter</td>
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<tr>
<td>Total</td>
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</tbody>
</table>

Conclusions: Majority of neonates were colonized with Enterobacteriaceae, often acquired from NICU environment, despite early exposure to MOBM and skin-to-skin contact. MOBM is unlikely source of Enterobacteriaceae.

Clinical Trial Registration: The study is not registrated yet
VANCOMYCIN THERAPEUTIC DRUG MONITORING IN NEONATES IN A THIRD LEVEL HOSPITAL

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**Background:** Pharmacokinetic monitoring of vancomycin in adult patients is a common practice to optimize such treatment. However, in neonatal population, mainly great inter- and intra-individual variability in pharmacokinetic parameters, information is scarcer. The objective is to describe the main clinical and pharmacokinetic characteristics of neonates treated with vancomycin by using therapeutic drug monitoring (TDM) in a tertiary hospital, from December, 2018 to January 2020.

**Methods:** All neonatal patients who were treated with vancomycin and in whom TDM were performed were registered. Study variables were: demographic data, beginning date and end date of treatment, reasons for antibiotherapy, minimum inhibitory concentration (MIC), initial and final dose, dosage adjustments, plasma levels and pharmacokinetic parameters (Vz, CL, T1/2, Cr). The digital clinical history and the prescription program were consulted.

**Results:** Fourteen patients were included:

<table>
<thead>
<tr>
<th>Gender</th>
<th>57.14% men</th>
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<tbody>
<tr>
<td>PA</td>
<td>33.14 weeks ± 6.83</td>
</tr>
<tr>
<td>Weight</td>
<td>1.87 kg ± 1.09</td>
</tr>
<tr>
<td>Duration of treatment</td>
<td>11.5 days (IQR: 10.25-17.75)</td>
</tr>
</tbody>
</table>

In 64.29% of the patients vancomycin treatment was targeted with pathogen MIC between 0.5-2mg/l. A total of 78.57% of the patients presented infratherapeutic levels prior to TDM, ranging from 1.5 to 9.6mcg/ml. After TDM, all patients achieved therapeutic levels (15-20mcg/ml) except for two, but with adequate clinical response. In 78.57% of the cases, the initial dose with respect to the final one required an increase that ranged between 50%-300%. The median pharmacokinetic parameters obtained were: 0.87 (IQR: 0.82-0.91) L/kg, 0.11 (IQR: 0.08-0.23) L/h, 6.28 (IQR: 4.75-9.16) h and 0.54 (IQR: 0.43-0.70) mg/dl.

**Conclusions:** Vancomycin TDM in neonates is critical to achieve optimal plasma levels, requiring in most cases a considerable dose increase except in those patients suffering from acute renal insufficiency, where a dose reduction is necessary. Larger sample size and further data collection is necessary to analyze and review the proposed vancomycin dosage guidelines for this population, to ensure that all neonates reach adequate plasma levels.
SAFETY AND PROTECTIVE EFFECTS OF MATERNAL INFLUENZA VACCINATION ON PREGNANCY AND BIRTH OUTCOMES.

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Background: Pregnant women are at increased risk of morbidity and mortality from influenza. Despite the broad recommendation to vaccinate pregnant women against influenza, uptake is often suboptimal and concern about safety was one of the main barriers cited. We aimed to assess whether maternal influenza vaccination was associated with adverse pregnancy and birth outcomes, and to identify potential protective effects of influenza vaccination in improving pregnancy or birth outcomes.

Methods: The study population comprised healthy nulliparous pregnant women in South Australia between 2015 to 2017. Participants were followed prospectively, with immunisation, pregnancy, and birth outcome data collected by research midwives. Vaccination status was confirmed. Log-binomial models and Cox proportional-hazards models were used to compare pregnancy and birth outcomes of vaccinated and unvaccinated mothers accounting for time-varying vaccine exposure within pregnancy.

Results: Of the final 1253 women, 48% had received influenza vaccination. Maternal influenza vaccination was not associated with increased risk of spontaneous abortion (adjusted hazard ratio aHR: 0.43; 95% CI: 0.12–1.51), chorioamnionitis (adjusted risk ratio aRR: 0.84; CI: 0.34–2.02), gestational hypertension (aRR: 0.82; CI: 0.49–1.36), preeclampsia (aRR: 0.84; CI 0.56–1.24), gestational diabetes (aRR:1.11; CI: 0.72–1.62), preterm birth (aHR: 0.95; CI: 0.59–1.53) and congenital anomalies (aRR:0.39; CI: 0.05–3.07). We observed a protective effect of maternal influenza vaccination on low birthweight at term (aRR:0.40; CI:0.17–0.96) and small for gestational age births (aHR: 0.64; CI: 0.40–1.04).

Conclusions: These results support the safety of influenza immunisation during pregnancy and suggest a protective effect against adverse birth outcomes.
ANTIMICROBIAL RESISTANCE IN SHIGELLA SPECIES IN A TERTIARY CARE PAEDIATRIC HOSPITAL IN SOUTH INDIA: A FIVE YEAR EXPERIENCE

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**Background:** This was a survey, a retrospective study. Emerging antimicrobial resistance in *Shigella species* poses a huge therapeutic challenge in children in India. MDR compounds the problem. This is an attempt at elucidating antimicrobial resistance mechanisms in *Shigella spp* seen over a five year period at a tertiary care paediatric hospital in South India, which would guide therapy of Shigellosis in children

**Methods:** A total of 286 *Shigella* species isolated from faeces of children with dysentery from 2013 to 2018 were identified using biochemical tests, serotyping using antisera (DENKASIEKEN). ABST was performed using disc diffusion, MIC’s, interpreted as per EUCAST guidelines. Screening, confirmatory tests were carried out to detect ESBL/AmpC. 25 isolates which showed ESBL/Amp C were tested for Carbapenamase genes (IMP, VIM, NDM-1, KPC, OXA-48) using GeneXpert system CARBA-R test.

**Results:** Of 286 isolates, *S.flexneri*, *S.sonnei*, *S.boydii*, *S.dysenteriae* accounted for 143(50%), 137(47.9%), 5(1.7%), 1(0.3%) respectively. ABST revealed resistance to Ampicillin (A-167/286-58.3%), Ciprofloxacin (Cf-270/286-94.4%), Cotrimaxozole(Co-273/286-95.45%), Chloramphenicol (C-90/286-31.4%), Nalidixic acid (Na-274/286-95.80%), Tetracycline (T-262/286-91.6%). Multidrug resistance (MDR- A+Cf+Co) was seen in 117/286(40.9%). All isolates were susceptible to Azithromycin. ESBL/AmpC seen in 43/286(15%) of isolates. ESBL alone (31/43-72.09%), ESBL+AmpC (12/43-27.90%), ESBL/AmpC+Cf+Co resistance (43/286-15%). NDM-1 carbapenamase gene detected in 6/25 (24%).

**Conclusions:** Increased resistance to ciprofloxacin and cotrimoxazole and 15% ESBL/AmpC resistance in our study limits the use of quinolones, cotrimoxazole, and cephalosporins for the treatment of shigellosis. Azithromycin may be the drug of choice to treat *Shigellosis*. Detection of NDM-1 carbapenamase genes in *Shigella species* signals horizontal transfer of resistance genes from other *Enterobacteriales* to *Shigella species* and could lead to carbapenem resistance in the future.
IS THERE A CORRELATION BETWEEN ASPERGILLUS FUMIGATUSS CHRONIC COLONIZATION, ALLERGIC BRONCHOPULMONARY ASPERGILLOSIS AND CYSTIC FIBROSIS TRANSMEMBRANE CONDUCTANCE REGULATOR GENOTYPE?

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Background: The clinical spectrum of Aspergillus fumigatus diseases in cystic fibrosis (CF) patients, including Aspergillus fumigatus chronic colonization and allergic bronchopulmonary aspergillosis (ABPA) has recently gained attention due to its association with the progression of lung disease. Our aim was to study whether cystic fibrosis transmembrane conductance regulator (CFTR) genotype could have a possible correlation with ABPA and A. fumigatus chronic colonization.

Methods: Forty-nine CF patients (median age: 12 years) with confirmed diagnosis of ABPA and / or A. fumigatus chronic colonization were included in the study. Patients were grouped according to their CFTR genotype. "Minimal" CFTR function was defined as carrying a combination of class I, II or III mutations and "residual" as carrying at least one class IV, V or VI mutation.

Results: Out of 49 patients, 29 had ABPA, 16 were chronically colonized by A. fumigatus and 4 had a history of both ABPA and A. fumigatus chronic colonization. Among the 98 CFTR alleles, 12 different CFTR mutations were detected. P.Phe508del mutation was the most common (60.63%), followed by c.489+1G>T (10.10.2%) and G542X (4.41%) mutations. Sixty-three (64.3%) mutations belonged to class II, and 24 (24.5%) to class I. No significant differences were detected among patients with ABPA and those who had only a positive history of A. fumigatus chronic colonization.

Conclusions: In our study population, no significant differences were detected in the type of CFTR mutation among CF patients diagnosed only with ABPA and those who had only a positive history of A. fumigatus colonization. As the nature of A. fumigatus diseases in CF patients remains complicated, further studies are necessary in order to identify specific mechanisms by which CFTR mutations influence host - Aspergillus interactions.
Cytokines and Chemokines Analysis for Detecting Bacterial Infection and Sepsis in Early Hours of Disease

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Background: Fever is one of the most common complaints of children presenting to the pediatric emergency department (PED). Most of them will have a self-limiting viral illness. However, a few will present with a serious bacterial infection (SBI). In this study, we have investigated the diagnostic value of various cytokines and chemokines analysis for discriminating bacterial from viral infection and predicting sepsis in feverish children during the first 12 hours of fever.

Methods: This prospective observational study included children under 5 years of age referred to our PED with febrile illness for less than 12 hours and being classified as having a high risk of SBI. Clinical examination and diagnostic tests were done according to the hospital’s standard of care. Additionally, all patients’ plasma samples were assayed for the same inflammatory cytokine and chemokine panels. According to final diagnosis, study population was categorized as following: into sepsis and non-sepsis groups; bacterial and viral infections groups.

Results: 70 children were eligible for the study. Out of 10 cytokines and chemokines, IL-6 showed to be the most sensitive biomarker to distinguish bacterial from viral infection (sensitivity of 69%). Meanwhile, the most specific biomarker (specificity of 90%) was IL-2. Comparing sepsis to non-sepsis groups, IL-10, at a best cut-off value of 10pg/mL exhibited a large area under the curve (0.837, 95% CI: 0.574-0.100 p<0.05) and showed high specificity (97%) and moderate sensitivity (75%).

Conclusions: Analysis of inflammatory cytokines and chemokines profiles may provide additional information in distinguishing bacterial from viral infection and determining sepsis in early hours. However additional analysis is necessary to predict SBI in older children. Moreover, biomarker testing could be expended with regard to identify some novel proteins as the early markers in SBI.

Clinical Trial Registration: Not a clinical trial. Permission to conduct this study was issued by Kaunas Regional Biomedical Research Ethics Committee (Protocol No.: BE-2-54).
T-CELL CROSS-REACTIVITY RESPONSES BOTH TO IAV AND EBV LEAD TO ALTERATIONS IN SEVERITY OF RESPIRATORY DISEASE.

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**Title of Case(s):** IAV Infection with Positive EBV Infection

**Background:** According to published data during EBV-associated IM IAV infection specific cross-reactive memory T cells are activated and play a role in disease severity. Research data confirms that during symptomatic IAV infection there is an expansion of EBV/IAV cross-reactive memory CD8 T cell responses. During 2017-2018 years influenza seasons in Georgia the most of cases with acute respiratory disorders characterized altered duration, severity, complications, recurrence. The study was designed to understand the mechanism of presented alterations.

**Case Presentation Summary:** During 2017-18 years winter-spring seasons in Tbilisi University Pediatric Hospital were observed average 2000 patients with pneumonia, bronchitis, bronchiolitis, vasculitis. There was 2 to 4 weeks history of upper respiratory infections, with recurrent high fever, fatigue. In most of them were identified positive Influenza A virus (70%). In hospitalized patients the main clinical manifestations for respiratory diseases there were recurrent fever, lymphadenopathy, serositis, skin rash. Patients were grouped for age, diagnosis, duration of disease, severity. According to clinical signs, in 744 patients were conducted investigation for EBV. 641 cases were positive for IgM EBV (86%). Under the national guidelines for treatment the CAP in children, the cases complicated with pneumonia were treated with antibiotics. As the known interactions between EBV with bete-lactam antibiotics, there were avoided the use of ampicillin or amoxicillin. Preference was given to i.v. ceftriaxone.

**Learning Points/Discussion:** High prevalence of EBV was confirmed in Georgia. During acute symptomatic IAV infection there is a preferential expansion of highly diverse cross-reactive responses between IAV and EBV, which leads to permanent changes in TCR repertoires to both of these two viruses. According to our research results in complicated cases with positive IAV recommended to avoid the use of β-lactam antibiotics.
CYTOMEGALOVIRUS SUBVERTS NATURAL CELLULAR IMMUNITY

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Background: Cytomegalovirus (CMV) has co-evolved with its respective mammalian host for millions of years, leading to remarkable host specificity and high infection prevalence. CMV is the most frequent cause of congenital infections. Yet, most children worldwide are infected in the first year of life without overt symptoms. Macrophages, which populate barrier tissues already in the embryo, are primary targets for CMV.

Methods: In vitro infections of macrophages and an experimental pneumonia model (mice) using a fluorescent mouse CMV were analysed (transcriptome, proteome, imaging, immunophenotyping, etc.). In most cases an unpaired t-test was used.

Results: Here we show that upon infection macrophages undergo a morphological, immunophenotypic and metabolic transformation process with features of stemness, altered migration, enhanced invasiveness and provision of the cell cycle machinery to viral proliferation. This complex process depends on Wnt signalling and the transcription factor ZEB1. In pulmonary infection, mouse CMV primarily targets and reprograms alveolar macrophages, which facilitates infection without provoking a proinflammatory response and immune cell infiltration.

Conclusions: Thus, CMV profoundly perturbs macrophage identity and rewrites specific differentiation processes, allowing for immune evasion.

Clinical Trial Registration: It's a basic study, i.e. not applicable
S. Pneumoniae Bacteremia in Children: Prevalence, Clinical, Laboratory Profile and Trends in Antimicrobial Susceptibility and Treatment

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Background: This was a survey, a retrospective study. Invasive S. pneumoniae infections are a challenge the world over. Few studies have focussed on invasive pneumococcal infections from India. This study reviews the clinical and laboratory profile, treatment and emerging trends of antimicrobial resistance of paediatric S. pneumoniae bacteremia as seen in a large tertiary care paediatric hospital in South India.

Methods: 75 patients with proven blood culture positive S. pneumoniae infections were included in a nine year period (2009-2017) retrospective study. The case records were screened for demographic and clinical details. The Isolates were identified using standard conventional tests. The Antimicrobial susceptibility testing (ABST) was done using disc diffusion and MIC’s, interpreted as per EUCAST / BSAC guidelines.

Results: Increased prevalence noted from 2015-2017. High prevalence found in pre-school age group (61/75-81.3%), median age (2yrs[25days-11yrs]), males (50/75-66.6%). Fever (66/75-88%), cough-coryza (35/75-46.6%), respiratory signs (45/75-60%) were major clinical features. Primary peritonitis with nephrotic syndrome (11/75-14.6%) noted. Major sources of bacteremia—pneumonia (23/75-30.6%), LRTI (18/75-24%). CNS complications (11/75-14.6%) and empyema (9/75-12%) were noted. The ABST revealed resistance to penicillin (2/75-2.6%), quinolones (17/75-22.65%), cotrimaxozole (33/75-44%). No cephalosporin resistant or MDR isolates were detected. Ceftriaxone/Vancomycin (56/75-74.6%), Meropenem (19/75-25.3%) were used for treatment. 71/75 (94.6%) had a favourable outcome. 4 children died due to MODS & shock.

Conclusions: Invasive S. pneumoniae infections are a huge disease burden in preschool children in South India. A low level penicillin resistance noted with higher levels of resistance to quinolones and cotrimoxazole. Ceftriaxone has been the drug of choice with or without vancomycin, followed by Meropenem. CNS complications followed by empyema thoracis necessitating decortication were the major complications noted in this study. Correlation of vaccine with clinical serotypes may be necessary.
RISK OF PNEUMOCOCCAL BACTEREMIA IN KENYAN CHILDREN WITH GLUCOSE-6-PHOSPHATE DEHYDROGENASE DEFICIENCY.

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Background: Glucose-6-phosphate dehydrogenase deficiency (G6PDd) is the most common enzyme deficiency state in humans. The clinical phenotype is variable and includes asymptomatic individuals, episodic haemolysis induced by oxidative stress and chronic haemolysis. G6PDd is common in malaria-endemic regions; an observation hypothesized to be due to balancing selection at the G6PD locus driven by malaria. G6PDd increases risk of severe malarial anaemia, a key determinant of invasive bacterial disease in malaria-endemic settings. The pneumococcus is a leading cause of invasive bacterial infection and death in African children. The effect of G6PDd on risk of pneumococcal disease is undefined. We hypothesized that G6PDd increases pneumococcal disease risk, and that this effect is dependent upon malaria.

Methods: We performed a genetic case-control study of pneumococcal bacteraemia in Kenyan children stratified across a period of falling malaria transmission between 1998 and 2010.

Results: 429 Kenyan children with pneumococcal bacteraemia and 2,677 control children were included in the study. G6PDd, secondary to the rs1050828 G>A mutation was common (11.2%; 301 of 2,677 controls). We found that G6PDd increased the risk of pneumococcal bacteraemia, but only during a period of high malaria transmission (P = 0.014; OR 2.33, 95% CI 1.19-4.57). We estimate that the population attributable fraction of G6PDd on risk of pneumococcal bacteraemia in areas under high malaria transmission is 0.129.

Conclusions: Our data demonstrate that G6PDd increases risk of pneumococcal bacteraemia in a manner dependent on malaria. At the population level, the impact of G6PDd on invasive pneumococcal disease risk in malaria endemic regions is substantial. Our study highlights the infection-associated morbidity and mortality conferred by G6PDd in malaria-endemic settings and adds to our understanding of the potential indirect health benefits of improved malaria control.

Clinical Trial Registration: Not applicable.
Background: Patients with cystic fibrosis (CF) are characterized by respiratory exacerbations, since the vast majority is colonized by different microorganisms. Lumacaftor/Ivacaftor is a recently approved drug for CF patients, which is expected to reduce the number of infectious respiratory exacerbations. The objective is to analyze the reduction of respiratory exacerbations, as well as the forced expiratory volume in the first second (FEV1) of Lumacaftor/Ivacaftor in the treatment of CF.

Methods: A retrospective observational survey including all patients treated with Lumacaftor/Ivacaftor in a regional hospital until August 2019 is presented. Assessed variables were: demographic data, date of start and end of treatment, baseline FEV1 at week 24, number of exacerbations during a year before undergoing the treatment, and number of exacerbations during the following year, once the treatment had begun.

Results: Eight patients were included: three (37.5%) were men (median age: 18 years [13-41]). A total of 23 exacerbations were recorded in the year prior to the start of treatment, while in the last year, after starting treatment, 35 episodes were recorded (52.17% increase). Only 1 patient experienced a reduction in the number of episodes (from 5 to 4), while the rest experienced an increase (1 episode in four patients, 2 episodes in one patient, 3 episodes in another patient and 4 episodes in the rest). The mean variation of FEV1 at 24 weeks was 2.17%±0.13 and at the end of the study 5.87%±0.20.

Conclusions: No improvement in the reduction of respiratory exacerbations with this new drug was observed. More studies with a larger sample size would be required to reliably assess the efficacy of this drug in reducing infectious exacerbations. In addition, respiratory physiotherapy and antibiotics are still used in these patients, so the action they exert in reducing exacerbations should be taken into account.
VERTICAL TRANSMISSION OF SALMONELLA ENTERICA SEROVAR TYPHI LEADING TO NEONATAL TYPHOID

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Title of Case(s): VERTICAL TRANSMISSION OF SALMONELLA ENTERICA SEROVAR TYPHI LEADING TO NEONATAL TYPHOID

Background: Salmonella Typhi causes typhoid fever, a systemic infection. Typhoid is an important public health problem in developing countries and is endemic in India. The disease when acquired during pregnancy can lead to uteroplacental infection causing abortion, still birth, premature labor and neonatal sepsis. Reports of maternal typhoid with fetal loss or neonatal typhoid without culture proven disease in mother are numerous. We report the first placental culture proven case of vertical transmission leading to culture positive typhoid in newborn.

Case Presentation Summary: A thirty two year old pregnant mother developed fever for four days, following which she had leaking per vaginum in the thirty fifth week of gestation. As the liquor was foul smelling and meconium stained, newborn was delivered by emergency caesarian section and placental membrane culture was sent. The baby was admitted to the neonatal intensive care unit with respiratory distress and required respiratory support in the form of CPAP (continuous positive airway pressure). He developed clinical features of sepsis in next forty eight hours. Blood investigations revealed a positive CRP (C reactive protein) and Placental membrane culture grew Salmonella typhi, hence, injection ceftriaxone was started. By day three of life, blood culture of the newborn also grew salmonella typhi and a diagnosis of neonatal typhoid was made. Parenteral antibiotics were continued for a total of fourteen days and baby was discharged in a stable condition on day sixteen of life.

Learning Points/Discussion: In developing countries, Salmonella typhi may be an important cause of neonatal sepsis in babies born to mothers with history of peripartum fever. Placental membrane cultures done routinely in such cases gives a clue to the etiologic organism of neonatal sepsis. Isolation of the same organism from the newborn confirms vertical transmission of salmonella. Early institution of appropriate antibiotic therapy improves neonatal survival rates.
CHANGES IN THE POPULATION OF PLASMACYTOID DENDRITIC CELLS IN CHRONIC HEPATITIS C IN CHILDREN

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Background: The risk of cirrhosis and the occurrence of hepatocellular carcinoma in the outcome of HCV actualizes the question of a deeper study of the pathogenesis of this disease in children. One of the directions in understanding the mechanisms of the immune response in HCV is the study of plasmacytoid dendritic cells (pDCs).

Methods: 58 children suffering from HCV and 16 healthy children (ad 1.5 to 18 y.) were examined. Quantitative indicators of pDCs were determined by flow cytometry, using specific markers of the pDCs (CD123 and CD303).

Results: In children with HCV, there is a decrease in both the absolute and percentage number of pDCs (13.9±1.0; 0.26±0.01) compared to healthy individuals (17.31±1.83 and 0.38±0.04; p<0.05 and p=0.05). In the group of children with no viral replication, the absolute number of pDCs was 2.2 times lower than in the group with a high level of virus replication (p=0.002). When comparing quantitative indicators of pDCs in groups with different virus genotype, it was found that the number of pDCs in 1B genotype was significantly lower than in 3A (p=0.001 and p=0.01). Gender does not have a noticeable effect on pDCs performance. It is shown that the absolute number of pDCs decreases by 1.4 times in the puberty period (p=0.02).

Conclusions: In children the quantitative indicators of pDCs are significantly reduced compared of healthy. Parameters of pDCs in children associated with the level of viral load, age and genotype of the virus. The lowest rates are observed in high viremia, in the puberty period and in patients with 1 genotype of the virus. The revealed regularities indicate a direct link between the state of the pDCs and clinical and laboratory indicators of HCV and its role in the pathogenesis of the disease.

Clinical Trial Registration: Not registered
DISSEMINATED MELIOIDOSIS IN CHILDREN

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Title of Case(s): Pediatric Melioidosis

Background: Melioidosis is a serious infectious disease which caused by gram negative bacteria Burkolderia Pseudomallei. This organism is mostly found in soil and surface water of regions including Southeast Asia, Northern Australia, and areas of South America. Melioidosis was classified as localized and disseminated. In septicemia patient, there is rapid deterioration to septic shock with mortality rate up to 80% of cases. In this case report, disseminated melioidosis in a child from Siem Reap, Cambodia, where is one of the regions with a high incidence of pediatric melioidosis, was presented.

Case Presentation Summary: A 12 year-old boy had been sick for 8 days with fever, right neck painful lump, painful and swelling on the right ankle on fourth day of illness following trauma. He lived in Sot Nikum district, Siem Reap Province. On examination, he looked toxic, feverish and chill. There was tender lump on right submandibular region. He had swelling, redness, warm, and tender on right ankle. He had tender on LUQ without hepatosplenomegaly. Imaging revealed right cervical suppurative adenitis, right ankle septic arthritis, and splenic microabscesses. Burkolderia Pseudomallei was isolated from throat swab, and pus from right ankle and right cervical lymph node. He was successfully treated with intravenous Ceftazidime for 21 days and put on maintenance therapy with oral Co-trimoxazole for 3 months. He is now doing well.

Learning Points/Discussion: Early recognition and treatment of melioidosis are important to improve outcome. Melioidosis germs have an intrinsic resistance to many commonly used antibiotics, which makes the disease difficult to treat. Appropriate treatment according to protocol includes at least 2 weeks of acute phase with IV Ceftazidime or Meropenem and at least 12 weeks of eradication phase with oral Cotrimoxazole or Co-amoxiclav must be implemented.
IS THERE A CONGENITAL PRION DISEASE? LITERATURE REVIEW, CASE REPORT, AND TWENTY YEARS FOLLOW-UP OF A SYMPTOMATIC INFANT WITH IN-UTERO EXPOSURE TO VARIANT CREUTZFELDT-JACOB DISEASE

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Title of Case(s): Is There Congenital Prion Disease? Literature review, case report and Seventeen years follow-up of a symptomatic infant with in-utero exposure to variant Creutzfeldt-Jacob disease

Background: Given the younger age of onset, most of reproductive age, and extra-neural isolation of pathologic prion proteins in variant Creutzfeldt-Jacob disease (vCJD), the possibility of vertical transmission has been proposed. Whilst the pathogenesis is more poorly understood than other infectious agents that readily cross the maternal-foetal interface, vertical transmission of prion diseases has the potential to have grave public health consequences even decades after the initial recognition of the disease process.

Case Presentation Summary: A case description of a female infant exposed in-utero to vCJD is presented along with 20 years of subsequent follow-up. A literature search was conducted surveying cases of in-utero exposure to vCJD and their associated outcomes along with exploration of potential biologic plausibility of vertically transmitted prion disease. Infant A was born at 37 weeks gestation to a mother diagnosed with vCJD, symptomatic early in pregnancy. Over the first four weeks of life, Infant A developed four limb hypertonia, hyper-reflexia and clonus. At six months of age dystonic features with decerebrate posturing and jerky limb movements were prominent. A diagnosis of cerebral palsy associated with significant neurological deficits was made. Abnormal prion proteins were not demonstrated in tonsillar tissue, lymph node, and salivary glands biopsies. Neurological deficits have remained static through twenty years of follow-up.

Learning Points/Discussion: Our case is of the first surviving symptomatic child exposed to vCJD in-utero. It is yet to be determined whether vCJD during pregnancy could result in prion embryopathy and/or whether prions passed transplacentally could have an effect in later life. Variations in clinical presentations of infants exposed to prion disease in-utero may be explained by: timing/onset and magnitude of exposure, prion-induced changes to the intrauterine environment, and/or direct pathologic effects on the developing foetus.
CLINICO-EPIDEMIOLOGICAL CHARACTERISTICS OF SCABIES IN CHILDREN. DO WE NEED MASS DRUG ADMINISTRATION?

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Background: Scabies is a neglected parasitic skin infestation. It is endemic in developing countries like Nepal and other rural communities. Although the burden of scabies is high, effective mass control strategies are lacking. Ivermectin is effective drug for treatment and control of scabies. The objective of this study was identifying clinical and epidemiological characteristic of scabies for mass drug administration with ivermectin.

Methods: This was cross-sectional hospital based, retrospective study conducted in out patient department of medical college in central Nepal, among children below 5 years of age, during Jan 2019 to June 2019. The clinical characteristics and epidemiological profile were retrieved from the central departmental records. Some patients were traced for interview when needed for clinical data if missing. The data recorded in preformed performa were analyzed using descriptive statistics.

Results: Prevalence of scabies in children was 5.1%. Among 342 patients, 222 were male and 120 were female. Mean age was 2.4 years. Majority were from rural areas (89.5%). Two third had low economic status. 90% had history of contact. Hindus constituted 75% and 25% were Muslims. Clustering of disease was seen in colder months. Common site of involvement was abdomen, fweb-space and genitalia. Pruritus was frequent symptom and secondary bacterial infections were seen in 10%. No patient reported septicemia or post streptococcal glomerulonephritis. None had received oral ivermectin.

Conclusions: Scabies is disease of public health importance with high prevalence and high socio-economic burden in community. High prevalence in children depicts high transmission rate and concurrent infestation in the family members. To improve the lower quality of life associated with scabies, there is need of primordial and primary prevention as public health campaign and mass drug administration of ivermectin in our communities.
FOCAL SEIZURE, NOT JUST EPILEPSY

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Title of Case(s): Focal seizure, not just epilepsy

Background: Early Tuberculous menigitis (TBM) diagnosis is the single most important factor influencing clinical outcome, but is difficult due to the non-specific signs and symptoms at disease onset. Late diagnosis is associated with high mortality and severe neurologic handicap, which emphasizes the value of TB preventive therapy in vulnerable young children with close TB contact.

Case Presentation Summary: A 5-month-old boy admitted because of prolonged seizure that had a left sided focal onset with secondary generalisation. On admission the seizure had stopped, having lasted more than 30 minutes, and he was fully conscious. The examination noted no focal neurological signs or bulging fontanel. Laboratory investigations were unremarkable for bacterial infection; CRP <6 mg/dl, PCT 0.3 ng/ml. His FBC showed raised neutrophils. CXR demonstrated bilateral nodular interstitial infiltration, highly suspicious of disseminated TB, with opacification of the left lower lobe. CSF was clear with a pleocytosis (207 cells/mm³, 75% neutrophils, 25% lymphocytes), increased protein (8.3 g/l), reduced glucose (0.7 mmol/l). Blood and CSF cultures were negative, but a Gene X-pert® test performed on CSF was positive for Mycobacterium tuberculosis complex. A rapid HIV test was negative. A CT scan of the brain confirmed hydrocephalus together with basal meningeal enhancement. His father was diagnosed with pulmonary TB 7 years ago, but was “lost to follow up” before treatment completion. In recent months, he developed a worsening cough. After the index case was diagnosed with TB, a CXR revealed a large cavity in the father’s left upper lobe and he was found to be 3+ sputum smear-positive. The mother and the 2-year-old sibling were commenced on isoniazid preventive therapy in the absence of symptoms and normal CXR. Clinical progress was summarised as below:
Key Learning Points: Xpert MTB/Rif® availability increases diagnostic access, but there remains an urgent need to optimise prevention strategies and improve the clinical management of TBM in children.
MULTI DRUG RESISTANT NONTYPHOIDAL SALMONELLA AS CAUSE OF CHILD DEATH: USING INNOVATIVE POST-MORTEM SAMPLING

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Background: The recent advent of minimally invasive tissue sampling (MITS) tries to overcome the limitations of currently used methodologies to infer cause of death (CoD) in resource-constrained settings by providing high quality data. Child health and mortality prevention surveillance aim to determine cause of death among stillbirth and under five children (U5) by using MITS and sophisticated laboratory technology in low-income countries, including Ethiopia.

Methods: a mortality surveillance of stillbirths and U5 started in Haramaya University demographic surveillance (DSS) area, Ethiopia, in February 2019. Death notification system was implemented to detect MITS eligible cases. Conventional microbiology, multiplex PCR (TAQman-Array) and histopathology including, immunohistochemistry and molecular pathology were done. A panel with experts in different medical fields gave a final CoD to each case by reviewing demographic and clinical information, laboratory results and verbal autopsy.

Results: from February-December 2019, 991 deaths were notified, 264 (26.8%) from DSS. Sixty-one (23.8%) were stillbirth, 97 (37.9%) neonates, 98 (38.3%) U5 infants and children. Hundred eighty-five (70%) happened at health facilities and 77 (29.2%) at home. 46/132 (34.1%) family approached consented. Twenty-three cases were given a CoD and ten had an infectious disease as underlying/immediate CoD. More common pathogens were a) nontyphoidal salmonella –SALS1 (NTS): two neonates and one infant, all admitted at hospital >72h; b) klebsiella pneumoniae: two neonates admitted >24h. All these five isolates were resistant to first-second line of antimicrobials.

Conclusions: Although representativeness still is a major challenge, MITS provides high quality data on CoD, being able to detect outbreaks of life-threatening microorganisms. Hospital-acquired nontyphoidal salmonella was the CoD of three cases. NTS is emerging as a major cause of morbidity and mortality among African children that could be reduced with the implementation of a vaccine like the one currently under development.
TITLE OF CASE(S): Respiratory Parasitic Emergency in a Refugee Minor

BACKGROUND: Cystic echinococcosis (CE), also known as hydatid disease, is a neglected tropical disease (NTD) caused by infection with the larval stage of *Echinococcus granulosus*. Incidence of this globally distributed parasitosis increased significantly in Germany after thousands of refugees arrived from war-torn regions of the Middle East. During the last 5 years several severe cases of CE have been treated at our university hospital.

CASE PRESENTATION SUMMARY: A fourteen-year old previously healthy refugee boy from Kurdistan felt discomfort in his chest, loss of appetite and weight in the months after his recent arrival in Germany. Doctors related his symptoms to posttraumatic stress disorder. One day he suddenly felt a painful sensation while playing soccer and experienced life-threatening respiratory distress, severe coughing and repetitive vomiting. With oxygen-dependent dyspnoea he was taken to the emergency room. His chest X-ray and CT scan showed a large fluid and air filled hydatid cyst with water-lily sign in his left lung after spontaneous rupture into the bronchial system. Therefore, the diagnosis of thoracic CE was made in the absence of eosinophilia or specific antibodies, although seroconversion was notified few weeks later. *Echinococcus granulosus* infection was confirmed by microscopy and molecular genotyping after open thoracothomical puncture, aspiration, hypertonic saline installation, re-aspiration and complete subtotal cystectomy under save-guarding high-dose albendazole treatment for at least 12 months.

LEARNING POINTS/DISCUSSION: Cystic echinococcosis is affecting refugees arriving in European Countries. Clinicians should be aware of CE and perform ultrasound and radiographic studies whenever needed, often allowing the diagnosis on the spot. Although most cases affect the liver, other organs like spleen, heart, CNS and the lungs can be involved. A multidisciplinary treatment approach involving experienced surgeons is mandatory for favorable outcome.
MATERNAL CERVICOVAGINAL UREAPLASMA SPP. COLONIZATION IS ASSOCIATED WITH BRONCHOPULMONARY DYSPALASIA IN PRETERM NEONATES.

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Background: Intra-amniotic, placental and cervicovaginal Ureaplasma spp. colonization is associated with adverse pregnancy- and neonatal outcome. The primary objective of this study was to evaluate the association of maternal cervicovaginal Ureaplasma spp. colonization with neonatal bronchopulmonary dysplasia (BPD) and/or mortality. The secondary objectives were to evaluate the impact of other cervicovaginal flora on these outcomes and to evaluate the potential protective role of maternal antimicrobial therapy.

Methods: This retrospective cohort study enrolled 480 neonates born prior to 32 weeks’ gestation and admitted to the neonatal intensive care department of the Antwerp University Hospital between January 2012 and December 2017. They were divided into four groups according to maternal cervicovaginal culture results. Multivariate logistic regression analysis was used to predict BPD and/or mortality based on these culture results, adjusted for perinatal risk factors and neonatal morbidities.

Results: Maternal cervicovaginal Ureaplasma spp. colonization was independently associated with moderate/severe BPD (OR 8.34; 95% CI 1.21-57.45). In neonates < 32 weeks’ gestation with and without maternal cervicovaginal Ureaplasma colonization moderate/severe BPD occurred in 12.3% and 3.8% respectively. There was no difference in mortality between neonates with and without maternal cervicovaginal Ureaplasma spp. colonization. Isolation of other microorganisms in maternal cervicovaginal cultures was associated with a higher neonatal mortality (p=0.002), lower gestational age (p=0.026) and lower birth weight (p=0.036).

Conclusions: This study underscores the role of the maternal cervicovaginal microbiome as a predictor of neonatal outcome in preterm neonates. Maternal cervicovaginal Ureaplasma spp. colonization seems not to be an innocent bystander in the multifactorial etiology of BPD. Although predictive factors for BPD are easy to identify, they are often difficult to modify. Whether eradication of maternal cervicovaginal colonization improves pregnancy and neonatal outcome should be studied in prospective randomized trials.
NICOLAU SYNDROME FOLLOWING INTRAMUSCULAR TREATMENT: BENZATHINE PENICILLIN–RELATED INJURY WITH CHRONIC PAIN SEQUELAE

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Title of Case(s): Benzathine penicillin–related injury with chronic pain sequelae

Background: Nicolau syndrome (NS) is a rare iatrogenic syndrome caused by intramuscular injection. It is impossible to be predicted and manifests as subtle and excruciating pain immediately after injection leading to necrosis of dermis and subcutaneous tissue. We describe a non-fatal case of Nicolau syndrome caused by intramuscular injection of benzathine penicillin, which resulted in complete resolution of cutaneous lesions but developed chronic pain.

Case Presentation Summary: A healthy 8-year-old boy was brought to our emergency department with a complaint of sudden pallor, reduced leg temperature, agonizing pain, and loss of consciousness minutes after receiving an intramuscular injection of benzathine penicillin in the right gluteal region for rhinosinusitis treatment. He was referred to our hospital with a diagnosis of arterial occlusion after intramuscular injection. On admission, he was well-appearing, alert and afebrile. He presented a purplish area in the gluteus and scrotum, significant pain in the right gluteus, receiving IV opioids every 4-6h. Laboratory exams revealed leukocytosis (19.200 cell/µl), C-reactive protein=2.7 (NV<0.5) and CPK=41.251 (NV<140). Doppler USG ruled out venous thrombosis. CT scan revealed muscular edema at the posterior hip compartment with intermingling gaseous foci and collection in the deep myofascial plane. Intravenous ceftriaxone and metronidazole plus anticoagulation were administered. No infectious complications occurred. After a prolonged hospitalization for neuropathic pain control, he’s being followed at our physiatry outpatient clinic.
Learning Points/Discussion: Despite rare, tissue ischemia and necrosis following intramuscular, intra-articular or subcutaneous injection, can lead to limb amputation, chronic pain, limb paresis, and urinary incontinence. Additional underlying muscular damage was supported by high serum levels of creatine kinase. Treatment is based on fluid expansion, intravenous steroids and anticoagulants, and antibiotic use should be restricted to cases with signs and symptoms of infection.
FUNCTION OF THE POPULATION OF PLASMACYTOID DENDRITIC CELLS (PDCS) IN CHRONIC HEPATITIS C IN CHILDREN.

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Background: Features of the course of HCV in children still remain the subject of active discussion and study. Understanding of the immune mechanisms that are implemented in response to the introduction of the HCV will help to shed light on important aspects of the pathogenesis of this disease. PDCs along with the production of a huge amount of IFN in response to the virus, are able to initiate the launch of cellular reactions that ensure the interaction of innate and acquired immune responses.

Methods: 74 children were examined: 16 healthy and 58 children with HCV at the age of 1.5 to 18 years. IFN in PDCs was determined by ELISA with cell stimulation.

Results: In healthy children the production of IFN in PDCs is recorded below the detection level of the method we use. In children with HCV, IFN in PDCs was significantly higher (113.3±21.7; p=0.0002). It is shown that the lower the production of IFN in PDCs, the higher the level of viral load (VL-10²-10⁴kop/ml-197.6±49.7; 10⁵ and more-75.8±20.7; p=0.03). The production of IFN in PDCs is higher at normal transaminase levels, than at their increase (p=0.01). It was found that children functional activity in PDCs in the group from 1.6 y. to 10 y. of age, is higher than in the group of children aged 11-18 y. (p=0.02). In boys and girls (p>0.05), the indicators of IFN production is significantly differed in the direction of higher interferonogenesis in girls.

Conclusions: The production of IFN in PDCs in healthy children is not normally determined, and in HCV there is an activation of the functional state of PDCs, which is naturally associated with the level of viral replication and cytolysis, which indicates the direct participation of PDCs in the immunopathogenesis of HCV.

Clinical Trial Registration: Not registry
HOW COMMON ARE ASPERGILLUS FUMIGATUS DISEASES IN CYSTIC FIBROSIS?

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Background: Recently, attention has increased regarding the clinical significance of fungi in cystic fibrosis (CF) patients. *Aspergillus fumigatus* is the main fungus cultured in the airways of patients with CF. CF patients might a) be colonized transiently or chronically, b) suffer from bronchitis, c) be sensitized and/or d) develop allergic bronchopulmonary aspergillosis (ABPA). Our aim was to study the spectrum of *Aspergillus fumigatus* diseases among Greek CF patients.

Methods: Medical records of 207 CF patients were retrospectively studied for a 20-year period in order to identify cases that belong to the spectrum of *Aspergillus fumigatus* diseases. Data regarding demographic characteristics, immunological status and clinical course were collected for each participant. All patients received their care at the CF center of "Aghia Sophia" Children's Hospital. Diagnosis of CF was confirmed by sweat chloride levels and genotyping.

Results: One hundred sixty-two (78.3%) patients experienced the clinical spectrum of *Aspergillus fumigatus* diseases. Thirty-six (17.3%) CF patients were transiently colonized by *A.fumigatus*, while 25 (12.1%) were chronically colonized. Sixty-one (29.5%) patients were sensitized to *A. fumigatus*, while 34 (16.4%) patients were diagnosed with ABPA during a 20-year period. Four (1.9%) patients experienced bronchitis due to *A. fumigatus* and 2 (0.9%) developed lung abscess due to *A. fumigatus*. Cases of aspergilloma or invasive aspergillosis were not detected during the study period.

Conclusions: Our study revealed the frequency of *A. fumigatus* isolation in respiratory samples as well as the frequency of sensitization to the fungi among Greek children with CF. Further follow-up studies are necessary, especially for asymptomatic cases that belong to the spectrum of *Aspergillus fumigatus* diseases, in order to study any possible effects on the progression of lung disease and to clarify the necessity of early antifungal treatment.
NEONATAL FUNGAEMIA IN A TERTIARY PAEDIATRIC HOSPITAL OF GREECE DURING A 21-YEAR PERIOD

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Background: Fungaemia is considered an important cause of morbidity and mortality in neonates characterized by multiple risk factors such as central venous catheter insertion, total parenteral nutrition, prolonged antibiotic treatment, low-birth-weight, etc. As limited data are available in Greece, our aim was to study the epidemiology and microbiology of neonatal fungaemia in the largest tertiary Greek pediatric hospital during a 21-year period.

Methods: A retrospective study of fungaemia in neonatal intensive care units (NICU) of “Aghia Sophia” Children’s Hospital was performed from January 1999 to December 2019. Identification of isolates was done using conventional API-AUX, API-yeast ID32, automated Vitek2(BioMérieux), RapIDYeast Plus System (Thermo Scientific™, Remel™) and molecular/proteomic techniques [D1/D2 region of 28S rDNA–sequencing/MALDI TOF-MS (BRUKER)]. Susceptibility testing was performed using gradient MIC strips (Liofilchem) and evaluated according to CLSI methodology.

Results: During a 21-year period, 159 cases were recorded with only 63 (39.6%) detected during 2010-2019. Candida albicans predominated (97;61.0%) followed by Candida parapsilosis (38;23.9%). Fifty-seven (35.8%) neonates had symptoms from gastrointestinal and 28 (17.6%) from cardiovascular system. Eighty-one (50.9%) neonates had undergone a surgery operation. Forty-two (26.4%) cases were fatal, mainly caused by C. albicans (31;73.8%). A significant increase was detected in cases caused by non-C. albicans species (50.8% vs 31.3%, P=0.013), during 2010-2019. No resistance to amphotericin, fluconazole, voriconazole ans echinocandins was detected for C. albicans.

Conclusions: C. albicans, followed by C. parapsilosis was the leading cause of neonatal fungaemia cases during a 21-year study period. The decrease in neonatal cases that was detected during 2010-1019, may reflect the increased awareness as well as the effective infection control initiatives and antifungal interventions. The changing epidemiology that was, also, detected is in accordance with the globally one and highlights the necessity of close monitoring and surveillance.
ATYPICAL PRESENTATIONS OF MYCOBACTERIUM TUBERCULOSIS

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Title of Case(s): Atypical Presentations of Mycobacterium Tuberculosis.

Background: In countries like India, where tuberculosis is very rampant the condition is generally considered in the differential diagnosis of most cases with fever and in any case with suspicion of an infectious disease. Despite this high index of suspicion, the disease often takes even the astute clinician by surprise and present itself in unexpected forms as illustrated by our case series

Case Presentation Summary: A healthy 6 month-old presented with tachypnoea. Genexpert positive for MTB. Screening done in-view of death in an infant sibling showed SCID. Good response to ATT. Underwent successful BMT. However, succumbed to measles one year later. 6 month-old brought with swelling over the thigh suspected to be vaccine-induced sterile abscess. Ultrasound revealed a thick-walled abscess. Genexpert was positive with intermediate-resistance. Line probe assay (LPA) confirmed rifampicin sensitivity. Good response to ATT. 14 year-old with deteriorating school performance. CXR showed effusion and MRI showed cortical lesions in the fronto-parietal lobe. CSF was abnormal. Genexpert from the pleural-fluid was positive for MTB. Good response to ATT. 9 month-old with one month fever. CXR showed consolidation. Gastric lavage genexpert was negative but LPA showed MTB. The child responded well to ATT but relapsed after six months. HRCT showed areas of cavitation. A third relapse resulted in destruction of the hip. LPA of hip tissue revealed rifampicin-resistant MTB. Immunodeficiency study done in view of repeated MTB revealed CGD.

Learning Points/Discussion: The myriad presentations of TB makes it essential to chase the diagnosis and make an attempt to isolate the organism. The availability of new real-time PCR techniques has improved the ability to detect MTB even in pauci-bacillary cases and detect antibiotic resistance in a matter of hours. Our case series emphasises the superiority of line probe assay over genexpert and even liquid cultures.
E-POSTER VIEWING

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CLINICAL VALUE OF CIRCULATING HDL-, LDL-, TOTAL-CHOLESTEROL AND APOLIPOPROTEIN-A1 (APO-A1) LEVELS IN NEONATAL SEPSIS: ASSOCIATIONS WITH C-REACTIVE PROTEIN, SERUM AMYLOID-A (SAA) AND CYTOKINES SERUM LEVELS

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Background: Studies in animals and human adults have shown that circulating levels of lipids and lipoproteins are influenced by sepsis, whereas SAA binds to HDL at the acute phase and becomes its major apolipoprotein by replacing Apo-A1. The diagnostic accuracy of lipid/lipoprotein levels in neonatal sepsis is not known. The aim of this study was to evaluate the value of serum HDL-, LDL-, total-Cholesterol (total-C) and Apo-A1 levels in the diagnosis and monitoring of neonatal sepsis and examine possible associations with serum CRP, SAA and cytokines levels.

Methods: Eighty-one neonates with clinical signs of sepsis and 45 healthy neonates (controls) were prospectively studied. Blood samples were drawn serially in all patients on day 1 (acute phase), 3 and 7 (recovery), whereas once in controls, for routine blood tests (including serum CRP levels), as well as for serum HDL-C, LDL-C, total-C, Apo-A1, SAA (immunonephelometry) and cytokines (IL-1b, IL-6, TNF-a) levels (Luminex technology). Anova or Kruskal-Wallis (with post hoc comparisons), correlation and ROC analyses were performed.

Results: HDL-C, total-C and Apo-A1 levels were lower in patients on Day1 in comparison with levels at recovery (p<0.007, p<0.0001 and p<0.0001, respectively) and controls (p<0.0001 for all). HDL-C and Apo-A1 levels were still significantly lower in patients on Day3 in comparison with levels at recovery and controls. On Day1, significant correlations were found among HDL-C, CRP, SAA and Apo-A1; total-C, SAA and Apo-A1; Apo-A1 and IL-6 levels. ROC analysis of HDL-C, total-C and Apo-A1 values on Day1 resulted in significant areas under the curve for detecting sepsis.

Conclusions: Serum HDL-C, total-C and/or Apo-A1 can be used as complementary biomarkers in the diagnostic work-up of neonatal infection. Further investigation is needed regarding the role of LDL-C and other apolipoproteins.
THREE MONTHS RIFAMPICIN PLUS ISONIAZIDE FOR TREATMENT OF LATENT TUBERCULOSIS AMONG MIGRANT UNACCOMPANIED ADOLESCENTS

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**Background:** The Spanish southern border is a hot-spot for illegal immigration to Europe, and the number of unaccompanied minors arriving to reception centers has risen rapidly. In this highly vulnerable population, tuberculosis (TB) and latent TB infection (LTBI) are major public health concerns. We aim to describe our experience using a combined regimen of 3 months of Isoniazide+Rifampicin (HR3m) for treatment of LTBI in this population.

**Methods:** Descriptive retrospective longitudinal study including all patients attended in a reference Unit for Pediatric Tropical Diseases in a tertiary hospital along almost 2 years, between January 2018 and October 2019. Those diagnosed with TB and/or LTBI were included in the analysis. Demographic and clinical variables were described (age, origin countries, diagnostic tests), as well as data regarding treatment and linkage to care.

**Results:** Out of 140 youths, 101 (72%) were diagnosed with LTBI and 4 with TB (2.8%) and were included. Median age was 16.8 (IQR:16.2-17.4). 57% came from Morocco; 43% from other subsaharian countries. TST and chest X-ray were performed in all, IGRA in 20 (discordant in 2). HR3m was prescribed in 93 and isoniazide for 6 months in 1 due to active HVB; 29 abandoned follow-up. 4 were diagnosed with TB: 2 were lost to follow, 1 is still on treatment and 1 completed treatment+follow up. Treatment were generally well tolerated.

**Conclusions:** Screening for TB should be mandatory at first evaluation of unaccompanied migrants-adolescents from endemic areas. Due to cultural and language barriers and social difficulties, loss to follow up is common. Combined regimens for LTBI were well tolerated and should be considered in order to shorter treatment. A multidisciplinary approach is required to ensure adherence to care in this vulnerable population.
Title of Case(s): IVIG-resistant intestinal pseudo-obstruction in course of Kawasaki disease – a case report

Background: Kawasaki disease (KD) is a systemic vasculitis of an unknown origin. Intestinal pseudo-obstruction (IPO) is a rare manifestation of KD. The majority of KD-related IPO cases was successfully treated with IVIG and aspirin.

Case Presentation Summary: A 2-years old girl with a 4-day history of fever, diarrhea and cough was admitted to our ward. The child had symptoms of tachypnea, tachycardia, meningeal signs, maculopapular rash, conjunctivitis, dry and fissured lips, erythema of oral mucosa, abdominal distension and feet edema. Laboratory tests showed neutrophilia, elevated inflammation markers, hypokalaemia and hypoalbuminemia. CSF examination revealed aseptic meningitis. The echocardiogram was normal. In abdomen plain X-ray dilated bowels with air-fluid levels were seen, and ultrasonography showed decreased peristalsis and enlarged lymph nodes. Anuria was noted, diuresis was successfully forced by furosemide. On the 6th day of fever KD was recognized and treated with IVIG and aspirin, resulting in permanent fever retreat. On subsequent days the child required potassium and albumins substitution and erythrocyte mass transfusion. However, despite normal potassium blood concentration, progressive abdomen distension, bowel dilation and disappearance of peristalsis were noted. On the 12th day of disease the KD-related intestinal pseudo-obstruction was recognized. Pulses of methylprednisolone were given for three days, sequencing in a retreat of pseudo-obstruction. The girl was discharged in good general medical condition on 15th day of disease (after 11 days of hospitalization). During a 12-month follow-up the echocardiogram remains normal.

Learning Points/Discussion: We present a case of KD with a multi-organ involvement. In this case, subileus, which initially was suspected to be related to hypokalaemia, proved to be KD-related pseudo-obstruction, which did not respond to IVIG treatment but ceased after methylprednisolone pulses.
RESPIRATORY MICROBIAL COLONIZATION IN CHILDREN WITH NEUROLOGICAL DISORDERS

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Background: Children with severe neurological disorders are at risk for respiratory infections significantly deteriorating quality of life and prognosis. Recurrent aspiration, impaired airway clearance, scoliosis, poor nutritional status and recurrent respiratory infections are the most important factors influencing the respiratory status of these patients. The study aimed to evaluate respiratory microbial colonization and factors associated with chronic lung disease in neurologic patients.

Methods: Children (1-18 years old) with neurological disorders were prospectively studied. Cough swabs obtained post inhaled hypertonic saline were sent for bacterial culture. Factors contributing to the airway microbial colonization and morbidity were evaluated. The Eating and Drinking Ability Classification System (EDACS) was used to measure eating and drinking ability, including safety, efficiency and the amount of assistance a person needs.

Results: A total of 65 children were enrolled. Thirty-eight (58.4%) were boys and the median age was 7 years. Twenty-three (35.4%) were diagnosed with epileptic encephalopathy, 8 (12.3%) with neurogenetic diseases and 34 (52.3%) with cerebral palsy. Eating and drinking disorders were observed in 84.6% and 16.9% had gastrostomy or jejunostomy. EDACS ≥3 was noted in 47 children (72.3%) and was associated with ≥3 respiratory infections and hospitalization ≥2 times within past 24 months. Airway microbial colonization was identified in 55.4%. EDACS was positively associated with positive sputum cultures (OR:2.36, CI:1.45-3.86, p<0.001).

Conclusions: The study results indicate that among pediatric patients with severe neurological diseases, the likelihood of a positive cough swab culture increases by 2.36 times higher for every unit increase in EDAC score and emphasizes the need for a multidisciplinary support. Early intervention with gastrostomy or jejunostomy as well as management of chronic purulent bronchitis are necessary to prevent respiratory failure.
A CASE OF UNILATERAL PINK EYE SYNDROME WITH IPSILATERAL LYMPHADENOPATHY IN AN ADOLESCENT

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Title of Case(s): A CASE OF UNILATERAL PINK EYE SYNDROME WITH IPSILATERAL LYMPHADENOPATHY IN AN ADOLESCENT

Background: A pink eye syndrome (acute conjunctivitis) in children is a clinical problem which primary care medical professionals encounter quite commonly. Differential diagnosis is broad and include causes of bacterial, viral, fungal, parasitic, chemical, and allergic origin. However, some causes are rare and not obvious both for patients and health care professionals, therefore important anamnestic clues could be missed during history collection.

Case Presentation Summary: We observed a case of unilateral purulent conjunctivitis associated with ipsilateral preauricular, submandibular and cervical adenopathy in a previously healthy 14 year old male. Other patient’s concerns were persistent subfebrile body temperature for the recent two weeks, malaise, swelling in periorbital area, and ptosis. The patient denied any allergy, trauma, infectious exposure or keeping pets at home and was fully immunized according to the national schedule. Ocular discharge culture revealed Streptococcus haemolyticus 1000 CU/ml; CBC demonstrated moderate leukocytosis. Two days later the patient's 6 year old sibling presented with moderate toxic signs, fever, rhinitis and tender unilateral inguinal adenopathy. Thorough physical examination revealed a solitary papule on the left genual area. After some targeted inquiries the brothers reported the recent episode of playing with a stray kitten. Parinaud oculoglandular syndrome associated with Bartonella henselae infection was confirmed. Three day course of azithromycin was effective.

Learning Points/Discussion: Parinaud oculoglandular syndrome is considered to be a rare atypical form of bartonellosis. Other infectious causes of Parinaud syndrome include Mycobacterium tuberculosis, Chlamydia trachomatis, etc. Transmission in this case probably occurred via ocular contamination with infected feline saliva through patient’s hands as no specific skin lesions were found in the relevant area. Bartonellosis should not be missed in the differential diagnosis for pediatric conjunctivitis and medical professionals should be alert to reveal a compatible history.
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NEONATAL SCREENING FOR CONGENITAL CYTOMEGALOVIRUS (CMV) INFECTION:
IDENTIFICATION OF A VIRAL DNA DIAGNOSTIC CUT-OFF VALUE IN SALIVA SAMPLES

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Background: CMV-PCR in saliva has excellent sensitivity for cCMV screening. However, viral
contamination of newborn saliva samples could happen throughout the peri- and post-partum period. This
is a prospective multicenter study aimed at determining: i) if a viral DNA cut-off value in saliva samples
can discriminate a congenitally infected newborn from a non-congenitally infected one (contamination);
ii) if a subsequent saliva sample is indicated as confirmatory testing for cCMV infection diagnosis or it is
mandatory to test a neonatal urine sample.

Methods: The study will analyze saliva swabs (COPAN UTM, IT) from a minimum of 3150 newborns up
to 21 days of age in order to obtain at least 20 congenitally CMV-infected newborns (Z-test at α=0.05;
power=0.80) in two Italian hospitals (Bologna and Legnano-MI). All infants will be evaluated at diagnosis
and classified as symptomatic or asymptomatic. The CMV-DNA search in saliva and urine samples will be
performed with a real time-PCR (ELITe InGenius-CMV-MGB Kit, ELITechGroup Molecular
Diagnostics, IT).

Results: To date, we have enrolled 2415 neonates and identified 17 infected infants (rate 0.7%). Thirty-
six (1.5%) saliva swabs were false positives, all with a number <250 CMV-DNA copies/mL. Out of 2415
mothers, 2285 (94.6%) knew their CMV serostatus. At birth, 15/17 (88.2%) cCMV infected newborns were
asymptomatic; 2/17 (11.8%) newborns had sensorineural hearing loss. cCMV infection resulted from
primary infections in 47.1% cases and from non-primary infections in 35.3%; in 17.6% cases maternal
CMV-serostatus was unknown.

Conclusions: Preliminary data on a large sample size demonstrate that saliva swabs with a number
<250 CMV-DNA copies/mL are likely related to contamination. Most cCMV infected infants were
asymptomatic at birth and born to mothers with a primary infection.

Clinical Trial Registration: Not applicable
PREVALENCE OF PNEUMONIA AND FACTORS ASSOCIATED AMONG CHILDREN 2-59 MONTHS OLD IN WONDO GENET DISTRICT, SIDAMA ZONE SNNPR ETHIOPIA

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Background: Acute respiratory tract infection is one of the leading causes of child morbidity and mortality in Ethiopia and throughout the world. Meanwhile, information on acute respiratory tract infection prevalence and associated factors is barely available in the study area. Therefore, this study was intended to determine pneumonia prevalence and associated factors among children 2-59 months old in Wondo Genet District.

Methods: Institution based cross-sectional study was employed on 206 child-mother or child-caregiver pairs to determine pneumonia prevalence and its associated factors. Data were collected by using pre-tested and structured questionnaire and analyzed by using Statistical Package for Social Sciences (SPSS) version 20 computer software. Odds Ratio along with 95% confidence interval was computed to determine significance and strength of association between independent and dependent variables.

Results: Prevalence of pneumonia among under-five children was 33.5%. The majority of children 190(92.2%) breastfed for more than 1 year. Fifty two (25.2%) of the children had history of diarrhea. Factors such as absence of separate kitchen, absence of window in the kitchen, breast feeding less than one year and children at age range of 2-12 months showed significance association at multivariable logistic analysis with prevalence of pneumonia.

Conclusions: Prevalence of pneumonia among under-five children was high. In this study children who breastfed for less than one year were 4.2 times higher chance to acquire pneumonia as compared to children who breastfed for more than a year. The identified determinates can be prevented and controlled through community mobilization on health benefits of ventilated and improved housing conditions, importance of separate kitchen, importance of kitchen which has windows and/or chimneys or hoods and importance of breast feeding to prevent under five pneumonia.
Background: Streptococcus pneumoniae (SP) is responsible for a wide spectrum of invasive infections. In Portugal, pneumococcal conjugate vaccine was licensed in 2001 (moderately high coverage) and included in the National Immunization Program in 2015. The aim of this study was to describe invasive pneumococcal disease (IPD) in a pediatric hospital in the last ten years.

Methods: Children <18 years with IPD occurring from 2009-2018 were identified from a retrospective study. Specimens of SP obtained from normally sterile sites were identified by culture and/or molecular biology. We evaluated demographic, clinical and microbiological data. Pneumococcal conjugate vaccine doses were counted if DIP occurred ≥2 weeks after a dose.

Results: Seventy nine cases were identified, median age 3 years. Antipneumococcal vaccination was completed in 47%. Most frequent diagnosis were pneumonia (63%), meningitis (18%), otomastoiditis (9%), occult bacteraemia (5%). Pneumococcus was identified in pleural fluid (40), blood (27), cerebrospinal fluid (13). Early complications occurred in 66%. Neurological sequelae were recorded in 5 patients, and 2 deaths occurred, in the context of meningitis. The serotype was obtained in 34%, 18 of them corresponding to a vaccine serotype. In 7 children with pneumonia and complete antipneumococcal vaccination, a serotype 3 pneumococcus was isolated.

Conclusions: Invasive infections due to S. pneumococcus remains a leading cause of morbidity and mortality. The knowledge of the serotype causing severe disease is important to allow updated vaccination recommendations. As in literature, serotype 3 was associated with complicated pneumonia despite previously vaccination.
**Background:** Infectious diseases display a primary cause of pediatric patients’ presentation in ED. Health and prevention surveillance is managed through reporting those infections to Disease Control and Prevention Center ("ΚΕΕΛΠΝΟ"). The purpose of this prospective study is to outline the epidemiological features of each infectious disease as they have been shaped over the past three years, in order to evaluate surveillance and improve prevention.

**Methods:** An archive of printed forms filled in over the years 2017-2019 was studied. The sample consists of 71 children (that were hospitalised) out of 80 examined in ED (46 boys and 34 girls, 54 of preschool age), representing 1.9% of admissions to our clinic. Data analysis was based on type of infection, vaccination profile and demographic criteria, then compared to those of previous years.

**Results:** The most frequent infectious disease was gastroenteritis (mostly salmonellosis, followed by shigellosis). An increase was detected during the fall of 2019. 21.5% was recorded among Roma and refugee groups. All 3 EHEC cases presented with HUS. Meningitis came second with 11 cases; 5 were partially vaccinated and only one was found with an infectious agent(Str.Agalactiae). 9 cases of measles (7 were hospitalised) were noted in unvaccinated Roma children during the latest epidemic. Other infections include Campylobacter coli in an infant with febrile seizures, and B.pertussis in a Roma infant.

**Conclusions:** The absence of Meningococcal or Pneumococcal meningitis and A or B Hepatitis, as well as the notable amount of measles cases both highlight the efficacy, but mostly the necessity of vaccination. The rise in foodborne infection incidence showcases the importance of adequate preventing measures, especially regarding refugee camps. A shift in seasonal epidemics has also been noted, presumably due to climate change.
A COMPARISON OF RESPIRATORY SYNCYTIAL VIRUS (RSV) PROPHYLAXIS IN MULTIPLE BIRTHS VERSUS SINGLETONS IN THE CANADIAN REGISTRY OF PALIVIZUMAB (CARESS) FROM 2012-2017

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Background: The use of palivizumab in multiple births remains controversial, despite the high risk of acquiring RSV infection through horizontal transmission.

Methods: Prospective study of infants aged < 2 years who received palivizumab and were recruited across 32 Canadian centers over 12 RSV seasons. Demographic data were collected at enrolment and respiratory illness-related hospitalization (RIH) events recorded monthly. We compared RIH and RSV-related hospitalization (RSVH) in multiple births (MBs) versus singletons.

Results: 25,003 infants were enrolled: 6,949 (27.8%) MBs; 18,054 (72.2%) singletons. A significantly larger proportion of MBs were premature (80.2%) versus singletons (56.8%). MBs had a lower gestational age (mean ± standard deviation): 31.2 ± 3.2 versus 33.2 ± 5.5 weeks) and birth weight (mean: 1590 ± 606.8 versus 2069.4 ±1068.5 g; both p<0.0005). They were younger at enrolment (4.5 ± 5.0 versus 6.1 ± 6.8 months), fewer attended daycare (1.9% versus 4.6%), and experienced exposure to smoking (24.5% vs. 29.9%), but more lived in crowded households (36.7% versus 19.4%; all p <0.0005. MBS had longer neonatal stay (51.1 ± 65.9 versus 47.9 ± 67.8 days), and more required respiratory support (65.7% vs. 57.7%), but for shorter duration (22.6 ± 32.9 vs. 24.7 ± 40.6 days); all p<0.001. RIH and RSVH rates in MBs versus singletons were 4.7%; 7.7% and 1.4%; 1.6% respectively. On Cox regression MBs had a lower risk of RIH compared to singletons (HR=0.616, 95%CI=0.543-0.698, p<0.0005), but not RSVH (HR=0.77, 95%CI=0.57-1.02, p=0.071).

Conclusions: MB infants had a significantly lower risk of RIH but not RSVH compared to singletons who received RSV prophylaxis during the RSV season. The results suggest that palivizumab may be useful in the prevention of RSV infection in MBs while concurrently reducing the risk for RIH.

Clinical Trial Registration: ClinicalTrials.gov Identifier: NCT00420966.
VARICELLA-ZOSTER VIRUS DNA DETECTED BY PCR IN HUMAN INTESTINE TISSUES FROM CHILDREN WITH GASTROINTESTINAL DISEASES

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Background: Varicella-Zoster virus (VZV) typically causes chickenpox, a rather benign disease. Following after primary infection or vaccination with live attenuated virus, the virus remains latent in dorsal root ganglions as well as ganglia of the enteric nervous system. Reactivation typically causes herpes zoster (HZ). Local reactivation of the virus in the bowel has been implicated in the pathogenesis of gastrointestinal (GI) diseases.

Methods: A pilot prospective study was conducted in order to investigate whether VZV reactivation is implicated in the pathogenesis of GI disorders. Pediatric patients, aged 2-16 years old, with chronic abdominal pain, inflammatory bowel disease (IBD) exacerbation, celiac disease or eosinophilic esophagitis (EoE), admitted for endoscopy in our department were included in the study. Detection of VZV DNA by PCR in biopsy tissue was carried out.

Results: Overall 21 children (median age 10.5 years) were enrolled; five (23.8%) with IBD exacerbation, 7 (33.3%) with celiac disease, 7 (33.3%) with EoE and 2 (9.6%) with nonspecific chronic abdominal pain. Twenty had been vaccinated with 2 doses of VZV vaccine, while 1 child had received one dose. None reported previous chickenpox or HZ. VZV DNA was detected by PCR in 6 patients (28.6%); in both children (100%) with chronic abdominal pain, 1 (20%) with IBD exacerbation, 1 (14.3%) with EoE and 2 (28.6%) with celiac disease.

Conclusions: The results from this pilot study suggest that VZV reactivation may be involved in the pathogenesis of chronic nonspecific abdominal pain in children. Moreover, while VZV DNA was detected in children with underlying GI disease, the role of VZV reactivation remains unclear. Further studies with larger number of children with chronic abdominal pain need to follow to support the pathogenetic role of VZV reactivation.
Background: In serious adverse event (SAE) data from the Prepare™ trial of maternal immunization with RSV-F nanoparticle vaccine, a ~50% reduction in SAEs coded as “pneumonia” (p<0.0001) was noted through 364 days among infants of vaccinated mothers. This analysis aimed to further characterize these cases.

Methods: SAEs coded to MedDRA terms including “pneumonia” or “bronchopneumonia” (excluding “congenital pneumonia” and “aspiration pneumonia”) were tabulated, including chest x-ray results (CXR, 64% of reports), RSV detections (active surveillance through day 180 only) and pulse oximetry from the trial’s pre-specified endpoints. A positive CXR was identified by the words “pneumonia,” “infiltrate,” or “consolidation” in radiology reports.

Results:

<table>
<thead>
<tr>
<th>Event, period</th>
<th>Safety Populations</th>
<th>Observed risk reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo n (%) N = 1561</td>
<td>Vaccine n (%) N = 3008</td>
</tr>
<tr>
<td>Pneumonia SAE, 0-180 d</td>
<td>66 (4.2)</td>
<td>65 (2.2)</td>
</tr>
<tr>
<td>Pneumonia SAE, (+)CXR, 0-180 d</td>
<td>42 (2.7)</td>
<td>34 (1.1)</td>
</tr>
<tr>
<td>Pneumonia SAE, (+)RSV, 0-180 d</td>
<td>37 (2.4)</td>
<td>25 (0.8)</td>
</tr>
<tr>
<td>Pneumonia SAE, (+)CXR &amp; RSV, 0-180 d</td>
<td>23 (1.5)</td>
<td>12 (0.4)</td>
</tr>
<tr>
<td>Pneumonia SAE, (+)RSV &amp; SpO₂&lt;92%, 0-180 d</td>
<td>19 (1.2)</td>
<td>6 (0.2)</td>
</tr>
<tr>
<td>Pneumonia SAE, 181-364 d</td>
<td>18 (1.2)</td>
<td>17 (0.6)</td>
</tr>
<tr>
<td>Pneumonia SAE, (+)CXR, 181-364 d</td>
<td>8 (0.5)</td>
<td>8 (0.3)</td>
</tr>
</tbody>
</table>
Conclusions: In this post-hoc analysis, SAEs coded as “pneumonia” were reduced in infants through 364 days of life in the vaccine group, with greatest reductions in SAEs associated with RSV, positive CXR, and/or hypoxemia. Impacts after 180 days suggest passive RSV immunization via maternal vaccination might modulate pulmonary health beyond the first RSV season and after vaccine-induced antibodies in infants would be expected to have waned.

Clinical Trial Registration: ClinicalTrials.gov NCT02624947
HPV NATIONAL IMMUNIZATION PROGRAMMES STATUS IN 53 WHO COUNTRIES

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Background and Objective: Since the introduction of HPV vaccination (HPVv), National immunization programmes in WHO Europe (WHO/ER) have rapidly evolved based on International and European recommendations. Several countries have recently decided to implement boys HPVv in addition to existing girls HPVv programmes. The objective of this research was to review the current status of recommendations, funding and program implementation of HPVv in WHO/ER.

Methods: A targeted literature review of WHO database and country websites (e.g. ministry of health, national authority) was conducted between August 2018-September 2019 across WHO/ER countries (n=53). Data included target HPVv population, vaccination schedule, setting (e.g. schools, healthcare center), and funding for primary (reported target-age group) and catch-up cohorts (individuals older than primary target-age). Funding was considered from patient’s perspective. HPVv was considered fully-funded if patient had no out-of-pocket pay, partially-funded if patient had to pay for part of vaccination and no-funding if vaccination was fully paid by the patient.

Learning Points/Discussion: In WHO/ER, 85% of countries (n=45/53) had national recommendations for HPVv among which 80% (n=36/45), 4% (n=2/45) and 16% (n=7/45) of countries had fully-funded, partially-funded and no-funding programs for the primary cohort, respectively. Fully-funded or partially-funded HPVv programs were available for girls only and girls & boys in 61% (n=23/38) and 39% (n=15/38) of countries, respectively. For catch-up cohorts, fully-funded or partially-funded HPVv programs were available in 26% (n=14/53) of countries. In fully-funded or partially-funded HPVv countries, vaccination occurred in healthcare centers (n=15/38), schools (n=16/38) or both schools and healthcare centers (n=3/38); with missing information regarding 4 countries. HPVv programs have been widely implemented in WHO/ER but 17 countries in the region still lack national recommendations and/or full funding. Substantial variations prevail across programmes including the target immunization population.
TREATMENT OF INVASIVE STAPHYLOCOCCAL INFECTIONS IN CHILDREN: IS MRSA DECREASING?

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Background: Management of invasive infections caused by methicillin-resistant *Staphylococcus aureus* (MRSA) may be challenging. However, in non life-threatening conditions, such as clinically stable patients with osteoarticular infections, and in areas with reduced rates of MRSA, initial therapy could probably cover only methicillin-susceptible strains. We retrospectively assessed rates of community-acquired MRSA among hospitalized children with invasive staphylococcal infections over the last years.

Methods: The microbiology records of 4 general hospitals with pediatric departments were reviewed for susceptibility results of *S. aureus* isolates from blood cultures of children aged 1 month–14 years with community-acquired infections, hospitalized between 1/1/2012-31/12/2019. Species identification and susceptibility testing were performed using VITEK 2 automated system. Oxacillin susceptibility and cefoxitin screen results were recorded. In addition, the outcome of all patients with culture-negative osteomyelitis/septic arthritis initially treated with non-MRSA-active agents was recorded.

Results: Eighteen patients with *S. aureus* bacteremia were retrieved, of whom 6 had MRSA isolated. All MRSA strains (6/11) were isolated during 2012-2015 period; from 2016-2019 the rate of MRSA was 0/7 (p=0.042, Fisher’s exact test). Seven patients with culture-negative osteoarticular infections were empirically treated with non-MRSA-active antimicrobials (2 during 2012-2015 and 5 during 2016-2019); they all had favorable outcome. By merging these data it appears that a non-MRSA-active regimen would succeed in 7/13 (53.8%) of these patients during 2012-2015 and in 12/12 (100%) of them during 2016-2019 (p=0.016).

Conclusions: These data suggest a trend for decreasing incidence of MRSA as a causative agent for community-acquired bloodstream and osteoarticular infections in children beyond the neonatal period, over the past years in our region. The use of non-MRSA-active antimicrobial agents for initial empirical treatment of non-critically ill children with presumed community-acquired invasive staphylococcal infections may be considered, under close monitoring.
A PROSPECTIVE STUDY OF PATIENTS WITH BRONCHIOLITIS ADMITTED TO THE PEDIATRIC INTENSIVE CARE UNIT IN A REGIONAL HOSPITAL (2017-2019) IN SPAIN

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Background: Acute bronchiolitis is the main cause of hospital admission among children under two years of age in our region. The most commonly identified agent is respiratory syncytial virus (RSV). Typically, pediatric intensive care unit (PICU) bronchiolitis admissions have been associated with comorbidities and an increase in antibiotic therapy. The objective of our study was to evaluate the differences in comorbidities, microbiology and management between the patients with bronchiolitis admitted to the PICU or to the hospitalization ward.

Methods: We conducted a prospective study of all children <2 years old who were admitted because of bronchiolitis at the hospital Universitari de Girona Dr. Josep Trueta, in Girona (Spain), during two and a half years (1st July 2017- 31th December 2019), who were treated as inpatients in the PICU (PICU group) or in the standard hospital setting (WARD group). Demographics, clinical and severity data (assessed by HSJD Score), complementary exams and antibiotics prescriptions were collected. Detection of respiratory viruses in nasopharyngeal swabs was accomplished by RT-PCR.

Results: We included 406 children (104 PICU, 302 WARD). The most frequently detected virus was RSV (55%, 226/406). In 50% (151/302) patients in the WARD group, no complementary exam was performed during hospitalization. Patient groups differed in HSJD Severity Score of bronchiolitis (P<0.001). No differences regarding the causative virus, age, comorbidities, blood test values (WBC, ANC, CRP and procalcitonin) were found. The two groups significantly differed in days of admission, supplementary oxygen, ventilator support and use of antibiotics. All blood cultures were negative in both groups.

Conclusions: In hospitalized infants, RSV was the most frequent agent causing bronchiolitis. Despite common use of antibiotics in PICU patients, there were no differences in blood test results between PICU and WARD patients.

Clinical Trial Registration: Our study doesn't need any clinical trial registration.
SEROLOGICAL REFLECTION OF THE STATE OF INTERFERON-MEDIATED ANTIVIRAL PROTECTION AND INTENSITY OF ALLERGIC INFLAMMATION IN ASTHMATIC CHILDREN DURING VIRAL UPPER RESPIRATORY TRACT INFECTIONS

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Background: Viral respiratory tract infections are the principal triggers of asthma exacerbations. Interferons (IFN) α and γ are crucial cytokines of Th1-type immune response with a distinct antiviral effect while interleukins (IL) 4, 5 and 13 are mediators of Th2-type response which support allergic inflammation.

The prospective cohort study aimed to investigate the serum interferon and interleukin response to viral upper respiratory tract infections (URTI) in preschool asthmatic children.

Methods: A total of 62 children, aged from 3 to 7 years, with mild (N=25) or moderate (N=37) allergic asthma constituted the main study group. Patients were enrolled on the first day of viral URTI. Non-allergic URTI patients, 33 in total, were the controls. Serum concentrations of IFN-α, IFN-γ, IL-4, IL-5, and IL-13 were compared at early, mid and late disease (Mann-Whitney U-test).

Results: Compared to non-allergic controls, the interferon response to URTI in asthmatics demonstrated lower levels of both studied IFNs from early to late disease. Simultaneously, an upsurge of IL-4 and IL-13 was registered. Particularly, IL-13 level spiked from 10.2 (3.2; 18.1) to 19.1 (8.7; 27.7) versus 2.6 (2.2; 2.9) to 2.9 (2.7; 3.1) pg/ml in controls; p< .001. In mild asthmatics basic depression of IFN concentrations were already present, and the increment of Th2-dependent ILs became comparable to moderate asthma subgroup values with the disease course.

Conclusions: Thus, systemic immune response to viral URTIs in asthmatic children is associated with depression of antiviral interferon-mediated protection in the form of a drop in serum IFN-α and IFN-γ concentrations at the onset of the disease with no considerable further growth, and progression of systemic Th2-mediated inflammation. Lower asthma severity ensures neither better interferon response nor lower intensity of interleukin-supported allergic inflammation in pediatric patients.

Clinical Trial Registration: Not applicable
CIRCULATING ANTIBODY-SECRETING CELL RESPONSE DURING MYCOPLASMA PNEUMONIAE CHILDHOOD PNEUMONIA

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Background: We recently demonstrated that the measurement of Mycoplasma pneumoniae (Mp)-specific IgM antibody-secreting cells (ASCs) improved diagnosis of Mp infection. Here, we aimed to describe Mp ASC response kinetics and duration in comparison to conventional measures such as pharyngeal Mp DNA and serum antibodies.

Methods: Prospective longitudinal study of 63 CAP patients and 21 healthy controls (HCs), 3–18 years of age, from 2016–2017. Mp ASCs measured by enzyme-linked immunospot (ELISpot) assay were assessed alongside Mp DNA and antibodies during 6-month follow-up.

Results: Mp ASCs of the isotype IgM were found in 29 (46%), IgG in 27 (43%), and IgA in 27 (43%) CAP patients. Mp ASCs were detected from 2 days to maximum 6 weeks after symptom onset, while Mp DNA and antibodies persisted until 4 months (p=0.03) and 6 months (p<0.01). Mp ASCs were undetectable in HCs, in contrast to detection of Mp DNA in 10 (48%) or antibodies in 6 (29%) controls for prolonged time. The Mp ASC response correlated with clinical disease, but did not differ between patients treated with or without antibiotics against Mp.

Conclusions: Mp-specific ASCs are short-lived and associated with clinical disease, making it an optimal resource for determining Mp pneumonia etiology.

Clinical Trial Registration: ClinicalTrials.gov NCT03613636
ERYTHEMA INDURATIVUM IN A 16-YEAR-OLD FEMALE ASSOCIATED TO MYCOBACTERIUM TUBERCULOSIS INFECTION: A CASE REPORT

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Title of Case(s): New onset rash as a sign of tuberculosis infection: a rare finding in paediatric TB

Background: Tuberculosis (TB) still is a major global disease burden, remaining the leading cause of death from an infectious disease worldwide. Although the lungs are most commonly affected, any organ can become a site of tuberculosis infection. Erythema indurativum is a rare cutaneous manifestation of TB.

Case Presentation Summary: This 16-year-old Somalian developed tender subcutaneous lesions on both her lower legs over the course of 6 weeks. Prior to presentation in our clinic, she received antibiotic therapy for one month with no effect under the suspected diagnosis of cellulitis. Skin biopsy was compatible with erythema indurativum of Bazin, showing panniculitis with tuberculoid granulomas. A tuberculin skin test resulted in 25 mm of induration and an interferon-gamma release assay was also markedly positive, indicating infection with Mycobacterium tuberculosis. She did not have any pulmonary symptoms. Computed tomography of the chest showed hilar lymphadenopathy without other pulmonary abnormalities. M. tuberculosis could not be confirmed by microbiology from samples of the skin or bronchoscopy. Also, several sputa remained PCR and culture negative. The patient was treated with anti-tuberculosis therapy resulting in complete remission of the skin changes.

Learning Points/Discussion: Presentation of TB is diverse and diagnosis, especially of extrapulmonary TB, can be challenging. TB is still prevalent in many developed countries, mainly due to international migration. This case underscores the importance of clinical knowledge in early identification and treatment of TB.
IMPACT OF 7- AND 13-VALENT PNEUMOCOCCAL CONJUGATED VACCINE (3+1 SCHEDULE) ON SEROTYPE VARIABILITY IN CRETE, GREECE

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Background: Introduction of pneumococcal conjugate vaccines PCV7 and PCV13 was related to decreased S. pneumoniae morbidity, serotype replacement, and changes in susceptibility to antibacterials (introduced in our area in 2004 and 2010, respectively). We have already shown that introduction of PCV7 considerably changed S. pneumoniae epidemiology in Crete. In this study, we explore trends following PCV13 introduction regarding S. pneumoniae serotype distribution.

Methods: This was a retrospective observational study that included all S. pneumoniae clinical isolates from children which were cultured, serotyped and tested for susceptibility to antimicrobials, in the referral healthcare facility of Crete, i.e., a well-defined area of high vaccination coverage (with the regimen 3+1 doses), during the 20-year period 1999-2019, divided in the pre-PCV (1999-2004), PCV7 (2005-2010) and PCV13 (2011-2019).

Results: A total of 396 isolates (54 invasive) were included, of whom 124 (25 invasive) in PCV13 period. Rates of serotypes included both in PCV7 and PCV13 continued to decline (p<0.0001 for all, p=0.023 for invasive). Rates of PCV13 serotypes were not similarly affected post-PCV13 (p=0.315 for all, p=0.579 for invasive); in particular a decline was shown for serotypes 1, 5, 6A, 7F (p=0.007) but not for 3 (p=0.07) and not for 19A (p=0.055). An increase of non-PCV serotypes was observed, both for the total (p<0.0001) and invasive (p=0.006) strains.

Conclusions: In the small population of our study area, after the introduction of PCV13, serotypes that were included both in PCV7 and PCV13 continued to significantly decline. However, decrease was not observed for all PCV13 serotypes (1, 5, 6A, and 7F were decreased, whereas 3 and 19A were not). Moreover, increase was confirmed for non-PCV serotypes. Hence, further surveillance is required.
SEVERE RSV-ASSOCIATED HOSPITALISATION IN THE FRENCH PAEDIATRIC POPULATION (LYON): INCIDENCE AND RISK FACTORS


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Background: Respiratory syncytial virus (RSV) infection is responsible for bronchiolitis in infants. RSV is the predominant cause of lower respiratory tract infection (LRTI) during the first year of life. We aimed to estimate the incidence of hospitalised LRTI, Severe LRTI, and Very Severe LRTI, and the birth variables associated with the risk of Severe LRTI in the paediatric population in a major metropolitan European area.

Methods: Data were collected from the 2016-birth-cohort from the University Hospital of Lyon with parents living in Metropolitan Lyon (1,370,678 inhabitants). From this cohort, hospitalisation with confirmed RSV-infection in the first year of life were identified using the diagnostic laboratory database on two successive RSV seasons (from 01/01/2016 to 01/03/2017). Severity was graded as LRTI, severe LRTI, and Very Severe LRTI according to the WHO case definitions.

Results: From the HCL-2016-birth-cohort (n=9,189), 116 less-than-1-year-old-infants were hospitalised for bronchiolitis with laboratory-confirmed-RSV-infection. Incidence of LRTI, Severe LRTI, and Very Severe LRTI per 1,000 births were respectively estimated at 2 (95%-CI 1–3), 1 (95%-CI 1-2) and 9 (95%-CI 7–11). Prematurity under 28 weeks of amenorrhea (OR 2.5 (95%-CI 1.3-4.6) p=0.006), multiparity (OR 1.9 (95%-CI 1.1-3.2) p=0.026), being born in September or December (OR 9.5 (95%-CI 3.6-24.7) p=0.000), and being born in October or November (OR 13.4 (95%-CI 5.3-34.3) p=0.000) were identified as independent risk factors for Very Severe RSV-LRTI.

Conclusions: The premature newborns, infants born during the months just before the RSV season, and the newborns having brotherhood have a high risk of Severe RSV-LRTI. Preventive pharmacological, i.e.
vaccine or antibodies, and non-pharmacological interventions (education for hand-wash, limitation of infectious contacts, e.g. avoiding crowds) should target the parents of at-risk infants during the pregnancy follow-up or during the birth hospitalisation.
A 5 YEAR REVIEW OF THE EPIDEMIOLOGY AND MANAGEMENT OF PAEDIATRIC MUSCULOSKELETAL INFECTIONS (MSKI) IN EAST MIDLANDS, UK.

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**Background:** Musculoskeletal infection (MSKI) is a common cause of hospitalisation in children worldwide. European data suggests that the prevalence of *Kingella kingae* is very high in some regions in Europe. This review aims to describe the epidemiology of MSKI in patients <16 years old in a large teaching hospital which serves the population in East Midlands, UK. Treatment and investigation results were reviewed to assess appropriateness of the current local empiric treatment.

**Methods:** A retrospective review over a 5 year period (01/01/2014-01/01/2019) of children aged <16 years old admitted with a diagnosis of MSKI was undertaken. Patients were identified using the hospital discharge clinical coding data. Baseline information including culture results, initial antibiotic choice and route, total treatment duration and documented complications were collected from electronic patient records, discharge summaries and medical notes.

**Results:** There were 86 children with a diagnosis of osteomyelitis, septic arthritis and/or myositis. *Staphylococcus aureus*(15%) was most commonly isolated, followed by *Streptococcus pyogenes*(10.5%). No cases of *Kingella kingae* were identified. Sites most commonly affected were knee and hip in septic arthritis and tibia in osteomyelitis. 13 samples had 16S rRNA PCR performed, of which one was positive for *Streptococcus pyogenes*. Most commonly prescribed antibiotics were intravenous flucloxacillin(48%) followed by intravenous ceftriaxone(18%). 9 patients developed complications, of which only 1 was attributed to treatment failure with empirical antimicrobial therapy.

**Conclusions:** In our centre, the commonest cause of MSKI in children under the age of 16 is *Staphylococcus aureus* followed by *Streptococcus pyogenes*. No cases of *Kingella kingae* MSKI was identified. Molecular techniques such as 16S rRNA PCR should be considered in all culture-negative cases, especially in those who has had antibiotic therapy prior obtaining microbiology samples or when fastidious organisms are suspected.
ETIOLOGICAL STRUCTURE OF INTESTINAL INFECTIONS IN 2017-2018 IN GEORGIA IN THE AGE OF CHILDREN

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Background: Despite improved standards of living and preventive measures, hospitalization with infectious diseases, including of intestinal infections, is still high compared to international data. Prevention of the spread of diarrhea pathogens is very important. As a result of rotavirus vaccination, the share of this pathogen has declined more frequent cases of norovirus. The aim was to determine the specific proportion of bacterial intestinal pathogens in diarrheal diseases.

Methods: At NCDC, bacteriological diagnosis of fecal samples from diarrhea was performed by genetic analysis of the material. Retrospectively we studied the medical records of 732 patients hospitalized at Acad.Vakhtang Bochorishvili Clinic 2017-2018 years. Analysis of features of disease progression on a wide range of clinical material, taking into account patient age, comorbid background and pathogen. Not a single case ended in a lethal solution.

Results: In Georgia between the age of 0-15 y. 56.1% of hospitalized due to infectious disease had intestinal infection, 64.1% were under the age of one year. Of the 732 patients hospitalized at the clinic, 72% (527pts) had bacterial intestinal infection. 26% (137 patients) had salmonellosis, 42% (221 pts) shigellosis and 14% (73 pts) E.coli. In the remaining cases, microbes could not be identified. From morbidity by E.coli, in few cases 0157 was detected. The main cause of hospitalization was bloody diarrhea. Fever that lasted for up to 4 days on average. In 2 cases, severe salmonellosis was detected, and the microbe was identified from blood.

Conclusions: The seasonal course of the pathogens of diarrheal diseases is still maintained, the structure has changed. Norovirus predominated among the viruses, and Shigella Sonnei was common among the microbes, instead of Shigella Flexneri, which was more common in the late 20th century. Azithromycin treatment was effective in bloody diarrhea, although azithromycin resistance was demonstrated during this period and ceftriaxone was used instead.
PROTECTIVE IMMUNITY AGAINST MEASLES IN PATIENTS WITH PRIMARY IMMUNODEFICIENCY

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**Background:** Patients with primary immunodeficiency (PID) are at increased risk of severe infection, including vaccine preventable. They have weak immune response after immunization; for some PID patients vaccines are contraindicated. Passive immunization with immunoglobulin replacement therapy can protect PID patients against the vaccine-preventable infections. There is a highest rate of measles incidence during last years in Ukraine. In such a situation, the issue of measles protection in PID patients becomes particularly relevant. The **aim** of the study was to evaluate the status of measles protection in children with primary immunodeficiency.

**Methods:** Laboratory evaluation of measles immunity by ELISA was performed in 3 groups of children: PID patients with preserved antibody production and mild antibody deficiencies (n = 25), PID patients with severe hypogammaglobulinemia on IVIG therapy (n = 18), and healthy controls (n = 20). The protective level of antibodies was assessed as 150 IU/ml.

**Results:** The vast majority of patients with PID have protective level of antibodies against measles. The level of anti-measles antibodies in vaccinated patients with preserved antibody production (2372±336 IU/ml) was significantly higher than in those receiving passive immunization by IVIG (1140±174 IU/ml) (p = 0.0021). The level of antibodies in vaccinated PID patients with preserved antibody production was lower than in the group of healthy children (9289±377 IU/ml), but the differences were not statistically significant (p = 0.07).

**Conclusions:** Both group of patients with PID who have received active immunization and who receive passive immunoprophylaxis with IVIG have a protective level of antibodies against measles. Active immunization against measles should be preferred in PID patients without contraindications. The effectiveness of IVIG in the protection against measles in patients with severe hypogammaglobulinemia is subject to further investigation.

**Clinical Trial Registration:** # 0118U001137
A CASE OF CO-INFECTED (CMV + STREPTOCOCCUS AGALACTIAE) MENINGOENCEPHALITIS IN A NEWBORN.

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Title of Case(s): A case of co-infected meningoencephalitis in a newborn.

Background: The problem of congenital infections is extremely difficult and various. Despite the modern possibilities of laboratory diagnostics, the identification of the pathogen and the degree of its significance in the development of the disease remains complicated. Particularly difficult situation in cases of co-infections. Combined virus-bacterial congenital infections, which are characterized by a severe and atypical course of the disease, often lead to mortality and disability of patients.

Case Presentation Summary: The child was born full-term, 8/9 on the Apgar score, in the first hours of life he developed dyspnea, respiratory failure, microcirculation disorder. Metabolic decompensated acidosis and congenital pneumonia were identified. Further, his condition worsened, he presented hyperthermia, hypotension and convulsions, septic shock developed, the child was started mechanical ventilation and transferred to ICU. Severe neutrophilic pleocytosis and isolated Streptococcus agalactiae in cerebrospinal fluid (CSF) confirmed the diagnoses of meningoencephalitis. The patient was treated with meropenem and vancomycin and almost recovered. His CSF analysis became normal. However, on the 15th day, the patient's condition worsened, seizure readiness appeared, the child became lethargic. Lumbar puncture was carried out again. Lymphocytic pleocytosis was found in CSF. Cytomegalovirus DNA was detected in blood and CSF by PCR. Ganciclovir was admitted and the patient recovered. Further follow-up of this child made possible to solve the vaccination issue and provide the rehabilitation, which improved his quality of life. As a result of the treatment and rehabilitation measures, the child grows and develops according to age, has no central nervous system disorders, hearing and vision impairment.

Learning Points/Discussion: This clinical case demonstrates the importance of screening for opportunistic infections in newborns with bacterial diseases. Timely diagnosis allows to prescribe the necessary therapy and improve the prognosis of patients.
INVASIVE MOLD INFECTIONS IN A PEDIATRIC HEMATO-ONCOLOGY UNIT: A 14-YEAR PERIOD REVIEW

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Background: Children receiving treatment for oncologic diseases or undergoing an hematopoietic stem cell transplant (HSCT) have a significant risk of developing an invasive fungal infection, especially caused by mold species. Clinical and radiologic manifestations may differ from those in adults. The aim is to describe epidemiology, diagnosis and outcome of invasive mold infections (IMI) in a pediatric hemato-oncology unit during the last 14-year period.

Methods: Descriptive retrospective study of cases of proven, probable and possible IMI in patients up to 18 years old admitted between 1st January 2006 and 31st December 2019 to the hemato-oncology unit of a public hospital (health area coverage around 47,000 children) in Madrid (Spain). Epidemiology, risk factors, microbiological and radiological findings leading to diagnosis, antifungal treatment and clinical outcome were analysed.

Results: Twenty-three patients were included (47.8% males, median age 10.8 years), all with bronchopulmonary infections. Baseline conditions: 13 had an hematological malignancy and 12 had undergone HSCT; 87% had received primary antifungal prophylaxis. Diagnosis: 1 proven IMI, by findings in a necropsy; 8 probable IMI (high galactomannan antigen level in serum [5 patients] or in bronchoalveolar lavage [3]); 14 possible IMI. Imaging techniques evidenced: nodules or pulmonary infiltrates (39.1% each), consolidation (34.8%); only 1 case showed a cavity and 3, the halo sign.

Outcome: 30.4% needed intensive care admission, 26.1% died.

Conclusions: IMI have a significant morbidity and mortality in immunocompromised children. Radiological manifestations in bronchopulmonary forms of IMI in children can be very variable and nonspecific, especially in neutropenic patients; classical cavitation, air crescent and halo signs are often absent. Blood cultures have a very low profitability and exposure to mold-active antifungals reduces galactomannan tests sensitivity; these can significantly impact diagnosis of proven and probable infections.
NOROVIRUS GII AS THE MAIN ETIOLOGICAL AGENT OF ACUTE DIARRHOEA IN SERGIPE STATE, NORTHEAST OF BRAZIL (2016 AND 2019)

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Background: Diarrhoea continues to be an important cause of morbidity, hospitalizations and, in less developed countries, childhood deaths. Rotavirus A (RVA) and Norovirus GII (NoV-GII) viruses are the most important causes for diarrhoea, but with variation of occurrence/subtypes on time. We studied the participation of both RVA and NoV-GII in acute gastroenteritis in the main emergency-public services of Sergipe between 2016 and 2019.

Methods: Faecal samples were collected from children <10 years old with diarrhoea in paediatric reference hospitals of Sergipe-State, Brazil. We have a four years of samples collection in the two main emergency services of Sergipe. Viral RNA was extracted and identified by RT-qPCR, using primers and probes specific to each virus. The samples were considered positive if amplified the two duplicates, had a cT less than 40 and a sigmoid characteristic curve.

Results: Between 2016-2019, 553 samples were collected. Of these, 38.5%(2016), 35.6%(2017), 10.0%(2018) and 15.9%(2019). A different behaviour was observed when dividing the study time in two. Between 2016-2017, 30.9% were positive for RVA and 8.3% positive for NoV-GII. During 2018-2019, 37.9% of the cases were NoV-GII, becoming the main etiological agent identified during the recent period. The RVA that in the previous years remained as the main cause of diarrhoea, was responsible for 12.1% of the cases identified in this study for the samples collected between 2018-2019.

Conclusions: Sergipe presented important epidemiological change, with the role of NoV-GII as the main cause of childhood diarrhoea currently, showed by the inversion of percentages from Rota to Norovirus aetiology. This is probably due to rotavirus vaccine introduction in Brazil. This data deserves attention especially with a virus that does not have a specific vaccine and is not capable of stimulating a prolonged immune response.
NEUROLOGIC MANIFESTATIONS OF CAT SCRATCH DISEASE - HOW TO RECOGNISE IT?

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**Background:** The most common neurologic manifestation of cat scratch disease (CSD) is encephalopathy. Transverse myelitis, radiculitis, cerebellar ataxia and seizures may develop. The aim of our study was to highlight the importance of including CSD encephalopathy (CSDE) in the differential diagnosis when a previously healthy child presents with refractory seizures and to assess diagnostic tools, management and outcomes of all children affected.

**Methods:** We retrospectively examined hospital records including clinical presentation, diagnostic tools, management and outcomes of all children with proven CSD and neurologic manifestations within the last 5 years. Diagnosis of CSD was confirmed by indirect immunofluorescence test (Bartonella henselae IgG titres > 512). We defined refractory seizures if seizures continued despite treatment with at least two antiepileptic drugs, either alone or in combination.

**Results:** We identified 4 children (age range 7–12) with neurologic manifestations of CSD. All children presented with fever, somnolence and refractory generalized tonic-clonic seizures. They all had previous contact with a cat. Meningeal signs were positive in 2 children. Pleocytosis ranged between 3-36 WBC/µL. All children had sterile cerebrospinal fluid (CSF), normal brain CT and MRI while electroencephalogram showed diffuse slowing. Diagnosis was confirmed by serology. Therapy included intensive care measures, antiepileptics and intravenous azithromycin for 5 to 7 days. Recovery was complete except in one child with residual cognitive impairment.

**Conclusions:** Refractory seizures can be neurologic manifestation of CSDE. One should suspect CSDE in a child who had contact with a cat, normal CSF findings or mild pleocytosis and normal CT and MRI findings. The diagnosis can be confirmed using serology methods. Since CSDE is self-limiting, the usage of intravenous azithromycin as the first line of treatment in children is hard to assess, but recommended.
SOCIAL DEPRIVATION AND UPPER RESPIRATORY TRACT INFECTION IN THE NORTH EAST OF THE UK

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Background: This prospective observational survey using data from the multicentre European MOFICHE and PERFORM study databases, aimed to 1. identify a relationship between social deprivation and patients presenting to Paediatric A&E (PED) with upper respiratory tract infection (URTI) in the North East of the UK, and 2. To analyse the geographic spread of URTI patients presenting to PED in the North East of the UK.

Methods: The postcodes of patients presenting to PED with a working diagnosis of URTI (n=1685) between April 2017 and March 2018 allowed classification of patients into Index of Multiple Deprivation (IMD) deciles using the English indices of deprivation 2015 tool. Individual patient postcodes were colour-coded by deprivation decile and pinned onto a visual map using the My Maps tool on Google Maps.

Results: 58.4% of URTI patients in PED came from the most, and 15.7% from the least deprived households. There was a general trend of decreasing patient presentation with decreasing levels of deprivation, but a slight increase in patients in IMD deciles 9 and 10. This trend remained the same for viral and bacterial URTIs. Patients from less deprived households were less likely to be discharged and more likely to be admitted, for both short (< 24 hours) and longer admissions (> 24 hours). Mapping of postcodes highlighted “hotspots” in the North-East.

Conclusions: There is a significant relationship between social deprivation and presentation to PED with URTI in the North East of the UK. Most patients presenting to PED with URTI came from more socially deprived backgrounds, which could also reflect local demographics. More research is needed to determine if the difference in outcome is due to differences in severity of URTI or care between IMD deciles.
EMPIRIC IN-HOSPITAL ANTIBIOTIC TREATMENT IN 1402 CHILDREN WITH PARAPNEUMONIC PLEURAL EFFUSION/EMPYEMA IN GERMANY

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Background: Parapneumonic effusion and pleural empyema (PPE/PE) are complications of community-acquired pneumonia (CAP) in children. Although causing bacterial pathogens are well known and antibiotic resistances are rare, treatment often remains controversial and challenging. The purpose of the study was to analyse the empirical in-hospital antibiotic therapy (EIH-ABT) of children with PPE/PE in Germany

Methods: Between 2010 and 2018, patients <18 years of age hospitalised with pneumonia-associated PPE/PE (>7 days or requiring drainage) were reported to the German Surveillance Unit for Rare Diseases in Childhood (ESPED) and clinical data was collected by questionnaire. Antibiotics for EIH-ABT were defined either as backbone therapy (BT) or as add-on therapy (AT).

Results: A total of 1402 hospitalised children with PPE/PE were included. In 64% of children, BT was started according to the German pCAP guideline with cefuroxime (46.6%) or aminopenicillin/beta-lactamase inhibitor (18.3%). In 36% of patients, BT differed from the guideline: Aminopenicillin (8.3%), combination of ≥ 2 beta-lactams (11.8%), beta-lactams with enhanced gram-negative activity (cefotaxime or ceftiraxone 5.8%) or activity against Pseudomonas spp. (piperacillin/tazobactam 2.6%, imipenem or meropenem 1.3%). The use of BT was mostly similar between children with and without underlying condition, besides an increased use of piperacillin/tazobactam, imipenem and meropenem. Although combination therapy is not recommended, the rate of children with AT was high (58%). Intention might have been to cover M. pneumoniae (macrolides, 24.5%), multi-drug resistant bacteria (aminoglycosides, 11.3%, glycopeptides, 2.9%) or a favorable tissue penetration (clindamycin, 7.4%).

Conclusions: Guideline adherence regarding antibiotic therapy was low, assumably due to the severe clinical presentation of children with PPE/PE. Antibiotic stewardship programs are necessary to increase guideline adherence and reduce unnecessary antibiotic combination therapy.

Clinical Trial Registration: Clinical trial registration: none
CD4 LEVELS IN RELATION TO THE SEVERITY OF IMMUNOSUPPRESSION AS A PREDICTOR OF THE HIV-RELATED CARDIOMYOPATHY IN CHILDREN WITH MOTHER-TO-CHILD HIV TRANSMISSION

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Background: HIV-related cardiomyopathy is associated with high mortality among children. The purpose of the study was to determine the association between the severity of immunosuppression (by world health organization) as a predictor of the HIV-related cardiomyopathy development in children, infected by perinatal transmission. This is a prospective cohort study of 187 consecutive children (mean age 5.6±3.6 years, 105 male and 82 female) born HIV positive (perinatal transmission) and had regular follow-up examinations at the National Research Center of Virology and the Republican Center of AIDS in the years 2010-2017.

Methods: The HIV infection was detected by the ELISA method following by Western Blot confirmation right after birth and during follow-up. The CD4 count was done on the Partec Flow Cytometry instrument (CyFlow) with a CD4% easy count kit-dry package. Cardiomyopathy was diagnosed by clinical findings, ECG, and echocardiography. The correlation and linear regression were conducted to determine the strength of association.

Results: In 34(18.2%) children, dilatation cardiomyopathy was diagnosed 5.32±2.6 years after birth. Not significant immunosuppression was observed in 35(18.7%) children, mild in 40(21.4%), advanced in 35(18.7%) and severe in 77(41.2%) cases. The severity of immunosuppression was positively related to cardiomyopathy development, $r=0.17$ ($p=0.007$), accounting for 3.2% of the total variance. A linear regression analysis was significant $F(1,185)=6.155$, $p=0.014$, $t=2.48$. The standardized coefficient beta=0.179, 95%CI for the slope was 0.012 to 0.072.

Conclusions: The severity of immunosuppression was highly related to cardiomyopathy development in children with perinatal HIV transmission (the more severe the immunosuppression the more likely the heart lesions occurred). Reducing the risk of mother to child vertical transmission, decrease the severity of the immunodeficiency by increasing CD4 count are the potential implications to decrease the incidence of cardiomyopathy and its related mortality.
DIFFERENCES IN LENGTH OF INPATIENT STAY IN CHILDREN WITH ACUTE RESPIRATORY INFECTIONS BETWEEN EUROPEAN COUNTRIES – RESULTS FROM THE PED-MERMAIDS PROSPECTIVE COHORT STUDY

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Background: Clinical management and outcome of acute respiratory infections (ARI) in children differ between countries globally. Comparative studies applying the same protocols across Europe are rare.

Methods: The EU-funded Paediatric Multi-centre EuRopean study of MAjor Infectious Disease Syndromes (PED-MERMAIDS) enrolled children ≤5 years hospitalised for ARI across 11 EU countries. Information on symptoms, course of disease and management was collected prospectively. Admission day nasopharyngeal swabs were analysed for viral and bacterial pathogens by multiplex PCR.

Results: 357 ARI children, median age 1.15 years (interquartile range, IQR 0.44-2.55) were enrolled over 2½ years. Children presented median 3 days after onset of symptoms (IQR 1-4). On admission, 113 (33.5%) presented with fever >39°C, 251 (70.7%) with poor feeding, 195 (54.8%) with chest recessions and 15 (4.2%) with prolonged capillary refill time. 210 ARI children (58.8%) received antibiotics, 149 (43.6%) required supplemental oxygen, 186 (53.8%) received intravenous fluids and 12 (3.6%) were managed on ICU. No child died after admission for ARI. Inpatient length of stay (LOS) ranged between <1 and 49 days (median 3 days, IQR 2-5 days) and was different by country of admission (see table, p<0.001). A potential respiratory pathogen was detected in 312 children (87.4%). Only bacterial pathogens were detected in 33 (9.2%), only viruses in 111 (31.1%) and viral-bacterial co-detection occurred in 168 (47.1%). Administration of antibiotics after admission was not associated with subsequent detection of potential bacterial pathogens. If RSV was detected (115, 35.2%), LOS was longer at median 4 days (IQR 3-5) compared to no RSV detected (3 days, IQR 1-4, p=0.001).

<table>
<thead>
<tr>
<th>Patient n</th>
<th>Spain</th>
<th>Italy</th>
<th>Greece</th>
<th>UK</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (IQR)</td>
<td>1.6 (0.7-3.9)</td>
<td>0.8 (0.2-1.3)</td>
<td>1.3 (0.4-3.0)</td>
<td>1.4 (0.9-2.6)</td>
<td>1.2 (0.4-2.5)</td>
</tr>
<tr>
<td>Prior days of symptoms (IQR)</td>
<td>3 (2-4)</td>
<td>2 (2-4)</td>
<td>2 (1-4)</td>
<td>2 (1-4)</td>
<td>3 (1-4)</td>
</tr>
<tr>
<td>Poor feeding</td>
<td>34 (61.8%)</td>
<td>82 (91.1%)</td>
<td>75 (59.1%)</td>
<td>47 (73.4%)</td>
<td>251 (70.3%)</td>
</tr>
<tr>
<td>Recessions</td>
<td>32 (58.2%)</td>
<td>58 (64.4%)</td>
<td>49 (38.6%)</td>
<td>47 (73.4%)</td>
<td>195 (54.6%)</td>
</tr>
<tr>
<td>Supp. oxygen</td>
<td>39 (70.9%)</td>
<td>39 (43.3%)</td>
<td>31 (24.4%)</td>
<td>28 (43.8%)</td>
<td>149 (41.7%)</td>
</tr>
<tr>
<td>IVF</td>
<td>28 (50.9%)</td>
<td>51 (56.7%)</td>
<td>84 (66.1%)</td>
<td>11 (17.2%)</td>
<td>186 (52.1%)</td>
</tr>
<tr>
<td>ICU</td>
<td>9 (16.4%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>2 (3.1%)</td>
<td>12 (3.4%)</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>43 (78.2%)</td>
<td>48 (53.3%)</td>
<td>76 (59.8%)</td>
<td>35 (54.3%)</td>
<td>210 (58.8%)</td>
</tr>
<tr>
<td>RSV detected</td>
<td>12 (21.8%)</td>
<td>37 (41.1%)</td>
<td>42 (33.1%)</td>
<td>17 (26.6%)</td>
<td>115 (32.2%)</td>
</tr>
<tr>
<td>LOS (IQR)</td>
<td>5 (3-7)</td>
<td>3 (1-5)</td>
<td>3 (2-5)</td>
<td>1 (1-3)</td>
<td>3 (2-5)</td>
</tr>
</tbody>
</table>

21 children were enrolled across 7 other participating countries and are not shown in the table except in the “total” column.

IQR: Interquartile range, IVF: Intravenous fluids, ICU: intensive care unit, RSV: respiratory syncytial virus, LOS: length of inpatient stay
Conclusions: Outcome of ARI in European countries is generally good. The difference in LOS is unadjusted for severity of disease at presentation, a multivariate analysis is in progress.
Clinical Trial Registration: observational, not registered
Background: Aim of the study is the presentation of epidemiological data on children with febrile seizures admitted to the Pediatric Department UHCT Mother Theresa during the period January 2018 – December 2019. Febrile seizures are common among children admitted in UHCT. There are children having febrile seizures not only once, but they have more than 1 episode during their childhood.

Methods: 320 children aged 1 month to 14 years, admitted to this service between January 2018 and December 2019 were enrolled in the study. Criteria of inclusion was the febrile seizure. Children admitted were from different areas. Descriptive analysis was performed after data were entered in EpilInfo. Criteria of inclusion was the febrile seizure. Confidence Interval was settled 95% for each calculation done.

Results: 6.42% of all hospitalizations during Jan2018 – Dec2019 had febrile seizures. Only 11.25% of febrile seizures patients were recurrent. 88.75% had the episode of seizure as first time. There was almost equal gender distribution (M:F = 56.87%; 43.13% or 1.31:1). Febrile seizure was more frequent among urban areas (63.75% vs 36.25% in rural areas. Frequency of seizure occurrence decreased by age. Family history associated with seizures in 25 children or 7.8%. More than half of the main diseases were viral infections 51.65%. Lower respiratory infections presented 16.6% of cases.

Conclusions: Main cause of febrile seizures in Albania are viral infections, affecting mostly the children aged 6 mo.-5 yrs. The disease is most common in males. The disease is most common in urban areas because of the higher density. The disease is most common in winter and spring. In the early stages, the disease is manifested by high fever and contractures. Temperature is septic with 3-4 peaks in 24 hours.
CASE DISCUSSION: MENINGOCOCCEMIA

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Title of Case(s): Meningococcal infection

Background: Meningococccemia as a dramatic example of fulminant septicemia is a permanent subject of interest for researches. Severe meningococcal infection is a sporadic disease in Georgia, although it is associated with the lowered recognition from healthcare providers and therefore delayed diagnosis. The presented case is interesting because of its urgency and potency of lethal outcome if the appropriate diagnosis and treatment is delayed.

Case Presentation Summary: 2 years old girl acutely developed hectic fever on 12.01.2020 10 pm. Antipyretic drugs were not effective. After 6 hours the parent noticed a pair of macular eruption behind the ear. During the next hours evolution of abundant blanching macular rash was seen firstly on lower extremities and sclera. The child also complained for leg pain. The patient was consulted by family physician and emergency doctor meningococcemia was not suspected. The misdiagnosis at the early stage of disease was related to the fact that the child had contact with family members infected with a respiratory viral infection on 01/01-07/01. After 14 hours from the onset only two dot-like haemorrhages were evolved on skin and sclera. was hospitalized at the infectious diseases clinic where the thoroughfull examination of the child meningococcemia was suspected. Laboratory tests showed following results: leukocytosis, neutrophyllosis, lymphopaenia, ESR 44 mm/hours, CRP 78 mg/l; Procalcitonin 10.92 ng/ml. Blood sera Real time PCR: St.pneumonia negative, H.influenza negative, N.meningitides positive. CSF general analysis was in normal range. Isolated meningococcemia without clinical evidence of meningitis was diagnosed. The patient recovered after 8 days.

Learning Points/Discussion: Early stage of meningococcemia the eruption may be blanching and macular, which may need differentiation with viral exanthema. Lower extremities pain is also a “red flag” which needs prompt attention. Other worrisome sign is dot-like hemorrhages on sclera as far as carefull examination of the patient may lead to early diagnosis and appropriate treatment which is essential for better outcome of meningococcemia.
THE DEVELOPMENT AND FEASIBILITY OF A NEW WHOLE BLOOD RNA-BASED DIAGNOSTIC TEST TO DIFFERENTIATE BACTERIAL FROM VIRAL INFECTION IN A HIGH RISK PAEDIATRIC POPULATION: A MIXED METHODS STUDY

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Background: Current clinical investigations cannot differentiate between bacterial and viral infections in >50% of febrile children, resulting in unnecessary antibiotic treatment and missed serious bacterial illness. Improved diagnostic tests are required, particularly for children at high risk of infection (HR).

Aims: To investigate the acceptability to patients and the feasibility of RNASeq in the development of a new ribonucleic acid (RNA)-based point-of-care test (POCT) for diagnosing infection in HR children

Methods: Design: Prospective cohort study and qualitative methodology

Subjects and setting: HR children with fever >38.0°C, presenting to the Emergency Department or other appropriate ward of 12 European hospitals; Patients and patients' families attending a Great North Children's Hospital, Newcastle Upon Tyne (GNCH) Bone Marrow Transplant Unit event. Main outcomes: White cell counts (WCCs) producing RNA yields of >1µg and >2µg; WCCs in subsets of HR children; The acceptability of a new POCT to HR patients and families

Results: 403 febrile episodes in 316 children were included. 59.0% had a diagnosis of malignancy. Infections remained undiagnosed after clinical investigation in 33.0%. The median WCC overall was 4.0x10⁹/L (IQR 0.9-9.6). RNAseq is feasible in 1.0ml samples with WCCs >0.9x10⁹/L. Many children with malignancy had WCCs <0.9x10⁹/L. Patients value at-home treatment and antibiotic minimization. They demonstrated trust in a POCT, particularly when offered in hospital; however, safety and reassurance were also important.

Conclusions: RNASeq analysis is feasible in 1.0ml samples from most HR children, except those with malignancy. For this group the standard tube (2.5 ml of blood) is required to obtain a sufficient RNA yield for signature discovery RNASeq analyses. Families would trust and accept a new POCT, with appropriate safety and reassurance. POCT could lead to reduction in cost for the NHS and families.
IMPORTED ENTERIC FEVER: EXTREMELY DRUG-RESISTANT CASES, EVEN IN SPAIN

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Title of Case(s): Fever in the returning traveler child: a new threat, and old enemy.

Background: Enteric fever is a potentially severe disease caused by Salmonella typhi. It carries a significant health burden worldwide, including imported cases: it affects 5,700 people in the US each year. Since 2016, Pakistan is experiencing a large outbreak of XDR S. typhi, which is only susceptible to carbapenems and macrolides. Outbreaks from imported XDR strains in travelers have been described in Europe and North America. We analyze twenty-seven typhoid cases since 2009 diagnosed in our hospital, including three caused by XDR strains, and the changes in the resistance pattern.

Case Presentation Summary: We studied twenty-seven patients with confirmed enteric fever admitted in our hospital since 2009. All cases came from Pakistan, India or Bangladesh, except for three of them (Morocco and Latin America). Three of the latest cases (2019 and 2020) from Pakistan had XDR Salmonella, resistant to third generation cephalosporins. There were also three (2019) MDR strains resistant to macrolides. Thirteen isolates were resistant to fluoroquinolones, most of them since 2016. The initial empiric treatment was a third generation cephalosporin in all cases except for the latest one from Pakistan, who was treated with meropenem since the beginning, given the risk of an XDR strain. On average, patients completed 10.3 days of i.v. antibiotic. Although five patients presented with complications, all of them finally recovered. All XDR strains were successfully treated with meropenem.

Learning Points/Discussion: The challenge of the increasing antibiotic resistance in enteric fever is a worldwide concern, and should be taken into account when choosing empiric treatment in suspected imported cases from Pakistan. In this case, it is advisable to start treatment with carbapenems and de-escalate according to antibiogram. It is expected that we encounter more XDR imported S. typhi in our area.
THE RATE OF INFECTIONS IN NEWBORNS FROM HIV-INFECTED MOTHERS

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Title of Case(s): The incidence of neonatal sepsis varies according to the literature data from 0.77 to 30 per 1000 live births.

Background: 54 newborns from 52 HIV positive mothers admitted in the HIV department during 2017-2019 were analyzed. Based on clinical signs, biological markers and positive blood culture diagnosis of neonatal sepsis was established. 12 mothers have been detected HIV positive during pregnancy or at birth, 40 mothers were known positive before pregnancy being on antiretroviral treatment. HIV infection was vertically transmitted in 2 cases.

Case Presentation Summary: Hepatitis B associated infection was present in 5 cases, one case was detected with hepatitis C virus and two mothers were diagnosed with syphilis. 9 cases had normal vaginal delivery. Newborns from the B and treponema infected group received specific therapy: hepatitis B vaccine and immunoglobulin; penicillin. Regarding bacterial infection - 46 newborns were classified as sepsis. Germs isolated during this period were Staphylococcus aureus (omphalitis - 4), enterobacter aerogenes (omphalitis - 1), enterococcus spp (omphalitis - 1, urinary - 1), Klebsiella (blood culture and otor - 1, omphalitis - 1). The antibiotics used were penicillin (2), Ampicillin (37) associated with gentamicin (24), cephalosporin (9), meropenem (8) associated with vancomycin (3), colistin (1). There were no deaths during this period.

Learning Points/Discussion: In our compartment rate of infections in newborns seems to be higher than the literature, possible as overreacting interpretation of clinical signs and biological markers. Furthermore microbiologically documented are only 9 cases. Omphalitis was the frequent localization of infection. All children delivered normal and more than half delivered by cesarean section showed signs of infection and needed antibiotic treatment; however, the use of antibiotics is still exaggerated.
THE ASSOCIATION OF HIV STAGE AND VIRAL LOAD AND THE DEVELOPMENT OF HIV-RELATED CARDIOMYOPATHY IN PERINATALLY HIV TRANSMITTED CHILDREN

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Background: Follow-up examination was conducted at the National Research Center of Virology and the Republican Center of AIDS in the years 2010-2017. The purpose of the study was to determine the association between the HIV stage and the viral load in children born HIV positive from HIV infected mothers on cardiomyopathy development. The HIV duration was over 3 years and all the patients were on antiretroviral therapy.

Methods: 187 consecutive children (mean age 5.6±3.6 years, 105 male and 82 female) born HIV positive were included in a prospective study cohort. HIV infection was detected by the ELISA method following by Western Blot confirmation. Viral load was determined by PCR (concentration of HIV RNA virus per 1 ml blood). Heart function was studied by ECG and echocardiography, and in 34(18.2%) children cardiomyopathy was detected.

Results: In 6(3.2%) children viral load was <50copies/ml, <1000 copies/ml were in 18(9.6%) kids, 1,000-10,000 copies/ml were in 31(16.6%), 10,000-100,000 copies/ml in 29(15.5%), 100,000-500,000 copies/ml in 34 (18.2%), 500,000-1million copies/ml in 39(20.9%) children, and >1million copies/ml were in 30(16.0) cases. Viral load was positively related to cardiomyopathy development, r=0.177, p=0.008, accounting 3.1% of total variance. A linear regression analysis between viral load and cardiomuopathy development was significant, F(1,185) =5.96, p=0.016, t=2.44. The 95%CI for the slope was 0.008 to 0.072. However, HIV stage did not show statistically significant difference, r=0.112, p=0.063.

Conclusions: The HIV viral load was positively associated and predicted the development of cardiomyopathy in children with perinatal HIV transmission in kids at least 3 years of age. Future studies are needed to determine if the decrease of the viral load on antiretroviral therapy (e.g. medication adherence, comorbidities, therapy) would be associated with the decreased incidence of heart disturbances in children.
Background: *Candida* species are the most common cause of systemic fungal infections in children. Risk factors for candidaemia vary in different patient populations, posing challenges for clinical prediction of infection. Characterising the local epidemiology of candidaemia is essential for directing therapy for prophylaxis and treatment to improve patient outcomes. In this retrospective audit, we describe the epidemiology of candidaemia in a tertiary centre, focusing on the role of prior colonisation as a risk factor.

Methods: We retrospectively reviewed the case notes of all children aged 18 years or less, with a positive blood culture with *Candida spp.* over a 16-year period at the Royal Children’s Hospital, Melbourne (2002–2018). Laboratory databases identified positive blood cultures. Clinical data on patient demographics, *Candida spp.*, antifungal susceptibility, prior colonisation with *Candida spp.*, and treatment outcome were collected.

Results: There were 139 episodes of candidaemia in 124 children. Predisposing factors included presence of central venous catheter (93.5%), prior antibiotic exposure (86.3%) and parenteral nutrition (43.2%). Colonisation with *Candida spp.* (30-days prior) occurred in 39.6% of episodes, 60.0% of these were the same species causing candidaemia. Of the 463 children admitted to the oncology ward with positive *Candida spp.* stool samples, 22 (4.8%, 95%CI 3.0–7.1%) developed candidaemia. Antifungal resistance was rare. 30-day mortality was 11.4% and risk factors for mortality were male sex, liver disease and mucositis.

Conclusions: Antifungal resistance remains low at our institution, however, with resistance emerging, ongoing surveillance for resistant strains remains important to guide antifungal therapy. Our retrospective study suggests that prior colonisation may be an important risk factor, however, this should be validated in large prospective studies. Further areas of study could include evaluating the role of pre-emptive antifungal therapy in colonised patients.
MEASLES CLINICAL PRESENTATION AND COMPLICATIONS DURING AN OUTBREAK IN BULGARIA IN 2019.

P. Velikov
Specialized Hospital for Active Treatment of Infectious and Parasitic Diseases "Prof. Ivan Kirov", First Childrens Department, Sofia, Bulgaria

Background: Measles is caused by one of the most contagious viruses known to man. Almost every infections is manifested clinically and frequently leads to serious complications. The aim of the present study is to review the clinical presentation and complications of measles during an outbreak in 2019 in Bulgaria.

Methods: Between February and August 2019 in our Institution, a total of 290 cases of children aged between 0 and 12 were hospitalized with measles and verified through IgM antibodies and/or through molecular confirmation for the presence of the virus. The prospective study analyzes the data, using Jamovi.

Results: 149 cases are male, 141 cases are female. The clinical presentation and complications can be seen in the following table:

<table>
<thead>
<tr>
<th>Symptom</th>
<th>&lt;13 m. (n=82)</th>
<th>1-3 y. (n=67)</th>
<th>4-12 y. (n=141)</th>
<th>Total (n=290)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rash</td>
<td>79</td>
<td>66</td>
<td>139</td>
<td>284</td>
</tr>
<tr>
<td>Pharingitis</td>
<td>75</td>
<td>60</td>
<td>131</td>
<td>266</td>
</tr>
<tr>
<td>Cough</td>
<td>71</td>
<td>62</td>
<td>128</td>
<td>261</td>
</tr>
<tr>
<td>Conjunctivities</td>
<td>72</td>
<td>58</td>
<td>124</td>
<td>254</td>
</tr>
<tr>
<td>Fever</td>
<td>70</td>
<td>46</td>
<td>82</td>
<td>198</td>
</tr>
<tr>
<td>Koplik’s spots</td>
<td>55</td>
<td>46</td>
<td>95</td>
<td>196</td>
</tr>
<tr>
<td>Coryza</td>
<td>50</td>
<td>39</td>
<td>80</td>
<td>169</td>
</tr>
<tr>
<td>Fatigue</td>
<td>41</td>
<td>31</td>
<td>66</td>
<td>138</td>
</tr>
<tr>
<td>Decrease in appetite</td>
<td>38</td>
<td>30</td>
<td>47</td>
<td>115</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>54</td>
<td>48</td>
<td>90</td>
<td>179</td>
</tr>
<tr>
<td>Vomitting</td>
<td>22</td>
<td>21</td>
<td>68</td>
<td>111</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>15</td>
<td>17</td>
<td>49</td>
<td>81</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>12</td>
<td>5</td>
<td>14</td>
<td>31</td>
</tr>
<tr>
<td>Otitis media</td>
<td>2</td>
<td>4</td>
<td>0</td>
<td>6</td>
</tr>
</tbody>
</table>
**Conclusions:** Our data shows that generally clinical manifestations during the outbreak in Bulgaria correspond to those, described in literature, regardless of the age group. High febrility was noted more frequently in younger patients – 85.4% (<13 m.) vs. 58.1% (4-12 y.). In regards to complications, vomiting was noted more frequently in older patients (4-12 y. 48.2%); bronchitis is more frequently noted in older children (4-12 y. 34.7%), while pneumonia is more frequently seen in younger patients (<13 m. 14.6%).

**Clinical Trial Registration:** This is not a controlled trial.
MEASLES EPIDEMIOLOGY DURING AN OUTBREAK IN BULGARIA IN 2019

P. Velikov
Specialized Hospital for Active Treatment of Infectious and Parasitic Diseases "Prof. Ivan Kirov", First Childrens Department, Sofia, Bulgaria

Background: Measles is caused by one of the most contagious viruses. Almost every infections is manifested clinically and frequently leads to serious complications. The aim of the present study is to review the epidemiology, incl. immunization status and first contact with the measles virus of cases during an outbreak in Bulgaria in 2019.

Methods: Between February and August 2019 in our Institution, a total of 290 cases of children aged between 0 and 12 were hospitalized with measles and verified through IgM antibodies and/or through molecular confirmation for the presence of the virus. The prospective study was performed though a questionnaire for family members of the patients. Data is analyzed using Jamovi.

Results: 149 cases are male, 141 cases are female. The immunization status of the patients can be seen below:

<table>
<thead>
<tr>
<th>Category</th>
<th>&lt;13 m. (n=82)</th>
<th>1-3 y. (n=67)</th>
<th>4-12 y. (n=141)</th>
<th>Total (n=290)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not immunized</td>
<td>82</td>
<td>35</td>
<td>45</td>
<td>162</td>
</tr>
<tr>
<td>Unknown</td>
<td>NA</td>
<td>13</td>
<td>59</td>
<td>72</td>
</tr>
<tr>
<td>1 dose of MMR</td>
<td>NA</td>
<td>9</td>
<td>22</td>
<td>31</td>
</tr>
</tbody>
</table>

In regards to the initial infection, in 68 cases this occurred through contact with a family member, while in 47 of the cases this occurred during a visit to a healthcare facility, incl. hospitalizations. For the remaining 174 cases, the first contact with the virus is unknown.

Conclusions: Measles affects primarily individuals who have not been immunized or who have unclear immunization status (89.3%). This leads to the necessity for implementation of further practices, aiming at increasing the procentage of immunized individuals in Bulgaria, as well as the need for easier information sharing between clinical physicians and general practitioners. A significant number of hospital-acquired infections (16.2%) was noted. This requires further evaluation of the methods for infection control in regards to highly contagious diseases.

Clinical Trial Registration: This is not a controlled trial.
EFFECTS OF CO-INFECTION WITH RESPIRATORY SYNCYTIAL VIRUS AND INFLUENZA A VIRUS ON VIRAL LOAD AND LUNG FUNCTION IN THE MOUSE MODEL

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Background: Respiratory syncytial virus (RSV) and influenza A virus (IAV) are responsible for many respiratory infections in children and are often detected as co-pathogens. To determine how co-infection with both viruses affects pathogenesis, we established a mouse model using RSV strain A2 and mouse-adapted IAV (PR8).

Methods: Mice were intranasally inoculated with either RSV, IAV, or with both viruses (RSV+IAV and IAV+RSV) administered sequentially 24 hours apart. Mouse body weight and survival were monitored. On days 3 and 7 post-infection (pi), lung, spleen and thymus were collected and weighed. Lung viral loads were measured. Lung function was evaluated using forced oscillation technique.

Results: Mortality rate in the IAV+RSV group was 50%. Body weight was significantly reduced in the IAV+RSV group compared to uninfected mice, Figure 1.

![Graph showing survival rate and body weight changes in co-infected mice](image)

Figure 1. Survival rate and body weight changes in co-infected mice

Mice were infected with RSV A2, IAV PR8, or one after the other at 24 hours interval (IAV+RSV and RSV+IAV) and monitored for (a) survival and (b) body weight for 7 days. Mice inoculated with PBS served as control. Values are mean ± SEM (in percentages) of the daily weight divided by the starting weight for each mouse. Survival data was derived from 2 independent experiments (n=6 mice per group). Body weight data was derived from 5 independent experiments (n=18 mice per group). Student’s T test was used for statistical analysis. Asterisks denote significant differences between the control and experimental groups; (*) p < 0.05, (**) p < 0.005.

Significant enlargement of lung and atrophy of the thymus and spleen were noticed in all infected mice except those infected with RSV alone. On day 3 pi, IAV viral loads in the lungs of the co-infected groups were much lower compared to the IAV alone group. However, on day 7 pi, IAV viral load was much higher in IAV+RSV group in comparison to IAV alone group. On day 3 pi, RSV showed a reverse trend with much higher titers in co-infected groups than RSV alone group. On day 7 pi, RSV clearance was observed in the IAV+RSV but not in RSV+IAV group. Impaired lung function was evident in both co-infected groups as demonstrated by increased airway resistance and reduced thoracic compliance.

Conclusions: In this model, infection with IAV followed by RSV promotes IAV replication and leads to severe morbidity and increased mortality. Moreover, infection with IAV prior to RSV results in early RSV
clearance.  
**Clinical Trial Registration:** Not applicable
THE ASSOCIATION BETWEEN PREGNANT WOMEN ADHERENCE TO ANTIRETROVIRAL THERAPY AND GIVING BIRTH TO AN HIV POSITIVE CHILD

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¹Tashkent Medical Academy, Department Of Infectious And Paediatric Infectious Diseases, Tashkent, Uzbekistan, ²Tashkent Medical Academy, Cardiology And Internal Medicine, Tashkent, Uzbekistan

Background: High adherence to the therapy is highly associated with decreased mortality and morbidity, improve outcomes, and decrease complications and disabilities. The purpose of the study was to determine the prediction of the mother’s adherence to antiretroviral therapy (ARVT) and giving birth to the HIV positive child. In 2007-2017, 148 HIV-positive pregnant women who were delivering babies at the National Specialized Center of Pediatrics, were included in the study cohort.

Methods: HIV infection was detected by the ELISA method following by Western Blot confirmation. The viral load was determined by PCR (concentration of HIV RNA virus per 1 ml blood). Among 148 women, 38 did not receive ARVT (all gave birth to HIV-positive child), 26 had low adherence (5(19.2%) HIV positive babies and 84 had high adherence (7(8.3%) babies were HIV-positive).

Results: The one-way ANOVA was conducted to evaluate the relationship between pregnant women ARVT adherence and giving birth to the HIV-positive child was significant, F(2,145)=157.09, p<0.001. The strength of the relationship was strong (r=0.779), accounting for 60.7% of the total variance. Follow-up tests were conducted to evaluate pairwise differences among the means. There was a significant difference between the group that did not receive ARVT therapy and groups with high and low adherence (p<0.001 for both associations), but no significant differences between low and high adherence groups (p=0.170).

Conclusions: Our findings suggest that the absence of ARVT therapy is the strong independent predictor of giving birth to HIV positive children from HIV positive mothers (vertical transmission). However, there was no statistically significant difference between low and high adherence to the ARVT. Possible confounding factors such as viral load, the severity of immunodeficiency, or the HIV stage may influence the results.
THE CHOICE OF OPTIMAL DELIVERY METHOD IN THE HIV POSITIVE PREGNANT WOMEN TO DECREASE MOTHER-TO-CHILD HIV TRANSMISSION IN UZBEKISTAN, MONOCENTRAL STUDY

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Tashkent Medical Academy, Department Of Infectious And Paediatric Infectious Diseases, Tashkent, Uzbekistan

Background: The choice of the optimal and safe delivery method is one of the key elements to reduce the risk of HIV mother-to-child vertical transmission. Most authors consider elective cesarean section (ECS) performed up to 38 weeks of gestation prior to the labor after informed consent) as the most acceptable choice. This is the first study to determine the association of the delivery method with the risk of mother-to-child HIV transmission.

Methods: In 2007-2017, 148 HIV-positive pregnant women delivering babies at the National Specialized Scientific-Practical Center of Pediatrics, were included in the study cohort. In 130(33.8%) women ECS was performed, and 18 women gave birth naturally. HIV infection was detected by the ELISA and Western Blot, PCR for viral load. Among 130 women undergoing C-section, 42(32.3%) children were HIV-positive compared to 8/18 women with a natural delivery.

Results: Natural birth was 1.37 times as likely to be associated with HIV-infected children as those who gave birth through ECS (RR=1.37). Vaginal delivery was positively related to HIV transmission, but not statistically significant, r=0.084, p=0.311. It suggests that the delivery method is shared only 0.007% of the total variance (HIV vertical transmission). These results may be explained that ECS was advised to the women with a higher HIV viral load in blood, and vaginal delivery was performed in 8/18 (44.4%) women with the viral load less than 10,000 copies/ml.

Conclusions: The type of delivery method in HIV pregnant women did not show a statistically significant difference in the mother to child HIV transmission. HIV viral load, antiretroviral therapy during pregnancy, HIV stage and the severity of immunodepression were the major factors influencing the preference of the delivery method, which were taken into consideration prior to any suggestions, as well as the pregnant women's choice and consent.
Background: There is not much information about the health of children travelling internationally. The aim of this study was to make a post-travel evaluation of the children who had received pre-travel medical advice in our centre.

Methods: A post-trip phone survey was applied to parents of under 18-years-old, who had been on a pre-travel consultation in 2018 in our hospital.

Results: There were 111 answers (241 travellers). The mean age was 8.0 years (1M-17Y). The most common visited continent was Africa (37.9%), 51.4% for tourism and 39.6% to visit friends and relatives. Vaccines were prescribed in 91%: only 3 weren’t vaccinated. 83.8% always drank from bottled water; 71.2% always avoided potentially dangerous food/drinks; 81.0% reported to always/almost always use mosquito repellent; 82.0% always/almost always used sunscreen. Sixteen (14.4%) children presented ≥1 symptom: fever (9), diarrhoea (4) and earache (3). Six of them received medical attention during the trip; 6 after returning.

Conclusions: A large number of children followed the recommendations. Very few had complications that could be associated with travelling. Parental education and counselling are central to a safe trip and post-travel surveys are important to assess the flaws and difficulties of travellers.
VACCINE HESITANCY ON THE INTERNET FOR GREEK-SPEAKING USERS

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¹University of Crete Medical School, Department Of Paediatrics, Heraklion Crete, Greece, ²University of Crete, Paediatrics, Heraklion, Greece

**Background:** The wide use of internet worldwide has had a profound effect on the diffusion of vaccine skepticism. Little is known on the content of vaccine-related websites on the internet for non-English users. The aim of this study was to investigate the content, means, accessibility and extent of dissemination of vaccine hesitancy through the internet for Greek-speaking users.

**Methods:** Web search through Google search engine and YouTube for Greek websites and videos with content that promotes vaccine hesitancy was performed.

**Results:** From a total of 27 websites, 33% contain original articles, while 67% reproduce articles from foreign websites. MMR and influenza vaccines are most commonly criticized (18.5%), followed by DTP (11%) and Hepatitis B (7.5%). The majority of webpages (81.5%) express opinions against all vaccines, 78% claim that vaccines contain dangerous ingredients, with aluminum and thiomersal being the most commonly cited. Average anti-vaccine YouTube videos views are higher than videos promoting vaccination (p=0.005) and have longer mean duration. Eighty-nine percent of videos state that vaccines cause serious diseases or even death.

**Conclusions:** Vaccine hesitancy on the internet for Greek and English-speaking users share similar characteristics in terms of content and means of expression. It is important to understand the current challenges that vaccine criticism poses both globally and at national level in order to address them.
Title of Case(s): Kawasaki disease in children - case presentation

Background: Kawasaki disease on child is a complex of symptoms that are based on an autoimmune determinant mechanism, characterized by inflammation of small and medium arterial vessels, prolonged febrile syndrome, inflammatory syndrome and multisystemic disorder: cutaneous-mucosal, cardiovascular, hematological, gastrointestinal, hepatic and renal. Cases with coronary artery disease are severe, with risk of complications and even death in the absence of proper treatment.

Case Presentation Summary: In this paper we present the case of a female child, aged 2 years admitted to our clinic, with the diagnosis of Kawasaki disease. At admission, we observed, a febrile child, with pale teguments, without eruptive elements, with conjunctival hyperemia, depapilated tongue, intensely congestive pharynx, laterocervical adenopathy, with no cardiorespiratory and digestive symptoms, but with hepatosplenomegaly. Laboratory investigations initially showed leukocytosis with neutrophils, inflammatory syndrome present, liver cytolysis syndrome. Initially, the ultrasound of the heart was within normal limits, and at 6 days after admission, she had bilateral coronary aneurysm dilatations. In evolution, the laboratory investigations highlighted thrombocytosis, regression liver cytolysis syndrome, hypochromic anemia. Under treatment with human i.v immunoglobulins and platelet antiaggregant, evolution was favorable with improvement of symptoms and general status, but with persistent thrombocytosis and anemia as well as coronary aneurysm dilatation. At cardiac ultrasound, coronary aneurysm dilations were diminished.

Learning Points/Discussion: The presented case, highlights a rare, but severe, pediatric condition when characteristic vasculitis affects the coronary arteries. The early treatment instituted did not prevent the installation of coronary aneurysms but the patient had rapidly favorable evolution. Treatment with platelet antiaggregant was continued and at 30 days after discharge the clinical examination and laboratory investigations were within normal limits, and the heart ultrasound showed a discrete dilatation at both coronary arteries.
BURDEN AND EPIDEMIOLOGICAL CHARACTERISTICS OF INFECTIOUS DISEASES AMONG REFUGEE CHILDREN PRESENTING AT A TERTIARY CARE CHILDREN’S HOSPITAL IN ATHENS, GREECE

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Background: Concerns about communicable disease risks associated with the high influx of refugees in Europe have been raised in the past few years. Greece is the country of first arrival in Europe. Data regarding infectious diseases (IDs) among refugee children are limited. We aimed to determine the burden of IDs among refugee children presenting at a tertiary care children’s hospital in Athens, Greece.

Methods: We retrospectively recorded and evaluated children (0-16 years) that presented to the Emergency Department and admitted in the general Paediatric wards during a 22-month period (03/2016-12/2017).

[RESULTS] A total of 2601 children (males 51.2%, n=1313) were examined. Most of them were infants (28.7%, n=746) and the main country of origin was Syria (44.1%, n=1146). Most of the visits were due to infectious diseases (78.2%, n=2029) and the main reason for admission was fever (51.3%, n=1334).

Results:

<table>
<thead>
<tr>
<th>Category</th>
<th>Percentage</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>URTis</td>
<td>30.4</td>
<td>28.4</td>
</tr>
<tr>
<td>LRTis</td>
<td>29.2</td>
<td>19.7</td>
</tr>
<tr>
<td>GTis</td>
<td>32.1</td>
<td>14.1</td>
</tr>
<tr>
<td>Skin infections</td>
<td>26.6</td>
<td>26.6</td>
</tr>
<tr>
<td>VPDs</td>
<td>33.7</td>
<td>29.2</td>
</tr>
<tr>
<td>UTIs</td>
<td>20.4</td>
<td>19.7</td>
</tr>
</tbody>
</table>

The commonest site of infection among non-hospitalized children was the upper respiratory tract (40.4%, n=1052). Vaccine preventable diseases (VPDs) were more frequent in year 2016 (7.5%; varicella n=70, hepatitis A n=20, measles n=6) than in 2017 (3.1%; varicella n=34, hepatitis A n=5, measles n=2) (p<0.001); children coming from Afghanistan were mainly diagnosed with VPDs (31.4%, n=43) (p<0.001). Infants and toddlers suffered mostly from lower respiratory tract infections (42.1%, n=122 & 32.1%, n=93 respectively, p<0.001) while preschoolers and school-age children/adolescents from skin infections (23.6%, n=21 & 33.7%, n=30 respectively, p<0.001). A case of active
tuberculosis and a case of brucellosis were recorded. A percent of 1.7% was diagnosed with parasitic infections (scabies n=20, cutaneous leishmaniasis n=4, oxyuriasis n=20).

**Conclusions:** Hospitalization rate was 25.9%(n=673) and median duration of hospitalization was 3 days(IQR: 2-5days). Infants were more frequently hospitalized(34.8%,n=216)(p<0.001) and for longer period(p<0.001). The commonest site of infection among hospitalized children was the lower respiratory tract(53.4%,n=155), followed by the urinary tract(44.3%,n=31). **[CONCLUSION]** Refugee children suffer from common and often vaccine preventable IDs. The risk of importation of rare and serious infectious diseases in Europe appears to be very low.
BACKGROUND: Carbapenem-resistant Enterobacteriaceae (CRE) have been classified as a critical threat by the World Health Organization (WHO) and an urgent threat by the Centers for Disease Control and Prevention (CDC). Rapid detection of CRE is needed to inform appropriate treatment. However, conventional methods of detection such as disk diffusion, broth micro-dilution and E-test can take up to 24 hours. While molecular detection methods such as PCR can decrease the turnaround time to a few hours, its typically laboratory based and/or require specialist equipment and expert users. The purpose of this study was to develop a rapid and sensitive detection tool, without the need for expensive equipment or expertise, in order to be suitable for point-of-care testing in low resource settings.

METHODS: Our approach utilized recombinase polymerase amplification (RPA) with lateral-flow detection (LFD) and was piloted for detection of \( \text{bla}^{\text{NDM-type}} \) carbapenemases. In brief, primers and probes were designed for sensitive and specific detection of NDM-encoding genes. The analytical sensitivity was determined by testing serial dilutions of plasmid harbouring \( \text{NDM} \) gene with known copy. The analytical specificity was determined by blindly testing 40 carbapenemase (e.g. NDM, KPC, OXA, VIM and IMP) and non-carbapenemase DNA extracts from previously characterized clinical samples.

RESULTS: The turnaround time for the developed assay was approximately 20 minutes. The limit of detection reached to 4.51 copies/µl for \( \text{bla}^{\text{NDM-type}} \). The sensitivity and specificity of the assay was 93.3% (14/15) and 100% (25/25) respectively.

CONCLUSIONS: This study demonstrates the effectiveness of RPA-based technology for providing rapid, sensitive and specific detection of \( \text{bla}^{\text{NDM-type}} \) gene. Combining the technology with the lateral-flow detection promotes a key advantage of this approach to make it suitable for point-of-care testing in low resource settings.

CLINICAL TRIAL REGISTRATION: No clinical trial have been conducted. Its a basic science study
EVALUATION OF THE IMPLEMENTATION OF ANTIMICROBIAL STEWARDSHIP MEASURES IN THE NEONATAL UNIT

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Background: Antimicrobial stewardship measures promote the rational use of antibiotics, including the creation of protocols avoiding their prolonged or unnecessary use. The main objective was to evaluate the changes in the admission rate, duration of antibiotic therapy and complementary tests done after the update of the protocol of early-onset neonatal sepsis in our hospital. The secondary objective was to detect derived complications.

Methods: Retrospective study of review of medical records since January 2019, date of protocol introduction that includes the elevation of the C-reactive protein cut-off point, the use of blood/CSF bacterial PCRs, and the different duration of empirical antibiotic therapy according to the evolution. Measures taken in case the previous protocol had been applied were analyzed. Definitions: meningitis (altered CSF), confirmed sepsis (positive blood culture or PCR), clinical/analytical sepsis (clinical or analytical alteration with negative microbiology).

Results: 227 neonates were included, 57.3% male. 45 admitted, 58.1% symptomatic. All blood cultures were negative, 5 with positive PCR. LP was performed in 25 (58%): in 2 the bacteria was isolated by PCR, 2 presented pleocytosis, no culture positivity. The average duration of antibiotherapy was 18 days (SD 7.13) in meningitis, 9.3 (SD 1.15) in confirmed sepsis and 5.03 (SD 1.5) in clinical/analytical sepsis. After applying the old protocol, we observed a 15% admission reduction, with 52.8% less LP, and a 2 days antibiotherapy reduction.

Conclusions: The implementation of this early-onset neonatal sepsis protocol has meant a reduction in the number of admissions, LP performance and duration of antibiotic therapy, as well as a reduction in hospital stay. The establishment of bacterial PCRs has allowed us to determine the causative microorganism in 14% of cases. After 1 year, there are no complications observed due to its application.
ARE INFANTS WITH SUSPECTED SEPSIS RECEIVING THE FIRST DOSE OF ANTIBIOTICS ON TIME?

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Background: Sepsis is associated with an increase in morbidity and mortality. Hence, the early administration of antibiotics is crucial in septic patients. The aim of this prospective study was to assess whether intravenous third generation cephalosporins are being administered within the golden hour in infants aged up to three months with suspected sepsis, as outlined in the paediatric sepsis six guidelines.

Methods: A representative sample of 80 infants aged up to 3 months who were admitted to hospital for a septic screen was recruited. The time from diagnosis to actual initiation of a third generation cephalosporin was noted from each infant’s treatment chart and medical records. The interval time between diagnosis and administration of antibiotics was then calculated. Student t-test was used to compare differences between antibiotic administration times.

Results: The study was carried out from July 2019 to January 2020. Of the 80 recruited infants (50 males, 30 females) with a mean age of 60 days (95% CI 54.2 - 66.5), 28% (23/80) were admitted in December. The average time of antibiotic administration was 139.6 minutes (95% CI 122.2 - 157.0) from sepsis diagnosis. Only eleven infants received antibiotics in the first hour (mean 39.6 minutes; 95% CI 30.0-49.2) compared to 69 infants who received antibiotics at a mean of 155.6 minutes (95% CI 138.2 - 172.9; p=<0.00001).

Conclusions: This study shows that although intravenous third generation cephalosporins are being administered to infants whenever sepsis is suspected, the paediatric sepsis six guidelines of administering antibiotics within the golden hour are still not being adhered to. Hence, there is the need for healthcare staff to recognise how important it is not to delay antibiotic administration in infants with suspected sepsis.
INVESTIGATIONS INTO VIRAL AND NASOPHARYNGEAL MICROBIOTA PROFILES DURING LOWER RTI IN CHILDREN AND THEIR ASSOCIATION WITH CLINICAL SYMPTOMS.

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Background: Lower respiratory tract infections (RTI) are a leading cause of death and morbidity in children, mainly as a result of infection-associated bronchiolitis and pneumonia. However, scientific research continues to provide insights into the pathogenesis of these diseases. Aim: To investigate viral / nasopharyngeal microbiota profiles and their possible association with the severity of clinical symptoms during lower RTI in children.

Methods: Data was collected from a prospective cohort of children (one month up to 5 years of age), presenting with fever and cough at the emergency departments (ED) of 7 hospitals in The Netherlands. Nasopharyngeal washes were analysed by semi-quantitative realtime PCR of respiratory viruses and Nanopore Sequencing to establish bacterial microbiota profiles. Viral and microbiota data was compared with clinical data at presentation.

Results: Viral and microbiota profile data was obtained from 158 and 68 children, respectively. Combined data was available for 59 children. Viral pathogens identifies included rhinovirus (40%), respiratory syncytial virus (25%), adenovirus and human metapneumovirus (both 13%). Bacterial pathogens included most frequently Moraxella spp., Haemophilus spp. and Streptococcus spp. Bocavirus cases had a higher severe initial presentation (73%) compared to the complete population (57%). Prolonged disease course was observed in 22% of all cases, but in a higher frequency observed in LRTI associated with Mycoplasma spp. (50%) and human coronavirus (43%).

Conclusions: This preliminary study provides insights into the pathogens associated with lower RTI in children with an emphasis on their role in the severity of disease. The early identification of such pathogens may be helpful in guiding treatment strategies during ED visits by children suffering from lower RTI.

Clinical Trial Registration: Netherlands Trial Register, NTR5326.
SEROPROTECTION RATES IN CHILDREN WITH JUVENILE IDEOPATHIC ARTHRITIS TREATED ANTI-RHEUMATIC DRUGS

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Background: Vaccination of children with juvenile ideopathic arthritis (JIA) remains a problem for pediatricians because many patients receive immunosuppressive therapy. Scientists discuss efficacy, immunogenicity and safety of vaccines for these patients nowadays. We studied an effect of anti-rheumatic drugs on the antibody response to vaccines.

Methods: We analyzed 158 blood serum of children (aged >6 years) with JIA received vaccines according to national guidelines (at least 1 dose for live vaccines, 3 dose for hepatitis B and 4 dose for diphtheria). There were two group of patients. The first group had children (101/158; 63.9%) under a wide range of immunosuppressive therapies at least 6 months (including glucocorticoids, methotrexate and biological disease-modifying anti-rheumatic drugs). The second group (control) had patients (57/158; 36.1%) without therapy. We used an enzyme immunoassay to detect an antigen-specific antibody concentration (IgG) to measles, rubella, mumps, hepatitis B and diphtheria.

Results: Seroprotection rates against these infections were higher in the control group than in children under immunosuppressive therapies (table).

<table>
<thead>
<tr>
<th></th>
<th>Measles (≥0.18 IU/ml)</th>
<th>Mumps (≥1,0)</th>
<th>Hepatitis B (≥10 mIU/ml)</th>
<th>Diphtheria (≥0.03 IUP/ml)</th>
<th>Rubella (≥25 IU/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Received anti-rheumatic drugs (101/158; 63.9%)</td>
<td>0.39±0.08*</td>
<td>3.12±0.24</td>
<td>45.89±12.45</td>
<td>0.2±0.03*</td>
<td>86.37±6.78*</td>
</tr>
<tr>
<td>Number of patients with non-protective antibody level (n; %)</td>
<td>50/101; 49.5%</td>
<td>20/101; 19.8%</td>
<td>49/101; 48.5%</td>
<td>23/101; 22.8%</td>
<td>18/101; 17.8%</td>
</tr>
<tr>
<td>Control (57/158; 36.1%)</td>
<td>0.85±0.19*</td>
<td>3.13±0.3</td>
<td>48.45±16.46</td>
<td>0.34±0.0*</td>
<td>122.13±8.59*</td>
</tr>
<tr>
<td>Number of patients with</td>
<td>17/57; 29.8%</td>
<td>10/57; 17.5%</td>
<td>34/57; 59.6%</td>
<td>5/57; 8.8%</td>
<td>0/57</td>
</tr>
</tbody>
</table>

* p < 0.05 compared to control group.
<table>
<thead>
<tr>
<th>non-protective antibody level (n; %)</th>
</tr>
</thead>
</table>

* - $p<0.05$ (Mann-Whitney test)

**Conclusions:** Patients treated with immunosuppressive drugs had significantly lower average antibody concentration against all infection. Number of patients with non-protective antibody titre to measles vaccination was 1.7 times less in the 1st group than in control. Further the vaccination schedule for these patients will be made up.

**Clinical Trial Registration:** Not registered
TRANSFER OF VACCINE-INDUCED ANTIBODIES VIA AMNIOTIC FLUID AS A POSSIBLE MECHANISM OF PROTECTION FOR MATERNAL VACCINATION AGAINST PERTUSSIS


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Background: Maternal immunization has emerged as an effective intervention to prevent infectious disease in the newborn. Antigen-specific neutralizing antibodies have been characterized in amniotic fluid, but it is not known if vaccine-induced antibodies exist in amniotic fluid. The relative antibody levels of different maternal and neonatal compartments and their role in maternal vaccination are unknown. We investigated whether vaccine-induced antibodies against pertussis are transferred to the amniotic fluid and whether they correlate with other compartments: maternal serum, cord blood and breast milk.

Methods: Amniotic fluid was collected at birth from a subset of 15 mothers (9 vaccinated, 6 controls) in an open-label, parallel, randomized controlled trial of maternal pertussis vaccination. Vaccine-specific antibodies were measured in amniotic fluid, cord blood, maternal serum and breast milk using a multiplex immunoassay.

Results: Pertussis-specific amniotic fluid IgG antibody titers were higher in vaccinated mothers compared to controls against Ptx (1.5 EU/ml 95% CI 0.93-2.0 vs 1.0 EU/ml 95% CI 0.58-1.6, p=0.55), FHA (4.9 EU/ml 95% CI 4.3-6.4 vs 1.1 EU/ml 95% CI 0.61-1.5, p=0.02) and PrN (5.2 EU/ml 95% CI 1.8-20.1 vs 1.9 EU/ml 95% CI 0.77-3.2, p=0.09). The correlation between amniotic fluid Prn-specific antibodies and Prn antibodies in other compartments was $r_s$ 0.84 (p<0.01) in maternal blood, $r_s$ 0.83 (p<0.001) in cord blood, and $r_s$ 0.64 (p<0.17) in breast milk.

Conclusions: Vaccine-induced antibodies are transferred to the amniotic fluid and correlate across different maternal and neonatal compartments. This study was limited by small sample size and warrants further exploration in future maternal vaccine trials. We present amniotic fluid antibodies conferred by maternal vaccines as a previously overlooked mechanism of infant protection against respiratory pathogens in the first weeks of life.

Clinical Trial Registration: EudraCT 2012-004006-9
Background: According to the Epidemiology National Center, there were over 300 children diagnosed with tuberculosis in Spain. The objective of this study was to describe children diagnosed with tuberculosis between 2007 and 2017 in a secondary hospital.

Methods: After the Ethics Committee approval, information was obtained from medical histories. We evaluated: home country, age, diagnostic tests, presence of household contact/index-case, symptoms, presence of overcrowding, treatment and adverse events.

Results: We retrieved 20 cases, 60% males, median of age: 72mo (IQR: 16-165mo), 11/20 had a known index-case, 13/20 were foreigners/foreign born-nationals. Most common symptoms: persistent cough under 24mo, and fever without source and unspecific respiratory infection over 24mo. We found one case of miliary tuberculosis with meningoencephalitis and choroiditis, three pleural diseases and one tuberculous lymphadenitis. The most frequent therapy was isoniazid, rifampin, pyrazinamide and ethambutol. No drug-resistance to isoniazid was documented. 2/20 had severe events: one paradoxical reaction that required hospitalization and steroids, and one acute hepatitis that needed pediatric intensive care and therapy changes.

Conclusions: Due to our small sample, inferences couldn't be made. Tuberculin skin-testing is a valuable diagnostic tool and should always be included in diagnostic algorithms, and more specifically when we are confronting unspecific symptoms such as persistent cough. A close follow-up is of great importance to discern adverse events.
STENOTROPHOMONAS MALTOPHILIA: THE PATIENT ENEMY

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Background: *Stenotrophomonas maltophilia* is an aerobic nonfermentative gram-negative bacillus. Despite its low virulence, it may cause severe opportunistic infections, particularly in Critical Care and Haematology Oncology Units. Prevalence is increasing in the last years due to a higher survival rate and invasive procedures performed in chronic complex patients. Central catheters and prolonged use of broad-spectrum antibiotics are well-known risk factors for infection.

Methods: Retrospective review of clinical and epidemiologic features of patients under 18 years-old with isolation of *S. maltophilia* in an hemoculture from January 2013 to December 2019 in a tertiary hospital. Identification and isolation were performed in Microbiology Department. Data were obtained from electronic clinical records and collected in an anonymized database. Statistical analysis was performed with SPSS Statistics version 25.

Results: We found 14 *S. maltophilia* bacteremias. There were 12 children under 24 months (85%) and 8 females (57%) at Critical Care Unit, because of post-operative of cardiac surgery(7), airway or lung disease(4), septic shock in oncologic patients(2), and bacterial meningitis(1). Clinical presentation was sepsis in 13 patients (93%) and 1 endocarditis. All of them carried central catheters and had received prolonged broad-spectrum antibiotics. Previous colonization in tracheal aspirate was present in 4 patients (28%). All strains were sensitive to trimethoprim-sulfamethoxazole and fluoroquinolones except for 1 indeterminate sensitivity to levofloxacin.

Conclusions: *S. maltophilia* bacteremia may be suspected in patients with central lines that had received broad-spectrum antibiotics. Early appropriate antibiotic treatment and removal of devices may influence the prognosis, as only 1 patient resolved the bacteremia without taking out the central line and in 1 patient, the bacteremia relapsed one month later. Treatment was trimethoprim-sulfamethoxazole for 15 days and 3 patients required combination with fluoroquinolones. Mortality rate was 28%.
VIABILITY OF CHILDREN BORN BY CESAREAN SECTION: IS IT LESS OR HIGH.

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\textbf{Background:} Babies born by caesarean section (CS) may have abnormal immunity, because CS usually is done at 38 week of gestation and it is well known that the fetus receives mean amount of maternal IgG from 38 to 40 weeks of gestation. Therefore they are more sensitive to infections. Our aim was to compare the morbidity of children was borne via CS and natural delivery and hospitalized during any time of infancy to Muratsan University Hospital Complex ICU.

\textbf{Methods:} A retrospective study was done in the Intensive Care Unit of Muratsan university hospital. We examined data of patients admitted from November of 2016 to August of 2017. Our research includes 121 medical charts. Inclusion criterion was age up to 28 days and exclusion criterion- fatal outcome. We filled questionnaires and then compared particularity of diseases depending on delivery type.

\textbf{Results:} The vast majority of patients 89(73.55\%) of 121 had respiratory tract infection, among them by CS was born 32(26.44\%), by vaginal delivery 69(57\%) and there is no data about delivery type of 20(16.52\%). The average age of infants delivered by CS was 3 months, mean length of stay were 12 days (max48, min1), mean gestation age-34 week average. The average age of hospitalized infants was born by vaginal delivery was 5.5 months, average length of stay were 8.3 (max24, min1) and mean gestation age-39 week.

\textbf{Conclusions:} As we suspected, Infants delivered by Cesarean Section compared to vaginal delivery have greater tendency to get infections in much more early period of life (3 month vs 5.5) and needed a longer duration of hospitalization (12 days vs 8.3). We suggest to be more careful with decision to do CS and avoid it if there are not strong indications.
A COMMON BUT DEADLY CAUSE OF RED EYES

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¹KK Women’s and Children’s Hospital, Paediatric Medicine, Singapore, Singapore, ²KK Women’s and Children’s Hospital, Paediatrics, Infectious Disease Service, Singapore, Singapore, ³Kandang Kerbau Women and Children's Hospital, Infectious Disease Service, Department Of Paediatric Medicine, Singapore, Singapore

Title of Case(s): A common but deadly cause of red eyes

Background: Adenovirus infection is a common viral illness in childhood. It is usually self-limiting in immunocompetent patients. However, it can cause significant morbidity and mortality in immunocompromised patients with multi-organ failure. Known risk factors for disseminated adenovirus infection include child less than 2 years old, chronic heart or lung diseases, genetic or metabolic diseases and immunodeficiency.

Case Presentation Summary: An immunocompetent 2.5 year old boy presented with 5 days of fever, red eyes, cough and rhinorrhea. Nasopharyngeal swab was positive for adenovirus. In view of persistent fever and increasing oxygen requirement, he was started on intravenous antibiotics for secondary bacterial pneumonia. However, he developed acute respiratory distress syndrome and required intubation and mechanical ventilation with lung protective strategy. During his admission to critical care unit, he had recurrent seizures. Cerebral spinal fluid and blood were positive for adenovirus via PCR testing. His condition was also complicated by septic shock and liver dysfunction. He was treated with one dose of intravenous cidofovir with probenecid for disseminated adenovirus infection. He responded well and his adenovirus PCR viral load was on a downward trend prior to extubation. He did not have any side effects from cidofovir infusion. Immunological evaluation did not reveal any significant abnormalities. He developed bronchiolitis obliterans and required prolonged hospitalization. His condition eventually improved and discharged with nocturnal oxygen supplement.

Learning Points/Discussion: Disseminated adenovirus infection is not common in immunocompetent children. Although there is a lack of evidence to guide cidofovir use in this group of patients, this case highlights the efficacy of cidofovir for disseminated adenovirus infection in an immunocompetent child. Further studies are required to evaluate the effectiveness and side effect profile of cidofovir for immunocompetent children.
M. Rigkos
National Health Center-General Hospital-Mental Institution of Leros, Microbiology Laboratory, Lakki, Greece

Title of Case(s): Case report of malaria in a refugee boy from the Reception and Identification Centre of Leros island, Greece, in July 2019

Background: Malaria is an endemic disease of tropical and paratropical countries, caused by protozoan parasites of *Plasmodium spp* and transmitted to humans by the female mosquito of the genus *Anopheles*. Although malaria has been eradicated in Greece many decades ago, there are new incidents associated with growing numbers of refugees coming from endemic places. This is a report of the first incident of malaria for the island of Leros, since the arrival of first refugees in 2015.

Case Presentation Summary: A young Somalian male from the refugee camp of the isle of Leros presented to the National Health Center-General Hospital-Mental Institution of Leros, mentioning afternoon fever, dysuria, myalgia and asthenia since a week. Clinical examination revealed high temperature, the ultrasound showed splenomegaly and the blood tests showed thrombocytopenia, moderate anemia, high CRP and hyponatremia. Malaria rapid immunochromatographic diagnostic test proved positive for non-falciparum *Plasmodium*. Microscopy revealed intraerythrocytic parasitic forms (mostly at the stage of schizont) characteristic for *Plasmodium vivax*, while the reticulocytes were within normal range. To confirm diagnosis, blood samples were sent to the National Malaria Reference Center of Greece, proceeding to multiplex PCR, which proved positive for *Plasmodium vivax*, while G6PD test was normal. After ten days of treatment with atovaquone/proguanil hydrochloride and doxycycline, patient's condition improved and he was discharged.

Learning Points/Discussion: Malaria is a severe and potentially fatal disease, making prompt diagnosis and treatment crucial. Even though malaria, since WW2, is not endemic in Greece anymore, the massive increase in traveling and immigration from endemic regions has resulted in growing numbers of sporadic incidents, especially among refugees hosted in the hotspots of Greek islands. Thus, increased vigilance and alertness among both clinical and laboratory doctors in health institutions is very important.
CORD BLOOD PRODUCES HIGHER AMOUNTS OF PRO-INFLAMMATORY CYTOKINES AFTER EXPOSURE TO SEPSIS-RELATED BACTERIA COMPARED TO ADULT BLOOD

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Laboratory of Pediatrics, Division of Pediatric Infectious Diseases and Immunology, Erasmus Mc - Sophia Children’s Hospital, Rotterdam, Netherlands

Background: Newborns are more susceptible to severe bacterial infections, such as sepsis, compared to adults. While an imbalanced inflammatory response is assumed to contribute to sepsis-induced morbidity and mortality in newborns, limited data is present to substantiate this hypothesis. In addition, insights into the cytokine response during neonatal sepsis could lead to targeted immune therapy. We therefore assessed the cytokine production of newborn blood upon exposure to sepsis-related bacteria.

Methods: Cord blood was derived from the placenta of cesarean sections with a gestational age from 37 to 42 weeks. Adult blood was derived from healthy adults. Cord (N=8) or adult (N=10) whole blood was incubated in vitro with E. coli, S. aureus, group B streptococcus and coagulase-negative staphylococci (CNS) at increasing concentrations. After 6 hours, the supernatant was removed and the amount of pro-inflammatory cytokines, such as tumor necrosis factor (TNF) and interleukin-6 (IL-6) was determined using enzyme-linked immunosorbent assay.

Results: E. coli induced higher amounts of IL-6 compared to S. aureus, GBS and CNS, whereas TNF was comparably induced by all bacteria. The production of TNF and IL-6 after exposure to E. coli or CNS was comparable between cord and adult blood. Interestingly, the production of TNF and IL-6 after exposure to GBS or S. aureus was significantly higher in cord blood compared to adult blood.
**Conclusions:** Our data shows that the production of TNF and IL-6 after exposure to bacteria is intact or even higher in cord blood compared to adults. Clinically, these high inflammatory responses could lead to inflammatory damage and could, thereby, contribute to the detrimental outcome of neonatal sepsis. Future research should further elucidate the induction of other cytokines by newborns, which could aid the development of targeted immunotherapy.

**Clinical Trial Registration:** Clinical trial registration: not applicable
Background:  Typhoid is a systemic illness with a high burden in low and middle income settings. In countries where improvements in hygiene and sanitation remain a challenge, vaccinations can be effective in disease prevention. TyVAC-Nepal is an ongoing double blinded randomized controlled trial taking place in Lalitpur, Nepal, which aims to determine the efficacy of a typhoid conjugate vaccine in children <16 years, to inform policymakers about vaccine introduction. Passive surveillance is being conducted to follow all febrile vaccinees and capture typhoid fever cases. The objective of this analysis is to describe the clinical presentations of study participants attending fever clinics.

Methods:  In a phase III trial, children aged 9 months to <16 years of age were individually randomized to either receive the typhoid conjugate vaccine (TCV) or a capsular group A meningococcal conjugate vaccine as a control. As a part of passive surveillance, 19 clinics were set up in a tertiary level hospital and the community. Febrile clinic attendees with fever ≥2 days, or a presenting temperature of ≥38°C were followed. Information recorded includes age and sex, presenting complaint, investigations and diagnosis.

Results:  Clinics started in November 2017, with attendance ongoing. Total 20,021 children were vaccinated and there were 11,217 clinic attendances over a one year period; 7,552 of these being study participants. There were 2005 febrile study participants (26.5%) out of whom 31 children developed culture positive typhoid fever. The mean age of febrile children was 4.7 years and there were 1,082 (53.9%) males. Data are currently being collected, cleaned, analyzed, and prepared for presentation.

Conclusions: Understanding attendee demographics, will help inform service planning. Clinics may be better adapted according to need and current public engagement and educational activities may be better targeted.

Clinical Trial Registration:  Trial Registration Number :ISRCTN43385161
DECREASED PROTECTION AGAINST MEASLES FOLLOWING A SINGLE DOSE OF MMR VACCINE IN CHILDREN WITH OLIGO-ARTICULAR JIA ON METHOTREXATE TREATMENT - A PROSPECTIVE CONTROLLED STUDY

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P.&A.Kyriakou Children's Hospital, Second Department Of Paediatrics, National And Kapodistrian University Of Athens, Athens, Greece

**Background:** Juvenile idiopathic arthritis (JIA), the most common paediatric rheumatic disease, renders patients susceptible to infections, including vaccine-preventable ones, due to their perturbing immunity and immunosuppressive treatment received. Data regarding response and long-term immunological memory to specific vaccines are limited. We aimed to determine the immune status against measles in children with oligo-articular JIA previously vaccinated with one dose of MMR, prior to commencement of methotrexate (MTX) treatment and at one and two years under treatment.

**Methods:** This was a prospective-controlled study including 54 oligo-JIA patients and 26 healthy controls. Seroprotection rates and measles-specific-IgG titers were measured by ELISA and expressed as GMCs. A second dose of the MMR vaccine was administered in all participants with non-protevtive antibody titers at 24 months-provided JIA patients were in clinical remission. Repeat vaccine-specific-IgG titers were measured six months post immunization.

**Results:** The two groups had similar demographic characteristics and immunization status. Although seroprotection rates decreased proportionally over time in both groups, they were significantly lower in the JIA-group at two years (p=0.04). Mean measles-IgG-antibodies were significantly lower in the JIA compared to the control group at one (p=0.036) and two (p<0.01) years' follow-up. Disease duration before MTX initiation, disease activity (JADAS-10), type of JIA, prior NSAIDs/steroids use, presence of uveitis or ANA-positivity didn't correlate to low seroprotection rates or enhanced antibody loss. Five patients and two controls with undetected measles-specific-IgG-antibodies at two years received a second MMR-dose and mounted a satisfactory antibody response; no adverse events/JIA-flare were reported.

**Conclusions:** Although seroprotection rates were similar between the two groups, measles-specific-IgG-titers were significantly lower in the oligo-JIA group after two years on MTX treatment. Further studies are required to address the question of long-term immunity conveyed by immunizations given at an early stage in children with rheumatic diseases on immunomodulating treatment and to assess the need for booster doses to subjects at risk.
COVARIATES OF AMIKACIN DISPOSITION IN A LARGE PEDIATRIC ONCOLOGY COHORT

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Background: The aminoglycoside amikacin is often used in children with neutropenic fever. It is a hydrophobic compound, displaying a concentration dependent efficacy, while the trough level is associated with toxicity. Amikacin pharmacokinetics (PK) in children displays large variability due to maturational and disease-related covariates. The aim of the current study was to explore amikacin PK in a large pediatric oncology cohort, taking into account within-patient changes.

Methods: Clinical data and amikacin therapeutic drug monitoring (TDM) observations were collected retrospectively from children with oncology diagnosis receiving amikacin as part of empiric therapy during febrile neutropenia episodes. Individual amikacin PK parameters were calculated using a one-compartment model with instantaneous input and first-order output. To explore covariates of clearance (Cl) and volume of distribution (Vd), linear mixed models were used, modelling a random effect for patient to account for clustering due to repeated measurements.

Results: Based on 188 amikacin treatment episodes in 114 patients, median (interquartile range) amikacin Cl was 1.37 (1.05; 2.46) L/h and Vd 7.98 (5.66; 12.73) L. Height and creatinemia were significant covariates for Cl (marginal R\textsuperscript{2} 71.1%), while weight, height and creatinemia determined Vd (marginal R\textsuperscript{2} 59.5%). Positive blood culture, oncology diagnosis and nephrotoxic chemotherapy were not retained as significant covariates.

Conclusions: We described extensive variability of amikacin PK in a large cohort of pediatric oncology patients, taking into account within-patient changes across treatment episodes. Maturational covariates and creatinemia determined amikacin Cl and Vd, while primary non-maturational covariates were not significant. Our observations, based on combined clinical and PK data in children with a specific disease condition, can be useful to feed dosing software programs. As a next step, prospective integrated PK/PD (pharmacodynamics) research is needed to optimize amikacin exposure.
EPIDEMIOLOGY OF FEBRILE SEIZURES IN THE CZECH REPUBLIC

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Background: Febrile seizures are the most common neurological disorder in childhood, affecting 2–5% of children. Febrile seizures are defined as seizures in association with a febrile illness occurring in child between 6 months and 5 years in the absence of a central nervous system infection. "The less is more" approach is endorsed in 2018 febrile seizures guideline from Czech-Society of Child Neurology. Epidemiology of febrile seizures in the Czech Republic has been unknown so far.

Methods: The analyses used for this epidemiologic survey were based on data managed by the Institute of Health Information and Statistics of the Czech Republic (IHIS CR). The primary database used was the National Register of Reimbursed Health Services (NRRHS). This database contains data from health insurance companies from both inpatient and outpatient facilities, including complete data on billed diagnoses, procedures and treatments currently available for 2010-2018.

Results: In average between 2012-2018 there were 2838 new patients with febrile seizures annually in the Czech Republic. In survey period, 27 130 unique patients with febrile seizures were treated. This cohort was used for detailed management-oriented analyses. The table shows changes in diagnostic methods use.

<table>
<thead>
<tr>
<th></th>
<th>2010</th>
<th>2018</th>
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<tbody>
<tr>
<td>EEG (% of patients)</td>
<td>40,8</td>
<td>33</td>
</tr>
<tr>
<td>Fundoscopy (% of patients)</td>
<td>19,4</td>
<td>7,6</td>
</tr>
<tr>
<td>Diazepam prophylaxis( % of patients)</td>
<td>49,1</td>
<td>32,1</td>
</tr>
<tr>
<td>Laboratory methods (% of patients)</td>
<td>30,8</td>
<td>42,7</td>
</tr>
</tbody>
</table>

Conclusions: Detailed epidemiology of febrile seizures and it's trends since 2010 in the Czech Republic were described. The prevalence and incidence were stable with no major changes. The decrease of use of EEG, fundoscopy and diazepam prophylaxis was apparent in last 2-3 years. Recent febrile seizures clinical practise guideline from Czech Society of Child Neurology could have positively influenced resource use.
THE STATE OF THE POPULATION OF PLASMOCYTOID DENDRITIC CELLS AGAINST THE BACKGROUND OF VARIOUS TYPES OF ANTIVIRAL THERAPY FOR CHRONIC HEPATITIS C IN CHILDREN.

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**Background:** Treatment of HCV in children is a multi-faceted, complex issue that requires additional study. Nowadays, treatment with interferon drugs (IFN) is not recommended, due to its insufficient effectiveness with a large number of side effects. The new treatment with direct-acting antiviral drugs (DAAD) in pediatrics is limited by age. At the same time, the problem of the impact of antiviral therapy (AT) on the child's immune system has been studied very little. Plasmocytoid dendritic cells (pDCs) specialize in instant production of IFN in response to virus. In this regard, the study of the effect of AT on pDCs in children with HCV is very relevant.

**Methods:** 11 people received IFN therapy, and 4 people-DAAD. Children were examined during treatment and at the end of it. IFN production in pDCs was determined by ELISA with cell stimulation.

**Results:** In patients examined against the background of IFN drugs, IFN- genesis in pDCs is higher than in the group without AT (492.6±228.8 and 134.4±27.2; p<0.0001). In patients who have used of DAAD, the production of IFN in pDCs was significantly lower than in the group receiving IFN (p=0.05) and lower than in patients without AT. Regardless of the type of therapy, at the time of its termination, the production of IFN in pDCs falls, remaining minimal, but higher than in the group of healthy (p=0.03; p<0.0001).

**Conclusions:** Changes of IFN in pDCs depends on the type of therapy and are multi directional. The sharply stimulating effect of the IFN function of pDCs with IFN preparations and its absence on the background of the use of DAAD were demonstrated. Further study of the effect of different types of AT on pDCs indicators will be possible in connection with the expected resolution of DAAD in children under 12.

**Clinical Trial Registration:** Not registration
DIPTHERIA IN INCOMPLETE VACCINATION CHILD

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Title of Case(s): Stridor in incomplete vaccination child

Background: Diphtheria is a potentially fatal, toxin-mediated, infectious disease of children caused by Corynebacterium diphtheriae, which may cause obstructive pseudo-membranes in the upper respiratory tract or damage to the myocardium and other tissues. Pediatric diphtheria is associated with myocarditis in 10–16.5% of cases. It is a preventable disease via vaccination. The child get high risk of infection when they have incomplete vaccination especially DPT

Case Presentation Summary: A 4-year-old girl presented with high fever, runny nose, frequently nonproductive cough, and fast breathing. It happened for 2 days, she developed gradually fast of breathing with noisy sound. She was 4th youngest child with previously healthy but incomplete vaccination DPT-Hep1-Hib1. On physical examination, she was very sick with moderate dyspnea, and stridor breathing sound, her bilateral tonsil swelling, erythema with the white patchy membrane. The cardiovascular and other system exam was normal. His initial lab revealed WBC:32.4x10⁹, ANC:26.2x10⁹, Hemoglobin:104g/L, Platelet:518x10⁹, CRP:196mg/dL, Throat swab (pending) Initially, he was diagnosed with severe Croup, treated with adrenaline nebulizer and Dexa IM. she still had a fever, dyspnea, and toxic appearance. After 48hours of throat swab culture, the result showed Corynebacterium Diphtheria. She was moved to the isolation room, promptly Erythromycin and Heart monitoring. The next day later she was afebrile, less stridor and no dyspnea. She was discharged home 5 days later without complication.

Learning Points/Discussion: Diphtheria is a preventable disease but highly mortality complication. In a child who has stridor with white patches tonsillitis and is Unvaccinated or incomplete vaccination should be considered diphtheria. In this case, the child got only one time of DTP vaccination and presented with white membrane tonsilitis. All children must have to complete all immunization in order to prevent life-threatening infectious diseases.
SYSTEMATIC LITERATURE REVIEW (SLR) ON ECONOMIC BURDEN AND QUALITY OF LIFE IN SELECTED SEQUELAE OF INVASIVE MENINGOCOCCAL DISEASE

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Background and Objective: Invasive meningococcal disease (IMD), a life-threatening disease caused by the bacteria Neisseria meningitides, primarily affects young children and adolescents. The objective of the review was to identify the economic burden and utilities of health-related quality of life of selected IMD sequelae.

Methods: Systematic literature reviews (SLRs) on utilities and economic burden of selected IMD sequelae were performed. Medline, Embase, NHS EED, HTA, and DARE databases were searched. Abstracts and full-texts were double screened (PICOS criteria), with extractions performed and quality checked.

Learning Points/Discussion: Summary: SLRs returned 7 publications reporting costs and resource use data for 10 IMD sequelae, with 2 publications reported utilities. Total direct costs of the sequelae in children were higher than in adults (Table 1). Cost of inpatient, outpatient care and rehabilitation in amentia/mental retardation and speech problems were higher in the 1st year than in subsequent years (€2,003 vs €82 and €1,921 vs €41, respectively). Total indirect cost of sequelae was €1,210/patient using friction capital approach, and €88,200/IMD survivor using human capital approach. Lifelong indirect medical costs due to neurological deficit in Spanish populations ranged from €1.18 million to €3.14 million. Utilities for mild hearing impairment and mental retardation in Canadian patients were better than utilities in patients with severe impairment (0.92 vs 0.86 for hearing impairment, 0.84 vs 0.59 for mental retardation). Utility of bilateral hearing impairment was lower than a unilateral (0.77 vs 0.89). Utility for neurological deficits among Dutch patients was 0.82. Implication: The SLRs revealed economic burden and utility data of IMD sequelae in children and adolescents. However, more studies are needed in this area to capture the true burdens of IMD.
<table>
<thead>
<tr>
<th>Sequelae</th>
<th>Aged 0-19 [Range]</th>
<th>Aged 20-&gt;80 [Range]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hearing impairment</td>
<td>Germany: €452,357 – €1,725,198 per age group</td>
<td>Germany: €18,272 – €364,455 per age group</td>
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<td></td>
<td>Brazil: $1.386 million over 17 years in children 0-1 years old</td>
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<tr>
<td>Cognitive impairment</td>
<td>Germany: €192,143 – €782,537 per age group</td>
<td>Germany: €9,886 - €235,228 per age group</td>
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<tr>
<td>Visual impairment</td>
<td>Germany: €3,400 – €15,065 per age group</td>
<td>Germany: €153 - €3,724 per age group</td>
</tr>
<tr>
<td>Skin scarring, skin</td>
<td>Germany: €9,058 - €42,320 per age group</td>
<td>Germany: €154 – €3,979 per age group</td>
</tr>
<tr>
<td>grafting, eczema</td>
<td>Brazil: $42,000 over 17 years in children 0-1 years old</td>
<td></td>
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<tr>
<td>Motor deficits</td>
<td>Germany: €41,185 - €119,337 per age group</td>
<td>Germany: €2,260 – €49,454 per age group</td>
</tr>
<tr>
<td></td>
<td>Brazil: $420,000 over 17 years in children 0-1 years old</td>
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<tr>
<td></td>
<td>France: €768,874 lifelong</td>
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<tr>
<td>Organ failure</td>
<td>Germany: €83,442 – €333,920 per age group</td>
<td>Germany: €4,521 – €104,334 per age group</td>
</tr>
<tr>
<td>Anxiety</td>
<td>Germany: €4,238 per IMD case</td>
<td>-</td>
</tr>
<tr>
<td>Seizures</td>
<td>Germany: €73,244 – €293,370 per age group</td>
<td>Germany: €3,764 – €349,433 per age group</td>
</tr>
<tr>
<td></td>
<td>Brazil: $252,000 over 17 years in children 0-1 years old</td>
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</table>
Background: Kawasaki Disease (KD) is an acute vasculitis of small and medium-sized vessels affecting mostly infants and young children. There is paucity of literature on Macrophage activation syndrome (MAS) in KD and virtually no studies from India. We herein review the clinical characteristics, laboratory profile, management and outcomes of patients with KD presented with MAS at tertiary care centre from North-West India.

Methods: We analyzed case records of 950 children with KD, registered between January 1994 - December 2019 at Pediatric Rheumatology Clinic, Advanced Paediatrics Centre, Postgraduate Institute of Medical Education and Research, Chandigarh, India. Medical records of the patients treated for KD and MAS in this period were reviewed. The demographics, clinical signs, laboratory values, coronary artery abnormalities, treatment and outcome of the patients having KD and MAS were noted.

Results: Of the 950 cases of KD, twelve (10 boys; 2 girls) (1.3%) children had MAS. The clinical characteristics and laboratory parameters are detailed in the table. The median age at diagnosis was 4 years (range: 9 months - 7.5 years). Coronary artery abnormalities were seen in five patients (45.4%). All patients received intravenous immunoglobulin (IVIg) – 2 g/kg as first-line therapy. Ten patients required additional therapy (methylprednisolone in eight; second dose IVIg in one; infliximab in four and cyclosporine in one). No mortality was noted in our cohort.
Conclusions: MAS is an unusual and under-recognized complication of KD. In our cohort of 950 patients of KD, 1.3% had developed MAS. KD with MAS is associated with significantly high levels of NT-ProBNP and an increased incidence of CAAs. There is a lack of standardized protocol for treatment of KD with MAS. In addition to IVIg, various agents like corticosteroids, cyclosporine A, cyclophosphamide, and biological drugs are used.
AETIOLOGY OF BACTERIAL MENINGITIS IN INFANTS AGED UNDER 90 DAYS: PROSPECTIVE SURVEILLANCE IN THE PAEDIATRIC HOSPITAL OF LUANDA, ANGOLA

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Background: Despite the availability of effective antibiotics and vaccines, bacterial meningitis (BM) remains a leading cause of high morbidity and mortality in young infants worldwide. The data for the aetiology and antibiotic susceptibility of BM are very limited in the Africa region. This study assessed the aetiology of BM in children <3 months of age in Luanda, the Angolan capital. The country launched conjugate vaccine against Haemophilus influenzae type b in 2006 and 13-valent pneumococcal vaccine in 2013.

Methods: We conducted a prospective, observational, single-site study from February 2016 to October 2017 in the Paediatric Hospital of Luanda and reviewed all cerebrospinal fluid samples (CSF) collected from infants aged <90 days with suspected BM or neonatal sepsis. The local laboratory performed microscopy, chemistry, culture and susceptibility testing; real-time polymerase chain reaction (PCR) of vaccine-preventable pathogens was performed in Johannesburg.

Results: Of the 1287 infants aged <90 days enrolled with CSF collected, 299 (23%) had confirmed or probable BM. 212 (16%) had bacteria detected: most commonly Klebsiella spp., Streptococcus pneumoniae, Streptococcus agalactiae, Escherichia coli, and Staphylococcus aureus (Figure). Of pneumococcus, 21% (3/14) had decreased susceptibility to penicillin, methicillin-resistant Staphylococcus aureus (MRSA) were encountered in 36% (4/11), and Gram-negative isolates resistant to gentamicin in 13% (6/45) and to third-generation cephalosporins in 34% (20/58). In infants with BM, the mortality rate was 20% (22/110).
Conclusions: We observed a high prevalence of BM among infants <90 days of age with suspicion of BM or sepsis in the Paediatric Hospital of Luanda. Gram-negative bacteria predominated and showed high rates of resistance to most commonly used antibiotics. Continued surveillance and evaluation of the antibiotic guidelines is needed for optimal therapy and to detect potential changes in the epidemiology of BM.
FROM COUGH TO CHRONIC HEPATITIS C: A 5-YEAR-OLD GIRL HOSPITAL COURSE

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¹Yerevan State Medical University after Mkhitar Heratsi, Infectious Diseases, Yerevan, Armenia, ²Yerevan State Medical University, Infectious Diseases, Yerevan, Armenia

Title of Case(s): From cough to chronic hepatitis C: a 5-year-old girl hospital course

Background: Liver disease due to chronic HCV infection generally progresses slowly in children, and cirrhosis and liver cancer occur infrequently. Although elevated serum aminotransferase levels are often noted, HCV-infected children younger than 3 years virtually never develop advanced liver disease. Direct-acting antiviral treatment is recommended for all children and adolescents with HCV infection aged ≥12 years. Our goal is to accent attention of pediatricians to possibility of infection with hepatitis C during medical care.

Case Presentation Summary: A 5-year-old girl presented to ICU on 16.12.2018, with dyspnea, cough and up to 40°C fever. According to clinical, laboratory and instrumental investigations the diagnosis of left lower lobe pneumonia was made. The next day thoracentesis was done. The cellular pathology corresponded to purulent inflammation.

25.12.2018-thoracoscopic decortication of left lung and pleural drainage was performed. 08.01.2019-thoracoscopic decortication and bronchoscopy was performed again. During hospitalisation polyetiological treatment with antibacterials, oseltamivir and fluconazole were administered.
19.01.2019- EBV(VCAIgM and IgG, EBNAIgG) was positive and PCR for parvovirus-B19-negative.
23.01.2019- the patient was discharged.
24.01.2019- the girl presented with cough and crackles. Left pleural space drainage was done. Azithromycin was started. 04.02.2019-discharge. 31.05.2019- the patient was admitted to hospital with fever, tachycardia, weakness and cough. History revealed that patient had urticaria during antibacterial treatment. EBV-VCA-IgM was positive(1,74S/CO;positive>1.00), ALT-58U/L, AST-56U/L, other liver function tests were normal. Elevation of liver enzymes persist 4 month. Anti-HCV-antibodies were positive, anti-HIV, HBsAg, HAV-IgM were negative.The diagnosis of chronic hepatitis C was made after HCV-positive PCR result.

Learning Points/Discussion: Patient history can be indicator for checking viral hepatitis. Although there is no evidence of source of virus, the long history of surgery is a risk for children to get hepatitis C and a reminder for pediatrician.
Title of Case(s): Kawasaki disease with atypical manifestation- acute febrile cholestatic hepatitis with jaundice. A case report.

Background: Kawasaki disease is a systemic vasculitis of unknown etiology. In most cases disease presents as self-limited acute febrile illness with additional characteristic signs. One of the main concerns is early diagnostics of disease because 20-25% of untreated children develop coronary artery abnormalities requiring lifelong follow-up. In rare cases Kawasaki disease manifests atypically, thereby delaying recognition and treatment. Acute febrile cholestatic hepatitis does not belong to the classic diagnostic criteria of Kawasaki disease but is important differential diagnosis in cases of acute hepatitis.

Case Presentation Summary: Boy (5 years old) was admitted to Children's Clinical Hospital with complains about spiking fever (>39.0°C), vomiting, diarrhoea. Fever was unresponsive to antipyretics. Objectively patient was presented with bilateral conjunctivitis, dry chapped lips, strawberry tongue, submandibular lymphadenopathy and jaundice. Liver edge was palpable 1.5 cm below the ribcage. Ultrasound of abdomen showed hepatomegaly with parapancreatic lymphadenopathy. Laboratory findings suggested bacterial infection of unknown origin (leukocytosis, thrombocytosis, CRP-117mg/L), with non-specific reactive hepatitis (ALAT-104.6U/L, total bilirubin 95.9 umol/L) and jaundice. Antibacterial treatment was initiated. After the re-evaluation of patients condition, there was high suspicion of Kawasaki disease. Additional therapy with Immunoglobulin and Aspirin was initiated. Echocardiography showed anatomically normal heart with maintained heart function. Other infectious causes of hepatitis were excluded. Received therapy with Immunoglobulin significantly improved patient’s condition and resolved jaundice.

Learning Points/Discussion: Kawasaki disease not always presents with classical signs and fulfills all the standard criteria for confirmation of diagnosis. In those rare cases the spectrum of differential diagnosis is wide, thereby delaying initial treatment. Kawasaki disease should be remembered as one of many differential diagnosis in cases of acute febrile cholestatic hepatitis with jaundice in order to initiate the necessary therapy timely and prevent possible complications, such as acquired heart disease.
Hospitalization for Acute Gastroenteritis in Children Under 5 Years in the Post-Vaccine Rotavirus Era: Preliminary Data

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¹Hospital São Luis Gonzaga, São Paulo, Brazil., Hospital Infection Control Service, São Paulo, Brazil,
²Santa Casa de São Paulo, Pediatric Infectious Diseases Unit, São Paulo, Brazil

Background: Acute gastroenteritis (AG) has been a major concern of public health in developing countries, leading to high morbidity and mortality in children. Rotavirus was the most common cause of hospitalizations associated with AG in children under 5 years before the vaccine introduction. Brazil had introduced rotavirus vaccine in the national immunization program in 2006. This study aimed to analyze the clinical findings and etiology of hospitalization for AG in children under 5 years after the introduction of the rotavirus vaccine.

Methods: A retrospective study, between January 2011 to December 2019, in Sentinel Hospital, located in São Paulo, Brazil. Only children under 5 years were selected. Were included only children who needed hospitalization or intravenous rehydration. All of them also had undergone routine tests to identify rotavirus (Elisa), norovirus (PCR) and Enteric pathogen (culture). Demographic, clinical characteristics and rotavirus vaccine were evaluated.

Results: 746 children with acute gastroenteritis were admitted: 60% were under 2 years. 214(30%) of them had a positive result for norovirus and 176(23%) for rotavirus. Co-infection by norovirus and rotavirus were present in 19 cases(2%). Overall, 338 children needed hospitalization, and 50% had received 2 doses of the vaccine. Rotavirus was more frequent in the winter, and norovirus had a peak over the summer. There was no difference in symptoms between norovirus and rotavirus. One rotavirus death occurred in a one-year-old child with Down syndrome.

Conclusions: After the rotavirus vaccine introduction, norovirus has been the main cause of hospitalization for acute gastroenteritis of children under 5 years. With the results of this study, we expect a vaccine development against norovirus. Certainly, the vaccine will have a potentially positive impact on reducing hospitalizations for acute gastroenteritis and also will reduce even more morbidity and mortality in young children.
CHOLESTATIC HEPATITIS A IN PEDIATRICS – A NOT SO COMMON PRESENTATION

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Title of Case(s): A Common Disease With An Uncommon Presentation

Background: Hepatitis A (HA) is an acute, usually self-limited liver infection, transmitted via the fecal-oral route. It is endemic in developing countries where infection is predominant in children. The clinical spectrum varies from asymptomatic to fulminant hepatitis, and most children under 6-years of age have no clinical manifestation. It can present with cholestasis, which accounts for a small number of these cases.

Case Presentation Summary: A four years old healthy female was admitted in the emergency department (ED) with a 2-day history of fever, headache and abdominal pain. Physical examination was unremarkable. Urine sample showed proteinuria and an elevated protein/creatinine ratio. Three days later, she was readmitted due to vomiting, the blood tests revealed a moderate elevation in liver enzymes and she was discharged with the indication to be reevaluated. One week later, she presented with jaundice and hepatomegaly; blood tests showed further elevation of liver enzymes, and increased biliary markers suggesting hepatic cholestasis. Abdominal ultrasonography showed hepatomegaly with a heterogeneous parenchyma and an enlarged gallbladder, without signs of cholelithiasis. She was admitted to the pediatric ward, treated with ursodeoxycholic acid and further investigation was consistent with hepatitis A.

Learning Points/Discussion: Only one third of the children with HA manifest with symptoms as fever, abdominal pain, vomiting and weight loss. Jaundice and mild hepatomegaly usually occur one week after symptoms’ onset. Conjugated bilirubin and aminotransferases return to normal within two to three months. The prognosis is excellent and treatment relies on supportive care. The authors expect to remind clinicians that HA is still prevalent even in developed countries. It has different forms of manifestation in children, being the cholestatic form, a rare one, occurring in about 5% of cases.
UNUSUAL CASES OF TUBERCULOUS MENINGITIS IN A PEDIATRIC INTENSIVE CARE UNIT

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AGHIA SOPHIA CHILDRENS’ HOSPITAL, Pediatric Intensive Care Unit, ATHENS, Greece

Title of Case(s): UNUSUAL CASES OF TUBERCULOUS MENINGITIS IN A PEDIATRIC INTENSIVE CARE UNIT

Background: Despite its low incidence, Tuberculous Meningitis (TBM) remains the most severe form of TB, especially in younger children. Early diagnosis is crucial since possible delay in diagnosis and therapy is associated with significant morbidity and mortality. The cornerstone for diagnosis remains the bacteriologic confirmation. However, due to disease’s paucibacillary nature and low accuracy of diagnostic tests this is often difficult.

Case Presentation Summary: We present two cases of TBM, admitted during 2019 in a single tertiary PICU in Athens. A 19-months girl with a 2-weeks history of fever and vomiting, presented with stupor, due to acute hydrocephalus. A ventricular drain was set. CSF analysis revealed mild leukocyttosis, normal protein and glucose. Chest CT scan showed mild lobar infiltrations. Extended testing for infections, as well as TST and CSF TB PCR were negative. She received wide-spectrum antibiotics, but soon after therapy she developed new onset of fever, visual impairment and tremor. A second CT scan revealed findings compatible with TB. The second case, a 11-months female infant vaccinated with BCG at birth and diagnosed with HHV-6 meningoencephalitis, was admitted due to seizures. Decreased CSF glucose raised suspicion of TBM. TST was positive, with negative IGRA’s. CT revealed hilar lymphadenopathy with concomitant pneumonitis. In both cases, family testing revealed parental active lung TB. Patients underwent bronchoscopy and MTb was isolated on BAL culture. After treatment they progressed gradual neurological recover.

Learning Points/Discussion: TB diagnosis remains challenging, despite technological advancements for Mtb detection, especially in children. Its subacute presentation, often causes delay in diagnosis and treatment, which is crucial to prevent adverse outcomes. It is essential for the clinicians to have a high degree of suspicion even in countries with lower incidence of the disease, and also in vaccinated infants of high-risk group.
CONGENITAL TOXOPLASMOSIS: A DIAGNOSIS CHALLENGE

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Title of Case(s): Congenital toxoplasmosis: a diagnosis challenge

Background: Congenital toxoplasmosis (CT) is unusual but can cause serious consequences. We reviewed all cases of confirmed CT in a tertiary hospital (2009-2019), according to the following criteria: detection of Toxoplasma gondii by PCR, presence of IgM/IgA antibodies, persistence of IgG beyond the first year or detection of newborn specific IgG (Western Blot). During the study period 55 infants born to mothers with seroconversion or IgM/low IgG avidity index during pregnancy were followed.

Case Presentation Summary: CT was ruled out in 46 after IgG negativization before 12 months (median time [IQR]: 4 months [3-6]). In this group, 26/26 had negative PCR results in blood and 3/3 negative Western Blot at birth. We found 9 infants with confirmed CT. Only 4 (44%) had been diagnosed by amniocentesis during pregnancy. Fetal ultrasound revealed abnormalities (hydrocephalus) in 2/9. At birth, Toxoplasma PCR resulted positive in 2/8 (25%) in CSF, 1/3 (33%) in urine and 0/6 in blood. IgM/IgA were positive in 6/9 (66%) and Western Blot in 2/3 (67%). 3 infants were diagnosed by persistence of IgG beyond 12 months. 55% (5/9) were symptomatic at birth: 4 ocular involvement, 2 intracranial calcifications, 2 hydrocephalus. 6/7 had hyperproteinorrachia (median [IQR]: 176 mg/dl [122-195]).

Learning Points/Discussion: CT is very unusual in our environment. Most cases are detected by maternal seroconversion with normal ultrasound findings. The low sensitivity of postnatal diagnostic tests hinders diagnosis after birth. All infants received pyrimethamine/sulfadiazine (median duration [IQR]: 363 days [330-458]). 4 developed neutropenia and 1 liver dysfunction. During follow up none developed chorioretinitis, 1 had epilepsy and 2 psychomotor delay (median of follow up [IQR]: 3 years [1.5-5]). Treatment should be implementing because improves prognosis, although half of infants develop neutropenia.
Title of Case(s): Generalize Exanthema a few days of birth

Background: Neonatal toxic shock syndrome, it rarely occurs in neonate if compare to adult and it caused by the bacterial superantigen, toxic shock syndrome toxin-1. It is a multisystem disease manifested by sudden onset of fever, chills, hypotension, and rash with desquamation, mental confusion, renal dysfunction, hepatic abnormalities, and thrombocytopenia. There are 5 categories for diagnosis and the treatment needs a combination of two antibiotics.

Case Presentation Summary: A 7 days old boy Prematurity, presented with poor sucking and poor activity for 5 days followed by skin exanthema and then develop peeling. On examination, he was floppy with moderate subcostal retraction. Skin a whole body with erythema and desquamation, the cardiovascular exam was bradycardia. Abdominal examination revealed 3cm hepatomegaly, otherwise, it is unremarkable. His initial lab revealed WBC: 3.5x10^9, ANC: 1.3x10^9, Hemoglobin: 137g/L, Platelet: 29x10^9, CRP: 165mg/dL, INR 1.6, APTT 42. CXR is normal. Blood Gas Metabolic Acidosis and Blood culture is pending. Initially, he was diagnosed with Neonatal sepsis, treated with Ceftriaxone, he developed shock, and got 3 times bolus of NSS and start to combine Inotrope dobutamine and adrenaline. His blood culture was Staphylococcus Aureus, he was stopped ceftriaxone and add Cloxacilline with Meropenem. Unfortunately, he got heart arrest and multiple Organs failures with no recovery after CPR 20 Minute.

Learning Points/Discussion: Neonatal toxic shock syndrome is rare to occur in neonate but high mortality, but should be considered if having 3 in 5 follow 5 categories in diagnosis such as (1) fever; (2) rash; (3) desquamation (1-2 wk after illness onset, involving palms and soles); (4) hypotension; and (5) evidence of multisystem involvement. The treatment must be a combination of Cloxacilline and Clindamycin, in this case, is 4 in 5 categories.
VARICELLA-VIRUS INFECTION TRIGGERING MILLER FISCHER’S SYNDROME IN AN OTHERWISE HEALTHY 6-YEAR OLD BOY

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Title of Case(s): Varicella-virus infection triggering Miller Fischer’s syndrome in an otherwise healthy 6-year old boy

Background: Miller Fisher’s syndrome (MFS) is a rare variant of Guillain Barre’s syndrome (GBS), characterized by the acute onset of ophthalmoplegia, ataxia and areflexia. MFS is highly associated with the presence of antibodies to GQ1b ganglioside (anti-GQ1b) in the acute phase. We report a case of MFS following a Varicella-zoster virus (VZV) infection in an otherwise healthy 6 year old child.

Case Presentation Summary: An otherwise healthy 6 year-old boy presented with acute diplopia, complaining also for frontal headache, photophobia and right ptosis during the last 24 hours. The initial physical examination revealed bilateral mydriasis. The deep tendon reflexes were normal as well as the rest of the clinical examination. An urgent brain Computed Tomography (CT) and brain CT venography did not reveal any abnormal findings. Further imaging with brain Magnetic Resonance Imaging (MRI) and Magnetic Resonance Angiography (MRA) revealed symmetric enhancement of the fifth cranial nerves bilaterally and clear enhancement of the right sixth nerve. A lumbar puncture was performed with normal findings, and no cytoalbuminologic dissociation. A nerve conduction study and electromyography revealed VI and V nerve dysfunction consistent with MFS. VZV IgM antibodies were positive by ELISA and anti–GQ1b antibodies were also positive strengthening the diagnosis of MFS. Under the working diagnosis of MFS, the patient was treated with Intravenous Immune Globulin (2gr/kg) with immediate clinical improvement.

Learning Points/Discussion: Our case report is the fourth in the literature presenting VZV as the antecedent factor in Miller Fischer’s syndrome. Campylobacter Jejuni has been reported as the most common antecedent agents for MFS. However, numerous infectious agents such as VZV have also been associated with the disease so far. Further case-control studies are needed in order to interpret the role of specific infectious agents.
CONFIRMED H1N1 INFLUENZA VIRUS CEREBELLITIS – MULTIFOCAL ENCEPHALITIS IN A PEDIATRIC PATIENT: FIRST CASE REPORT FROM GREECE.

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Title of Case(s): Confirmed H1N1 influenza virus cerebellitis – multifocal encephalitis in a pediatric patient: First case report from Greece.

Background: Influenza has long been associated with neurological manifestations, especially in children. The burden of influenza-associated neurological disease became more apparent after the Influenza A/H1N1 2009 pandemic when an increased frequency of neurological complications had been observed from cohorts among different pediatric populations worldwide.

Case Presentation Summary: A previously healthy 6-year-old boy was admitted because of progressively worsening ataxia, slurred speech and decreasing level of consciousness starting 24 hours before admission. The patient’s parents reported high-grade fever and flu-like symptoms with mild vomiting for 5 days. A lumbar puncture was performed, which revealed lymphocytic pleocytosis. A brain MRI showed the presence of increased signal T2W/FLAIR lesions on bilateral cerebellar hemispheres and left temporal lobe. Resting EEG presented generalized background slow-wave activity, indicative of a diffuse encephalopathic process. Molecular CSF analysis with a rapid multiplex PCR meningitis/encephalitis panel was negative, while a nasopharyngeal swab specimen tested positive for Influenza A/H1N1 pdm2009 strain. Molecular analysis for pdm2009 H1N1 RNA in CSF also yielded a positive result, directly confirming the diagnosis of H1N1pdm2009 CNS infection. The patient was treated with a 5-day-course of oral oseltamivir with the gradual improvement of his neurological status. Follow-up MRI imaging was suggestive of mild cerebellar atrophy, while the patient still exhibited mild learning and behavioral abnormalities 14 months post-discharge.

Learning Points/Discussion: Despite the increasing awareness regarding influenza-related neurological disorders, only a few cases with confirmed molecular detection of influenza in CSF samples are reported in the literature maintaining the hypothesis that these disorders most probably occur due to an inflammatory, cytokine-mediated response rather than direct invasion of the virus in the central nervous system. To our knowledge, this is the first reported case of molecularly confirmed H1N1 cerebellitis – multifocal encephalitis in Greece.
FACTORS CONTRIBUTING TO NON-COMPLIANCE WITH SURGICAL ANTIBIOTIC PROPHYLAXIS IN PEDIATRIC CARDIAC SURGERY PATIENTS

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Background: Perioperative antibiotic prophylaxis (AP) has proved to reduce Surgical Site Infections (SSI) in pediatric cardiac surgery patients, but adherence to International Guidelines remains low. Children with Congenital Heart Disease are often critically ill, requiring long hospitalization before surgery. The aim of this study was to identify the factors associated with low adherence to these guidelines and establish potential areas of improvement.

Methods: This is a retrospective observational study of pediatric patients that underwent cardiac surgery and admitted in a single tertiary Cardiac Intensive Care Unit (PCICU) in Athens, Greece from 01/01/2017 to 30/06/2018. Antimicrobial prophylaxis agent, duration, dose, dosing interval, and time appropriateness were studied in the patients’ group, while compliance was assessed according to Guidelines for Antibiotic Prophylaxis in Cardiac Surgery of ASHP.

Results: 79 patients were enrolled, with a median age of 5,3 months (IQR 1,6-63 months), with 64,6% of patients previously hospitalized. The mean adherence rate was 66,3% (SD=22,5%), with prolonged antibiotic prophylaxis documented in 65,8%. Factors associated with non-compliance (p<0,05) were the use of Cardio Pulmonary Bypass, postoperative mechanical ventilation and the need for re-operation. Duration of operation, longer use of Central Venous Catheter and length of stay (LOS) were also associated with lower adherence to the guidelines. Operation complexity (RACHS-1 score) was found to have significant negative correlation (p<0,100) to the compliance.

Conclusions: In this study, findings indicate low adherence to surgical prophylaxis guidelines in pediatric cardiac patients. Factors such as the severity of the Congenital Heart Disease and the cardiac surgical intervention appears to influence the adherence while previous antibiotic exposure or the presence of antibiotic resistant pathogens in patients’ colonization were not recognised as significant factors contributing in non compliance, in the critically ill patients.
Title of Case(s): Promoting Global Awareness of RSV Mortality: 3 million views within 24 hours

Background: RSV is the second cause of death in young children after malaria and 700 children die every day from RSV. More than 99% of these deaths occur in lower-income countries. However, in contrast to malaria these numbers are not sufficient for general RSV awareness. Several vaccines are in clinical development for RSV, but lack of awareness may hamper future vaccine uptake.

Case Presentation Summary: The aim of the mortality awareness campaign was to increase awareness on the global burden of RSV by having a short film viewed more than 100,000 times within 24 hours. Together with the independent RSV patient advisory board, we produced a video to put a face to this global health threat by sharing the story of a mother who lost her child to fatal RSV infection. Ethical approval was obtained, the consent process was reviewed by the legal department and a participant was recruited via the Child Health and Mortality Prevention Surveillance study (CHAMPS). The film was produced by a communication agency, Beyond Borders Media, with experience in health development aid. A communication plan was developed to identify the target population and create an action plan with content planning for the video launch.

Learning Points/Discussion: Social media analysis software registered 3,229,637 views and 353 messages within 24 hours. The video was shared by public health organizations such as the Bill & Melinda Gates Foundation as well as national radio, newspapers and television. A local viewing in Soweto was organized to reach approximately 450 people of the local population. The RSV mortality awareness campaign exceeded its goal with more than 3 million views within 24 hours. Sharing a personal story can be used to increase vaccine impact for diseases when awareness is lacking.
MELIOIDOSIS IN CHILDREN

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**Title of Case(s):** Dyspnea after playing in the water canal

**Background:** Melioidosis, caused by the soil saprophyte *Burkholderia pseudomallei*, is endemic in South-East Asia. Parotid abscess and suppurative parotitis are very common in Thailand and Cambodia where up to 40% of children present with a localized disease in the head and neck. The majority of infections are asymptomatic; however, in the susceptible host, the infection can result in overwhelming sepsis and death.

**Case Presentation Summary:** A 6-year-old boy presented with high fever, cough, dyspnea, and weakness for 3 days without vomiting or headache. Mum gave only paracetamol at home. He had a history of playing in the water canal 2 days before the symptoms started without associated choking or drowning. On examination, he had a fever, looked unwell with dyspnea and crackles on the left side. The cardiovascular exam was normal except tachycardia. An abdominal examination revealed 3cm hepatomegaly. His initial lab revealed WBC:12x 10⁹, ANC:5.4x10⁹, Hemoglobin:88g/L, Platelet:523x10⁹, Na:138mmol/L, K:3.4mmol/L, CRP:41mg/dL, ALT:32U/L, Negative Malaria, CXR showed left upper lobe density. He was diagnosed with bacterial pneumonia, treated with ceftriaxone. He was getting worse with dyspnea and continued high fever and was transferred to PICU. The second lab showed CRP 174mg/dL and worsen chest X-Ray. His blood culture reported positive Burkholderia Pseudomallei. Antibiotic therapy was changed to Meropenem. He developed septic shock and was intubated with inotrope infusion. Unfortunately, he died in PICU.

**Learning Points/Discussion:** Melioidosis commonly causes local infection with associated high mortality in bacteremia, it usually the following exposure to contaminated water in the endemic area. In this case, probably acquired the infection through near-drowning in drain water. In a child with prolonged fever, a history of water exposure and clinical toxicity Melioidosis must be considered. Delayed diagnosis and management can result in poor prognosis.
ANTIBIOTIC THERAPY ON THE PAEDIATRIC ENVIN-HELICS DATA BASE

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Background: Healthcare-associated infections (HAI) are a major public-health problem. The aim of this study is to compare the evolution of antibiotics used for HAI diagnosed in Paediatric Intensive Care Units (PICU) from the Spanish registry Paediatric-ENVIN-HELICS.

Methods: Multicentre, prospective and observational study of HAI diagnosed in 26 Spanish PICU, during a three-month period (April to June) of 2013–2019. The ENVIN diagnostic criteria adapted to paediatrics were used, based on CDC recommendations.

Results: Total number of patients 10469. Rate of antibiotics use 73%. Comparing 2019 with 2013, this rate decreased 5% (p>0.05). Eight PICU (30%) had Antimicrobial Stewardship Program (ASP) in 2019, compared with none in 2013 (p<0.001). Antibiotic stewardship was 18.6% higher (p<0.001). Early suspension antibiotic rate increased (3.9%, p<0.001). Antibiotic modifications due to side effects decreased (0.3%, p>0.05), as well as modifications due to resistances (0.1%, p>0.05). There was a decrease on meropenem use comparing with 2018: for HAI previous PICU admission of 5% (p>0.05) and for PICU HAI of 1.7% (p>0.05).

Conclusions: The rate of antibiotics use was high, but results showed a decreasing trend during 2019. The implementation of ASP probably has led to a better use of carbapenems for HAI, as well as to an increase of antibiotic de-escalation and early suspension rate. In 2019 there was a reduction on the modifications of the antibiotic regime due to adverse event, and also due to non-susceptible microorganisms.
DILI (DRUG INDUCED LIVER INJURY) IN A CHILD RECEIVING ANTITUBERCULAR MEDICATIONS: DILEMMA IN DIAGNOSIS AND MANAGEMENT.

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Title of Case(s): DILI (Drug induced liver injury) in a child receiving Antitubercular medications: Dilemma in diagnosis and management.

Background: A 15-year-old with background of Crohn’s disease being treated with infliximab and Azathioprine was diagnosed with pulmonary tuberculosis with significant weight loss, fever and night sweats. (QuantiFERON test negative prior to start of immunosuppressant had now turned positive) This was a challenge both in terms of diagnosis as well as management. Stopping the immunosuppressant would mean flare up of Crohns but if not stopped then risk of worsening TB.

Case Presentation Summary: Child was started on intensive phase of antitubercular therapy (ATT) after stopping his infliximab comprising of Rifampicin, Isoniazid, pyrazinamide and ethambutol. Liver functions(LFT) showed evidence of injury (elevated ALT levels >3 times the upper limit) by 4th week. ATT was stopped and gradually reintroduced after the recovery of LFT as per the BTS guidelines (British Thoracic Society). Cause of DILI was attributed to Isoniazid, Pyrazinamide. Child was hospitalised for phased re-introduction of drugs as the disease got worse and lost more weight. These included second line Amikacin, Clofazimine and Moxifloxacin. Patient also spiked fever, chest xray revealed military tuberculosis. Oral intake was a challenge for which parenteral route was chosen (Nasogastric). Difficulty at this point was to understand if symptoms were secondary to flare up of Tuberculosis or sensitivity to isoniazid which presents similarly with fever.

Learning Points/Discussion: DILI secondary to ATT remains a significant problem. New evidence include various mechanism of liver injury including the recent Isoniazid induced immune mediated injury which is rapid and fatal. Being a major component of ATT, this is hurdle to efficiently treat Tuberculosis world-wide. It is more common than is accounted for hence prior knowledge is important for early identification, management of DILI. This further improves efficacy and significantly reduces drug resistance secondary to poor compliance.
Background: Lumbar puncture is a valuable tool in the diagnosis of central nervous system infections. In the UK, LPs have been actually performed less frequently since the 1960s. Recommendations on when to obtain cerebrospinal fluid have been published, but it is unclear whether they are being followed. The aim of this study was to explore the opinions of paediatric trainees towards LPs.

Methods: A written questionnaire was compiled and data collected from 32 paediatric trainees (all levels of training). 25 questionnaires answered on a regional teaching day of the West Midlands Paediatric trainees and 7 obtained during a national study day (pilot study). A variety of questions was to measure how and when the paediatric trainees used the LP as a diagnostic tool.

Results: 23% of trainees were not sure whether LP is an acute diagnostic tool. Only one stated “not confident” with the technique. 31% believed that LP microscopy (cell count) remains accurate after 24 hours of IV antibiotics, whilst 21.8% correctly identified not. On average, they knew 3 LP contraindications. 10% stated reasons such as workload or night shifts which deter them from undertaking an acute LP. Only 15.6% would delay antibiotic administration in a stable patient to complete the septic screen.

Conclusions: Our study suggests that current recommendations are not being followed as many trainees have incorrect information regarding LP accuracy and would often defer or delay it. Empirical antibiotic treatment, can give falsely reassuring results, mislead or complicate decisions around length of antibiotic course. Our suggestion is the introduction of a simple low-cost LP pack and teaching sessions to increase awareness of the importance of a timely LP; aiming to improve the diagnosis and targeted management of CNS infections.
STOP, THINK SCORTCH: RE-THINKING THE TRADITIONAL ‘TORCH’ SCREEN IN AN ERA OF RE-EMERGING SYPHILIS

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Background and Objective: The epidemiology of congenital infections is ever changing, with a recent resurgence in syphilis infection rates. Testing modalities and investigations are often limited, leading to missed diagnostic opportunities. Identification of congenital infection is often delayed; early recognition of congenital infections remains the cornerstone of management and coordination of care, as perinatally acquired infections can be associated with significant long term sequelae if not recognised promptly.

Methods: The SCORTCH (Syphilis, Cytomegalovirus, Other, Rubella, Toxoplasmosis, Chickenpox, HSV and blood-borne viruses) acronym increases the awareness of clinicians to the increased risk of congenital syphilis, whilst considering other infectious aetiologies including: Zika, Chagas, Parvovirus, Enterovirus, HIV, Hepatitis B/C, and HTLV-1, in addition to the classic congenital infections recognised in the ‘TORCH screen’. The SCORTCH diagnostic approach describes common signs and symptoms present in infants with congenital infection, details serological testing for mother and infant, and important direct diagnostic testing.

Learning Points/Discussion: We advocate a low threshold of consideration for all possible antenatal infections given the consequences of failing to diagnose and treat perinatally-acquired infections early. The traditional ‘TORCH screen’ focuses on serology-specific investigations, which has the potential to omit important direct diagnostic testing of the infant, and fails to consider emerging/re-emerging congenital infections. In recognition of syphilis as a re-emerging pathogen and the overlapping clinical presentations of various other infectious aetiologies, we advocate for a broader outlook, investigating congenital infections utilising the SCORTCH approach. Our SCORTCH tool utilises a multimodality strategy for investigations by including radiology, ophthalmology, audiology, microbiology, and histology, as well as highly effective molecular techniques. This toolkit and associated educational materials aims to serve as an important model for educating medical professionals in the recognition of all congenital infections and rationalise the diagnostic approach.
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EPIDEMIOLOGY AND CLINICAL CHARACTERISTICS OF KAWASAKI DISEASE IN CYPRUS

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Background: Kawasaki disease (KD) is one of the most common vasculitides of early childhood. Diagnosis depends on clinical criteria. Without treatment, it is a self-limited condition which however, may result into a high frequency of complications mainly from the coronary vessels. There are no previous studies on KD in Cyprus. This is a retrospective study on the epidemiology and clinical characteristics of Kawasaki disease in the Cyprus population.

Methods: This is a retrospective study of all patients less than 15 years of age, diagnosed with typical and atypical Kawasaki Disease and admitted to major hospitals in Cyprus, between January 1992 and December 2019. Demographic, clinical and laboratory data were retrieved from hospital records and analysed. Patients were followed up for at least one year after diagnosis for cardiology outcome.

Results: 136 patients were included in this study, 55% of them were male. 133 cases (83%) were under 5-years of age. 88 children (69%) were classified as typical KD. Changes of lips and oral cavity were the most commonly met criterion (89.0%), followed by skin rash (83.2%) and conjunctivitis (80.5%). IVIG therapy was given between the 5th and the 10th day of illness to 73% of patients. 12% presented after 10th day of illness. 22 patients (15%) were non responders. Coronary artery abnormalities (ectasia or aneurysm) developed in 31 patients (23%).

Conclusions: Epidemiologic and clinical characteristics of Kawasaki Disease in the Cyprus population were very similar to those reported in other countries. Although the majority of cases received appropriate treatment, based on International guidelines on time, coronary artery abnormalities still occurred. However, a significant percentage of cases present late. Therefore increased awareness of Physicians for earlier recognition of Kawasaki Disease is needed.
EXOTIC CAUSE OF FEVER IN A LESS THAN 3 MONTHS-OLD BELGIAN BOY

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Title of Case(s): Crawling and exotic cause of fever in a 2.5 month-old Belgian boy

Background: Reptiles are frequently colonised by Salmonella enterica and therefore a potential source of invasive infections especially in children younger than 5 years old. Numerous serotypes of Salmonella enterica exist. Salmonella ser. Tel-el-kebir, a relatively rare serotype, has been reported in only 3 clinical cases describing invasive infection incriminating pet reptiles. Such serotypes are otherwise infrequent in the general population.

Case Presentation Summary: A 2.5 month-old boy was admitted for pyrexia and poor general state. Three blood cultures on two different days revealed the presence of Salmonella ser. Tel-el-kebir resistant to ciprofloxacin. The same serotype was also found in the patient’s stools. Lumbar puncture was not inflammatory and bacterial culture was negative. Cefotaxim 50mg/kg q6h was successfully continued for 14 days after first negative blood culture. The patient recovered quickly and was discharged at day 16th. The admission history reveals the presence of a chameleon at home and two pogonas at the grandparent’s house. Salmonella ser. Tel-el-kebir caused 3 bacteraemia in Belgium during the last 14 years. Over the last 7 years in Belgium, non-typhoid salmonella have been isolated in 19 160 clinical samples. Among those, Salmonella ser. Tel-el-kebir was overrepresented in bacteraemia (3/15; 20%) compared to all other serotypes (461/19 160; 2.4%).

Learning Points/Discussion: People, even paediatricians, are poorly informed about the risk that reptiles may represent for children. Salmonella ser. Tel-el-kebir is a rare serotype in Europe but seems particularly prone to be associated with bacteraemia compared to other non-typhoid salmonella. Its presence in a clinical sample should stimulate the search of a reptile in the patient’s surroundings. The virulence of Salmonella ser. Tel-el-kebir should be further investigated.
INVASIVE DISEASE DUE TO HAEMOPHILUS INFLUENZAE IN THE POST-VACCINE ERA: EXPERIENCE OF PAEDIATRIC PUBLIC HOSPITAL

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Background: During the pre-Haemophilus influenzae serotype b (Hib) conjugate vaccine era, Hib was the cause of more than 95% of invasive H.influenzae disease among younger children, especially meningitis. The universal recommendation for the immunization of infants in Brazil started in 1999, with a very significantly reduced the incidence of invasive Hib disease. This study aimed to analyze the epidemiological profile of invasive disease by Haemophilus influenzae (Hi) in a paediatric public hospital located in São Paulo, Brazil.

Methods: Retrospective study, between January 2012 and December 2019, in a state public Hospital. The cases were selected from a public notified meningitis database form and positive microbiological culture database from Nosocomial Infection Control Service. Patients from 0 to 18 years were included. We evaluated age, comorbidity, vaccination against pneumococcal and Hib, length of stay, diagnostic methods used, classification of invasive disease by topography, mortality and microbiological serotype.

Results: We identified 14 cases. Pneumonia and meningitis were the main causes. Patientes were aged between 30 days through 6 years. None of the cases developed through the neonatal period, although 70% occurred with children under 1 year. We found 7 cases of meningitis in this period, 6 of them in 2018, representing 40% of the bacterial meningitis. Typeable Hi was identified in all the Haemophilus meningitis and serotype A was the most prevalent, Hib was detected once. Non typeable Hi was more prevalent over the cases of pneumonia. The mortality global rate was 30% and among the meningitis cases was 50%.

Conclusions: After the introduction of vaccine against Haemophilus influenzae b there was a major reduction of the number of invasive disease by this agent. The results of our study showed an expressive number of Non-Type B and non-typable Haemophilus influenzae cases, especially serotype A, as a cause of invasive disease, with high morbidity and mortality.
A STUDY OF ABNORMAL HEMATOLOGICAL PARAMETERS IN CHILDREN WITH DENGUE FEVER
–A HOSPITAL BASED STUDY

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Background: Dengue, an arboviral infection is mainly found in the tropical and sub-tropical regions around the world. Apart from platelet count, the other hematology parameters like total white cell count, differential white cell count, haematocrit too aid in diagnosis and prognosis. The aim of study was to assess utility of hematology parameters (total leucocyte count, differential counts, platelet counts & haematocrit) in children hospitalized with dengue.

Methods: In this study all the consecutive children admitted in the department of pediatrics, Dayanand medical college & hospital, Ludhiana as cases of dengue fever (as per WHO definition) were prospectively studied from August to December 2020. In all the cases blood samples were obtained for hematological parameters and repeated where ever required. The results obtained were entered in a proforma and data was statistically analysed.

Results: A total of 220 children with dengue fever were hospitalized during 5 months from August – December 2019. Youngest was a 22 days old neonate. Male to female ratio was 2.7:1. Among the various hematological parameters-leucopenia was seen in 29.5%, leucocytosis in 15.9%, neutrophilia in 26.3%, lymphocytosis in 41.8%, monocytosis in 70%, raised hematocrit in 36.3% and low hematocrit in 23.6% of children. Out of 220 cases low platelet counts were seen in 89.6%. In 21.6% cases platelet count was less than 20000. Out of 220 cases, 174 were dengue serology or NS1 antigen positive. Overall mortality was 8.6%.

Conclusions: Dengue is a self limiting condition, severe forms if not detected early and treated properly are lethal in 5-10% of cases. Our study focusses on the utility of these hematology parameters including platelet counts, but where platelet count is not an early indicator of dengue, the total leucocyte counts-leucopenia & lymphocytosis are earlier and prominent events in dengue along with haematocrit in resource limited rural set ups.
Background: Bacterial pneumonia is a common disease in children. With microbiological tests mostly negative, empirical treatment is guided by available microbiological isolates and their antibiotic susceptibility. Our current guidelines recommend penicillin for uncomplicated bacterial pneumonia, amoxicillin/clavulanic acid for secondary pneumonia and mydekamycin for atypical pneumonia. The purpose of our survey was to review the aetiology, diagnostics and treatment of children with pneumonia in our centre.

Methods: We reviewed the medical records of 440 children with pneumonia that were hospitalized in the paediatric ward of the Department of Infectious Diseases Ljubljana between February 2017 and January 2019. Based on clinical and microbiological data patients were divided in three groups: typical pneumonia, secondary pneumonia and atypical pneumonia. Data on treatment was collected for each group and reviewed for adherence to guidelines and treatment success/failure.

Results: Of 338 children with typical bacterial pneumonia 286 (84.6%) were treated with penicillin G; in case of allergy cefuroxim or clindamycin was used. Amoxicillin/clavulanic acid was started in 73/75 (97.3%) patients with secondary pneumonia and midekamycin in 19/27 (70.3%) cases of atypical pneumonia. Pathogen was confirmed in 49/440 (11.1%) cases, most common being S. pneumoniae and M. pneumoniae. Treatment was conforming with the guidelines in 380 (86.3%) cases. Only 10/286 (3.5%) children on penicillin G required change of antibiotic due to various reasons (allergy, treatment failure, co-infections).

Conclusions: Microbiological confirmation of bacteria causing pneumonia is rare, with S. pneumoniae and M. pneumoniae being most commonly identified in our cohort. High adherence to the guidelines and low rate of antibiotic failure suggest that narrow spectrum penicillins are still the appropriate empiric therapy for uncomplicated typical bacterial pneumonia in children in Slovenia, even in the era of raising antimicrobial resistance.
A COMMON INFECTION TAKES AN UNCOMMON COURSE

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Title of Case(s): A COMMON INFECTION TAKES AN UNCOMMON COURSE

Background: Lemierre syndrome (LS) is a rare complication of oropharyngeal infections, caused by Fusobacterium necrophorum or mixed anaerobic flora, that typically affects previously healthy adolescents and young adults. It is characterized by septic thrombophlebitis of the internal jugular vein, septicemia and pulmonary lesions associated with septic emboli. The mainstay of treatment are antibiotics; the role of anticoagulation remains controversial.

Case Presentation Summary: A 9yo girl was evaluated for 3 weeks of fever, sore throat and asthenia and 3 days of chills, anorexia, cough and right dorsolumbar pain; 18 days before she had been diagnosed with infectious mononucleosis. Physical examination revealed pale mucous membranes, palpable spleen tip and was otherwise unremarkable. Chest radiograph showed a right lower lung opacity. Blood tests showed hemoglobin 42 g/L, platelets 344 x10^9/L, WBC 14.3 x10^9/L, CRP 28.7mg/dL. She was admitted with the diagnostic hypotheses of pneumonia and anemia associated with acute infection, was started on ampicillin and received a red blood cell transfusion. However, fever persisted, and she had aggravating odynophagia and left cervical pain. Thirty-six hours after admission a left cervical swelling developed, which prompted a cervical ultrasound that revealed massive left jugular vein thrombosis. Anticoagulation therapy was started, and the antibiotic switched to amoxicillin/clavulanate and clindamycin. Chest CT confirmed multiple septic emboli to lungs. She clinically improved and was discharged on amoxicillin/clavulanate and warfarin. On 3-month follow-up she was asymptomatic, having completed 6-weeks of antibiotics and due to complete 6-months of anticoagulation.
Learning Points/Discussion: LS should be suspected in patients with worsening oropharyngeal symptoms, respiratory distress, neck pain and/or sepsis despite adequate treatment for an underlying oropharyngeal infection. Although rare nowadays, it remains a disease of considerable morbidity. In this case we opted to use 6 months anticoagulation.
HIGH DIVERSITY OF STAPHYLOCOCCUS EPIDERMIDIS IN FAMILY CENTERED NEONATAL INTENSIVE CARE UNIT

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Background: We have previously demonstrated low diversity and high meca prevalence of S. epidermidis in gut of preterm neonates admitted to mixed neonatal/paediatric intensive care unit (NICU). Aim: To describe diversity of S. epidermidis MLVA types (MT) and presence of meca gene in neonatal gut, mother’s own breast milk (MOBM) and parents’ skin (PS) in a hospital providing family centered care.

Methods: Neonatal stool (F), MOBM and PS samples were collected from parents-neonatal pairs (gestational age (GA) <34wk) after delivery, at age of one and four weeks; environmental swabs from nCPAP prongs and incubator-linen at 48h of admission. From mannitol salt agar five staphylococcal colonies were identified to species level by MALDI-TOF-MS. S. epidermidis was typed by MLVA, diversity was described by Simpson’s Diversity Index (SDI) and presence of meca gene determined by PCR.

Results:

Figure. Genetic relatedness of MTs. Each node represents a distinct MT, and the size of the node is proportional to the number of isolates of the MT.
**Results.** We included 32 neonate-parents pairs (median (IQR) GA 29 (26-33) weeks, birth weight 1.41 (0.80-2.49)kg, length of NICU stay 16 (9-28) days. Two neonates (6%) had late onset sepsis caused by coagulase-negative staphylococci. Overall, 480/1567 (31%) *S.epidermidis* isolates were *mecA* positive and 348 MTs were identified. *MecA* prevalence increased over time in MOBM (41%→62%→60%; p=0.002) but not in F (50%→83%→67%; p=0.115) and PS (30%→37%→43%; p=0.173). On prongs and linen *mecA* prevalence was 89%. SDI (95% CI) was ≥0.993 in MOBM, F and PS throughout, on prongs 0.767 (0.677-0.856) and linen 0.942 (0.893-0.999). Phylogenetic analysis confirmed diversity (Figure).

**Conclusions:** Diversity of colonizing *S. epidermidis* in preterm neonates in our NICU suggests the role of NICU type or family centered care routines.

**Clinical Trial Registration:** No clinical trial registration
AUDIT ON THE MANAGEMENT OF CONGENITAL CMV CASES – A SINGLE CENTRE EXPERIENCE.

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Background: Congenital CMV (cCMV) is the commonest congenital infection in the high-income countries. Although most infants will remain symptom-free, ~15% develop hearing, vision and/or neurodevelopmental sequelae. We aimed to audit the management of infants with cCMV against local guidelines that recommend PID review of all referred infants within 30 days, and clinical examination and confirmed virology testing within 21 days of life.

Methods: Details of infants with cCMV diagnosed between January 2018 and December 2019 were obtained from the congenital infection database and patients' notes were reviewed. This was the first audit performed on clinical management of cCMV cases as local guidelines were updated in December 2018. A repeat audit has been scheduled for December 2020 after communicating the results of the present audit.

Results: 13 infants were included (7 [54%] female, median gestational age 39.5 weeks). A positive CMV result was obtained within 21 days in 11 (85%) infants and 2 infants had a result obtained at 21-28 days. Eleven (85%) infants received valganciclovir treatment, 2 initially commenced IV ganciclovir. All infants had safety bloods checked 2 weeks after starting oral valganciclovir treatment. All infants had regular audiology and ophthalmology follow-up. Four (31%) infants had signs of developmental delay in follow-up reviews. The clinical and imaging findings and valganciclovir side effects are showed in Table 1.

Conclusions: All infants were reviewed by the PID team in the first month of life and symptomatic cases started antiviral treatment, in an appropriate timeframe. Subsequent close monitoring for adverse events of valganciclovir is crucial as treatment interruptions were frequent (55%). Regular auditing of our PID service on cCMV management, along with the clinical guidelines review ensures prompt diagnosis and treatment of our patients.
A WORM IN MY LEG – A CASE OF UNEXPECTED TRAVELLERS

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Title of Case(s): A WORM IN MY LEG – A CASE OF UNEXPECTED TRAVELLERS

Background: Human myiasis is the infestation of humans with dipterous larvae. Rare cases reported in developed countries are mostly imported from tropical areas with inadequate sanitary conditions. The infestation can affect skin, dead tissues or natural cavities of living people. Chronic skin diseases and wounds are predisposing factors to cutaneous myiasis, which is unusual in intact skin.

Case Presentation Summary: A 17-month-old boy presented with a 6-day history of painful swellings on his left thigh and scrotum and his grandmother stated she had seen a “worm” appear from one of the lesions that morning. He had travelled to Portugal from Guinea-Bissau 7-days earlier. Trauma or skin lesions were denied. On examination the patient was afebrile and appeared healthy. Two red, hot and painful furuncle-like swellings were noted: 3x5cm with a 0.2cm central ulcer in the medial aspect of his left thigh and 3x3cm in the base of the scrotum; there was no drainage upon squeezing. While on observation, a larva emerged from the thigh ulcer and a second one was pulled using tweezers, suggesting cutaneous myiasis. Plastic bandages were applied to asphyxiate any other larvae but no more were found. The patient was discharged on amoxicillin/clavulanate and reevaluated 3 days later without further complications. Definitive diagnosis was made by macroscopic analysis that revealed Cordylobia anthropophaga larvae.
Learning Points/Discussion: Cutaneous myiasis is uncommon in developed countries and should be suspected when observing furuncle or boil-like skin lesions in patients travelling from endemic regions. *Cordylobia anthropophaga* is endemic to the subtropics of Africa and commonly infects humans by laying eggs on wet clothes, despite humans being an accidental host. Treatment may involve application of toxic substances to larvae, localized hypoxia to compel their emergence or surgical removal.
A CASE OF SEVERE INFECTION CAUSED BY CONSPIRACY BETWEEN AUTOINFLAMMATION, AUTOIMMUNITY AND IMMUNODEFICIENCY

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Title of Case(s): A case of severe infection caused by conspiracy between autoinflammation, autoimmunity and immunodeficiency

Background: Deficiency of ADA2 (DADA2) is an early-onset vasculitis syndrome caused by bi-allelic hypomorphic mutations of ADA2. The most common presenting features are rash, vasculitis, fever and stroke although B-cell immunodeficiency has been described. Haematopoietic stem cell transplant (HSCT) can be curative. We describe a child with a novel homozygous missense mutation in ADA2 presenting with severe neutropenia and enterocolitis.

Case Presentation Summary: A 5-year-old boy born to consanguineous parents presented with fever, mouth ulcers, abdominal pain and diarrhoea. He had severe neutropenia (<500 cells/mm³); low B cell (90 cells/mm³) count; low NK cell (23 cells/mm³) counts; elevated serum IgG (30g/L); and detectable serum IgM and IgG anti-granulocyte antibodies on multiple occasions. Stool examination suggested pancreatic exocrine insufficiency. He also developed enterocolitis and colonoscopy demonstrated deep colonic ulceration which flared with neutropenia. Neutropenia initially recovered with granulocyte colony stimulating factor (G-CSF), rituximab and mycophenolate mofetil, but was eventually refractory to treatment. Whole genome sequencing revealed a bi-parentally inherited homozygous missense mutation in ADA2, and protein functional activity was confirmed to be completely absent. At 11 years old, he suffered an episode of persistent fever and abdominal pain. Imaging revealed diverticulitis of the descending colon and colonoscopy confirmed refractory enterocolitis. He received broad spectrum antibiotic, antifungal and antiviral treatment, alongside immunosuppressive treatments including steroids and infliximab. His condition deteriorated, and repeat imaging revealed an intra-abdominal collection, which was surgically drained. His recovery was complicated by wound dehiscence and Enterobacter cloacae complex bacteremia. Despite appropriate antibiotic treatment, the child died before HSCT could be performed.

Key Learning Points: DADA2 can manifest with features of autoimmunity, autoinflammation and immunodeficiency that together conspire to cause severe infection. Next generation genomic testing facilitates the early diagnosis and treatment of children with atypical clinical phenotypes, such as DADA2 without clinical evidence of vasculitis
Background and Objective: Kawasaki disease (KD) is a complex, limited, systemic vasculitic syndrome of unknown etiology that mainly occurs in infants and toddlers, and potentially causes severe coronary artery aneurysms. The pathogenesis of KD commonly ascribed to an exaggerated immunologic response to an unidentified environmental or infectious trigger in susceptible children. In this study, we sought to determine the environmental factors associated with individual risk of KD.

Methods: For this Review, we used the standard search strategy of the Cochrane Neonatal Review group to search the Cochrane Central Register of Controlled Trials; MEDLINE via PubMed (2015 to 25 January 2020); Embase (2010 to January 2020); and CINAHL (2015 to January 2020). We also searched clinical trials' databases, conference proceedings, and the reference lists of retrieved articles for randomized controlled trials and quasi-randomized trials.

Learning Points/Discussion: The high incidence of KD in Asian populations globally is strong evidence of a genetic contribution to disease susceptibility. The prominent seasonal and temporal/spatial distribution of KD cases has led to many theories suggesting an infectious trigger to the disease. A disease caused by mercury toxicity, led to proposals that mercury might play a causative role in KD. The etiology may be a previously unidentified infectious agent and a few environmental factors, for instance, dust mites, rug shampoo, and pollen release may be effected in the trigger of KD. Seasonal variations in epidemics of KD suggested the probability of an airborne antigenic as a trigger to increase rate of KD. Inflammatory reaction leads to vascular damage, therefore the role of immunity is suggested. In addition, like other pediatric vasculitis such as IgA vasculitis, KD may occur in genetically susceptible individuals following exposure to any of a variety of infectious and/or environmental triggers.
Title of Case(s): Altered Mental Status - What should be investigated?

**Background:** Altered mental status associated with generalized or focal seizures can be a form of presentation of several conditions, such as epilepsy, encephalitis or meningitis. Human Herpesvirus (HHV)-6 is a neutrotropic agent that has been associated with some of these disorders. Therefore, a comprehensive and structured diagnostic approach is essential to achieve a correct diagnosis, allowing to timely start the proper treatment, if necessary.

**Case Presentation Summary:** A 15-months old healthy female was admitted to the emergency department (ED) due to a febrile seizure, with generalized tonic-clonic movements, facial cyanosis and ocular reversion that lasted around 2 minutes. Physical examination was unremarkable. During her observation period at the ED, she had a complex febrile seizure, which only stopped after the administration of intravenous antiepileptic drugs (diazepam and phenytoin). She had a normal blood gas analysis, no leukocytosis, and C-reactive protein was 25.3mg/L. Despite having a normal head computed tomography scan, she remained lethargic, and further investigation ended with a lumbar puncture (no pleocytosis). She was admitted to the pediatric ward, completed 5-days of ceftriaxone and acyclovir, with a favorable evolution and a normal electroencephalogram. The definitive diagnosis of viral encephalitis was made, as further results from the cerebrospinal fluid revealed a HHV-6 infection.

**Learning Points/Discussion:** HHV-6 has been directly or indirectly associated with neurological diseases like encephalitis in cases of primary infection in immunocompetent young children. Mental status variations and simple or complex seizures are among the most frequent symptoms associated with fever and without exanthem. The non-specificity of these symptoms makes it a challenge to correctly identify HHV-6 encephalitis in these patients and the diagnosis requires a high index of suspicion. The role of this virus in neurological symptoms in young immunocompetent hosts needs further investigation.
PRETERM NEONATAL ENTEROPATHY: FOCUS ON GUT MICROBIOTA, MICROBIOME AND FAECAL METABOLOME.

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Background: Necrotizing enterocolitis (NEC) is the most serious intestinal pathology in preterm infants. No clinical trial or cohort studies included only stage I of NEC (NEC-1).

Methods: We analysed stool samples collected from infants under 34 weeks of gestational age, including 11 infants who developed enteropathy (NEC-1 group) and 21 matched controls. Fecal bacterial communities were profiled by sequencing the 16S rRNA bacterial gene. Faecal metabolomic profiles were analysed by NMR.

Results: During the first ten days of life (d1-10), samples from NEC-1 infants showed a lower alpha diversity than controls with a significant difference in the distribution of bacterial communities but not in faecal metabolome. Between d11-d20, microbiome did not differ between NEC-1 infants and controls, but metabolomic analysis showed a significant decrease in serine levels in NEC-1 infants. Between d21 and d30, Bacillus, Staphylococcus, Bacteroidetes and Streptococcus bacterial groups were more abundant in NEC-1 infants than in controls, whereas Klebsiella and Raoultella species were more abundant in controls. Beyond 30 days of life, controls showed a microbiota richer in Klebsiella and Enterobacter than NEC-1 infants. Leucine levels in faeces were lower in NEC-1 infants.

Conclusions: The modifications of gut microbiota and microbiome during NEC-1 development appear more distinguishable by the third decade of life, when compared to healthy children. These data may suggest new microbial targets to fight/blunt the progression of NEC as early as by stage 1.

Clinical Trial Registration: no Clinical trial registration, only CPP validation DC-2016-2804
IMPACT OF ROTAVIRUS VACCINATION AFTER 10 YEARS OF A NATIONAL IMMUNIZATION PROGRAM IN FINLAND (2009-2018)

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Background: Rotavirus (RV) vaccination was included in the Finnish National immunization Program (NIP) in 2009. RotaTeq (RV5) has been used exclusively with a national average vaccination coverage rate (VCR) of > 90%. While previous studies have demonstrated RV incidence reduction of up to 96% in children ≤ 5 years old, we analyze here RV incidence in all children <10 years old.

Methods: We describe the incidence of rotavirus gastroenteritis (RVGE), viral gastroenteritis, and acute gastroenteritis (AGE) using national inpatient register data for all Finnish children up to 9 years and eligible for RV5 in the NIP (study groups: 0-3y; 3-5y; 5-7y; 7-9y). All children were born after July 2009 and followed from September 2009 to June 2018. We also estimate health care resource utilization (HCRU) and variation of RVGE and AGE incidence over regions characterized by different vaccination coverage, VCR (high VCR: VCR>90%; lower VCR: VCR 80 to 90%).

Results: RVGE incidence decreased significantly in the younger age-groups after RV vaccine introduction in the NIP and remained at very low levels in all age groups studied throughout the study period. Declines in other viral gastroenteritis and in all AGE cases were also observed across all age groups over time. Additionally, HCRU due to viral gastroenteritis and all-cause gastroenteritis decreased in the youngest age group during 2012-2018. Across all age-groups, regions with high VCR had lower incidence of RVGE and AGE than regions with lower VCR.

Conclusions: Conclusion: Incidence of rotavirus gastroenteritis has remained low in all children during the 10 years after RV vaccine was introduced in the Finnish NIP. Differences in RVGE incidence were observed in regions with high and lower VCR, further highlighting the benefits of maintaining high vaccination coverage.
E-POSTER VIEWING
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10-28-2020 8:00 AM - 7:00 PM

EPIDEMIOLOGICAL CHARACTERISTICS OF CHILDREN TESTED FOR COVID-19 IN A TERTIARY HOSPITAL

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Background: Preliminary data suggest that children are as likely as adults to become infected with COVID-19 but are less likely to be symptomatic or develop severe symptoms. Aim of our study was to identify epidemiological characteristics of children with possible and confirmed COVID-19.

Methods: Retrospective study of children<18 years old, who were tested for COVID-19 in the largest tertiary Children's Hospital in Greece during January-June 2020. Eligible for screening were children with symptoms of COVID-19, who visited the emergency unit and/or were hospitalized as well as asymptomatic children with exposure history to COVID-19 or undergoing an operative procedure. Nasopharyngeal swab was collected by each child and was further tested for SARS-CoV-2 by real time RT-PCR. Epidemiological data were also collected.

Results: Totally 1185 children were tested for COVID-19. Symptomatic were 603/1185 (0,93%). Range of their age was 11 days-12 years old. Most of the children with COVID-19 (10/11) presented with mild symptoms (fever, cough, diarrhea) and 7/11 needed hospitalization due to their young age. Asymptomatic was found one toddler, who was the sister of an infant hospitalized with COVID-19. Transmission route of COVID-19 in 10/11 children was close contact with another case within the family and one infant had history of recent travel in South Africa.

Conclusions: Incidence of COVID-19 in children is low. All age groups can equally be infected mostly by previously infected adults. Continuous epidemiological surveillance is important to conquer better knowledge of possible implications of COVID-19 in children.
APPENDICULAR INFECTIONS IN CHILDREN

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Background: Appendicular infections are very common in children. In fact, appendicitis is the first abdominal surgical emergency in children. Accurate diagnosis is challenging due to atypical presentations. In some areas, complicated forms such as peritonitis and abscesses predominate and are due to diagnostic delay. The aim of our study is to report the epidemiological, diagnostic, therapeutical and evolutive aspects of these infections.

Methods: This is a descriptive retrospective study involving 86 children who were treated for an appendicular infection over a period of 6 months. The mean age was 10.4 years, with extremes of 2 and 15 years. The sex ratio was 2.9. We studied the clinical presentations of these infections, the ultrasound contribution to the diagnosis and the results of the treatment.

Results: The consultation period varied between 1 day and 21 days with an average of 4.7 days. Abdominal pain was the first functional sign found (n = 86/86). Physical examination revealed abdominal pain in all cases. In more than half of the cases, abdominal ultrasound confirmed the diagnosis (n = 49/86). We recorded 36 cases of acute appendicitis, 25 cases of appendicular peritonitis, 23 cases of appendicular abscess and 2 cases of appendix plastron. All patients underwent appendectomy and triple antibiotic therapy. The evolution was good in all cases.

Conclusions: Appendicular infections are frequent. Clinical presentations of these infections are various and dominated by complicated forms, especially abscesses and peritonitis. Appendicitis remains as the most frequent form and a clinical diagnosis. Ultrasound contributes moderately to diagnosis. Surgical treatment consisting on appendectomy is always necessary associated to a triple antibioc therapy. Despite of late diagnosis, outcomes are good even in complicated forms.
Background: The current COVID-19 epidemic is rapidly reaching every corner of our world. Although much progress has been made to understand its effects on the human body, our understanding of pediatric infections remains limited. This study’s objective is to explore the course and characteristics of COVID-19-infections in the Breda area, one of the first affected Western-European areas.

Methods: Pediatric patients who received COVID-19 PCR-testing as advised by local guidelines in the Breda-area during March-April 2020 were included. Clinical data gathered at presentation were supplemented with laboratory and imaging studies and data from a questionnaire monitoring disease recovery. COVID-19 testing was performed by the local Hospital and Municipal Health service. A total of 107 children were seen of which 78 were referred to the local hospital.

Results: 7 tested positive of which three were hospitalized: a newborn, a 15-year-old and 17-year-old. All three reported fever, rhinitis, 2/3 needed oxygen therapy and one was transferred to ICU. All showed infectious markers such as raised CRP and lymphopenia. Of the 75 negative patients seen in hospital, 5 had a history of a strong cough/dyspnea/fever, a prolonged course of disease and close-contact with (suspected) COVID-19-cases raising the likelihood of COVID-19-infection despite negative results. In total, 5 patients received a CT chest; only one was suspicious for COVID-19 related disease.

Conclusions: This study confirms the suspicion that COVID-19 infections are less prevalent in children compared to adults. However, the suspected false negative rate of PCR, especially in children\(^1\) and the low sensitivity of CT-imaging\(^2\) might indicate that COVID-19 infections can be underestimated. Data on COVID-19 tested cases without referral to the hospital are still being analyzed in this study.
Background: Pediatric Inflammatory Multisystem Syndrome (PIMS) is an emerging phenomenon connected with the COVID-19 pandemic. Characteristic features are fever, overlapping Kawasaki disease (KD), and toxic shock syndrome symptoms, with predominant gastrointestinal and cardiac involvement. The majority of described patients had rapid progression to shock, required administration of inotropic drugs or vasopressors, and treatment in the intensive care unit (ICU). However, severe cases - representing the majority of the reported ones - may indicate the iceberg's tip, and we should expect a broad spectrum of patients with fever and inflammatory disease.

Methods: Poland (population over thirty-seven mln citizens, a highly homogenous society with the predominance of the caucasian race) is a country with a low incidence rate of COVID-19. On May 25th we established a national registry of PIMS patients in Poland (MOIS CoR study) to collect retrospective (since March 2020) and prospective PIMS surveillance. As of July 14th, 31 hospitals from 18 cities have joined the study and reported thirty-seven patients, 35 of them fulfilled the inclusion criteria.

Results: Thirty patients met KD or incomplete KD criteria, and 5 had other presentations. Together six patients had either laboratory (4) or epidemiology (4) confirmation of COVID-19 disease - only one child required ICU treatment; 4 patients - oxygen supply. Gastrointestinal, musculoskeletal, and neurological involvement was frequent (20, 18, and 26 patients, respectively). Four children developed coronary arteries aneurysms; two had impaired heart contractility, and 3 - pericardial effusion.

Conclusions: PIMS cases are rare in Poland and the proportion of severe cases is lower than reported from other countries. We expect to gather valuable data that would give an insight into the nature of PIMS cases in Poland.
Background: Measles is a highly contagious disease, that although primarily affects children, people of all ages can be infected. Between 2015 and 2019 there was a measles outbreak in Europe. Newborns were exposed to measles virus, with sole protection the maternal IgG antibodies that passively pass to newborn via the placenta. The aim of this study was to examine the seropositivity of mothers and newborns for measles and the factors that influence the IgG titre in these two groups.

Methods: A prospective study was performed in General Hospital of Lakonia Greece, from January to November 2018. 206 mothers and their newborns participated in the study. Blood samples were obtained and tested for IgG antibody titre for measles. The serum samples were analysed via quantitative ELISA and were considered to be positive when concentration was more than 200 U/mL. Data were collected in the form of a questionnaire via personal interview with mothers.

Results: The majority of both mothers and newborns had protective titre of IgG antibodies for measles (180/206 (87.4%) mothers and 183/205 neonates (89.5%)), but a significant percentage was found to have non-protective serology (approximately 12%). The factor that was found to be statistically significant associated with the number of measles antibodies in neonates was maternal antibody levels (p=0.001). Neonates whose mothers had positive antibody levels had more antibodies (geometric mean 804.8) than neonates whose mothers had negative or intermediate levels (geometric mean 97.7). Similarly, the association between maternal-neonatal antibodies was found to be statistically significant strong positive linear (rho=0.994).

Conclusions: A significant percentage of mothers and newborns were found not to be protected for measles. Vaccination coverage in women of reproductive age has to be increased, as newborns will be subjectively protected. Further studies need to be conducted in order to determine the age of maternal IgG protection loss and suggest safe vaccination schemes.
IDIOPATHIC POST INFECTIOUS PURPURA FULMINANS ASSOCIATED WITH ANTI-PS ANTIBODIES IN CHILDREN: FRENCH MULTICENTRIC RETROSPECTIVE STUDY ABOUT 18 PATIENTS

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Background: Post Viral Acquired Protein S deficiency (pv-APSD) is a rare but severe coagulation disorder occurring after viral infection, in particular chickenpox virus or HHV6. This thromboembolic pathology leads to a decrease in the plasma concentration of protein S by autoantibodies against protein S. Pv-APDS has mainly been described by case reports to date, there are no diagnostic or management recommendations.

Methods: We conducted a retrospective multicentric study. Patients were selected from 13 pediatric French centers. All data were collected via patient records including clinic and biology at diagnosis, care and outcome of patients. Eighteen patients were included.

Results: Median age at diagnosis was 4.3 years. Time to diagnosis was 6 days. Clinical presentation was ecchymotic purpura in 13 patients, necrotic purpura in 6 patients. There was legs impairment in 16 cases, limited to the calves in 3 of cases. Median level of PS at diagnosis was 6.5%. The diagnosis of viral infection was confirmed in 88% of patients, 11 cases of chickenpox and 3 cases of HHV6 infection. Most patients received heparin and fresh frozen plasma transfusions, severe patients were treated with polyvalent immunoglobulins or plasmapheresis.

Conclusions: No deaths were recorded, 10 children present severe necrosis, 6 necessitated amputations and 5 a skin graft. This study described the largest cohort of pv-APDS, we precise clinical and biological characteristics and details on the management and the outcome of patients.
ANTIBIOTIC CONSUMPTION DURING A 30-MONTH PERIOD IN A TERTIARY GREEK PEDIATRIC HOSPITAL WITH AN ANTIMICROBIAL STEWARDSHIP PROGRAM

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Background: The excessive use of antibiotics in children has multiple negative effects, including drug-related adverse events, the emergence of multidrug resistant pathogens, etc. As limited data are available in Greece, our aim was to evaluate the trends of antibiotic consumption in pediatric patients by using an antimicrobial stewardship program

Methods: A retrospective study was performed in “Aghia Sophia” Children’s Hospital from January 2017 to June 2019. The monitoring of antimicrobial consumption was performed through pharmacy records and presented as Daily Defined Dose (DDD) by 100 patient-days. Consumption was evaluated in pathological (PU), surgical (SU) and intensive care unit (ICU).

Results: A significant decrease in penicillins use (p=0.058), but not in cephalosporins (p=0.268) was observed. In PU, penicillins were the most frequently prescribed antibiotics, followed by 2nd generation cephalosporins. Penicillins use increased from 7.6 DDDs in 2017 to 8 DDDs in 2018 and then decreased to 4.4 DDDs in 2019 (p=0.026). In SU, 3rd generation cephalosporins were the most frequently prescribed antibiotics. Regarding penicillins, their use increased from 7.7 DDDs in 2017 to 9.1 DDDs in 2018 and then decreased in 4 DDDs in 2019 (p=0.034). In ICU, no remarkable change in penicillins and cephalosporins use was detected (p=0.199 and p=0.743, respectively).

Conclusions: The declining trend in penicillins use that was detected in both PU and SU during the first half of 2019 is quite promising. However, the increased use of cephalosporins, especially in SU, highlights the necessity of antibiotic stewardship program in order to establish a strict and evidence-based antibiotic prescribing policy in the hospital.
ANTIBIOFILM EFFECTS OF HUMAN NEUTROPHILS IN COMBINATION WITH AMPHOTERICIN B FORMULATIONS OR VORICONAZOLE AGAINST FUSARIUM SPP.

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Background: *Fusarium* species are important emerging pathogens, especially among immunocompromised hosts, including children. They are able to cause superficial, invasive or disseminated infections. Biofilms are resistant to innate defense mechanisms. We assessed the antifungal activity of polymorphonuclear neutrophils (PMN) against *Fusarium* planktonic cells (PL) and biofilms (BF) with deoxycholate amphotericin-B (D-AMB), liposomal amphotericin-B (L-AMB) and voriconazole (VRC).

Methods: *Fusarium* BF and PL were incubated at 37°C in a 5% CO₂ incubator with PMN from healthy volunteers at effector-to-target ratios 5:1 or 2:1 alone or in combination with D-AMB, L-AMB, VRC for 24h. Antifungal activity was assessed by the XTT reduction assay. MIC50 was determined as ≥50% BF/PL damage. The % damage of the PMN+drug treatment was compared to that of PMN or drug alone by ANOVA (n=8; P<0.05). Additivity was defined as significantly greater damage by the combination than by either PMN or drug. Antagonism was defined as an antimicrobial effect of the combination that was significantly less than the effect produced by either PMN or drug.

Results: PMN-mediated damage was greater against PL than BF. Regarding PL, an additive effect was observed between 0.5mg/l D-AMB+PMN vs D-AMB. Antagonistic effects were observed between 1mg/l L-AMB+PMN vs L-AMB and 1mg/l and 4mg/l VRC+PMN vs VRC. Additive effect against BF was demonstrated between 2mg/l L-AMB+PMN vs L-AMB. Antagonism against BF damage was found at selective drug concentrations: 0.5mg/l and 4mg/l D-AMB+PMN vs DAMB, 32 mg/l L-AMB+PMN vs L-AMB and 64mg/l VRC+PMN vs VRC.

Conclusions: *Fusarium* BF are more resistant to VRC than D-AMB or L-AMB. The combined treatment of PMN with D-AMB, L-AMB or VRC shows antagonistic activities at certain concentrations against BF, which may explain the difficulty to confront invasive fusariosis.

Clinical Trial Registration: Not a clinical trial
INDIVIDUAL RISK FACTORS FOR STREPTOCOCCUS PNEUMONIAE NASOPHARYNGEAL CARRIAGE IN THE PNEUMOCOCCAL CONJUGATE VACCINES (PCV) ERA IN CHILDREN. A META-ANALYSIS OF REAL WORLD DATA.

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Background: Streptococcus pneumoniae nasopharyngeal carriage (Spnc) precedes invasive disease, and colonised individuals serve as a reservoir for horizontal spread in the community. Although there is evidence of the impact of individual risk factors on Spnc such as age, day care attendance (DCA) or young siblings, there are scarce data on the influence of these factors after the implementation of pneumococcal conjugate vaccine (PCV).

Methods: We evaluated the impact of individual risk factors on Spnc in generally healthy 0-7 year-old children, by performing a meta-analysis of non-Randomised Controlled studies, retrieved from Medline, Cochrane and Trip databases published from 01/2000 to 07/2019. The quality of studies was assessed using the Newcastle-Ottawa-Scale. A random effects model using odds ratio (OR) as effect measure, was used. Statistical analysis was performed using the generic reverse variance approach in Cochrane Review Manager v5.3. Pooled OR were presented with forest plots and between-study heterogeneity was quantified using the I² statistics.

Results: We included eleven cross-sectional and cohort studies that met predefined inclusion criteria with a total of 15,865 patients. Spnc ranged from 23.0%-54.2%. Age >2 years, DCA and having siblings were significantly associated with increased risk of Spnc (figure 1). Other factors including male gender, smoke exposure, breastfeeding, recent antibiotic consumption and hospitalisation were not associated with increased risk in random-effect meta-analysis.

Conclusions: Age more than two years, attending nursery and living with young siblings remain strong predictors of pneumococcal carriage despite the sequential introduction of PCV7 and PCV13. Children’s nasopharynx persists as a natural habitat of Streptococcus pneumoniae and crowding facilitates colonization; targeted surveillance studies and informed decision-making in the vaccine production process remain a powerful tool in the armamentarium against pneumococcus’ dynamic epidemiology.

Systematic Review Registration: N/A
INVASIVE MENINGOCOCCAL DISEASE - A WIDE CLINICAL SPECTRUM

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Title of Case(s): Non-blanching rash - clinical approach

Background: The clinical approach to the febrile child with rash can often pose a diagnostic challenge in distinguishing what may be a benign from a potentially fatal presentation. Despite being rare, meningococcal infection in children is associated with a high rate of morbidity and mortality. The author’s objective was to describe 3 clinical cases that illustrate the possible spectrum of presentation of this infection.

Case Presentation Summary: Case 1: A 9-month-old male infant presenting a 6-hour fever, vomiting and prostration; no leukocytosis and C-reactive protein (CRP) of 23 mg/L. Cerebrospinal fluid (CSF) culture was negative, but the blood culture was positive for Neisseria meningitidis serogroup Y. Case 2: A 12-month-old male toddler attended the emergency room with 24-hour fever and maculopapular rash, with progressive worsening and appearance of scattered petechiae in the limbs. Additionally, he had leukocytosis (28000/µL), CRP of 131 mg/L, and evidence of Neisseria meningitidis serogroup W, in the CSF and blood cultures. Case 3: A 4-year-old girl, with 2-day fever, had since that morning petechiae and purpuric rash. Analytically, had leukocytosis (26430/µL) with CRP of 242 mg/L and Neisseria meningitidis serogroup B growth in bacteriological CSF despite sterile blood culture. All cases had updated vaccination program with no additional vaccine, and all were diagnosed within January 2019. After 7-day course of intravenous ceftriaxone and support treatment, they presented favourable evolution.

Learning Points/Discussion: Currently, although serogroup B is the most frequently identified agent in Europe, the incidence of other serogroups such as C, W and Y has been increasing. Due to the rapid progression of this infection, an accurate and early diagnosis, and therapeutic initiation, are essential for a favourable prognosis. Authors’ main objective is to draw attention to this disease clinical spectrum.
A STUDY ON EPIDEMIOLOGY AND ETIOLOGY OF ACUTE GASTROENTERITIS

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Background: Acute gastroenteritis (AGE) remains an important cause of child morbidity and mortality worldwide. Therefore, it is essential to understand which information should be gathered (e.g. symptoms, risk factors, immunization), in order to distinguish between a viral and bacterial infection. Specifically, as the latter has a higher risk of ward admission and dehydration, with consequent higher costs and longer hospital admissions.

Methods: Retrospective analysis of the clinical records of all patients admitted to the pediatric ward with AGE at a level two hospital over the last 4 years. Statistical analysis was performed using SPSS Statistics V26.0, and p<0.05 was considered statistically significant. Five hundred and six patients were included in this sample, with a median age of 18 months (P25-P75: 9-49 months) and 55% were male.

Results: Oral intolerance was admission criterion in 81% patients, mean (sd) length of hospitalization was 5 days (4.1). Stool sample analysis was performed in 420 patients and 251 had a positive result (46% bacteria). Symptoms as, temperature above 39.5ºC, vomiting, abdominal pain and blood or mucus stool in bacterial AGE was statistically significant (p<0.001). Bacterial infection was more prevalent than viral in children > 3 years old, as well as in patients with contaminated water consumption (p<0.001). Bacterial AGE presented higher neutrophils count (μ=7176, p=0.016) and C-reactive protein (CRP) (μ=76.1, p<0.001).

Conclusions: In our sample, as stated in the literature, high fever, blood or mucus in the stool are more likely to be present in bacterial infection, as well as neutrophilia and an elevated CRP. Bacterial AGE was more prevalent in patients with contaminated water and on those with a complete immunization against rotavirus. Viral infection seems to me most common in the first three years of life.
Laboratory data evaluation of perinatal infected HIV children and adolescents at a teaching hospital in Ghana

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Background: The 2019 consolidated guidelines for HIV care in Ghana recommend at least yearly laboratory investigation for patients on antiretroviral therapy to monitor treatment for success or failure. This study evaluates the laboratory data of children and adolescents perinatally infected with HIV in order to ascertain their compliance with the recommended national guidelines for HIV care with respect to laboratory tests.

Methods: The medical records of 69 children and adolescents who attended the HIV Clinic between October and December 2019 were assessed for availability of laboratory test results. The laboratory tests considered in this study were viral load, renal function and full blood count. The reasons for the patients’ inability to undergo prescribed laboratory tests were also assessed by interviewing the patients and their caregivers.

Results: Out of the 69 patients, 45 (65%) had viral load data for 2019. There was viral suppression for 33% of the patients with viral load data. Also, 25 out of 37 patients on tenofovir based regimen had renal function data available in their medical records. Furthermore, full blood count data were available for 35% of patients on zidovudine based regimen. Barriers to undergoing prescribed laboratory tests were high cost of some of the tests and frequent breakdown of viral load testing machine.

Conclusions: There were significant numbers of patients whose laboratory data were not available in their medical records. High cost of some laboratory tests and frequent breakdown of the viral load machine were identified as barriers to patients’ ability to undergo prescribed laboratory tests. Clinic based interventions and subsidies for laboratory tests should be introduced to address the barriers identified and ensure monitoring of patients on antiretroviral therapy.
Background: Clinical trials for vaccine development are a critical step to generate efficacy/safety information for licensure and decision-making process. Conducting these trials involves complex set-up to guarantee adequate recruitment, retention and follow-up of participants. In recent years, electronic tools (e-tools) have been developed to overcome some of these challenges. We evaluated the performance for using three validated e-tools at a research center (Cevaxin) in Panama over protocol compliance, efficacy endpoints surveillance and adverse events reporting.

Methods: Three e-tools were implemented following ethical and regulatory approvals: 1) Patient Follow-up System (PFS): a web-based system to schedule and complete study visits as per-protocol definitions; 2) Vigilant-E: a mobile-app for subjects to report their health status including specific clinical outcomes, such as respiratory or gastrointestinal symptoms, under surveillance over time; 3) Vax e-Diary, a mobile-app to monitor immunization reactions, reported by the participants. We estimated indicators on protocol compliance, retention and outcomes/adverse reactions reports using these e-tools.

Results: From 2013 to 2019, we conducted 21 vaccine trials enrolling 10,290 participants. All of them used PFS: 64,689 visits were scheduled, 97% were completed according to protocol and overall retention rate was 95%; Vigilant-E was used in 5 studies with a weekly reporting rate ≥85%. This e-tool was the primary source for reporting targeted outcomes as indicated in the protocol in 56% of cases; E-diary was employed in 6 trials with a daily reporting rate by the participants ≥90%. Data were automatically transferred into the study database in real-time.

Conclusions: Implementing e-tools has the potential to strengthen the performance of vaccine clinical trials, making them more efficient and acceptable for study participants, and assure confidence and privacy requirements. These validated e-tools can enable timely data accessibility to expedite results availability.
Title of Case(s): A SEVERE OSTEOARTICULAR INFECTION: AN ATYPICAL CASE

Background: Fusobacterium necrophorum is a common agent of disease in humans, but the occurrence of primary infections outside the head and neck area is extremely rare. Here, we report the case of septic arthritis, pyomyositis and fasciitis of the left thigh in an otherwise healthy adolescent.

Case Presentation Summary: Previously healthy 15-year-old male presented with 12-hour history of fever and sudden severe pain in the left thigh and groin. Upper respiratory tract infection was referred the week before. Hip was flexed in external rotation with a limited range of motion and intense tenderness. Initial laboratory results revealed leukocytosis (19,580/µL) with 94% neutrophils and CRP of 281mg/L. MRI showed left coxofemoral 14mm effusion with extensive psoas, proximal adductors and obturators pyomyositis, and multiple muscle abscesses. Started empirical antibiotics (ceftriaxone and clindamycin), and was submitted to arthrocentesis and arthrotomy. Due to worsening, with suspecting fasciitis, vancomycin was added, and underwent multiple interventions for abscess drainage and debridement. At day-20 Bacterial DNA-PCR was positive for Fusobacterium necrophorum, while synovial fluid grew oxacillin-susceptible Staphylococcus lugdunensis. Thorax-CT revealed bilateral ovular lesions with central cavitation. Tuberculosis was excluded. Echocardiography was normal, neck ultrasonography disclosed any thrombosis. Fever persisted for 50 days, and treatment was changed to meropenem. Left femur head avascular necrosis was diagnosed and underwent decompression surgery, followed by hyperbaric oxygen therapy. At 6 months follow-up, needs crutches for gait maintenance with limited hip mobility.

Learning Points/Discussion: Fusobacterium species are anaerobic, gram-negative bacilli that can cause metastatic osteoarticular infections. Coinfection with aerobic bacteria is a poor prognostic factor. Septic arthritis can be rapidly progressing and potentially fatal, requiring a high level of suspicion in patients with previous upper respiratory infections. In this case, despite intensive treatment with debridement, the patient progressed to avascular necrosis.
Background: Influenza infection is very common and usually considered benign in healthy children. In Portugal, the vaccine is not part of the national immunization programme. The Directorate General of Health (DGS) defined risk groups for whom vaccination and/or oseltamivir are indicated. The objective of this study is to characterize this infection over 6 seasons in a pediatric hospital.


Results: Median age was 4Y (1.6–8.4) and 173 had risk factors. 34% were admitted (median length of stay of 4D). Complications were observed in 35%, mainly lobar pneumonia, acute otitis media, and myositis. Severe complications, such as encephalitis (6), bacteremia (S. aureus, H. influenza), sepsis (S. pneumoniae, GAS), occurred in children with no risk factors. 5 children died (1 previously healthy). Children with risk factors were older (p=0.015), had higher admission rates (p<0.010) and longer hospital stay (p=0.030), but there was no difference in the rate of complications (p=0.052).

Conclusions: Influenza infection is responsible for a significant consumption of health resources and can cause a serious illness not only in children with risk factors but also in previously healthy children, in whom the rate of severe complications was higher.
NEURODEVELOPMENT OUTCOMES OF INFECTIOUS ENCEPHALITIS

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Background: Encephalitis in paediatric age might impair neurodevelopment with variable severity. If there are any acute predictors of neurodevelopment sequelae is not well established. We aimed to characterize the neurodevelopment outcomes of encephalitis patients to optimize follow-up and early intervention in these patients.

Methods: Retrospective study in paediatric patients (0-18 years old) with infectious encephalitis between January 2013 and December 2018 and follow-up until November 2019. Neurodevelopment accessed through Schedule of Growing Skills II.

Results: 80 cases with median age 3 years old - Varicella zoster (8), influenza A virus (11), EBV (6), Mycomplasma pneumoniae (3), HVS2 (2), HV6 (2), others (4). 21 (26%) admitted to the intensive care unit. Neurodevelopment assessed in 79% (56). 31/56 (55%) shown neurodevelopment disability – learning (11), communication (10), intellectual (9), motor (7), cerebral palsy (4), hyperactivity and attention deficit (4), behaviour (2), auditive (1), visual (1) compromise). 22/31 (71%) submitted to intervention. Neurodevelopmental impairment was more frequent if age 12-24months (p 0.03), temporal slowed EEG (p 0.02) and leucocytes in LCR (p 0.03).

Conclusions: Neurodevelopment impairment is not predictable during the acute course of the disease, even though it occurs during the second year of life, in patients with temporal slowing, and moderate raise in LCR lymphocytes. All efforts should be done to adequately follow up and early support these patients so the effects of encephalitis can be minimised.
SUCCESSFUL TRANSCATHETER ARTERIAL ANTIMICROBIAL AND STEROID THERAPY FOR LIVER ABSCESSSES IN CHRONIC GRANULOMATOUS DISEASE: A CASE REPORT

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Title of Case(s): Successful transcatheter arterial antimicrobial and steroid therapy for liver abscesses in chronic granulomatous disease: a case report

Background: Chronic Granulomatous Disease (CGD) is a primary immunodeficiency disorder in which phagocytes are not able to destroy catalase-positive microorganisms. Liver abscess is a common manifestation of CGD, its optimal management in these patients is unknown. We describe the case of multiple hepatic abscesses in CGD patient successfully treated with systemic antibiotic therapy and transcatheter arterial (TA) antimicrobial and steroid therapy.

Case Presentation Summary: A 31-year-old male affected by CGD, diagnosed at 6 months of age, was admitted in our hospital with fever. The abdominal ultrasound and computed tomography (CT) showed multiple lesions in the liver with the main involvement of the II (d max 4 cm) and VII (d max 4.3 cm) segment. Laboratory tests were positive for cholangitis. Aspiration of the main lesion resulted positive for S. aureus (MSSA). After two months of systemic therapy with Meropenem, Tigecyclin, Daptomycin and steroids no clinical and radiological improvement were achieved. The surgical treatment was discarded because of the diffuse liver involvement. As salvage therapy, TA antimicrobial and steroid therapy was decided: Meropenem (1.5 g) and Methylprednisolone (30 mg) were administrated every two weeks for 4 months. The CT scan showed a clear improvement with reduction of all lesions described previously (Fig). Therefore we performed 3 more TA infusions. All the procedures were well tolerated with no signs of cytolysis and an improvement of cholangitis markers. The systemic antibiotic therapy was continued throughout.
Learning Points/Discussion: In conclusion, this is the second case reported showing that TA antimicrobial and steroid therapy can be one of the treatment options for refractory hepatic abscess, especially in patients who are not candidates for surgical intervention. More data are needed to validate the use of other antimicrobials with this new treatment.
Title of Case(s): GAIT UNSTEADINESS AND PARAESTHESIA ON AN 12-YEAR-OLD-GIRL: A RARE COMPLICATION OF INFECTIOUS MONONUCLEOSIS

Background: Infectious mononucleosis is a common clinical syndrome in paediatric age, particularly in adolescence, caused by the Epstein-Barr virus. Guillain-Barré syndrome (GBS) is a term encompassing the several variants of acute immune-mediated polyneuropathies. Typically, there is history of an antecedent infection, thought to trigger the immune response that leads to peripheral nerve damage. GBS following infectious mononucleosis has been rarely reported.

Case Presentation Summary: A 12-year-old girl presented with bilateral paraesthesia in her toes, associated with calf and plantar pain, resulting in trouble to walk. She had been diagnosed with infectious mononucleosis 2 weeks earlier. Neurological exam revealed only mild gait unsteadiness. Electromyography (EMG) was normal. Cerebrospinal fluid revealed pleocytosis 34/μL and proteins 148.8mg/dL. She started empiric ceftriaxone and acyclovir, as well as intravenous immunoglobulin (IVIG) 400mg/day for 5 days. A couple days later, it was difficult to elicit lower limbs deep tendon reflexes and was evident a mild paresis of the right lower limb (score 4-/5 on foot and hallux plantar flexion and dorsiflexion; score 4/5 on leg flexion and extension). Spinal MRI revealed signal enhancement after gadolinium on some roots of cauda equina. She repeated EMG, revealing a motor demyelinating pattern consistent with GBS. PCR for Epstein-Barr virus was positive in cerebrospinal fluid. The remaining laboratory work was negative, including antiganglioside antibodies. The sensory symptoms improved completely until patient discharge.

Learning Points/Discussion: GBS in paediatric patients can present with subtle clinical manifestations early in its course; moreover, all supportive features in diagnostic testing may not be present at first, making the clinical suspicion the key to adequate diagnosis. Some data suggest that IVIG shortens the time to recovery compared with supportive care alone, but large randomized controlled trials are needed to support this data.
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Background: It is known that the maintenance of viral suppression is not an easy task for vertically HIV-infected adolescents. Hence to assess clinical benefits and difficulties associated with this aim is of upmost importance.

Methods: Thirty adolescents were prospectively followed-up over 45 months: 16 ART-treated individuals on viral suppression (VL<40 copies/mL) during the whole period and 14 adolescents without viral suppression (median log10 VL 3.3/mL) despite ART-treatment. All individuals had CD4 T cells over 200/mm$^3$ at enrolment. They were closely followed-up and assessed for CD4 T cell numbers, HIV viral load, clinical signs and symptoms (Table). Immune activation (CD38+HLA-DR+) and PD-1 expression on CD8+ T cells were evaluated by flow cytometry at study entry.

Results: Adolescents with non-suppressed VL had lower CD4 T cells, higher activation markers and PD-1 expression on CD8 T cells than those on viral suppression. Infections were more frequently observed in non-suppressed individuals, but that was not statistically significantly (Table). Over 40% of non-viral suppressed women got pregnant during the 45-month period. By contrast, 25% of individuals on viral suppression reported depressive symptoms. Linear regression analysis showed that CD4 T cell numbers was the only factor associated with infectious episodes, after controlling for immune activation, PD-1 expression and viral suppression ($p=0.011$).

Conclusions: Clinical benefits of viral suppression were evident and low CD4 T cells are associated with the development of infections. Despite that, viral suppression is a challenge and those who manage to achieve it must be closely observed because they are the ones who report more frequently depressive symptoms.
A MULTIETHNIC CHILDREN POPULATION WITH HIV INFECTION IN ITALY. PSYCHOLOGICAL STUDY OF EMOTIONS AND BEHAVIORS

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Background: Even though the progress of HIV ARV have improved 1.800.000 of children live with HIV in the world. Particularly difficult is live with this disease when patients and their family live in a poor condition and became migrant people. In the last 15 years many families have come from poorest countries to Italy. They brought different ethnicities, beliefs and cultures related to body pathology and stigma education. We propose a retrospective and prospective study to Identify obstacles and facilities to harmonize the communication strategy and understand how different ethnic groups conceive HIV infection.

Methods: cohort: 33 children 1-13aa; average 8aa; 17 girls; 16 boys. Geographical areas: Asia 3.1; East-Europe 28.1%; Italy 28.1%; South-America 6.3 %; Africa 34.4 %. Phase I Patients meet immunologist and psychologist every two months during the clinical follow-up. Consider anthropological differences, quality of life, HIV identity.. Phase II a-Child assessment : Raven-Color-Progressive-Matrices-47; Cognitive Bayley-III Scale; Raven-Progressive-Matrices-38; Strengths and Difficulties Questionnaire; Social emotional Bayley-III Scale; Pediatric Quality of life inventory. b-Parents assessment: Patient Health Questionnaire-9; General Anxiety Disorder-7; Physical and Mental Health Summary Scales-12. Phase III: Analysis tests and life stories, organize individualized interviews, counseling and first "disclosure". Phase IV: Selecting parenting support group.

Results: Fluid intelligence show a range score of QI69,5- QI130. Early traded children QI>95. PedsQL highlighted emotional end scholar problems. PHQ9 and GAD7 of mothers show score above cut off in 60% of case. SDQ show 50% children behavior problems, emotional symptoms, prosocial problems.

Conclusions: Pediatric HIV clinical path in Europe have to include the respect of child personal history with his anthropological history. Work towards the personal identity of the child is guiding him towards greater responsibility in self-care throughout his life

Clinical Trial Registration: no unique identifying number
ULCER OF LIPSCHUTZ – DESCRIPTION OF A RARE AND UNKNOWN CAUSE OF GENITAL ULCERATION

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Title of Case(s): Description of a rare and unknown cause of genital ulceration

Background: Lipschütz ulcer is a rare condition that leads to painful ulceration in the vulva, typically occurring in sexually inactive young women. In the setting of fever and acute onset of genital ulcers in girls and women, the term Lipschütz ulcer is used to describe ulcers associated with an immunologic reaction to a distant source of infection/inflammation. Triggers include bacteria and viruses, especially EBV.

Case Presentation Summary: Case 1: 25-months old girl with Down syndrome, presenting fever and flu-like symptoms. Azithromycin and prednisolone were started and after five days of persisting symptoms, a pustular then ulcerative lesion in the perineum was identified: a single and painful ulcer with flat erythematous edges and a clean granulation bottom. Intravenous oxacillin+clindamycin were given for three days. Blood count revealed left shift and elevated C-reactive protein. The lesion is improving until present day. Case 2: 3-year old asthmatic girl, presenting fever and upper-respiratory symptoms. On the 10th day of amoxicillin treatment, she presented fever. There was an elevated C-reactive protein, but the blood count was suggestive of viral infection. On the 6th day of fever, a single genital ulcer plus maculopapular lesions in arms, hands and mouth developed. As vulvar cellulitis was suspected, intravenous ceftriaxone and clindamycin was used for four days. The wound improved quickly, at complete healing occurred after ten days.

Learning Points/Discussion: Lipschütz ulcer is an uncommon entity, but recognising and including it in the differential diagnosis of vulvar ulcerations is imperative for diagnosis. Influenza or mononucleosis-like symptoms usually preceded the lesion and treatment is mainly supportive with pain relief (topical anaesthetics/oral analgesics). In case of multiple, large or deep necrotic ulcerations, topical or a short course of systemic corticosteroids may be considered.
Background: Hyperbaric Oxygen Therapy (HBOT) is increasingly being used in the pediatric population due to its immunomodulatory properties. It combines action of hyperoxia and hyperbaric pressure, leading to significant improvement in tissue oxygenation and mitochondrial metabolism, with bactericidal and pro-healing anti-inflammatory effects. This study aims to analyze the indications, outcomes, and complications of HBOT in children with infection.

Methods: Descriptive analysis of pediatric patients with infectious pathology, hospitalized in a tertiary care hospital, who underwent adjunctive therapy with HBOT, between January 2010 and December 2019 (10 years). Epidemiological, clinical, and laboratory data were collected.

Results: Thirty-two patients were included: median age of 10.4 years, 53% males, average of 34 sessions/patient. 40% had chronic disease, most commonly sickle cell disease (n=5). Indications were refractory osteomyelitis (n=14), chronic infected ulcers (n=9), necrotizing soft tissue infections (n=8), skeletal muscle-compartment syndrome (n=2), and acute thermal burn injury (n=2). Most frequently isolated pathogens were *Staphylococcus aureus* (n=9) – MSSA(n=6) and MRSA(n=3), and *Pseudomonas aeruginosa* (n=8). All patients had antibiotics and surgical interventions. In 93% of cases, there was improvement and cure without recurrence. Middle ear barotrauma was the only reported side effect (12.5%).

Conclusions: Available evidence supports a beneficial role of adjunctive HBOT when combined with culture-directed antibiotics and thorough surgical treatment, especially in refractory cases of chronic osteomyelitis and enhancement of healing in problem wounds. By creating a sustained increase in the arterial perfusion of previously hypoxic bone and soft tissues, HBOT can also reduce the susceptibility to recurrence. Although there is strong evidence of synergic results, there is still a pressing need for well-defined protocols.
MYCOPLASMA PNEUMONIAE-INDUCED RASH AND MUCOSITIS

Title of Case(s): Mycoplasma pneumoniae-induced rash and mucositis

Background: Mycoplasma pneumoniae-induced rash and mucositis (MIRM) is a newly characterized entity, described in 2015. It is clinically distinct from Steven-Johnson syndrome as there is significant mucosal involvement with minimal (if any) skin lesions, reduced systemic symptoms, and is more common in children and young adults. Since diagnosing MIRM is limited to serology or PCR, clinical diagnosis can be challenging and lead to treatment delays.

Case Presentation Summary: Case 1 - 8-year-old boy presented with a 5-day history of fever, dry cough, sore throat, and adynamia, evolving with mucocutaneous lesions. There were painful erosions on the lips and oral mucosa, bilateral conjunctival hyperemia, erythema and edema of the glans penis and prepuce. He received clarithromycin for ten days. Case 2 - 12-year-old boy presented with a 5-day history of fever, dry cough, sore throat, and headache, as well as progressive mucocutaneous lesions. There were painful erosions on the lips and oral mucosa, bilateral conjunctival hyperemia, erythema and edema of the glans penis and prepuce, and target on the trunk, palms, and plants. He received azithromycin and prednisone for ten days. Both patients presented a resolution of pulmonary symptoms and gradual improvement of mucocutaneous lesions. Chest radiography showed diffuse interstitial infiltrate. Serology was positive for M. pneumoniae (IgM and IgG) and negative for herpes simplex virus, cytomegalovirus and EBV.

Learning Points/Discussion: Pneumonia, accompanied by ocular and mucocutaneous eruptions, and particularly in young patients, should raise clinical suspicion of MIRM. There is no standard treatment, but antibiotics with or without steroids are often used. Recognition of MIRM as a clinical entity distinct from other mucocutaneous eruptions may be clinically beneficial as treatment options, disease prognosis, and patient education of MIRM will be different from that of the latter.
FATHER AND 12-YEAR-OLD SON PRESENTING CONCURRENTLY WITH FEVER AND SPLENOMEGALY

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Title of Case(s): Father and 12-year-old son presenting concurrently with fever and splenomegaly

Background: Malaria was a common disease in Greece since antiquity. Following eradication program, Greece achieved malaria-free status in 1974. Since then, malaria has been mostly imported, possibly due to the massive influx of immigrants from Africa and Asia, with the identity of imported strains reflecting the area of original infection.

Case Presentation Summary: A 12-year-old Greek boy presented with a week history of high fever, shaking chills and non-productive cough. Fever appeared daily during afternoon and persisted for about 12 hours despite administration of antipyretics. He reported headache, loss of appetite, abdominal pain and prostration. His past medical history was unremarkable with no recent travel. He lives in the Marathon area in East Attica, in a small village ~40 km from the center of Athens, which is a wetland area. His father also had similar symptoms starting on the same day. His liver and spleen were palpable. Laboratory evaluation revealed anemia, thrombocytopenia, elevated ESR and CRP. Cultures and tests for EBV, CMV, Brucella, Toxoplasma and Leishmania were negative. A rapid test and microscopy for malaria yielded a positive result for *Plasmodium vivax*, which was confirmed by PCR. Chloroquine and Primaquine therapy was initiated. On the third day of treatment, decreased oxygen saturation with facial pallor, but no dyspnea was observed. He developed methemoglobinemia treated with ascorbic acid and had uneventful recovery. His father, a farmer, was diagnosed with *P. vivax* infection and treated with antimalarial treatment.

Key Learning Points: Malaria should be included in the differential diagnosis of febrile patients without travel history and even in the absence of a typical tertian or quartan fever pattern, especially in case of residence or visit to areas of known recent local malaria transmission. Pallor during primaquine treatment should prompt oxygen saturation testing and methemoglobin in cases with desaturation to prevent this potentially severe side effect.
A REVISIT TO KOCHER’S CRITERIA IN REFERENCE TO NEW GENERATION SERUM BIOMARKER TO DIFFERENTIATE SEPTIC ARTHRITIS WITH TRANSIENT SYNOVITIS HIP – A COHORT STUDY.

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Background: Sensitivity of kocher’s four variables criteria and its modification by (Cavied et. al.) decreased to 59% (against 95% as claimed) on external validation. In the present study, we planned to make a prediction model for septic arthritis on basis of CD64 on neutrophils (nCD64) as an adjunct parameter to Kocher’s criteria.

Methods: Children (n=34) below 18 years of either gender (M=22/F=12) below 18 years presenting with acute, new onset, non – traumatic limp or joint pain were enrolled (as per inclusion-exclusion criterion) as cases and otherwise normal age-sex matched children as controls (n=35). Full clinical work-up including kocher’s criteria [Non weight-bearing; Temperature; Erythrocyte Sedimentation Rate(ESR) and Total Leucocyte count(TLC) in addition to C-reactive protein(CRP) and CD64 count on neutrophils(nCD64) were done. X-ray, sonography of joint was done to confirm presence or absence of joint effusion. Arthrocentesis was done in effusion positive cases. Cases were divided into septic arthritis (polymorph>50,000cells/mm3) and transient synovitis (polymorph <50,000 cells/mm3).

Results: We analyses 34 cases [septic arthritis (n=19), transient synovitis (n=15)] and controls (n=35). Statistically significant differences were found in parameters (Non-weight bearing, temperature, ESR, CRP, TLC and nCD64 count) between cases and controls (<0.0001). In cases, except the nCD64 count (p= 0.0007), all the four kocher’s criteria tests including CRP showed insignificant difference between septic arthritis and transient synovitis cases. ROC maximum area was 0.8316 and found to be significant (P=0.0010). Addition of nCD64 count in kocher’s criteria had increase their sensitivity, specificity and AUC from 57.77, 70.17 and 0.63 to 58.33, 76.31 and 0.6851 respectively.

Conclusions: The nCD64 count was the potential diagnostic biomarker to differentiate septic arthritis from transient synovitis and should be used as an adjuvant to kocher’s criteria to increase its reliability.

Clinical Trial Registration: Not Applicable
RISK FACTORS OF UTI IN CHILDREN WITH NEPHROTIC SYNDROME

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Background: Urinary tract infection is a common complication in children with nephrotic syndrome. Many children with nephrotic syndrome suffer from UTI and leads to so many mortality & morbidity in developing country like Bangladesh. Many risk factors are responsible for development of UTI. Many etiological agent causes UTI. For this background, we did this study to see risk factors of UTI in children with nephrotic syndrome.

Methods: A case control study was done in the department nephrology ward of Mymensingh medical college hospital from July 2017 to June 2019 to identify the risk factors of UTI in children with nephrotic syndrome. Totally 90 patients of nephrotic syndrome children aged 2-10 years who fulfilling the inclusion & exclusion criteria are selected as group I (Case) and group II (Control) according to urine culture report. Group I was UTI positive & Group II was UTI negative.

Results: Mean age of group I was 5.26 ±3.18 year & group II was 6.03±2.85 years. Male predominance in both groups. No significant difference was found in age & sex both the groups (p-value >.005). Fever, dysuria, abdominal pain, anasarca, vomiting, & pallor were found as common presentation in group I. Children with dysuria and abdominal pain were significantly higher in group I than group II (p-value<.001). UTI was found more in relapsed cases than the initial attack. E.coli is the most common etiological agent (37.8%).

Conclusions: UTI & Nephrotic syndrome closely related with each other. All the patient of nephrotic syndrome have UTI both 1st attack or relapse cases. UTI is the most common cause of relapse of nephrotic syndrome. Elimination of risk factors of UTI like Constipation, Circumcision & Proper management of UTI in children with nephrotic syndrome reduce the risk of mortality & morbidity of children.
MEASLES ANTIBODIES IN VERTICALLY AND HORIZONTALLY HIV-INFECTED INDIVIDUALS AND RESPONSE TO A BOOSTER DOSE IN THOSE WITH SERONEGATIVE RESULTS

R. Simakawa¹, M.I. De Moraes-Pinto², B. Araujo², E. Ono², F. Carmo², A. Gouvea², D. Machado², S. Beltrão², R. Succi²
¹Federal University of São Paulo, Paediatrics, São Paulo, Brazil, ²Federal University of Sao Paulo, Pediatrics, São Paulo, Brazil

Background: Global measles re-emergence in the last years has brought back into discussion if people living with HIV (PLHIV) are well protected with routine vaccination and which factors could be related to it. At this concerning scenario, assessing measles vaccination adequacy and measles immunological status of PLHIV might be of interest.

Methods: A prospective, cohort study approved by the local ethics committee was conducted from July 2018 to December 2019. The study was done on four groups of patients: 96 vertically HIV-1-infected individuals, 69 horizontally HIV-1-infected individuals, 89 healthy vaccinated controls and 20 controls with history of measles disease. Data on epidemiology and past medical history, including measles vaccination status, was analyzed. A blood sample was collected to measure measles antibodies by ELISA. An extra MMR vaccine dose was offered to those with seronegative results, with a subsequent test at least 30 days after.

Results: Measles seropositivity was significantly lower among vertically HIV-infected individuals in comparison to horizontally HIV-infected and controls (table). All seronegative individuals to whom an extra MMR vaccine dose was given (17/17) seroconverted. Virological suppression at assessment was more prevalent among horizontally HIV-infected compared to vertically HIV-infected and it was correlated to higher measles seropositivity prevalence and higher median measles IgG titers (table).

<table>
<thead>
<tr>
<th></th>
<th>Vertical HIV (n=96)</th>
<th>Horizontal HIV (n=69)</th>
<th>Vaccinated controls (n=89)</th>
<th>Control with history of measles disease (n=20)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female gender</td>
<td>34 (35%)</td>
<td>33 (48%)</td>
<td>72 (80%)</td>
<td>15 (75%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Median age in years (range)</td>
<td>21.1 - 32.1</td>
<td>26.4 - 52.0</td>
<td>26.0 - 42.0</td>
<td>61.8 - 71.8</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Measles Qb-7+ cell conversion at assessment (range)</td>
<td>6/15 (40%)</td>
<td>60/65 (92%)</td>
<td>n.a.</td>
<td>n.a.</td>
<td>0.014</td>
</tr>
<tr>
<td>Number of individuals with virological suppression at assessment</td>
<td>50/86 (58%)</td>
<td>93/87%</td>
<td>n.a.</td>
<td>n.a.</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Measles antibody v/real time determined in virological assessment (range)</td>
<td>12.0 - 24.1</td>
<td>4.5 - 16.2</td>
<td>n.a.</td>
<td>n.a.</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Number of individuals with virological suppression at assessment</td>
<td>51/85 (60%)</td>
<td>95/95%</td>
<td>n.a.</td>
<td>n.a.</td>
<td>0.391</td>
</tr>
<tr>
<td>Number of individuals with measles antibody v/real time at assessment (range)</td>
<td>17 (18%)</td>
<td>25-30%</td>
<td>35-37%</td>
<td>25-37%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Median time (months) between last measles vaccine dose and assessment (range)</td>
<td>10 (9 - 35)</td>
<td>11 (7 - 29)</td>
<td>11 (7 - 29)</td>
<td>n.a.</td>
<td>0.153</td>
</tr>
<tr>
<td>Number of individuals with seropositive measles antibody v/real time at assessment</td>
<td>55 (55%)</td>
<td>55 (99%)</td>
<td>85 (97%)</td>
<td>85 (97%)</td>
<td>0.004*</td>
</tr>
<tr>
<td>Measles antibodies IgG time (10/10/10) (range)</td>
<td>1.55 (1.0 - 1.1)</td>
<td>779 (27 - 3232)</td>
<td>358 (71 - 4052)</td>
<td>1229 (741 - 1955)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Number of individuals with seropositive measles antibody v/real time at assessment (range)</td>
<td>1.54 (1.0)</td>
<td>1.1</td>
<td>0.5 (0.05)</td>
<td>n.a.</td>
<td>0.360</td>
</tr>
</tbody>
</table>

n.a. - not applicable
* p < 0.05 between vertical HIV and horizontal HIV, vertical HIV and vaccinated controls, vertical HIV and control with history of measles disease, vaccinated control and control with history of measles disease.
Conclusions: At the present context of vaccine hesitancy and measles re-emergence, it is important to understand which factors may be involved in better responses to MMR vaccine among PLHIV. This study suggests that an extra MMR vaccine dose may be considered to PLHIV during outbreaks, especially to the ones vertically infected and already immunocompromised at the time of routine vaccination.
BACKGROUND: Pediatric Clostridium difficile-associated diarrhea (PCDAD) is increasingly diagnosed worldwide; consequently, the increasing need to have a proper isolation space in hospitals is challenging even more. This aims of this study was to assess the features of the hospitalized cases of Pediatric Clostridium difficile with associated diarrhea that might be assigned as predictors for the empirical preemptive guidance of isolation.

METHODS: Children with Pediatric Clostridium difficile-associated diarrhea cases diagnosed in our nearly 100 hospitals during the year 2019 were included. Data on demographics, medication exposure, and hospital healthcare encounters were collected from the EpiInfo7 database software that we use to centralize all the data. Percentages with 95% CI were performed to identify predictors of pediatric Pediatric Clostridium difficile-associated diarrhea.

RESULTS: The study group includes 52 PCDAD cases with a median age of 5 years (IQR: 3–15 yrs), male/female rate: 0.52. Exposures found: (a) 63.5%; CI95%: (49.0%–76.4%) hospitalized in the last year; (b) 82.4% (69.1%–91.6%) had antibiotic exposure within 3 month of illness. From all 45 antimicrobial cures prescribed, 66.7% were cephalosporin and carbapenems. Finally, 90.4% (79.0%–99.8%) of cases were exposed to hospitalization or antimicrobial treatment prior to current admission. Prevalence was similar by gender (RR:0.93 (0.79–1.10), p: 0.81) and by age groups (RR: 0.89 (0.72–1.06); p:0.44).

CONCLUSIONS: It appears that preemptively establishing of contact precautions for the children that were admitted at the hospital with acute diarrheal syndrome and with a history of recent hospitalization might be an effective measure to prevent the transmission of the Clostridium difficile infection in health settings. Such a measure may also be effective to children with a history of systemic antimicrobial treatment.
FETAL VARICELLA SYNDROME AND HOSPITALISED NEONATAL VARICELLA: A CASE FOR SURVEILLANCE

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²Public Health England, Immunisation And Countermeasures Division, London, United Kingdom,
³Hospital Pediátrico, Centro Hospitalar e Universitário de Coimbra, Faculdade De Medicina, Universidade De Coimbra, Coimbra, Portugal

Background and Objective: Young babies and non-immune pregnant women are at risk of severe complications of varicella. Although rare, the impact of an infection during pregnancy can be devastating for both the mother and baby. Two percent of babies born to pregnant women infected between the 13th and 20th weeks will develop fetal varicella syndrome (FVS). A literature review was conducted to identify data on the incidence of FVS and hospitalised neonatal varicella in the UK.

Methods: A literature review was conducted using Medline to identify publications on FVS and neonatal varicella incidence. The search was limited to publications in the English language. The search terms included fetal or congenital varicella syndrome, neonatal varicella, epidemiology, burden and incidence. Abstracts were reviewed for relevance and the reference lists from studies reviewed were used to identify additional publications.

Learning Points/Discussion: There are limited data regarding incidence of FVS and neonatal varicella in the UK as varicella is not a notifiable condition. A recent surveillance study utilising Hospital Episode Statistics data for all admissions in England demonstrated that in 2016, there was a person-based rate of varicella of 31.1 per 100 000 infant population. This data looked at any diagnosis of VZV in neonates under 28 days and did not distinguish between FVS and neonatal varicella. Estimates based on surveillance data from sentinel GP practices in England and Wales estimate that varicella affects 3 in 1000 pregnancies resulting in an estimated incidence of fetal varicella syndrome of 1.6 per 100,000 births. An ESPID/INOPSU grant has been awarded to conduct surveillance for fetal varicella syndrome (FVS) and hospitalised neonatal varicella in the United Kingdom and Portugal. This upcoming study will provide critical data on disease burden required to inform vaccination policies.
MOLECULAR EPIDEMIOLOGY OF GRAM-NEGATIVE BLOODSTREAM INFECTIONS IN QUEENSLAND CHILDREN

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¹The University of Queensland, Uq Centre For Clinical Research, Brisbane, Australia, ²The University of Queensland, School Of Chemistry And Molecular Biosciences, Brisbane, Australia, ³Pathology Queensland, Microbiology, Brisbane, Australia

Background: Establishing new therapeutic options for the treatment of antimicrobial resistance (AMR) in Gram-negative infections is a global priority. A detailed understanding of the molecular mechanisms of AMR complicating invasive childhood infections would facilitate the development of new therapeutic agents, but surveillance studies of AMR focus overwhelmingly on adults. We describe the molecular epidemiology of Gram-negative bloodstream infections (GNBSI) in Queensland.

Methods: A study of the mechanisms of AMR in bacteria causing GNBSI in children in Queensland, Australia. Illumina whole genome sequencing (WGS) was performed on Gram-negative bloodstream isolates collected from 26 hospitals between 2018 and 2019. Raw sequence data was analysed using an infectious disease genomics pipeline developed in collaboration with the microbial genomics laboratory at the UQ School of Chemistry and Molecular Biosciences.

Results: 146 isolates consisting of E. coli (64%), Pseudomonas spp. (16%), Klebsiella spp. (10%), and Enterobacter spp. (8%) were analysed. WGS identified blaTEM-1 as the most common beta-lactamase in E. coli (23%), followed by aph gene variants encoding aminoglycoside resistance (27%). blaSHV-1 was present in 4% of isolates, and fosA encoding fosfomycin resistance was found in 25% of all isolates. Only one E. coli isolate contained an extended-spectrum beta-lactamase (blaCTX-M-15) and 3% contained single nucleotide polymorphisms within gyrA and parC associated with fluoroquinolone resistance.

Conclusions: We illustrate the predominant mechanisms of AMR from a state-wide study of invasive Gram-negative infections in Queensland children. Few isolates carried ESBLs, and no carbapenemases were observed. The distribution of fosA may have implications for treatment. Data are emerging to support new agents targeting resistant Gram-negative infections in adults. Systematic reporting of the molecular epidemiology of AMR in children will help establish which agents should be prioritised for translation into paediatric clinical practice.
ECONOMIC BURDEN OF PNEUMOCOCCAL AND POTENTIALLY RELATED DISEASES IN CHILDREN IN THE LIGURIA REGION, ITALY

D. Amicizia1, M. Astengo2, C. Paganino2, C. Trucchi2, A. Orsi1, F. Varlese2, T. Hu3, T. Petigara4, C. Alimenti2, G.M. Prandi6, G. Icardi1, F. Ansaldi2
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Background: Streptococcus pneumonia (SP) can cause invasive (i.e. meningitis, bacteremia and bacteremic pneumonia) and non-invasive pneumococcal diseases (i.e. acute otitis media (AOM) and non-bacteremic pneumonia) with a substantial economic burden in children. Since May 2003, a large-scale programme of vaccination against SP started in Liguria. All newborns were invited to receive PCV. This analysis assessed the economic burden of pneumococcal and potentially related diseases among children aged <15 years from 2012 to 2018.

Methods: A retrospective observational analysis was conducted to assess costs associated with emergency department (ED) visits and hospitalizations for bacteremia, meningitis, pneumonia, and AOM in children <15 years in the Liguria region from 2012-2018. Pneumococcal and potentially related diseases were identified using pneumococcal-specific and non-specific ICD9 codes in the Ligurian Regional Administrative Databases. Total costs and cost per ED and hospital admissions were also calculated from Regional Administrative Databases.

Results: Average annual total cost associated with ED visits and hospitalizations (2012-2018) for pneumococcal and potentially related diseases amounted to €2,067,000; 96% of costs were due to hospitalizations. The percentages of total hospital costs attributable to pneumococcal and unspecified pneumonia, bacteremia and AOM were 59%, 22% and 16%, respectively. Cost for each hospitalization over the analysis period amounted to €4,174 for meningitis, €3,515 for bacteremia, €3,199 for pneumonia and €1,535 for AOM.

Conclusions: The economic burden of pneumococcal and potentially related diseases continues to be substantial in children aged <15 years in Liguria. Hospitalizations for pneumococcal and unspecified pneumonia caused majority of the burden. Vaccination remains the most important and effective public health tool that can reduce the burden of pneumococcal disease, particularly in infants, subjects at high risk of severe disease or associated complications.
RETROSPECTIVE STUDY TO EVALUATE THE FREQUENCY, FEATURES AND COSTS OF ROTAVIRUS HOSPITAL INFECTIONS IN SPAIN AMONG REGIONS WITH DIFFERENT VACCINATION COVERAGE RATES. THE FHOROS STUDY.


¹Hospital de Basurto, Pediatrics, Bilbao, Spain, ²Hospital Germans Trias i Pujol, Paediatrics, Badalona, Spain, ³Hospital Universitario Clínico San Carlos, Paediatrics, Madrid, Spain, ⁴Hospital 12 de Octubre, Pediatrics, Madrid, Spain, ⁵Hospital de Donostia, Pediatrics, San Sebastián, Spain, ⁶Hospital Juan Ramón Jiménez, Pediatrics, Huelva, Spain, ⁷Hospital Virgen de la Arrixaca, Pediatrics, Murcia, Spain, ⁸Hospital Central de Asturias, Pediatrics, Oviedo, Spain, ⁹Complejo Hospitalario de Navarra, Pediatrics, Pamplona, Spain, ¹⁰Hospital Regional de Málaga, Pediatrics, Málaga, Spain, ¹¹Hospital La Fe, Pediatrics, Valencia, Spain, ¹²Hospital Universitario Río Hortega, Paediatrics, Valladolid, Spain, ¹³MSD, Medical Affairs Department, Madrid, Spain

Background: In Spain rotavirus (RV) vaccination is not included in the National Immunization Program but it is recommended by paediatricians with heterogeneous vaccination coverage rates among regions (VCR). This study aims to evaluate the frequency, characteristics and costs of RV Gastroenteritis (RVGE) hospitalizations in children <5 years old during a 5-year period (2013-2018). Preliminary results on frequencya and features are showed in this abstract.

Methods: Observational, multicentre, retrospective study performed at 12 hospitals of regions with different VCR (low: <30%, moderate: 30-60%, high: >60%). All children <5 years admitted to with microbiological-confirmed RVGE were identified from hospital databases for hospitalization rate estimation. Odds ratios (OR) for hospitalizations rates between regions were calculated. For RVGE characteristics evaluation patient clinical records were reviewed. A total of 1,731 RVGE episodes were recorded; 16.7% were nosocomial infections.

Results: 70.5% occurred between January-April. Average [SD] age was 13.69 [11.73] months; 59.2% were boys. Only 14.7% (147/546) were attending day-care. Most frequent previous medical conditions were prematurity (13.1%) and low birth weight (9.9%). Chronic diseases were reported in 19.5% of episodes. Most frequent complications included dehydration (48.2%; moderate-serious: 59.4%), hydroelectrolytic alteration (37.7%), seizures (5.0%). 2.1% were admitted to ICU. Table. Percentage of RVGE related to total hospitalizations in children <5 years among VCR groups.

<table>
<thead>
<tr>
<th>VCR</th>
<th>Total 2013-2018</th>
<th>OR (IC 95%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30%</td>
<td>3.98</td>
<td>Ref.</td>
</tr>
<tr>
<td>30-60%</td>
<td>2.96</td>
<td>0.73 (0.66-0.82)</td>
</tr>
<tr>
<td>&gt;60%</td>
<td>1.78</td>
<td>0.44 (0.39-0.49)</td>
</tr>
</tbody>
</table>
**Conclusions:** RVGE hospitalization rates are still significant in Spain, but inversely dependent on the VCR. Most frequent chronic diseases recorded include pneumopathy, gastrointestinal disorders, cardiopathy, encephalopathy, nephropathy, and failure to thrive. Complications related to RVGE are frequent, specially dehydration in almost 50% of hospitalizations.
E-POSTER VIEWING
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10-28-2020 8:00 AM - 7:00 PM

PROSPECTIVE VALIDATION OF INDIVIDUALIZED BAYESIAN DOSE OPTIMIZATION TOOL DOSOPT FOR VANCOMYCIN TREATMENT IN NEONATES

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Background: Despite numerous accepted dosing schedules only about 25% of initial and 40% of all subsequent vancomycin trough concentrations (C_tr) are within the desired range in neonates. Our aim was to prospectively validate whether DosOpt-based individual dosing is safe and more likely to achieve therapeutic drug concentrations than conventional dosing.

Methods: 50 neonates with Gram-positive late onset sepsis treated with vancomycin will be recruited in 3 Estonian NICUs. Initial vancomycin dose is based on a population model. Thereafter dose will be adjusted every 36-48h with Bayesian software DosOpt (https://biit.cs.ut.ee/dosopt_ss/) based on C_tr value(s) and using optimization target of C_tr 10-15mg/l. Dose variation between 5-30 mg/kg and interval 6-24h are allowed. The proportion of neonates attaining the optimization target and clinically acceptable target of C_tr 8-17mg/l in current study is compared with historical group treated between January 2016 and May 2019.

Results: By January 10th 2020, 14 neonates with median current weight of 870g and postnatal age 14 days have been recruited. A total of 29 C_tr ranging between 5-22.4mg/L have been measured; 14 C_tr after initial (model-based) and 15 after customized (Bayesian) dosing. Based on primary data, DosOpt improves the probability of target attainment (PTA) by around 10-20% (Table). No dangerously high or low concentrations were observed. Tabel. Demographic characteristics and measured vancomycin concentrations

<table>
<thead>
<tr>
<th></th>
<th>Historical group (01.01.2016-16.05.2019)</th>
<th>DosOpt group (29.05.2019-10.01.2020)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nr of patients</td>
<td>99</td>
<td>14</td>
</tr>
<tr>
<td>Body weight in grams: median (range)</td>
<td>1250 (450-5045)</td>
<td>870 (550-3690)</td>
</tr>
<tr>
<td>Postnatal age in days: median (range)</td>
<td>16 (1-84)</td>
<td>14 (4-31)</td>
</tr>
<tr>
<td>Initial vancomycin C_tr (Nr)</td>
<td>99</td>
<td>14</td>
</tr>
<tr>
<td>PTA of C_tr 10-15mg/l</td>
<td>26.3%</td>
<td>35.7%</td>
</tr>
<tr>
<td>PTA of C_tr 8-17mg/l</td>
<td>52.5%</td>
<td>78.5%</td>
</tr>
<tr>
<td>All vancomycin C_tr (Nr)</td>
<td>250</td>
<td>29</td>
</tr>
<tr>
<td>Median C_tr (range) mg/l</td>
<td>11.5 (2-57.5)</td>
<td>12.3 (5-22.4)</td>
</tr>
<tr>
<td>PTA of C_tr 10-15mg/l</td>
<td>34.8%</td>
<td>44.8%</td>
</tr>
<tr>
<td>PTA of C_tr 8-17mg/l</td>
<td>61.6%</td>
<td>82.8%</td>
</tr>
</tbody>
</table>

Conclusions: Based on current limited data, DosOpt appears safe and may ensure improved hitting of targeted C_tr of Vancomycin in neonates. Continuing the study is justified.

Clinical Trial Registration: Eudra CT no: 2019-000668-14
Background: Limited data are available for Kawasaki disease (KD) under 12 months of age, especially in Caucasians. We aim to analyze the clinical and laboratory features of infant KD.

Methods: This retrospective study included infants with KD who were younger than 12 months. Epidemiological, clinical and laboratory features were recorded as well as treatments and outcomes. Patients with incomplete and complete KD (iKD and cKD) were compared.

Results: A total of 42 infant KD patients [27 (65%) male] were evaluated that 32 (76%) of them were iKD. Twelve patients aged below 6 months, and three below 3 months. The median age was 9 (range: 1-12 months) months. Twenty (48%) patients had coronary involvement of whom 15 (75%) were iKD. The mean duration of fever was 7.74 ± 3.88 days and the length of hospitalization was 8.09 ± 4.23 days. The frequency of mucosal changes, conjunctivitis, extremity edema, periungual desquamation, and gallbladder hydrops was significantly higher in cKD, whereas lymphadenopathy was more common in iKD. There were no differences between the two groups in terms of length of hospital stay, fever duration, and laboratory results. However, platelet distribution width (PDW) was higher in infants with coronary involvement (p=0.015). Treatment was successful with one dose IVIG in 38 infants, four required a second dose and two of these also required steroids.

Conclusions: These findings support the lack of defining characteristics in KD among infants. Even so, it is feasible to suggest that increased PDW levels may be a warning factor for coronary involvement in infant KD.

Clinical Trial Registration: It is not a clinical trial study
APPOINTMENT FOR PRE-IMMUNOSUPPRESSIVE THERAPY SCREENING FOR INFECTIOUS DISEASES IN PEDIATRICS

B. Sousa Nunes, T. Milheiro Silva, F. Candeias
Hospital Dona Estefânia, Centro Hospitalar Universitário Lisboa Central, Infectious Diseases Unit, Lisbon, Portugal

Background: Providing health-care to children undergoing immunosuppressive therapy is challenging and increasingly common. The CRIPTO initiative (Portuguese acronym for appointment for pre-immunosuppressive therapy screening for infectious diseases) was created to try to prevent infectious complications of immunosuppressive therapy, and tackle the current suboptimal immunisation rates in this population. The aim of the present study is to characterise the population followed in CRIPTO.

Methods: We retrospectively analysed data from patients undergoing CRIPTO appointments, scheduled between February 2016 and December 2019 (47 months). The parameters included demographics, clinical information, immunisation status, infectious disease screening and the recommended vaccination schedule. Descriptive statistics were computed for all parameters.

Results: 110 patients, with an average age of 11.5 years (SD 5.2) and an average of 2.8 visits/patient (SD 1.6). Only 39.1% were assessed before starting immunosuppressants; the remaining were under corticotherapy (71.6%), immunomodulators (56.7%), calcineurin inhibitors (17.9%), biological agents (13.4%). The main causes of referral were inflammatory bowel disease (24.5%) and atopic dermatitis (9.1%), with 3 newborns enrolled for in-uterus immunosuppressant exposure. The screening identified tuberculosis (n=9) and Strongyloides infection (n=3), with no cases of HIV or hepatitis B/C. The immunisation schedule was incomplete in 19%; 481 vaccines were recommended.

Conclusions: Children undergoing immunosuppressive therapy have increased susceptibility to infections. The infectious disease screening and vaccination of this specific-risk group should be considered a priority, ideally performed before the beginning of treatment and following a consistent protocol. The cost of non-subsidised vaccination in this population is (expected to be) elevated.
MANAGEMENT OF PEDIATRIC SOIL-TRANSMITTED HELMINTHIASIS IN A NON-ENDEMIC AREA: A TWICE-NEGLECTED DISEASE.

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¹Hospital Universitari Vall d’Hebron, PROSICS Barcelona, Universitat Autònoma Barcelona, Spain., Pediatric Infectious Diseases And Immunodeficiencies Unit, Barcelona, Spain., ²Hospital Universitari Vall d’Hebron, PROSICS Barcelona, Universitat Autònoma Barcelona, Spain., Microbiology Department, Barcelona, Spain

Background: Soil-transmitted helminthiasis are widely distributed in tropical and subtropical areas causing substantial disease and disability. Current therapeutic options show limited efficacy, particularly against *Trichuris trichiura*. Some groups propose an epidemiological approach to patients coming from endemic countries (empirically treat all patients), instead of an individual one (diagnose, treat and confirm curation). The aim of this study is to describe patients’ demographic, clinical and analytical characteristics, treatment and outcome in a non-endemic cohort.

Methods: We performed a descriptive retrospective study including all paediatric patients (0-16 years) visited in an International Health Unit in a non-endemic area with soil-transmitted helminthiasis (2014-2018). We included patients with infections caused by *Trichiuris trichiura*, hookworm (*Necator americanus* and *Ancylostoma duodenale*), *Ascaris lumbricoides* and *Strongyloides stercoralis*, diagnosed microbiologically using the formol-ether or Ritchie technique, and culture or positive serology to *S. stercoralis*.

Results: Forty-nine patients from 17 countries were included, with 63 samples testing positive for soil-transmitted helminths. Seventy-five percent of patients were immigrants and long-period travellers (mean time 11.9 months). Twenty-four patients (48.9%) had been previously tested (automatic concentration test) obtaining a negative result for helminths (100%). All patients but one received treatment according to current guidelines. Curation rates with the first line treatment were 83% for *A. lumbricoides*, 40% for hookworm, 72% for *T. trichiura* and 100% for *S. stercoralis*. Only 53% of patients were followed up until microbiological curation.

Conclusions: Curation rates in our cohort are variable according to the species, similarly to those published in studies conducted in endemic areas. The limited effectiveness of treatments suggests that after the first line treatment, a follow-up must be done until confirming curation. The efficacy of available treatment schedules is not good enough to recommend an empiric approach in our health-care system.
HIV ASSOCIATED NEPHROPATHY – EXPERIENCY OF A TERTIARY HOSPITAL

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Background: Children with Human immunodeficiency virus-associated nephropathy (HIVAN) may present with the classical features of nephrotic syndrome or with isolated and persistent proteinuria. The renal histological lesions are typically characterized by evidence of focal and segmental collapsing glomerulosclerosis and microcystic tubular dilatation. The exact prevalence of HIVAN in children is unknown as the definitive diagnosis requires renal biopsy, which is not routinely performed. The aim of the present study is to characterise the population of a tertiary hospital with respect to the diagnosis of HIVAN.

Methods: Cross-sectional descriptive study of HIV-infected children, followed in immunodeficiency appointments between January and December 2019 (12 months), with the diagnosis of HIVAN.

Results: We report 4 cases of HIVAN (5.3%), all in HIV-1 infected children of African ancestry. Average age at diagnosis of 3 years (SD1). Clinical and immunological categories B1 (n=2), B2 (n=1), B3 (n=1). HIV load exceeded 400 copies/mL in 2 patients and CD4 cell count nadir was lower than 30/mL in 1 child. 2 patients had already begun anti-retroviral therapy, with poor compliance. All had significant proteinuria (urine protein/creatinine ratio within 0.22-1.70), with normal kidney function. No history of diabetes, hypertension, acute kidney injury or exposure to other nephrotoxic drugs registered.

Conclusions: Effective anti-retroviral therapy is associated with a marked improvement of HIVAN and its early use may prevent progression to end-stage renal disease. Proteinuria and renal function should therefore be routinely monitored. In the study population, monitoring seems to be of particular relevance in children of African ancestry and children with low adherence to anti-retroviral therapy.
RARE CASE OF INTRACRANIAL INFECTION- COULD HAVE BEEN DIAGNOSED EARLY?

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Title of Case(s): Rare Case Of Intracranial infection- could have been diagnosed early?

Background: Amoebic encephalitis is an infrequently encountered, fatal infection of the CNS seen mostly in immunocompromised individuals. Granulomatous Amebic encephalitis (GAE) is a subacute to chronic infection caused by Acanthamoeba spp. and Balamuthia mandrillaris. The symptoms are nonspecific which can be easily mistaken for other bacterial, viral disease, with no definite diagnostic test its diagnosis is most often made post-mortem. The prospect for successful treatment of GAE remains poor with nearly 90% case fatality rate. Here we describe a GAE caused by Acanthamoeba.

Case Presentation Summary: 9 month old girl adopted by an orphanage, when she was found in the garbage with animal bite marks. She presented with fever, reduced activity and sensorium, nodular swelling in the left parotid area, LMN-facial, 9th and 10th cranial nerve palsy and stable vitals. She was immunised for age, thriving well and developmentally normal. MRI Brain showed multiple cortical, subcortical, basal ganglionic and left inferior cerebellar peduncle lesions with eccentric nodular focus of enhancement. CSF analysis showed 44 WBC with 36 lymphocytes, low sugar. Toxoplasma PCR, Biofire meningitis-PCR, geneXpert and fungal study on CSF were negative. She was managed with Meropenem and Vancomycin initially. With possible differential of toxoplasma and fungal infection, Clindamycin, pyrimethamine and liposomal amphotericin B were initiated. Even with the above measures child deteriorated and expired after 12 days of hospital stay with severe brain stem dysfunction. Postmortem brain tissue biopsy was positive for Acanthamoeba.
Learning Points/Discussion: Acanthamoeba is a pathogenic free-living amoeba in air, soil, water. It is transmitted by cuts, skin wounds, aerosols. The yield of the organism on CSF is very low. A combination of Pentamidine, azole (Fluconazole + Itraconazole), Sulfadiazine, Flucytosine can be used for treatment. GAE has to be considered in patients with chronic/acute/sub-acute CNS syndrome with no apparent cause. A high index of suspicion should be maintained even in immunocompetent persons as delay in diagnosis and therapy is main reason for the increased fatalities.
SUCCESSFUL TREATMENT OF A CHILD ON ECMO WITH KLEBSIELLA PNEUMONIAE BACTEREMIA WITH FOSFOMYCIN AND MEROPENEM

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Title of Case(s): Successful treatment of a child on ECMO with Klebsiella pneumoniae bacteremia with fosfomycin and meropenem

Background: Fosfomycin is a broad-spectrum bactericidal antibiotic, with activity against Gram-positive and Gram-negative microorganisms, including multidrug-resistant bacteria. In vitro studies have reported a synergistic effect with many antimicrobials and an effective biofilm penetration. Nevertheless, there isn’t a clear indication for treatment of life-threatening bacteremia. We describe the case of a child on ECMO who developed a Klebsiella pneumoniae sepsis and was successfully treated with a combination therapy of meropenem and fosfomycin.

Case Presentation Summary: A 10-year-old girl with pleuroparenchymal fibroelastosis secondary to chemotherapy awaiting lungs transplant developed severe respiratory failure requiring veno-venous extracorporeal membrane oxygenation (ECMO) support. She presented a septic shock with need to switch to a veno-arterial ECMO. Blood cultures from central venous catheter (CVC) resulted positive for Klebsiella pneumoniae not MDR. Given the patient’s severe clinical conditions and the numerous vascular accesses, treatment with meropenem was started. Substitution of vascular accesses was discussed, but it was deemed excessively dangerous in this clinical setting. CVC local lock therapy with amikacin was implemented. Furthermore, since a good synergistic action with carbapenems has been described, intravenous fosfomycin (100 mg/kg every 6 hours) was added. Despite no clinical studies have been carried out in patients on ECMO, fosfomycin has also the ability to penetrate into biofilms, reducing the bacterial density and modifying biofilm structure. After 10 days of this combination therapy, blood cultures resulted negative.

Learning Points/Discussion: In conclusion, in our patient the combination of fosfomycin and a carbapenem was effective in sterilizing blood cultures; this association should be considered in treating Gram-negative bacteremia. More data from clinical trials are needed to confirm efficacy of treatment with fosfomycin in life-threatening infections. Also pharmacodynamics and pharmacokinetics studies are required to optimize fosfomycin use in the pediatric setting.
Background: Diphtheria is an acute infectious disease caused by Corynebacterium diphtheriae. It was one of the leading causes of mortality in pre-vaccination era. Incidence of In India diphtheria continues to be endemic in several states and one of them being Karnataka especially the northern districts of Kalaburgi and Vijayapura. The objective of the present study was to recognize the clinical profile, morbidity and mortality pattern of diphtheria, paediatric intensive care unit of Dr. Bidari’s Ashwini Hospital.

Methods: The data was recovered from the case files, of children diagnosed as diphtheria from the Medical Record Section and Statistical Service of the institute from the period of June 2017 to October 2019. A protocol was formed after approval from the ethical committee. The study consisted of suspected, probable and confirmed cases of diphtheria as per the WHO definition. All the available data regarding age, gender, immunization status, clinical details, complications, and treatment provided, and outcome were recorded.

Results: Amongst 25 children, 60% were >5 years, with male preponderance. Only 1 child (4%) was completely immunized, 13 (52%) were partially immunized and 11 (44.2%) were not immunized. All patients presented with fever and membrane in throat, throat pain 73%, enlarged/congested tonsils 80.85%, respiratory difficulty 44%, dysphagia 56% bull neck 48.94%. complications during management anaphylaxis to ADS (64%), Dyselectrolytemia (72%). Myocarditis was the commonest (59.55%) complication, septicaemia and acute renal failure (4.25%), DIC & shock (1.25%) and conduction blocks (1.25%) were observed. Case fatality rate was 32%.

Conclusions: Most common presentation of Diphtheria was in the age group of 5-15 years, and most of them were poorly immunized suggesting the need to improve and strengthen the immunization activity.
THE MULTICOMPONENT MENINGOCOCCAL SEROGROUP B VACCINE 4CMENB ELICITS CROSS-REACTIVE IMMUNITY AGAINST A, C, W, X AND Y STRAINS: REVIEW OF AVAILABLE DATA

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Background and Objective: Invasive meningococcal disease (IMD), caused by Neisseria meningitidis, remains a major public health concern worldwide and has the highest incidence in infants and adolescents. The multicomponent meningococcal serogroup B (MenB) vaccine (4CMenB, GSK) is currently indicated against MenB-caused IMD. However, 4CMenB vaccine antigens are also expressed in meningococci belonging to other serogroups. We provide an overview of studies assessing the ability of antibodies raised by 4CMenB immunisation to induce complement-mediated killing of non-MenB strains.

Methods: We reviewed available information on cross-reactive immunity elicited by 4CMenB against MenA, MenC, MenW, MenX and MenY strains. We collected all available data from peer-reviewed publications and communications from relevant worldwide conferences/congresses. In the identified studies, sera from individuals immunised with 4CMenB according to various schedules, were tested in serum bactericidal antibody assay using human complement (hSBA) against non-MenB strains. An hSBA titer ≥4 is the accepted correlate of protection.

Learning Points/Discussion: Pooled/individual sera from 4CMenB immunized infants (2+1 or 3+1 doses) and/or adolescents/adults (2/3 doses) display bactericidal activity against: • 6 (out of 6) MenW strains collected from England and Wales during 2010–2013 (hSBA titers ≥32). • 9 (out of 9) MenX strains from different African countries (hSBA titers ≥32) and 2 (out of 2) MenX strains from France for adolescent/adult sera only (hSBA titers ≥4), collected during 1995–2007. • 4 MenA strains selected from 1046 isolates collected from different countries (2000–2016): 58–92% of adolescents had hSBA titers ≥4. • 109 (74%) and 91 (62%) out of 147 non-MenB strains collected from Europe (2007–2008) and Brazil (2012) for infant and adolescent sera, respectively (hSBA titers ≥4). These results support the assumption that 4CMenB vaccination may have an impact on non-MenB-caused IMD. Funding: GlaxoSmithKline Biologicals SA
IMMUNE INTERFERENCE (BLUNTING) IN THE CONTEXT OF MATERNAL IMMUNIZATION WITH TDAP-CONTAINING VACCINES: IS IT A CLASS EFFECT?

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Background and Objective: Maternal immunization with reduced antigen content tetanus-diphtheria-acellular pertussis (Tdap)-containing vaccines is currently recommended in >40 countries to prevent pertussis in young infants. However, maternal antibodies may interfere with infant immune responses to routine immunization with diphtheria-tetanus-acellular pertussis (DTaP)-containing vaccines (blunting), raising concerns of suboptimal protection, especially for pertussis which lacks defined correlates of protection. Our review aimed to assess whether blunting occurs regardless of the manufacturer/brand of Tdap- and DTaP-containing vaccines.

Methods: We undertook a narrative literature review using the search terms ‘(maternal immunization AND pertussis AND blunting)’ for articles in English in PubMed published until 1 March 2019. Randomized clinical trials or observational studies describing antibody titers post-DTaP vaccination in infants from Tdap-vaccinated and non-Tdap-vaccinated mothers were included. Additional references and unpublished data were also included. Blunting was defined as statistically significant lower geometric mean concentration levels against DTaP antigens in infants from Tdap-vaccinated mothers compared to infants from non-Tdap-vaccinated mothers after primary immunization and/or booster dose.

Learning Points/Discussion: Our search identified 14 studies. Most studies reported blunting of humoral immune responses to ≥1 DTaP-antigen in infants after primary and booster vaccination. Blunting occurred regardless of the brands and combinations of Tdap- and DTaP-containing vaccines administered for maternal and pediatric immunization. We conclude that blunting can be considered as a class effect. The exact mechanism of blunting is not fully understood. Limited knowledge indicates that maternal antibodies allow priming of infant cellular and humoral immune responses. Available evidence does not support an observable impact of blunting on protection. Further investigations of the blunting mechanism and determination of long-term impact are needed to help optimize the timing of maternal and infant immunization and support future vaccine development. Funding: GlaxoSmithKline Biologicals SA
LONG TERM FOLLOW-UP OF CHILDREN BORN POST DOCUMENTED PRIMARY TOXOPLASMA INFECTION DURING PREGNANCY

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Background: Toxoplasma gondii is an obligate intracellular parasite. Congenital toxoplasmosis post transplacental transmission may result in severe complications, mainly retinochoroiditis. Most infections are asymptomatic at birth. High-risk neonates should be tested to rule out infection, while administration of treatment significantly decreases the incidence of long-term complications. The aim of this retrospective cohort study was to collect medical data on the long-term follow-up of children born after documented primary toxoplasma infection during gestation.

Methods: Data was collected from two outpatient clinics on gestational infections in Athens (01/2008 - 10/2019). Women with confirmed primary toxoplasmosis during pregnancy were interviewed by phone and asked about their offspring. Questions focused on the clinical management and follow up of their child. Most recent toxoplasma immunoglobulin G (IgG) test results and results from the latest ocular examination (fundoscopy) were noted.

Results: Overall, 71/93 identified women responded and 72 children were enrolled. All mothers (50 infected during 1st trimester) received treatment and 57 underwent amniocentesis. Interestingly although 7 amniocentesis were positive by PCR, none was confirmed by culture and all 72 children were tested negative for toxo-IgG antibodies and had normal fundoscopy at evaluation. All children were tested as neonates for toxoplasmosis and 8 children received treatment for a median of 3.5 months (only one for 12 months).

Conclusions: Transmission of acute toxoplasmosis during pregnancy is rare in Greece. Since all children in this cohort lost transplacentally transferred maternal antibodies, one may postulate that toxoplasma DNA detection in amniotic fluid was false positive. Referral of such cases to specialized clinics to ensure appropriate treatment and longitudinal follow up is needed. The development of a National registry may improve management.
EVALUATION OF EAZYPLEX® SUPERBUG CRE TO DETECT EXTENDED-SPECTRUM BETALACTAMASES DIRECTLY FROM POSITIVE PEDIATRIC BLOOD CULTURE BOTTLES

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Background: Bacteremia caused by extended-spectrum beta-lactamase (ESBL)-producing organisms is associated with increased morbidity and mortality, particularly when conventional antimicrobial susceptibility methods delay ESBL recognition and appropriate therapy. Easyplex\textsuperscript{®} Superbug CRE is a loop-mediated isothermal amplification based technique that can rapidly detect selected antimicrobial resistance genes directly on positive blood culture bottles, reducing the time to optimal therapy. We aim to determine the accuracy of Eazyplex\textsuperscript{®} Superbug CRE for the detection of \textit{bla}\textsubscript{CTX-M} genes directly from positive pediatric blood culture bottles.

Methods: Eazyplex\textsuperscript{®} Superbug CRE was performed prospectively on positive BD BACTEC Peds Plus/F bottles (June 2019 to January 2020). Antimicrobial susceptibility was performed on colonies using the BD Phoenix\textsuperscript{™} automated system. ESBL phenotype was inferred from the antibiogram.

Results: Thirty-three unique positive blood culture bottles collected from children with septic episodes caused by Enterobacteriaceae were assessed. Thirty-eight organisms were identified: 
- \textit{Klebsiella pneumoniae} (16 isolates; 42.1%),
- \textit{Escherichia coli} (11 isolates; 28.9%),
- \textit{Salmonella} spp. (3 isolates; 7.9%),
- \textit{Enterobacter cloacae} and \textit{Klebsiella oxytoca} (2 isolates; 5.3% each),
- \textit{Klebsiella aerogenes}, \textit{Citrobacter freundii}, \textit{Pantoea} spp. and \textit{Serratia marcescens} (1 isolate each; 2.6% each).

Genes encoding CTX-M enzymes were detected in 8 bottles by Eazyplex\textsuperscript{®} SuperBug CRE; 6 CTX-M-1 group and 2 CTX-M-9 group. The overall concordance of positive and negative test results with phenotype data was 100%. Furthermore, the assay accurately detected the presence of CTX-M ESBLs in 4 bottles that eventually grew mixed coliforms on solid media.

Conclusions: Eazyplex\textsuperscript{®} CRE Superbug is a rapid and reliable method for the detection of CTX-M type ESBLs in pediatric blood culture bottles. Additionally, it could be used as a carbapenem-sparing tool since patients with negative results could be treated with narrower spectrum agents.

Clinical Trial Registration: N/A0000000000
THE INFLUENCE OF EARLY-LIFE GUT MICROBIOME DEVELOPMENT ON VACCINE RESPONSES

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Background: Immune responses to vaccination vary considerably between individuals and populations, thereby limiting the performance of existing vaccines. Lifestyle and environmental exposures in infancy may impact development of both the immune system and the gut microbiota, a recognised immune modulator that may consequently influence vaccine immunogenicity.

Methods: In a prospective cohort of 120 healthy infants (NTR3986), we characterized gut microbiota development from birth using 16S rRNA gene sequencing, and measured post-vaccination salivary immunoglobulin G (IgG) concentrations specific to pneumococcal vaccine serotypes (Ps) at 12 months of age (1 month after the PCV-10 booster), as well as meningococcus type C (MenC) at 18 months of age (4 months after vaccination) by a fluorescent bead-based multiplex immunoassay.

Results: Natural birth and breastfeeding were associated with higher vaccine responses as opposed to birth by caesarean section and formula feeding. Moreover, we observed that a characteristic microbial succession pattern of gut microbes in the first 2 months of life linked vaginal birth and breastfeeding with especially higher pneumococcal vaccine responses at 12 months of age. For instance, higher abundance of *Escherichia coli*, and several *Bifidobacterium* and *Bacteroides* species and lower abundance of *Clostridium*, *Streptococcus* and *Prevotella* species in early life were associated with higher levels of Ps6b antibodies. We observed a similar correlation between higher abundance of *E. coli* and higher MenC antibody responses, as well as between higher abundances of *Veillonella* and *Clostridium* species and lower MenC antibody responses at 18 months of age.

Conclusions: Our results suggest that early-life exposures affect gut microbiota development, which in turn is associated with antibody responses to routine immunization. Mechanistic studies are required to establish causality and potentially provide input for clinical studies to improve vaccine efficacy.

Clinical Trial Registration: Netherlands Trial Register: trialregister.nl NTR3986
A RETROSPECTIVE STUDY OF IMMUNIZATION TRENDS IN ROMANIA

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Background: As global immunization levels are decreasing, the threat of severe endemics of preventable diseases is becoming a considerable danger. The US and Europe have been exposed to measles epidemics, most of them driven by the lack of herd immunity. Although the Romanian population states to have an overall positive opinion about vaccination the ongoing measles outbreak demonstrates the opposite.

Methods: We collected data between 2010 until 2018 from the official site of the National Institute of Public Health of Romania and the Romanian Institute for Evaluation and Strategy.

Results: The cohort contained around 86% of the newborns in each year, 33.85% were incompletely vaccinated, in 2011 representing the majority (66%). The optimal immunization rate is achieved for the BCG vaccine, which through 9 years was above 95%. DTaP, IPV and Hib levels were under 70%, with the main decrease in 2011. Hepatitis B (87.36%) and MMR (73.55%) ranked under the threshold. Parents failing to comply with the immunization schedule (34.93%), medical contraindications (26.42%), shortages in vaccines (26.96%) and refusals to vaccinate (8.63%) are the pillars of low vaccination rates.

Conclusions: The ongoing awareness campaign fails to make an impact, because of the lack of public knowledge about it. The law for mandatory vaccination could not be passed, as public resistance overthrew it. In conclusion, even though some acute measures seemed promising, overall the failure in public health policies is and will continue to be a treat for migrating outbreaks.
ADENOVIRUS-INDUCED IMMUNE RESPONSE IN IMMUNOCOMPETENT CHILDREN AFFECTED BY UPPER RESPIRATORY TRACT INFECTIONS

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Background: Adenoviruses are known to cause morbidity due to an enhanced inflammatory response in the host. When causing upper respiratory tract infections (URI), severe clinical presentation, elevation of white blood cell (WBC) and C-reactive protein (CRP) often lead to hospital admission and an overuse of antibiotics. A clear biological background sustaining this clinical presentation has not been fully elucidated in pediatric literature.

Methods: We enrolled consecutive febrile patients aged <14 admitted to our Institution with acute URI. Infection etiology was tested with naso-pharyngeal swabs, serology and DNA-PCR. WBC count, CRP, inflammatory cytokines and lymphocyte subset populations were assessed during fever and subsequent recovery and compared with 2-tailed t-test.

Results: We included 41 patients with viral URIs, 21 of which by Adenovirus. Compared to other viral infections, Adenovirus URIs showed higher B and T-lymphocyte count (avg: 1350 vs 236/mcL and 3301 vs 598/mcL, respectively). Among T-cell compartment, a higher number of T-cd4+ naïve and T-cd8+ naïve were found (avg: 1547 vs 259/mcL and 855 vs 432/mcL, respectively). In patients recovering from Adenovirus URIs (mean time to recovery, MTTR: 6.2 days), proportion of T-cd8+ memory was 4.2% vs 3.4% compared to other URIs (MTTR: 6.6 days). Finally, in Adenovirus URIs, IL-10 was significantly higher in the acute phase (avg: 3.8 vs 1.75pg/mL), compared to convalescence (All p<0.05).

Conclusions: Acute Adenovirus-induced response provides a stronger stimulation of B and T-cells. The activation of T-cd8+ lead by Adenovirus is confirmed by the switch to T-cd8+ memory during convalescence. Moreover, the elevation of IL-10, a proliferative stimulant produced by T-cd4+, speaks towards the increase of B lymphocytes. Primary acute Adenovirus infection seems to activate significantly both humoral and cell-mediated immunity more than other common viruses in URIs.

Clinical Trial Registration: CE number 391/2019/Sper/AOUBo
A RETROSPECTIVE DATABASE ANALYSIS TO ESTIMATE THE BURDEN OF ACUTE OTITIS MEDIA IN CHILDREN 0-14 YEARS IN THE VENETO REGION, ITALY

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Background: Acute Otitis Media (AOM) causes substantial healthcare resource utilization in children, with Streptococcus pneumoniae as an important pathogen. PCV13 was introduced into the Veneto immunization schedule in 2010 but is not mandatory. The full-series vaccination coverage rate (VCR) was 67.5% for the 2010 birth cohort. This analysis assessed AOM incidence, time trends and costs in children followed up by primary care pediatricians.

Methods: AOM episodes in children <15 years residing in the Veneto region were identified in Pedianet (pediatric primary healthcare database) from 2010-2017 searching ICD9-CM codes (381.x, 382.x) and free-text fields. Expenditures were calculated multiplying the average cost/episode with the age-standardized regional IR. Incidence rates (IR) were numbers of episodes/1,000 person-years. Interrupted time series (ITS) analysis compared annual IRs in early and late PCV13 (2010-2013, 2014-2017) periods.

Results: IRs declined from 126 to 79/1,000 person-years (2010-2017). Incidence was highest in 2-4 years, followed by <2 and 5-14 years. ITS analysis showed annual rates declining by 5.8% and 5.9% during early (p=0.003) and late PCV13 periods (p<0.0001). In children 5-14 years, rates declined by 2.7% and 2.8% in early (p=0.03) and late PCV13 periods (p<0.0001). While incidence was lower after PCV13 introduction in 2-4 years, in <2 years varied from 119 to 129/1,000 person-years (2010-2017). Antibiotic prescriptions/episode varied from 0.93 to 0.91 (2010-2017). AOM-associated costs declined from €3.8 to €2.8 million (2010-2017).

Conclusions: AOM incidence decreased in children <15 years after PCV13 introduction with greater benefits in older children. Incidence did not decline in the target population of children <2 years. Moreover, considering that Italian children start attending nursery schools later in age than children living in other European countries, it may explain why AOM IRs was higher in children 2-4 years than children <2 years.
MEASLES, MUMPS, RUBELLA (MMR): WHY IS ERADICATION SO DIFFICULT?

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Background and Objective: The burden of MMR diseases decreased notably worldwide between 2000-2018, following implementation of vaccination programs. However, resurgence and recurrent outbreaks (particularly for measles and mumps) continue to occur, suggesting that preventive public health strategies have failed, and corrective systematic measures must be taken. Immediate initiatives following outbreaks are mostly symptomatic and don’t address the underlying causes. Countries are challenged to find an impactful approach for controlling these measles/mumps infections. We appraise the existing literature to clarify the current challenges and the interventions needed to reduce the number of MMR outbreaks.

Methods: This is a rapid evidence appraisal of the challenges and solutions to help policy makers achieve elimination of MMR diseases. We executed a comprehensive search of the available literature published up to 2019 in English. We developed search terms for separate questions on public perspectives and hesitancy, challenges in vaccination service delivery, environmental/societal challenges and logistical challenges (e.g. waning immunity and secondary vaccine failure).

Learning Points/Discussion: To overcome the current challenges, the following actions should be considered: • Mandatory vaccination of the target population. • Implementing shorter interval between vaccine administration to improve herd immunity during an outbreak (MMR vaccines administered at 6-weeks interval are as effective as administered at longer interval). • Increased knowledge of diseases amongst the public (this increases likelihood of vaccinations). • Patient invite/reminder systems. • Supplementary immunisation campaigns targeting under-served/unvaccinated populations. • Regularly revised protocols for outbreak preparedness, clinical management of measles cases, outbreak response. • Optimising surveillance systems and diagnosis. • Implementation of a third dose during mumps outbreaks. MMR vaccination programmes have failed due to suboptimal implementation (not to faulty vaccines). An urgent pro-active approach is needed to avoid putting global health at risk with vaccine-preventable diseases like MMR. Funding: GlaxoSmithKline Biologicals SA
Background: Human challenge studies have the ability to prevent colonisation with pathogens by the introduction of commensal organisms into an individual's microbiome. To date these studies have been conducted exclusively in healthy adults. Human challenge studies offer a potential novel strategy to protect pregnant and neonatal populations against invasive infection. However, it is unclear whether these studies would be acceptable to pregnant women. Therefore, we undertook an interview study to investigate whether human challenge studies would be acceptable to a pregnant population.

Methods: Healthy pregnant women were recruited from a maternity hospital and invited to take part in a semi-structured interview. These interviews explored perceptions of risk and acceptability of a hypothetical human challenge study in pregnancy. We conducted thematic analysis of interview transcripts to identify common themes and patterns.

Results: Overall, participants considered a human challenge study to be acceptable in pregnancy. Factors that would encourage participation in such a study included: potential benefits to the participant’s child, utilisation of a method less invasive than injection, benefit to the public, and the requirement to pass strict eligibility criteria. Perceived risks included: uncertainty about potential harms, and a reluctance to take part in research during pregnancy. Opinions about acceptability of this research method were polarised and formed early in the interview; once formed reassurance did not alter these initial impressions of acceptability.

Conclusions: Conducting a human challenge study in pregnancy would be acceptable to some pregnant women and offers novel means to investigate and manipulate the neonatal microbiome. This may provide infants new avenues of protection from invasive infection.

Clinical Trial Registration: Clinical trial registration: n/a
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**Background:** In recent years, pediatric urinary tract infections (UTI) caused by extended-spectrum beta-lactamase (ESBL) producing enterobacteria have increased in frequency. These infections have been classically treated with intravenous broad-spectrum antibiotics, contributing to greater bacterial resistance and increasing morbidity and healthcare costs associated to hospital admission. The objective of this study is to describe the prevalence, clinical outcomes and adequacy of treatment of UTI caused by ESBL producing bacteria in a third-level pediatric hospital.

**Methods:** A retrospective analysis of all cases of UTI with positive urine culture for ESBL producing enterobacteria diagnosed in children between 0 and 18 years in a third-level pediatric hospital was performed between April 2016 and April 2019.

**Results:** Ninety-six cases were recorded (62.5% girls, median age 47.2 months); 43.7% had nephro-urological or immune risk factors and 15.6% of them were receiving antibiotic prophylaxis. At diagnosis, 72.9% had fever. The most frequently isolated pathogens were *E. coli* (82.3%) and *K. pneumoniae* (14.6%). The most commonly used antibiotics for empirical and targeted therapy were cefixime (39.6%) and carbapenems (51%), respectively. No significant differences were observed between groups with/without risk factors in terms clinical outcome and recurrences, the last observed in 23 patients (24%) of the total sample after an interval of 2.5 months (95%CI, 1.5-3.5).

**Conclusions:** Although carbapenems remain the cornerstone of treatment in patients with previous pathology or in severe infections, it is worth considering alternatives in uncomplicated UTI in order to reduce hospitalization and microbial resistances. On this series we found a wide variability in the use of antibiotic treatment. Further studies with longer follow-up are needed.
INCREASING CONTRIBUTION OF NEW HIV DIAGNOSES IN ADOLESCENTS IN SPANISH ADULT AND PEDIATRIC COHORTS (CORIS-CORISPE)

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**Background:** A specific approach of HIV in adolescence is of global concern. Data about new HIV diagnoses in adolescents is scarce, especially in Europe. Describing this population will contribute to better approach this problematic situation.

**Methods:** Description of new HIV diagnoses in patients 12-20 years-old included in CoRIS (adult, accounting with more than 40 centers actually) and CoRISpe (pediatric) Spanish cohorts until end 2017. Demographic, clinical, biological data and way of transmission were analysed. Contribution of new diagnoses in adolescents to total diagnoses is analysed from 1997 using a segmented regression.

**Results:** Contribution of adolescents in new HIV diagnoses in CoRIS-CoRISpe increased from 2005 (95%CI 2000-2009,p=0.025, figure1), with 357 adolescents diagnosed. Adolescents before-after 2005 differed: increasing sexual transmission (37.8% vs 93.6%;p<0.001), men-having-sex-with-men (20.8% vs 67.3%) and heterosexual (17.0% vs 26.3%), proportion of men (66.0% vs 79.3%,p=0.012) and foreigners (17.9% vs 44.6%,p<0.001). Medium adolescents (15-17 years-old) increased in the last 5 years (16.8% in 2008-2012 vs 25.2% in 2013-2017,p=0.030). Late presenter adolescents (CD4<350/mm³ or AIDS at diagnosis) decreased after 2005 (46.2% vs 30.0%,p=0.005) but this rate remained unchanged in the last 15 years.
Conclusions: Contribution of adolescents in new HIV diagnoses increased from 2005, possibly related to the increase of sexual transmission, men and foreign adolescents. About 1/3 are late presenters and did not decrease in the last 15 years. This emphasizes the vulnerability of this population and the need to develop more effective actions.
SCREENING STUDY OF BLOOD SERUM OF PATIENTS–CHILDREN WITH ARTHRITIS FOR THE PRESENCE OF ANTIBODIES TO BORRELLIOSIS.

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Background: Lyme disease (LD) is the most common transmissible infectious disease, caused by Borrelia burgdorferi senso lato. That is a serious medical problem because of the possibility of damage to many organs and systems, joint pain, fatigue, malaise, headache, swollen lymph nodes, erythema migrans, fever, lesions of the central nervous system, hearth and the seriously tendency to chronic process and disability.

Methods: We reviewed charts of 150 patients with diagnosis of Ternopil region aged 7 to 16 years who was admitted with clinic of arthritis. This diagnosis was confirmed by patients complaints, history, laboratory data (increase in anti-borrelia Antibodies to complex antigens B. Burgdorferi senso lato IgM in ELISA), all positive results were confirmed by using more specific Western Blot test

Results: Arthritis and non-localized pain of bones, joints and muscles were found in 13 sick children. Analysis of serological examination from blood serum for the presence of specific antibodies IgM and IgG for B. Burgdorferi senso lato. 13(8.6%) from 150 children (6 girls and 7 boys) were diagnosed with Lyme arthritis. High specificity of Ig M to VlSE 13 % OspC B. afzelii (13 %) and OspC B. garinii (6 %), and Ig G to Ospc B. afzelii (13 %), P41 16% for arthritis.

Conclusions: During two-stage diagnostics of arthritis, fluctuations in the content and immunoglobulins were found - from 20.8% for IgM to 66.6% in IgG, which indicates the chronicity of the process. Serological detection by IgA antibodies of IgM and IgG classes to B. Burgdorferi senso lato showed positive or intermediate results in 8.6% of patients with signs of arthritis.

Clinical Trial Registration: no aplicapableN/A
CLINICAL CHARACTERISTICS AND MOLECULAR GENOTYPING OF HUMAN PARECHOVIRUSES CAUSING CENTRAL NERVOUS SYSTEM INFECTIONS IN NEONATES

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Background: Human parechoviruses (HPeVs) are single-stranded RNA viruses which cause infections in neonates presenting as febrile exanthematic illness, sepsis-like illness, meningoencephalitis. In the present study we describe the clinical and molecular characteristics of neonates with HPeV Central Nervous System (CNS) infections.

Methods: Cerebrospinal fluid (CSF) from neonates with suspected CNS infections was tested by a multiplex PCR panel (Biofire® FilmArray® Meningitis/Encephalitis panel) in a tertiary pediatric hospital of Athens during a 1-year period. Genotyping was performed in positive HPeV samples using Sanger Sequencing.

Results: HPeVs were detected in 5/180 CSFs from neonates with suspected CNS infection. All of the neonates were under 30 days old, 4/5 male. Neonates presented with prolonged fever, 2/5 with a rash and 1/5 with seizures. CSF analysis found no pleocytosis and normal levels of protein and glucose. HPeV-3 was detected in all analyzed samples. No other causative agents were detected. One neonate was presented with a sepsis like illness and was treated with intravenous immunoglobulin, considering the possibility of severe systemic inflammatory responses. In 3/5 the empirical antibiotic treatment was stopped. All neonates recovered without obvious sequelae.

Conclusions: HPeV infection is a possible pathogen in neonatal CNS infection. The rapid detection of parechoviral RNA in CSF should be included in the routine diagnostics in neonates with febrile illness, as it could probably reduce unnecessary empirical antibiotic treatment and shorten hospital stay.
Background: In countries where varicella vaccination is not routine, chickenpox is an almost universal disease of childhood. Data regarding hospitalisation are sparse and may represent only the severest cases. However such information is needed to permit accurate cost-benefit assessment regarding universal varicella vaccination in childhood.

Methods: All patients admitted to Bristol Children’s Hospital, from February 2018 ongoing, are asked about their contact with chickenpox. Children identified as having recent chickenpox are assessed to see if their admission could be related. Data are collected on all varicella related admissions, which will be used to undertake a health economic analysis to calculate the cost of these admissions. Annual crude age-specific rates were calculated using mid-year population (0-5 years) estimates as the denominator and are expressed as rates per 100,000 0-5 years population.

Results: From Feb 2018 to Oct 2019 172 children were admitted with recent chickenpox infection, in 145 of whom the presenting complaint was considered directly or possibly attributable to varicella. Median age at admission was 2 years (range 0–15 years), and median length of stay 2 days (range 0–42 days). 47 children were admitted with soft tissue infections, including cellulitis, 23 with uncomplicated varicella requiring admission, of whom 10 were aged less than one. The annual varicella hospitalisation rate is estimated at 179 per 100,000 (0-5 years).
Conclusions: Complications of varicella severe enough to warrant admission to hospital are common, costly and burdensome to families. We discuss the secondary health care utilisation associated with admissions due to varicella. Uncomplicated varicella can still cause concern in early stages due to diagnostic uncertainty, with children under one being particularly affected. Most children affected are <5 years but older children with comorbidities also affected.
Title of Case(s): How travel history helped diagnosing a child with focal seizures

Background: Neurocysticercosis is a clinical syndrome caused by the larval stage of Taenia solium. Approximately 29% of seizures in endemic areas are caused by neurocysticercosis. We report a case of neurocysticercosis successfully treated in a child presenting focal seizures.

Case Presentation Summary: A two-year-old girl of Indian origin was taken to the emergency department in Italy for a nonfebrile focal seizure. Patient history was negative and physical examination was normal. A CT scan was performed, which showed in the right occipital lobe and in the left parietal lobe two hypodense round lesions (max diameter 5 mm and 7 mm) with a small hyperdensity within, associated with perilesional edema. The MRI scan confirmed the lesions (fig A-B) and suggested a cystic infectious process. Laboratory findings, including cultural exams on blood, liquor and stool, were negative for infection. Also serology for cysticercosis on blood and liquor was negative. Chest X-ray and abdominal ultrasound did not demonstrate other localizations of infection. A more focused travel history revealed that the patient had travelled to a rural area in India one week before. The neuroimages were reviewed and, despite negative serology, neurocysticercosis was diagnosed. Treatment with Albendazole (7.5 mg/kg every 12 hours for 15 days) and Prednisone (10 mg for 7 days, then decalage) was therefore stared. In addition, seizure prophylaxis with Carbamazepine was administered. One year later, MRI images (fig. C-D) showed a substantial decrease in size of the lesions. The patient did not experience other seizures, Carbamazepine was therefore discontinued.
Learning Points/Discussion: In conclusion, when confronted with infectious diseases an accurate travel history is of the utmost importance, especially in patients originally from tropical regions. Neurocysticercosis must be considered in the presence of suggestive neuroimaging, even with negative serology.
CENTRAL-LINE ASSOCIATED BLOODSTREAM INFECTIONS IN CHILDREN WITH LONG-TERM PARENTERAL NUTRITION: A 2-YEARS RETROSPECTIVE OBSERVATION.

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Background: The central-line associated bloodstream infections (CLABSI) are common but severe healthcare-associated infections in childhood. Children on parenteral nutrition (PN) have high risk of CLABSI (CVC) due to the use of long dwelling central line, multiple daily manipulations and infusion of nutrients. The aim of our study was to evaluate rates of clinical sepsis episodes and CLABSI in children on long-term PN.

Methods: A 2-years retrospective study was performed at “Federico II” University of Naples. Primary outcome was the rate of sepsis and CLABSI/1000 CL-days. Data of children on PN were collected. CLABSI was defined according to the US Center for Diseases Control definitions. 17 children on PN were enrolled (11 males, median-age 86±94 months): 10 (58.8%) had post-resection short bowel, 5 (29.4%) intestinal motility disorders, 2 (11.8%) primary villous disorders.

Results: 4 (23.6%) patients reported at least 1 episode of fever and 16 sepsis episodes were observed (sepsis-rate: 1.61/1000 CL-days). 13 episodes satisfied CLABSI’s criteria (CLABSI-rate:1,43/1000 CL-days). Coagulase-Negative Staphylococci (62.5%), E. Coli (6.25%) and E. Faecalis (6.25%) were isolated. CVC was removed in 3 cases (18.75%), one because of endocarditis. Antibiotic treatment, hospitalization and fever had a mean duration of respectively 19, 21.75 and 5.06 days. No correlation between underlying disease and CLABSI risk was observed (2,67±2.65, p<0,003). 3/4 children with CLABSI and 2/13 among those without CLABSI have a gastro/enterostomy.

Conclusions: Children on Total-PN had a higher risk of CLABSI than those on Partial-PN (4,33±2,51vs 0,21±0,8, p <0.0001). Patient’s age is not a risk factor for CLABSI (2,5±3,32, p<0.07), but there is a higher trend under 3-years age. Infections are a major cause of morbidity in PN. Gastro/enterostomy is a risk factors for CLABSI, but the improvement in management could reduce the infection-rate.
CONGENITAL TOXOPLASMOSIS IN A TEACHING HOSPITAL’S OUTPATIENT CLINIC: A FIVE-YEAR SURVEY

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Background: Congenital toxoplasmosis is a serious condition that can lead to lifelong sequelae. Brazil’s Ministry of Health recommend universal screening for toxoplasmosis during pregnancy and there is a public poll currently underway to assess the implementation of toxoplasmosis IgM testing in the national neonatal screening programme. There was a symptomatic toxoplasmosis outbreak in São Paulo in the beginning of 2019. The aim of this study was to identify a possible increase in cases of congenital toxoplasmosis in São Paulo.

Methods: In this retrospective epidemiological study we analyzed patient chart data of infants with confirmed or suspected congenital toxoplasmosis who attended our clinic between 2014 and 2019. We included infants born to women with positive toxoplasmosis screening in pregnancy and/or infants with documented congenital toxoplasmosis. We assessed maternal serology and treatment as well as infant serology, molecular testing, treatment and symptomatic disease.

Results: Of 96 patients included, 20 presented symptomatic congenital toxoplasmosis. Of these, 18 had a positive IgM testing at birth. All cases were evenly distributed across the years. Nine patients were diagnosed due to symptomatic disease. The other 11 were diagnosed due to pre-natal screening: six mother seroconverted during pregnancy and another six presented positive IgM testing on the first screening. The most common symptoms were chorioretinitis (85%) and periventricular calcifications (75%).

Conclusions: Symptomatic congenital toxoplasmosis was fairly common in our study, with patients developing lasting sequelae. Our assessment did not show an increase in symptomatic cases over the last few months. Antenatal screening is important to prevent vertical transmission and to identify infants at risk of congenital toxoplasmosis. Neonatal screening may be important, but a negative IgM at birth does not exclude congenital toxoplasmosis.
COMPARATIVE DIAGNOSTIC ACCURACY OF SINGLE HRP2/PLDH (PAN) RAPID DETECTION TEST AND PAIRED BLOOD FILM FOR DIAGNOSING MALARIA IN CHILDREN

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Background: Misdiagnosis of Malaria could result in significant morbidity and mortality. Rapid, accurate and accessible detection of falciparum and non-falciparum malaria parasites through the use of combined HRP2/pLDH (Pan) Rapid Detection Test (RDT) with a paired blood film has an important role in diagnosis. This retrospective study aims to support evidence on the diagnostic accuracy of both tests in children travelling from areas with low prevalence of human P. Knowlesi infection.

Methods: Non-concurrent database analysis was undertaken of children suspected of malaria disease at a tertiary paediatric hospital in the UK over a 5-year period (2014-19). All included children had at least one RDT, blood film and Full blood count. The gold standard was discharge diagnosis of malaria by clinical and diagnostic testing. 2x2 tables were constructed and analysis undertaken using Medcalc® software.

Results: 197 investigated hospital attendances were included, with 17 cases (8.63%, 95% CI 5.1 -13.5) of malaria diagnosed. The Sensitivities (95% CI) of RDT, thin film and combined RDT/film were 100% (80.5-100), 88.2% (63.6-98.5) and 100% (80.5-100) respectively. Specificities (95% CI) were 100% (98-100), 100% (98-100) and 98.9 (96.4-99.9) respectively. All confirmed cases travelled from African countries and were symptomatic.

Conclusions: The use of a single RDT could be sufficient to rule out malaria in children returning from African countries. Serial combined HRP2/pLDH (Pan) RDT and blood films do not seem to increase the overall diagnostic accuracy. Nevertheless, there are known limitations to the efficacy of RDTs for the recognition of Plasmodium Knowlesi, currently prevalent in some countries of South East Asia. Hence, serial films should still be obtained to exclude malaria in travellers coming from that geographical region.
OFF-LABEL USE OF GROUP A STREPTOCOCCUS RAPID DIAGNOSTIC FOR PERIANAL AND PARONYCHIA INFECTIONS

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Background: In addition to pharyngitis, Group A Streptococcus (GAS) plays a major role in several diseases seen in pediatric ambulatory care. Rapid antigen detection tests (RDT) have been well studied for pharyngitis but not for extrapharyngeal infections such as perianal infections and paronychia. The use of RDT in this context is off-label but probably very useful.

Methods: By automated data extraction, we daily prospectively collect anonymized data (age, sex, height, weight, daycare attendance, vaccines, diagnosis and prescriptions) of children with infectious diseases in 100 primary-care-pediatric-offices using the same software (Axi5-Infansoft®, CompuGroup Medical): PARI study (Pediatric Ambulatory Research In Infectious Diseases). The pediatricians of this network have to participate to e-learning and face to face meetings in order to improve their diagnosis and management of infectious diseases. Here, we analyze the data of extrapharyngeal GAS-infections.

Results: Between September 2017 and November 2019, RDT was performed for 93% of 298 perianal infections and for 46% of 249 paronychia, about 3 cases per year per pediatrician.

<table>
<thead>
<tr>
<th></th>
<th>Perianal (n=298)</th>
<th>Paronychia (n=249)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex M</td>
<td>70%</td>
<td>62%</td>
</tr>
<tr>
<td>Mean age ±SD (years) Median</td>
<td>4.2±2.4 4.0</td>
<td>4.7±3.9 3.7</td>
</tr>
<tr>
<td>RDT</td>
<td>277 (93%)</td>
<td>114 (46%)</td>
</tr>
<tr>
<td>RDT+ Antibiotic prescription Amoxicillin</td>
<td>169 (61%) 95% 28% 59% 8%</td>
<td>57 (50%) 96% 63% 33% 0</td>
</tr>
<tr>
<td>Amoxicillin clavulanic acid Other</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RDT- Antibiotic prescription Amoxicillin</td>
<td>108 (39%) 18% 1% 16% 1%</td>
<td>57 (50%) 37% 4% 33% 0</td>
</tr>
<tr>
<td>Amoxicillin clavulanic acid Other</td>
<td></td>
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Conclusions: Off-label use of RDT in extrapharyngeal infections such as perianal infections and paronychia could be helpful in pediatric ambulatory settings. This study confirms the major role of GAS in these infections and could improve the antibiotic prescriptions in these settings.
A RETROSPECTIVE DATABASE ANALYSIS TO ESTIMATE THE BURDEN OF RECURRENT ACUTE OTITIS MEDIA IN CHILDREN 0-14 YEARS IN THE VENETO REGION, ITALY

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Background: Acute Otitis Media (AOM) is one of the most prevalent infectious diseases in childhood causing substantial healthcare utilization, especially in primary care setting. Different studies have suggested that replacement of PCV7 with PCV13 in 2010 has resulted AOM epidemiology change. This analysis assessed incidence and regional expenditures associated with recurrent AOM (rAOM) following PCV13 introduction in the Veneto (not mandatory-) immunization schedule.

Methods: AOM episodes in children <15 years residing in Veneto were identified in the Pedianet (pediatric primary healthcare database) from 2010-2017. Incidence rates (IRs) were numbers of episodes/1,000 person-years. rAOM was defined as at least three episodes in 6 months, or four or more episodes in 12 months. Total regional expenditures were calculated by multiplying the average cost/episode with the age-standardized regional IR. Interrupted time series (ITS) analyses compared annual IRs in early and late PCV13 (2010-2013, 2014-2017) periods.

Results: In 2010-2017 rAOM IRs declined from 16 to 11/1,000 person-years [95%CI:15-17 to 10-11]. Children with rAOM out-of-all AOM varied from 5.8% to 1.3% (2010-2017). In ITS analyses, rAOM-IRs did not change (in all age groups) in the early PCV13 period, however it declined annually by 2.7% in the late PCV13 period (p=0.0008). The number of antibiotic prescriptions/episode of rAOM varied from 1.46 to 1.27 (2010-2017). Costs associated with rAOM declined from €464,365 to €383,688 (2010-2017).

Conclusions: Recurrent AOM incidence declined across all age groups in the late PCV13 period (2014-2017). This is the first analysis that report rAOM costs using primary care real world data in Italy showing a decrease in regional expenditures over the analysis period. However further analysis regarding PCV13 impact on all costs, including out of pocket expenditures and societal costs, from patient-payer prospective are needed.
Background: Bronchiolitis is one of the main cause of hospitalization in the first 12 months of life. The aim of this study is to evaluate the acute hospitalization cost related to bronchiolitis in children admitted in 2017 to Bambino Gesù Children Hospital (BGCH), Rome, Italy.

Methods: Patients aged up to 1 year with diagnosis of bronchiolitis hospitalized at BGCH from January 1\textsuperscript{st} to December 31\textsuperscript{st}, 2017, entered the study. Health records were extracted from the digital database of the hospital and bronchiolitis diagnosis was defined according to ICD-10 codes.

Results: In 2017, 531 children were hospitalized. The direct cost of a single patient accessing the ED (Emergency Department) was of 309.87 euros. The 3.57% of patient required intensive care. The hospitalization cost of patients requiring intensive care was significantly higher (mean cost 9094.32 ± 2626.15 euros), than those admitted at Pediatric Infectious Unit (5489.09 ± 1972.46 euros). Mean costs of hospitalization did not differ significantly between children infected with RSV and those with other etiological causes. The total cost of bronchiolitis hospitalization was 2.983.204 euros (mean of 5618.09 ± 2105.06 euros per patient) (Figure 1).
Conclusions: Hospital costs related to a disease are relevant end-point in economic evaluation. These studies estimate eventually cost saving that can support decision makers in planning appropriate immunization strategies and vaccination programs. We only analyzed direct cost associated with in-patient services in the acute phase. Following analysis will consider indirect costs, such as missing working days for parents who assist children.

Clinical Trial Registration: not applicable
MOLECULAR CHARACTERIZATION OF CARBAPENEMASE-PRODUCING ENTEROBACTERIACEAE IN THE PEDIATRIC POPULATION IN QATAR

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Background: Although infections caused by carbapenemase-producing Enterobacteriaceae (CPE) are increasing in the Arabian Peninsula, the molecular epidemiology of these enzymes in children is unknown. Carbapenemase genes and sequence types (ST) of CPE recovered from clinical and surveillance specimens from pediatric patients were characterized during a 2-year period at Sidra Medicine, a tertiary care children’s and women’s hospital in Qatar.

Methods: Whole genome sequencing of carbapenem-resistant Enterobacteriaceae (January 2018 to December 2019) was performed on Illumina Miseq platform. STs were determined by in silico multilocus sequence typing and resistance gene analysis was performed using ResFinder pipeline. Antimicrobial susceptibility testing was performed using the BD Phoenix™ and susceptibility breakpoints determined using Clinical and Laboratory Standards Institute guidelines.

Results: Overall, 67 CPEs recovered from 50 patients were sequenced during the study period. Among them, 59 strains (88%) were isolated from surveillance specimens. Only NDM-type (38 isolates; 53.5%) and OXA-48-type (33 isolates; 46.5%) carbapenemases were identified. NDM-5 (22 isolates; 30.1%) and OXA-181 (13 isolates; 18.3%) were the most common representatives within both types. Twenty-two (75.8%) OXA-48-type producers were susceptible to meropenem. By contrast, all NDM producers displayed high-level resistance to this agent. CPEs belonged to 4 species: Escherichia coli (42 isolates; 62.7%), Klebsiella pneumoniae (22 isolates; 32.8%), Citrobacter spp (2 isolates; 3%) and Klebsiella oxytoca (1 isolate; 1.5%). Among E. coli, ST 38 was the most prevalent clone (9 isolates; 21.4%) followed by ST 410 (5 isolates; 11.9%). K. pneumoniae ST 73 was the only clone identified repeatedly in this species (3 isolates; 13.6%). \( \text{bla}_{\text{CTX-M-15}} \) gene was co-carried by 47.8% (32 isolates) of isolates.

Conclusions: Our data suggest that the epidemiology of CPE in the pediatric population in Qatar is primarily dominated by OXA-48-type and NDM-type carbapenemases.

Clinical Trial Registration: N/A000000000
VACCINE HESITANCY AMONG HEALTHCARE WORKERS IN AL AIN CITY, UNITED ARAB EMIRATES: A QUALITATIVE STUDY

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Background: Healthcare workers (HCWs) are at the frontline to curb the spread of vaccine hesitancy (VH) in the community. However, there is a growing concern pointing that HCWs themselves are becoming vaccine-hesitant. This research aims to explore VH among HCWs in the United Arab Emirates (UAE).

Methods: The study consisted of 32 semi-structured face-to-face interviews with randomly selected HCWs involved in recommending and/or administering vaccination at 7 primary healthcare centers, Al Ain city, UAE. Participants included doctors, nurses and pharmacists; one third were Emiratis. The interview guide of the European Centre for Disease Prevention and Control on VH among HCWs and the Precede-Proceed Model: Predisposing, Enabling and Reinforcing Factors (PERF) were integrated and used for the study. Each interview was recorded and lasted ~20-40 minutes. Thematic analysis was performed after verbatim transcription of all interviews.

Results: Major themes based on PERF that positively influence HCWs’ attitudes toward vaccination included trust in the healthcare system and the government’s immunization policies, previous practices and cultural/religious factors that make people careful about their own and their children’s health. Other themes included concerns about unnecessary vaccines and vaccine safety. HCWs who believe in complementary medicine were more vaccine-hesitant. Many HCWs were concerned that social media might have a strong influence on people’s attitudes toward vaccination. Most HCWs claimed they never received a proper training on how to address VH.

Conclusions: HCWs in the UAE are complying with local immunization policies. However, the social media’s negative influence on people’s practices toward vaccination is a major concern that requires an urgent attention. Training HCWs on how to address VH among patients and the public must be a priority.
HOST IMMUNE RESPONSES AGAINST PNEUMOCOCCAL PROTEINS FOR PREVENTION OF NASOPHARYNGEAL CARRIAGE

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1National and Kapodistrian University of Athens, Faculty of Medicine, Immunobiology And Vaccine Research Laboratory, Athens, Greece, 2Radboud University Medical Center, Radboud Center for Infectious Diseases, Nijmegen, Section Pediatric Infectious Diseases, Laboratory Of Medical Immunology, Nijmegen, Netherlands, 3Athens Medical School, Department Of Microbiology, Athens, Greece

Background and Objective: Background/Objective: Pneumococcus colonizes the human nasopharynx leading to asymptomatic carriage or disease. In this study, we reviewed the complex immune dynamics of host responses against several pneumococcal proteins in the nasopharynx, aiming to elucidate the protective mechanisms against nasopharyngeal colonization. Such information is essential for the selection of proteins with the potential to be used for the development of serotype-independent protein-based pneumococcal vaccines.

Methods: Peer-reviewed papers in English reporting immunological mechanisms involved in host immune response to pneumococcal proteins in the nasopharynx were retrieved through a PubMed search using the terms ‘pneumococcal proteins’, ‘nasopharyngeal colonization’ and/or ‘cellular and humoral host immune response’.

Learning Points/Discussion: -Several pneumococcal proteins have been studied regarding their effectiveness in the elimination of carriage. -In humans, high antibody titers against the proteins: Ply, PhtD, PhtE, PcpA, PspC were found to correlate with lower carriage, whereas in mice, high antibody titers against PsA, PspA and PnrA offered protection against colonization. -Anti-protein antibodies have been demonstrated to eliminate pneumococcus mainly through bacterial agglutination (e.g. PspA), prevention of bacterial adherence to nasopharyngeal cells (e.g. PsA, PsrR) and dysregulation of zinc concentration homeostasis in the bacterial environment (Pht-family). -Cellular response to pneumococcal proteins is increasingly recognized as an important mediator of immunity against colonization. Mice lacking functional CD4+ T cells failed to show protection against subsequent carriage. In humans, T cell–mediated immune response, alone, although interfering with pathogen clearance in the nasopharynx, was not associated with the absolute interruption of subsequent pneumococcal carriage. -The crucial point for a possible induction of a protective effect may be the combination of different proteins able to induce a synergistic immune response (humoral and cellular), reinforcing their potential as antigens of novel protein-based pneumococcal vaccines against nasopharyngeal colonization.
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¹National Institute for Public Health and the Environment (RIVM), Centre For Infectious Disease Control, Bilthoven, Netherlands, ²Domus Medica, Perined, Utrecht, Netherlands, ³University Medical Centre Utrecht, Division Of Mother And Child, Utrecht, Netherlands

Background: Maternal vaccination is an effective and safe intervention to protect newborns against infectious diseases in early life. We assessed background rates of adverse pregnancy outcomes, collected in The Netherlands Perinatal Registry prior to the implementation of a maternal pertussis immunisation programme in the Netherlands. We aimed to put legitimate safety concerns about adverse events following immunization into perspective.

Methods: The Netherlands Perinatal Registry holds a validated linkage of national registries of four professional organizations that provide perinatal care in the Netherlands, covering approximately 98% of all deliveries in The Netherlands. Yearly numbers of pregnancy outcomes, divided by the total number of pregnancies or births each year for maternal and infant outcomes, respectively, were used to calculate incidence rates per 10,000 between 2006-2018. We only included viable cases, which were defined as ≥500g birth weight and ≥24+0w gestational age.

Results: The total number of pregnancies between 2006 and 2018 ranged between 158,868 and 175,710. Those women gave birth to 161,307 to 178,874 infants. Table 1 shows incidence rates of included maternal and infant outcomes per 10,000 between 2006 and 2018.
Conclusions: Background rates provide important information to guide safety surveillance after implementation of maternal vaccination programmes in the Netherlands. Changes in routine care and case definitions should be taken into account when time series of adverse pregnancy outcomes are analysed.

Table 1. Incidence rates per 10,000 of adverse pregnancy and birth outcomes for 2006-2018

<table>
<thead>
<tr>
<th></th>
<th>Mean incidence rate per 10,000 (median; range)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Maternal level</strong></td>
<td></td>
</tr>
<tr>
<td>Maternal mortality</td>
<td>0.4 (0.4; 0.2-0.7)</td>
</tr>
<tr>
<td>Placental abruption</td>
<td>17 (17; 15-19)</td>
</tr>
<tr>
<td>Hypertension/toxicosis</td>
<td>599 (604; 535-663)</td>
</tr>
<tr>
<td>(Pre-) eclampsia</td>
<td>34 (29; 22-51)</td>
</tr>
<tr>
<td>Prelabour rupture of membranes (≥24h)</td>
<td>658 (658; 613-709)</td>
</tr>
<tr>
<td>Inducing labour*</td>
<td>1853 (2028; 1228-2148)</td>
</tr>
<tr>
<td>Uterine rupture</td>
<td>0.9 (0.8; 0.5-1.4)</td>
</tr>
<tr>
<td>Total artificial labour or caesarean section*</td>
<td>2453 (2495; 2194-2672)</td>
</tr>
<tr>
<td>Vacuum extraction</td>
<td>891 (908; 695-1012)</td>
</tr>
<tr>
<td>Forceps extraction</td>
<td>28 (27; 11-5)</td>
</tr>
<tr>
<td>Caesarean section*</td>
<td>1578 (1596; 1470-1679)</td>
</tr>
<tr>
<td>Postpartum hemorrhage (&gt;1000ml)*</td>
<td>609 (6229; 505-646)</td>
</tr>
<tr>
<td><strong>Infant level</strong></td>
<td></td>
</tr>
<tr>
<td>Fetal mortality*</td>
<td>36 (35; 27-51)</td>
</tr>
<tr>
<td>Neonatal mortality (up to 28d postpartum)*</td>
<td>22 (22; 17-28)</td>
</tr>
<tr>
<td>Perinatal mortality (up to 7d postpartum)*</td>
<td>53 (50; 43-73)</td>
</tr>
<tr>
<td>Perinatal mortality (up to 28d postpartum)*</td>
<td>59 (56; 47-79)</td>
</tr>
<tr>
<td>Prematurity &lt;28+0 weeks</td>
<td>38 (38; 35-40)</td>
</tr>
<tr>
<td>Prematurity &lt;37+0 weeks</td>
<td>735 (739; 679-782)</td>
</tr>
<tr>
<td>SGA (&lt;10th percentile of Hoftiezer)</td>
<td>1085 (1073; 1035-1176)</td>
</tr>
<tr>
<td>LGA (&gt;90th percentile of Hoftiezer)</td>
<td>1030 (1020; 968-1114)</td>
</tr>
<tr>
<td>Lethal congenital disorders*</td>
<td>24 (25; 16-29)</td>
</tr>
<tr>
<td>Low Apgar score (&lt;7 at 5min)*</td>
<td>183 (187;162-203)</td>
</tr>
<tr>
<td>Neonatal hospital admission*</td>
<td>1683 (1683; 1186-2209)</td>
</tr>
<tr>
<td>NICU admission</td>
<td>355 (385; 207-467)</td>
</tr>
<tr>
<td>Intracranial bleeding</td>
<td>32 (31; 27-40)</td>
</tr>
<tr>
<td>Resuscitation</td>
<td>284 (286; 210-348)</td>
</tr>
</tbody>
</table>

* outcomes of which trends are partially explained based on the opinion or clinical experts

* specific and multiple and syndromic congenital disorders combined

* excluding admission after caesarean section without other diagnosis
10-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PHID-CV) IMPACT ON PNEUMONIA MORTALITY

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**Background:** Pneumococcus is estimated to have caused 294,000 deaths worldwide in children <5 years; and 81% of those infections were accompanied by pneumonia. Respiratory illnesses were the second main cause of hospitalizations at all ages in Brazil, with 375,214 hospital admissions and 56,175 associated deaths in 2017. In 2010, Brazil introduced the PHID-CV in its National Immunization Program (NIP).

**Methods:** Ecological study (2002-2017) of all ages prior to and after vaccine implementation in the Brazilian NIP. Data collection was performed from a National open-access database. A time series analysis of pre versus post-vaccinal periods was performed (R software). This ecologic study consists of data analysis of death associated with hospital admission diagnosis of pneumonia in the population assisted by the Brazilian Public Health system (SUS). The Pneumonia code is resumed to primary diagnosis at admission and it didn’t distinguish pathogens. All mortality data refers only to in-hospital death.

**Results:**

<table>
<thead>
<tr>
<th>Age group</th>
<th>2002-2009</th>
<th>2011-2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>(years)</td>
<td>Trend</td>
<td>Min.</td>
</tr>
<tr>
<td>&lt; 1</td>
<td>-0.0006</td>
<td>-0.0002</td>
</tr>
<tr>
<td>1 to 4</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>5 to 9</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>10 to 14</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>15 to 19</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>20 to 29</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>30 to 39</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>40 to 49</td>
<td>0.0002*</td>
<td>0.0003</td>
</tr>
<tr>
<td>50 to 59</td>
<td>0.0004*</td>
<td>0.0006</td>
</tr>
<tr>
<td>60 to 69</td>
<td>0.0015*</td>
<td>0.0011</td>
</tr>
<tr>
<td>70 to 79</td>
<td>0.0045*</td>
<td>0.0034</td>
</tr>
<tr>
<td>&gt;80</td>
<td>0.0118*</td>
<td>0.0072</td>
</tr>
</tbody>
</table>

* Statistically significant with confidence level of 95%

In the time series analysis the impact of the vaccine was shown to significantly influence the death rate trend leading to a death decline on those ≥5 years old. This reduction was not significant in the groups <1 year, and 1 to 4 years. Children under 1 year had a decreasing death rate even before the beginning of the new vaccination schedule. The reduction on mortality rate was consistent among the whole population above 5 years.
**Conclusions**: The PHiD-CV in Brazilian National Immunization Program reduced all-cause pneumonia death in the vaccinated and non-vaccinated inhabitants in a sustained and progressive manner, and reinforce PHiD-CV impact. This is an ecological study and there is no information regarding Pneumococcal serotypes in the analysis. The mortality impact of this time series regression is consistent with previous studies.
MOLECULAR GENOTYPING OF ENTEROVIRUSES ASSOCIATED WITH CENTRAL NERVOUS SYSTEM INFECTIONS IN ATHENS, GREECE

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Background: Human Enteroviruses cause a wide range of clinical syndromes, ranging from asymptomatic infection and hand, foot, and mouth disease, to meningitis, encephalitis, acute flaccid paralysis, and myocarditis. The aim of this study was to identify and characterize the EV associated with central nervous system (CNS) infections.

Methods: Cerebrospinal fluid (CSF) was obtained from children and neonates with suspected CNS infection, and tested by a multiplex PCR panel (Biofire® FilmArray® Meningitis/Encephalitis) over a 2-year period (2018-2019) in a tertiary pediatric hospital of Athens. Genotyping was performed in positive Enterovirus (EV) samples employing Sanger Sequencing.

Results: A total of 38/180 (21.1%) CSF samples were tested positive for EV. 63.2%(24/38) were males and the median age was 3 months (IQR: 1-75). Sufficient volume of CSF for genotyping was available in 17/38 samples. Eight different serotypes were identified: E11 (5/17), CV-B5 (4/17), E30 (3/17), E6 (1/17), E13 (1/17), CV- A14 (1/17), CV- A16 (1/17), CV- A8 (1/17). The most severe case was an 18-month old child, who was presented to ED with fever, status epilepticus and coma and CV- A8 was detected in CSF. All children recovered without obvious sequelae.

Conclusions: The predominant enteroviral serotypes circulating in our region associated with aseptic meningitis are E30, E11 and CV-B5. No unusual neurologic manifestations were observed during the study period.
UNCOMMON INFECTIONS IN EARLY INFANThOOD

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Second Pediatric Clinic of National & Kapodistrian University of Athens, P. & a. kyriakou Athens Children Hospital, ATHENS, Greece

Title of Case(s): UNCOMMON RECURRENT INFECTIONS IN EARLY INFANThOOD

Background: Chronic granulomatous disease (CGD) is a group of rare X-linked or autosomal recessive genetic disorders of the phagocytic nicotinamide adenine dinucleotide phosphate (NADPH) oxidase system causing recurrent bacterial and fungal infections with excessive inflammation and granuloma formation. The patterns of presentation differ from patient to patient in CGD. As shown in this case, abscesses are a common initial presentation of CGD and can occur at any site. Alternatively, dermatitis, pneumonia, lymphadenitis, liver abscess or osteomyelitis may be the prominent clinical problem in CGD.

Case Presentation Summary: A 12-day-old baby boy was presented in our Neonatal Department with fever, vomiting and impetigo-like skin infection in lower extremities. He is a first-born, 40 weeks of gestation via an uncomplicated vaginal delivery, following an unremarkable antenatal period. There is no maternal history of miscarriages. Complete blood count revealed a WBC count of 27000/mm3 (N: 80%, L: 20%) and elevated inflammation factors (CRP: 222mg/l). Blood culture was positive for Serratia marcessens, while CSF, urine and skin cultures were sterile. A step-up of adding meropenem to the antibiotic therapy was made without any significant clinical amelioration. Fever persisted and S.marcessens was also cultured from the percutaneous skin abscess drainage pus sample. An immunology control approach, including dihydrorhodamine (DHR) testing, confirmed the diagnosis of CGD. Immunomodulatory therapy (subcutaneous INF-γ administration) was added to the patient's regimen as well as antifungal and antibacterial prophylaxis. Molecular techniques including gene sequencing and mutation analyses for subtype were also considered, Clinical revaluation showed complete resolution of the previous findings. Seeking for HLA-identical family donor, peripheral blood stem cell transplantation is the next therapeutic step for our patient.

Key Learning Points: CGD is a primary immunodeficiency disorder which requires a high index of suspicion along with prompt and aggressive treatment of infections. The presentation of this patient with uncommon infections in early infancy pointed towards a primary immunodeficiency.
EVALUATION OF HEPATITIS A VACCINATION: EXAMPLES OF SAUDI ARABIA AND TURKEY

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¹GSK, Medical & Clinical Emerging Markets, Istanbul, Turkey, ²GSK, Medical Vaccines, Jeddah, Saudi Arabia, ³GSK, Medical & Clinical Emerging Markets, Wavre, Belgium, ⁴University of Antwerp, Vaccine & Infectious Disease Institute, Antwerpen, Belgium

Background and Objective: In Saudi Arabia and Turkey, improvements in socio-economic status and hygiene have contributed to decrease endemicity of hepatitis A (HepA). Additionally, an HepA virus (HAV) vaccine was included in the universal vaccination programs of Saudi Arabia and Turkey in 2008 and 2012, respectively. This literature review is intended to see the endemicity shift in HepA infection in the population of both countries.

Methods: We screened the peer-reviewed scientific literature and official online databases to retrieve information on HepA disease epidemiology (i.e., case numbers, age-group incidence, incidence by years) in Saudi Arabia and Turkey, before and after the HAV vaccine was introduced. Here, we present a summary of the epidemiology data from different articles and data on impact from the Ministries of Health of the two countries (i.e., case numbers evolution).

Learning Points/Discussion: Following the implementation of universal HAV vaccination with a two-dose regimen at 12 and 18 months of age with coverage rates >94% in Saudi Arabia and >91% in Turkey, HepA prevalence has decreased in both countries (see Figure). These important declines are observed in all age groups, highlighting a marked herd immunity effect. However, despite improved sanitary conditions and vaccination programs, virus circulation cannot be excluded in intermediate endemicity level countries. The adolescent and adult populations are becoming susceptible to HAV, due to e.g. altered eating habits and increased children day care attendance. HAV infection in those groups is associated with a higher rate of severe clinical manifestations. High vaccination coverage in children offers obvious reduction in HAV incidence in all age groups. Acknowledgements: Amandine Radziejwoski (Business & Decision Life Sciences platform) for publication coordination.

Figure 1: Evolution of HepA cases in Saudi Arabia and in Turkey
IMPACT OF SURVEILLANCE ON HEALTH CARE ASSOCIATED INFECTIONS IN TERTIARY CARE NEONATAL UNIT: AN EXPERIENCE OF MORE THAN 10 YEARS

D.M. Jajoo
Chacha Nehru Bal Chikitsalaya(Affiliated to Maulana Azad Medical College), Pediatrics, India, India

**Background:** Prevention and control of Health Care Associated Infections (HCAIs) is fast gaining prime importance in health care settings. The present study was done to know the prevalence and Impact of surveillance on decreasing the HCAIs.

**Methods:** Active as well as passive surveillance for HCAIs was started in Tertiary level Neonatal intensive care unit of Chacha Nehru Bal Chikitsalaya Delhi N from May 2008. For active surveillance clinicians and Infection Control Nurses were provided with training and proforma. The NIs were identified as per definitions as per CDC guidelines. Hospital Infection Control data was analysed on daily, weekly and monthly basis. All positive cultures were traced back for potential NIs (passive Surveillance) using specially designed forms.

**Results:** A total of 89913 patient days were observed during period of May 2008 to June 2019. There were 352 cases of HAI (HAI rate per 1000 patient days:4.0). Blood stream infections (BSI) were commonest, 61 % of HAI (215 cases) then Ventilator associated Pneumonia (VAP) 33.8% (119 cases), VAP rate was 11.9/ 1000 ventilator days. The rest 5 % (18 cases) were CRBSI & UTI. Acinetobacter spp. (26.3%), Klebseilla spp. (22.7%), were commonest organisms,then yeasts (18.4 %), E.coli (10.5%) and Enterococcus spp. (7.8%). The gram negatives were susceptible to colistin (92.3%), and imipenem (47%).

**Conclusions:** Surveillance of NIs is imperative for quality care. Constant training and monitoring are important tools to reduce these infections. Microbiological diagnosis along with clinical spectrum can help identify most of the HAI. Hand Hygiene is single most steps towards minimizing NIs in our setup.
**Background:** Infective endocarditis (IE) is a rare disease, difficult to diagnose and associated with high morbidity and mortality. Here, we present the clinical and microbiological characteristics and treatment of IE in children admitted in hospitals from the southern Spanish region.

**Methods:** Retrospective study of the cases diagnosed between 2008 and 2018 in three hospitals (Sevilla, Malaga, Cadiz). The clinical presentations, presence of previous congenital heart defect, infectious complications, diagnosis delay and treatment were reviewed.

**Results:** 34 IE episodes (IEE) from 29 patients; median age 10.9 years (IQR 3.6-14.5). 21/29 had a congenital heart defect. 26/34 had fever; median time of diagnosis 9 days (IQR 4.5-21), CRP 126 mg/L (IQR 59-189), neutrophils 7840/mm³ (IQR 4500-12715). PET-CT was performed in 8/34 IEE; infectious complications occurred in 7/34 (lung), 4/34 (cerebrovascular), 2/34 (renal), ocular/hepatosplenic embolism (1/34 each). Median treatment duration was 45 days (IQR 38-56). The most used antibiotics were β-lactams + gentamicin (15/34). Surgical treatment was required in 14/34. Recurrent episode or death in 4/34 each.

<table>
<thead>
<tr>
<th>CNS</th>
<th>9</th>
</tr>
</thead>
<tbody>
<tr>
<td>S.epidermidis</td>
<td>4</td>
</tr>
<tr>
<td>S.aureus</td>
<td>7</td>
</tr>
<tr>
<td>MRSA</td>
<td>1</td>
</tr>
<tr>
<td>S.viridans</td>
<td>4</td>
</tr>
<tr>
<td>HACEK</td>
<td>2</td>
</tr>
<tr>
<td>Others</td>
<td>9</td>
</tr>
<tr>
<td>Negative</td>
<td>3</td>
</tr>
</tbody>
</table>

**Conclusions:** With the exemption of cases with severe presentations, diagnosis of IE continues to be delayed, requiring a high suspicion for children with risk factors and fever. The microbiological etiology in our environment was similar compared to other regions. PET-CT was useful to identify infectious metastatic complications, however its utility to improve time of diagnosis remains to be determined. High
variability on IE treatment was observed. An ongoing prospective study of the REPA-GAIP group will address the above in order to improve diagnosis and treatment in children with IEE.
**Background:** A high percentage of the population in Latin America lives with intestinal parasitic infections, neglected tropical diseases frequently not treated. Intestinal parasitism is associated with nutritional diseases but the information about the epidemiological situation in countries like Bolivia is scarce. The environmental conditions play an important role in the prevalence of certain parasites. The main objective was to know the current situation of parasitic infections among children under twelve years old from different geographical areas of the department of Cochabamba – Bolivia.

**Methods:** We retrospectively analysed the laboratory reports of four second line hospitals of different areas and the Tertiary Care Hospital. Results of stool examinations performed between 2011 and 2015 in children under twelve years of age were collected.

**Results:** We gathered the results of 23221 examinations. The 89 % of children were less than five years old. Pathogenic parasites were found in 31 %. *Entamoeba histolytica* and *Giardia lamblia* were the two most prevalent parasites in all areas. Helminths were found in only 19% of positive samples and *Ascaris lumbricoides* was the most prevalent. Parasitic infections are more frequent in the tropical area and helminths are quite exclusively of this area.

**Conclusions:** Parasitic infections in children are still highly prevalent in Bolivia. Protozoan infections are the major problem while the prevalence of helminths is decreasing. The most vulnerable population is still concentrated in tropical areas where the risk of parasitic infection is increased due to the environmental conditions. Our results will enable the planning of more efficient policies to control parasitic diseases.
RESPIRATORY TRACT INFECTIONS IN CHILDREN, 3 YEARS TIMELINE OF BRONCHIOLITIS, INFLUENZA, OTITIS AND PNEUMONIA IN AMBULATORY SETTINGS

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**Background:** Few studies allow to analyze the timeline of potentially bacterial respiratory tract infections (acute otitis media and pneumonia) with viral epidemics: RSV (for which best marker is bronchiolitis) and influenza in ambulatory settings.

**Methods:** By automated data extraction, we daily prospectively collect anonymized data (age, sex, height, weight, daycare attendance, vaccines, diagnosis and prescriptions) of children with infectious diseases in 100 primary-care pediatricians using the same software (Axi5-Infansoft®, CompuGroup Medical): PARI study (Pediatric Ambulatory Research In Infectious Diseases). The pediatricians of this network had to participate to e-learning and face to face meetings in order to improve their diagnosis and management of infectious diseases. Here, we aim to analyze the data of respiratory tract infections.

**Results:** Between September 2017 and January 2020, we reported 38,266 otitis, 9,514 bronchiolitis, 8,002 influenza, and 1,251 pneumonia. Children with bronchiolitis were significantly younger (mean age 1.1 y ±1.2 y.) than those with otitis (2.4 y ±2.2 y), pneumonia (3.7 y ±2.6 y) or influenza (4.6 y ±3.3 y). Main peaks of otitis and pneumonia fitted with bronchiolitis and preceded influenza peaks (Figure).

**Conclusions:** The timeline we observed with this 3-years surveillance supports strong interaction between viruses and bacteria in respiratory tract infections. Moreover, such data provide real time epidemiology of the main respiratory diseases in ambulatory settings.
COMPLICATIONS IN PEDIATRIC PATIENTS AFFECTED BY MENINGITIS

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Bambino Gesù Children Hospital, Pediatric Infectious Diseases Unit, Roma, Italy

Background: Mortality and morbidity may affect patients with meningitis even if an adequate and prompt treatment is started. Meningitis complications can be severe and may include amputations, neurological damage, hearing loss, learning disabilities, visual impairment, seizures. The aim of the study is to identify the incidence of complications in patients with meningitis.

Methods: Patients aged 1-18 years, admitted to the Bambino Gesù Children Hospital, Rome, Italy for meningitis were included. The study period ranged from 1st February 2001 and 31th December 2017.

Results: In the study period, 408 patients were enrolled. Out of them, 124 developed a complication (Group A). The other 284 patients (group B) did not present any sequelae even at the follow-up evaluation. There was neither gender nor age difference between group A and B. The hospitalization was significantly higher in group A (38.7±42.4 days) than in group B (18.9±12 days). As for disease onset, seizures and lethargy were significantly more frequent in group A than in group B. As for blood exams, platelets and ESR were significantly higher in patients with complications than in the others. As for the etiology, the main isolated pathogens were Streptococcus Pneumoniae (20.16% in group A and 10.21% in group B) and Neisseria Meningitidis (12.90% in group A and 17.95% in group B)

Conclusions: Vaccination is one of the most cost-effective public health tools. As most of the meningitidis may be prevent by immunization, vaccination programs among pediatric population should be enforced in all countries.

Clinical Trial Registration: NOT APPLICABLE
EVALUATION OF KNOWLEDGE, BEHAVIOR AND PERCEPTIONS OF THE PEDIATRICIAN IN THE INDICATION OF THE HPV VACCINE - THE FINAL REPORT

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Background: AUDIT Background and aims: The HPV vaccine is an essential strategy for cervical cancer prevention. The physician is a crucial instrument for disease education and vaccine indication to patients and their families. However, worldwide low vaccination coverage has raised questions about the pediatrician's role in these unsatisfactory numbers.

Methods: Methods: During 2018 a questionnaire was applied to pediatricians at a tertiary hospital in São Paulo, Brazil. Knowledge about the disease and vaccine, behavior and perceptions of the physician regarding barriers and strategies for better vaccination coverage were evaluated.

Results: Results: Of 136, 30% achieved a high level of knowledge in HPV disease and vaccine. Although 73% always recommend vaccine and 55% believe to provide strong recommendation, 72% feel their knowledge is partial/null for proper vaccine orientation. Only 20% know the age indication of HPV vaccination schedule and 2/3 are not aware the vaccines available in Brazil. Most doctors believe updating medical professional is an adequate strategy. 58% prefer focusing on HPV vaccination as a cancer prevention strategy than STDs and 18% believe promoting vaccination campaigns in schools is a viable strategy.

Conclusions: Conclusions: The study found 70% of doctors with low knowledge about the disease caused by HPV and the indication of HPV vaccine. Low knowledge can compromise the quality of the vaccine recommendation and consequently the vaccine acceptance by the patient and family, contributing to low HPV vaccine coverage.
TARGET TRIAL DESIGN FOR TESTING AZITHROMYCIN FOR COMMUNITY-ACQUIRED PNEUMONIA (CAP) ASSOCIATED WITH MYCOPLASMA PNEUMONIAE AND TO DIFFERENT MICROORGANISMS


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Background: The efficacy of macrolides in Community Acquired Pneumonia (CAP) associated with M.pneumoniae is controversial. Causal inference analysis with a “target trial” design can help to reduce the bias of the observational studies by emulating a clinical trial. Our aim was to evaluate the effect of azithromycin on CAP by M.pneumoniae and on "other infiltrate/non-consolidation" pneumonia by other microorganisms, through a target trial.

Methods: An observational, prospective study was performed in 15 hospitals. Patients with CAP and PCR positive for M.pneumoniae in nasopharyngeal aspirate were included in this analysis. Using the “target trial” methodology, patients on azithromycin in the first 24 hours of admission were compared with those who did not receive azithromycin. The same analysis was performed on patients who had "other infiltrates/non-consolidation" on the radiograph, regardless of the etiology.

Results: From 344 patients with CAP, 27 with M.pneumoniae CAP were analyzed. 55% received azithromycin early and 45% not. There were no differences in admission (5 vs. 4.5 days, p=0.7), necessity and duration of oxygen (33% vs. 50%, p=0.7 ; 2 vs. 2 days, p=0.84). From 73/344 patients with "other infiltrate/non-consolidation" pneumonia, five were associated with M.pneumoniae, 36 with virus and 31 with unknown/not highly pathogenic virus. 24% patients received early azithromycin. Azithromycin predicted shorter admission (3.3 vs. 4.5 days, p=0.003) regardless of etiology, antibiotic or oxygen. No other effects were found.

Conclusions: In this small study, azithromycin had no effect on the outcomes of CAP associated with M.pneumoniae in children. However, it seems that azithromycin had an effect on the admission time of children with CAP with "other infiltrates" and without condensation, regardless of etiology. Whether the reason is related with the anti-inflammatory, immunomodulatory or antimicrobial effect of azithromycin, remains to be determined.
Title of Case(s): Bordetella pertussis: experience of Parma Children’s Hospital, Italy

Background: Pertussis has been resurging worldwide as a major health problem. The clinical spectrum of Bordetella pertussis illness extends from a trivial illness to a death causing condition, most frequently in infants aged ≤ 3 months. In this study, we present all cases aged ≤ 3 months admitted to Parma's Children Hospital from 2017 to 2019.

Case Presentation Summary: In this period, 8 patients < 3 months old were admitted with a diagnosis of laboratory-confirmed pertussis. A total of 2/8 were late preterm and 1/8 was small for gestational age (SGA). 7/8 were unimmunized, because too young to be vaccinated. In one case, the mother had been vaccinated during pregnancy. The age at onset varied between 20 and 104 days (mean: 52.9 days) and their weight was between 1600 gr and 3830 gr (mean 2857 gr). At admission, the symptoms varied between mild rhinitis and whooping cough with respiratory distress. When performed, the blood cell count showed marked lymphocytosis and C reactive protein was elevated in 3/8 cases. Diagnosis was confirmed in all cases by polymerase chain reaction for B. pertussis on naso-pharyngeal aspirate turned positive in 100% of cases. Despite prompt start of antibiotic therapy with macrolides and oxygen administration, 3/8 patients needed invasive respiratory support. One of these recovered well after ECMO, whereas one died due to cardiorespiratory arrest.

Learning Points/Discussion: Pertussis in young infants is a reemerging cough illness, associated with significant morbidity and mortality. Extreme leukocytosis and birth weight < 2500 gr are correlated to more severe forms. A prompt suspect and rapid diagnosis are fundamental for clinical management and for preventing complications. More effort is needed to improve prevention strategies such as maternal immunization and cocooning.
AUDIOLOGICAL COMPLICATIONS IN PEDIATRIC PATIENTS AFFECTED BY MENINGITIS: PROSPECTIVE AND FOLLOW-UP STUDY

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Background: Audiological complications are frequent long-term sequelae of meningitis. The aim of the study is to identify a combination of parameters predicting long-term audiological complications in patients with meningitis.

Methods: Patients aged 1-18 years, admitted to the Bambino Gesù Children Hospital, Rome, Italy for meningitis were included. The study period ranged from 1st March 2001 and 28th February 2019. Patients underwent an audiological examination before dismissal and within 4 weeks after discharge.

Results: 425 patients entered the study. An audiological complication was found out in 11% of cases (46 patients). A significant association between hearing impairment and pneumococcal etiology was observed (41% of cases) (p <0.001). Moreover, at the onset of meningitis, letargy was most frequently reported among patients with an audiological complication (p = 0.027). As for laboratory, a reduced glucose (26.18 mg / dL) in cerebral spinal liquid was detected in patients with hearing impairment (p = 0.004); as well as an higher RCP (17.77 mg/dL) (p=0.01) and ESR (106.3 mm/h) (p=0.04). At follow-up, 19 patients still had hearing impairment. Treatment was required in 16 patients: external hearing prosthesis in 6 cases, cochlear implant in 10 cases. Unfortunately, in 4 out of 10 cases, in which audiological screening was delayed, cochlear fibrosis and/or ossification was observed, with a definitive hearing damage.

Conclusions: Audiological complications may be promptly investigated in children affected by meningitis, in order to reduce the risk of major sequelae and facilitate the possible recovery of auditory function.

Clinical Trial Registration: NOT APPLICABLE
LIVE-VIRAL VACCINE SAFETY AND EFFECTIVENESS IN CHILDREN WITH AUTOIMMUNE DISEASES ON IMMUNOSUPPRESSIVE TREATMENT: A REVIEW OF THE LITERATURE

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Background and Objective: According to the EULAR and ESPGHAN guidelines, live-vaccines are contraindicated in children receiving high-dose corticosteroids, non-biological immunosuppressants and biologicals and they should be administered prior to treatment initiation. Live-vaccination coverage in these children ranges from 18.4% to 93.5% and in a multicenter European study in IBD children, live-vaccine-coverage was suboptimal for MMR (89.3%) and disappointing for VZV (18.4%). During measles epidemics in Europe and due to lack of universal varicella vaccination, many of these children are unprotected and at increased risk of complications. Live-vaccines, such as MMR and VZV, in these patients raise concerns regarding live-vaccination side-effects (SEs), underlying disease-flares and low effectiveness.

Methods: Herein, we reviewed 13 published studies on safety and effectiveness of MMR and VZV vaccines in pediatric patients under immunosuppressive treatment. We searched for relevant literature in PubMed using keywords: "live-vaccination; immunosuppressive; treatment", "live-vaccines; infection", "vaccination; coverage; autoimmune", "biologicals; live-vaccination", "varicella; immunosuppression", "immunosuppressive; treatment; measles".

Learning Points/Discussion: Safety studies, regarding MMR and VZV vaccine-strain infections and vaccine-related disease-flares are limited. In one small randomized trial, MMR and VZV vaccines appear to be generally safe and well-tolerated for children receiving immunosuppressive treatment. The frequency of SEs in this patient group was also comparable to the frequency in healthy children. Infections caused by vaccine-strains, have been reported after MMR and VZV, but they appear to be extremely rare (4/743 patients in all the studies reviewed) and mostly in patients on IL-1 (anakinra, canakinumab, rilonacept) and IL-6 blockades (tocilizumab). Vaccinations with MMR and VZV appear to be adequately effective, eliciting both humoral and cellular responses in these patients. Children receiving combined immunosuppressive and anti-TNF-a treatments demonstrated lower rates of antibody persistence. Existing data suggest that when necessary, live vaccines can be used in patients on immunosuppressive treatment. However, the implementation of vaccination guidelines should be enhanced in all patients before the initiation of immunosuppressive therapy and research is required for determination of immunological surrogates of live-vaccine safety.
MICROORGANISMS INVOLVED AND RESISTANCE PROFILE OF NOSOCOMIAL INFECTIONS IN PEDIATRIC INTENSIVE CARE UNITS ACCORDING TO 2019 ENVIN REGISTRATION.

A.C. Izurieta¹, E. Fresan Ruiz², S. Bobillo Pérez², A. Bustinza Arriortua³, P. García Soler⁴, S. Belda⁵, A. Solé⁵, I. Jordan², S.G. Paediatric Envin Registry⁶

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Background: To describe the microorganisms responsible of nosocomial infections and their resistance profile to antibiotics in pediatric intensive care units (PICU) in Spain.

Methods: A multicenter, prospective and observational study based on the pediatric ENVIN registry, which includes 29 PICU of Spain. Nosocomial infections from April 1st to June 20th, 2019 were included. The types of infections as well as the microorganisms involved with their antibiotic resistance profile were analyzed.

Results: 1752 patients were included and 68 (3.88%) had at least one nosocomial infection. In 52 (76.4%) the microorganism was isolated. The most frequent infection was urinary tract infection (5.7/1000) followed by central line-associated bloodstream infection (2.34/1000) and ventilator-associated pneumonia (2.3/1000). Gram negative were the most frequently isolated (32; 61.5%), being *Escherichia coli* (10; 31.2%) and *Klebsiella* (9; 28.1%) the most frequent in this group. Gram positive (13; 25%) were *Staphylococcus epidermidis* (5; 38.5%) and *Enterococcus faecalis* (4; 30%). All fungal infections (8; 15.4%) were caused by *Candida*. Carbapenemases-producing enterobacteria were not recorded.

Conclusions: The nosocomial infection rate in Spanish PICUs during 2018 remains low and similar to the previous year. The microorganisms most frequently involved are Gram negative, most of them being sensible to the usual antibiotics.
IMMUNOLOGICAL STATUS EXAMINATION AND SPECIFIC PATHOGENS IN ACUTE CEREBRAL NERVOUS SYSTEM INFECTIONS

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Background: Acute central nervous system (ACNS) infections may cause mortality and morbidity among children even if an adequate therapy is promptly prescribed. Aim of this study is to study the immune system in children who experienced an ACNS infection.

Methods: Patients admitted to the Bambino Gesù Children Hospital for ACNS infection between January 2006 and June 2016 entered the study. Exclusion criteria were major comorbidities and previously detected immunodeficiencies.

Results: The sample size included 97 patients, with a mean age of 4 years. At least an immunological alteration was found out in most of our patients (74%). Out of them, 51.4% had an altered B cell proliferation test, and 23% a B cell phenotype alteration (23%). Analysing pathogens, patients were divided into two groups: children older than 3 years old (Group A, n= 57) and children younger than 3 years old (Group B, n=40). In group B, Escherichia Coli, Haemophilus Influenzae, Klebsiella Pneumoniae were exclusive of patients affected by immunological alteration (p< 0.001). In group B, we also observed lower values of IgG, IgM, CD3, CD4, CD8 (P <0.05).

Conclusions: A potential limit of our study is the small sample size. Further researches are required to confirm our results. Nevertheless, we suggest that an immunological evaluations may be useful in patients affected by an ACNS infection.

Clinical Trial Registration: not applicable
Background: Respiratory syncitial virus (RSV) is a common cause of respiratory infections in children. In developed countries, mortality due to RSV is <0.1%; this value rises in patients with comorbidities. None of the therapies tested for RSV has proven effective; supportive care is the only recommended therapy. Ribavirin is a purine-analogue active against Paramyxoviridae. Its use is almost exclusively limited to immunocompromised patients with positive outcome. Side-effects include: anemia, insomnia, dyspnea, irritability. We describe a series of pediatric patients affected by RSV infection requiring ICU-admission not responsive to conventional ventilatory support treated with oral ribavirin.

Methods: All children aged between 0 and 18 months admitted to the Bambino Gesù Children’s Hospital in Rome over a six-year period (2015-2020) receiving oral ribavirin associated or not to intravenous immunoglobulines because of a severe RSV respiratory infection were included.

Results: Among the 125 patients admitted to the ICU because of a PCR-proven RSV infection, 27.2% received oral ribavirin. None of the patients had life-threatening side effects. In two patients an increase of serum ALT and GGT were described; in four patients an isolated increase of GGT was observed. One patient had an increase of LDH. Anemia occurred in one patient. Rhabdomyolysis occurred in one patient, although a single case of rhabdomyolysis related to ribavirin treatment is reported in literature but associated with other drugs. In none of these cases the drug was discontinued.

Conclusions: Ribavirin was well-tolerated in our cohort of patients and no deaths have been recorded, thus it might be considered in severe RSV infections not responding to supportive care. However, randomized trials are needed to assess the efficacy and safety of this treatment for RSV infections in children.
Background: Preterm birth is a well-known risk factor for RSVH in children ≤2 years. This study describes the burden of RSVH in children born <29wGA using national data from Scotland over a 12-year period.

Methods: All live births between 2000-2011 from NHS Scotland Information Services Division (ISD) databases were followed until 2 years of age and RSVHs (ICD-10 codes J12.1, J20.5 & J21.0) assessed in children born <29wGA versus those born 29-35wGA and ≥36wGA.

Results: RSVH incidence was 12.8% (277/2,168) for <29wGA children compared to 5.5% (1,433/25,821) for 29-35wGA (relative risk [RR] <29wGA vs. 29-35wGA: 2.29, 95% confidence interval [CI] 2.05-2.56; p<0.0001) and 2.0% (11,633/595,384) for ≥36wGA (RR <29wGA vs. ≥36wGA: 6.54, 95% CI 5.86-7.30; p<0.0001). RSVH rates were 149/1,000, 62/1,000, and 21/1,000, respectively (both p<0.0001 vs. <29wGA). Median age at first RSVH was higher (p<0.0001) for <29wGA children (247 [interquartile range 143-411] days) versus 29-35wGA (150 [75-284] days) and ≥36wGA (139 [60-272] days). Intensive care unit admission rates were 13.4% (43/322) for <29wGA, 10.1% (162/1,605; p=0.057) for 29-35wGA, and 3.6% (457/12,687; p=0.0001) for ≥36wGA. Children <29wGA spent longer in hospital (median 5 [2-9] days) than 29-35wGA (3 [1-6] days; p=0.0024) and ≥36wGA (2 [1-4] days; p<0.0001). Of <29wGA children with RSVH, 46.9% did not have bronchopulmonary dysplasia (BPD) or congenital heart disease (CHD). Male sex (p=0.322) and multiple birth (p=0.273) were not risk factors for RSVH in <29wGA children, while lower birth weight was borderline significant (p=0.0483).
**Conclusions:** Birth <29wGA is a significant risk factor for RSVH irrespective of BPD/CHD or other risk factors, with these children having an increased burden of disease compared to those born ≥29wGA.

**Acknowledgements** Matthew Freddi (Strategen Ltd) – editorial services.

**Systematic Review Registration:**

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<th>≥36wGA</th>
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<td><strong>Number of children</strong></td>
<td>2,168</td>
<td>25,281</td>
<td>595,384</td>
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<td><strong>Number with ≥1 RSVH (%)</strong></td>
<td>277 (12.8%)</td>
<td>1,433 (5.5%)</td>
<td>11,633 (2.0%)</td>
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<td><strong>Admission rate</strong> Rate per 1,000 (number of admissions)</td>
<td>148.5 (322)</td>
<td>62.2 (1,605)</td>
<td>21.3 (12,687)</td>
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<td><strong>Number of children with RSVH with &gt;1 admission (%)</strong></td>
<td>38 (13.7%)</td>
<td>151 (10.5%)</td>
<td>961 (8.3%)</td>
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<tr>
<td><strong>Age at first admission</strong> Median [IQR]</td>
<td>247 [143-411]</td>
<td>150 [75-284]</td>
<td>139 [60-272]</td>
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<td><strong>Mean (SD)</strong></td>
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<td><strong>Number with ICU admission (%)</strong></td>
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ICU: intensive care unit; IQR: interquartile range; LOS: length of stay; RSVH: respiratory syncytial virus hospitalisation; SD: standard deviation; wGA: weeks’ gestational age.
ANTENATAL AND CONGENITAL SYPHILIS SCREENING - A LARGE UK TEACHING HOSPITALS EXPERIENCE OVER THREE YEARS

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Background: Congenital syphilis (CS) is a significant public health problem, complicating an estimated one million pregnancies per year worldwide. Screening and treatment for pregnant women is an effective approach for reducing CS, but requires effective communication between clinical teams to ensure both mother and child are managed appropriately. We assessed if pregnant women in our trust with positive syphilis serology and their children had appropriate investigation and management as per our local guidelines.

Methods: A retrospective review of all women screening positive for syphilis in pregnancy in our hospital from January 2016 to February 2019 was conducted. Women were identified from a local antenatal blood born infection database, and blood results were obtained from our electronic reporting system. We reviewed the clinical notes and serology results of both mother and child (where available) and compared investigations, treatment and followup against our local guidelines.

Results: In the time period covered, there were 34491 pregnancies leading to 31059 live births. 37 women had positive syphilis serology. 15 women had no documented previous treatment, indicating a local prevalence of 0.04%. Among these women 2 miscarriages and 1 stillbirth occurred (20%), and 6 women were treated for syphilis, leaving 6 neonates requiring screening. This occurred in 5, and one neonate was empirically treated.

Conclusions: Our local prevalence of antenatal syphilis is 0.04%, which is slightly lower than estimated national prevalence of 0.05%. All neonates were either screened or treated in line with our local protocol. Whilst our current system for referring and monitoring pregnant women with positive syphilis serology potentially duplicates work, it ensures appropriate management for both the mother and child. We encourage other hospitals to audit their rate of antenatal syphilis screening and to ensure their referral systems are equally robust.
THE HUMAN GUT ORGANOIDS, A PROMISING MODEL TO STUDY ENTEROVIRUS INFECTION AND DISEASE PATHOGENESIS

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Background: Enteroviruses (EVs) are a major source of human infections worldwide, with a broad spectrum of disease symptoms, from diarrhea and skin rash to more severe disease like meningitis and paralysis. Elucidating EV pathogenesis has been limited by the lack of suitable models that faithfully mirror normal human physiology and pathophysiology. Organoids are stem cell-derived in vitro 3D organ models and an excellent system that has potential for studying on EV-host interaction, virus evolution, and antiviral compound testing on a human system.

Methods: The 3D fetal gut organoids are an “inside out” representation of human physiology with the basal side on the outside facing the environment and the apical side facing the inwards. During culture, the proximal and distal organoids are “opened up” and cultured as a monolayer on transwell inserts to establish viral infection. The monolayers were apically exposed to enterovirus A71 (EV-A71) and subsequent viral replication was assessed by quantifying the production of viral RNA and virus replication at several time points over a course of six days.

Results: Using the monolayer transwell system we show that EV-A71 infects the epithelium monolayers from the apical surface. We will present data on infection of the monolayer model with EV-A71, cell tropism of the virus, and monolayer permeability after infection.

Conclusions: The human fetal gut derived intestinal organoid model is a powerful model for studying enterovirus infection and related disease pathogenesis. Continued development of the organoids cultures by including components of the normal host tissue microenvironment such as immune cells and blood vessels, will facilitate and simplify studies on human viral pathogenesis, and improve the development of platforms for pre-clinical evaluation of vaccines, antivirals and therapeutics.

Clinical Trial Registration: ClinicalTrials.gov 0123456789
DILEMMAS IN THE DISCLOSURE OF HIV INFECTION IN CHILDREN AND ADOLESCENTS - THE FINAL REPORT

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Background: HAART reduced morbimortality of HIV, allowing infected children to achieve late adulthood. The WHO recommends that diagnostic disclosure should begin during school age in a gradual, continuous and individualized approach. We aimed to evaluate the knowledge, feelings and difficulties involved diagnostic disclosure in a tertiary hospital in São Paulo, Brazil.

Methods: We prospectively applied three different questionnaires for HIV-infected patients with revealed diagnosis, their caregivers and the health professionals involved in their regular care, including epidemiological data, clinical data and the disclosure.

Results: Caregivers (n=18): 88% were mothers; 57% were living with HIV, 40% had already revealed the disease to their children. In their opinion, the ideal age for disclosure is ±13 years old. HIV-infected adolescents (n=10): 60% were girls; 80% acquired infection through vertical transmission. Mean age at disclosure was 12.9 years. 60% think that there is a ideal moment for disclosure, especially when the patient starts questioning the disease. Healthcare professionals (n=72): Most are already trained pediatricians, average age of 26-30 years. 80% think there is no ideal age for disclosure.

Conclusions: Understanding the challenges involved in HIV disclosure can lead to improved approach methods, increased adherence and disease control. Training is important for healthcare professionals. A careful follow-up after disclosure is fundamental, since many patients experience negative feelings.
Title of Case(s): A case of measles in a vaccinated person.

Background: The incidence of measles remains an actual problem for European region. It's known that measles virus can also circulate in vaccinated people, causing atypical forms of infection. Due to this facts, a positive history of vaccination cannot completely exclude the diagnosis of measles.

Case Presentation Summary: A 15-years old girl sought medical attention due to running nose, dry cough, fever up to 38.6 °C, itchy eyes, feeling of sand in the eyes, rash. The disease started from respiratory symptoms for 2 days. On the 3rd day rash on the face appeared and spread to chest and hands on the 4rd day. As she had been vaccinated due to schedule (she got 2 doses of MMR) she was diagnosed as an acute respiratory infection. But during patient history taking became known that girl's mother had laboratory confirmed measles 15 days ago. The girl was admitted to the hospital and managed as measles. She had fever for 2 days, on the 5th day of the disease isolated elements of a maculopapular rash appeared on the buttocks, hips and legs. On the 8th day of the disease pigmentation appeared, nasal breathing improved, and the cough disappeared. In laboratory tests she had negative IgM, positive IgG, PCR of nasopharyngeal specimen was negative, but urine positive. She completely recovered and was discharged from the hospital with diagnoses: Atypical measles, mild course.

Learning Points/Discussion: This case shows that measles can occur in vaccinated persons. Atypical and mild course is more common and can lead to incorrect diagnosis. Only a sufficient vaccination rate can provide complete protection from measles for the population.
A NOVEL OUTPATIENT PARENTERAL ANTIBIOTIC THERAPY SERVICE FOR NEONATES AT A TERTIARY UNIVERSITY HOSPITAL IN LONDON: A TWO YEAR REVIEW

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¹St George’s University Hospitals NHS Foundation Trust, Paediatric Infectious Diseases, London, United Kingdom, ²St George's University Hospitals NHS Foundation Trust, Neonatal Unit, London, United Kingdom, ³St George's University Hospitals NHS Foundation Trust, Wandsworth Children's Continuing Care, London, United Kingdom

Background: Neonatal infections can require prolonged intravenous antibiotic treatment leading to prolonged hospitalisation. Paediatric outpatient parental antibiotic therapy (POPAT) is well established in paediatrics, but not in neonates. This survey aimed to determine the feasibility of a neonatal POPAT (nPOPAT) service and identify the patient groups that would benefit.

Methods: Retrospective review of the nPOPAT service from 2017 – 2019. Neonates aged 0-28 days at time of referral were included. Data was collected using REDCap. STATA was used for descriptive analysis.

Results: 50 patients completed antibiotic therapy: 34(68%) referred from the postnatal ward, 5(10%) from the infectious disease ward, 5(10%) from the neonatal unit, 6(12%) from medical/surgical wards. Median age was 4 days (IQR 2,6). The most common diagnoses were early onset sepsis (EOS) in 24(50%), bacteraemia in 8(17%) and bacterial meningitis in 6(13%). 48(96%) of neonates were treated with once daily Ceftriaxone. Median antibiotic duration was 5 days (IQR 3,8). 41(82%) utilised peripheral cannulas, 8(16%) midline catheters and 1(2%) a central line. Overall, 350 bed days were saved.

Conclusions: Providing this service more widely can result in significant reductions in in-patient bed utilisation for this common neonatal condition, and consequently reduce treatment costs.
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EARLY DIAGNOSIS OF CHRONIC GRANULOMATOUS DISEASE IN A NEONATE

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Title of Case(s): Early diagnosis of Chronic Granulomatous Disease in a Neonate

Background: Chronic Granulomatous Disease (CGD) is one of the classic primary immunodeficiencies of childhood, although its presentation in neonatal period with some uncommon features may be easily overlooked. CGD is characterized by recurrent life-threatening bacterial and fungal infections with a high mortality rate.

Case Presentation Summary: A 12-day-old boy was referred to our hospital, due to rash over the last three days. On admission, he was febrile and had bullous impetigo in the genital area-intact and crusted impetigo on the face. He also had conjunctivitis with purulent discharge, dactylitis in the right foot and cellulitis in the dorsum and planum of left and right foot, respectively. Ultrasonography revealed abscesses under the cellulitis site. He was treated with IV vancomycin. Bacterial culture of the nares was positive for MRSA, whereas cultures from blood, skin lesions and pus grew Serratia marcescens. According to this, meropenem was added. From the second day, the fever was subsided, and the abscesses were laid down in size. Due to suspected CGD, DHR test was performed that came up pathological. Subsequently, administration of prophylactic cotrimoxazole and itraconazole was started. The neonate was discharged after 18 days but 2 days later he presented with new abscesses and he was treated again with IV antibiotics. He was also given IFN gamma and was planned for hematopoietic cell transplantation (HCT).

Learning Points/Discussion: CGD disease is rarely seen in neonates, however neonates with multiple abscesses, especially caused Serratia marcescens, must be investigated for CGD. Prompt diagnosis and treatment with broad spectrum antibiotics are crucial.
GLOBAL MOLECULAR DIVERSITY OF RSV – THE “INFORM RSV” STUDY


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Background: Respiratory syncytial virus (RSV) is a global cause of severe respiratory morbidity in infants. Preventive and therapeutic interventions are being developed, including antivirals, vaccines and next generation monoclonal antibodies. The International Network For Optimal Resistance Monitoring of RSV (INFORM-RSV) is a prospective, multicenter, global observational study performed by ReSViNET to investigate the molecular diversity of RSV isolates from more than 15 countries in children < 5 years of age visiting a hospital who have confirmed RSV.

Methods: Over a five-year period approximately 4,000 RSV-positive respiratory samples will be collected and whole RSV genomes sequenced to assess temporal and geographical molecular patterns. RSV will be cultured to study the functional implications of specific amino acid polymorphisms, including viral fitness and susceptibility to different monoclonal antibodies. In addition, a repository of globally collected RSV sequences will be created.

Results: During the pilot season (2017-2018), 410 of 476 RSV-positive nasal samples obtained from eight countries (Australia, Brazil, Finland, Japan, the Netherlands, South Africa, Spain and the United Kingdom) were successfully sequenced. Subtype B was more prevalent than subtype A and polymorphic changes were observed in all five antigenic sites of RSV F protein.

Conclusions: Although sample collection was non-uniform in this first year of study, minimal global variation of RSV glycoproteins was observed across countries studied.

Clinical Trial Registration: Not applicable
MORTALITY AND MORBIDITY IN COMMUNITY ACQUIRED LOWER RESPIRATORY TRACT INFECTIONS IN EUROPEAN PAEDIATRIC INTENSIVE CARE UNITS


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Background: Lower respiratory tract infection (LRTI) in children is a frequent reason for hospital admission. Data on the outcome of children with community acquired LRTI admitted to the Paediatric Intensive Care Unit (PICU) are scarce.

Methods: Data were collected as part of the prospective cohort study from the European Childhood Life-threatening Infectious Disease study (EUCLIDS). We collected data from children (age 28 days to 18 years) admitted to the PICU with severe community acquired LRTIs in 7 European countries from July 2012 to January 2016. Variables included clinical presentation, laboratory and radiological tests, diagnosis, treatment and outcome.

Results: Median age of 323 patients at admission was 3.1 years (range 28 days – 17 years). Overall, 49.5% of all children had a comorbidity. Pulmonary complications such as pleural empyema, lung necrosis or pneumothorax were present in 38.7%. The median number of days of PICU hospitalization was 7 days (range 1-134 days). Overall mortality was 5.4%. Fatal cases had a median age of 8.4 years and 82.4% had comorbidity. In 246/306 patients who survived, the overall performance at hospital
discharge was recorded and 75 (30.5%) were discharged with some disability.

**Conclusions:** Almost half of all children admitted to PICU with severe community acquired LRTI had comorbidity. Overall mortality was 5.4%. Patients who died were older children with a significant comorbidity. More knowledge about the clinical characteristics of children at risk of mortality or complications following admission to PICU for severe LRTI, might help in development of personalised monitoring and treatment strategies.
UNEXPECTED REACTIONS DURING TUBERCULOSIS TREATMENT: WHAT WE SHOULD NEVER FORGET.

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Title of Case(s): Unexpected reactions during tuberculosis treatment: what we should never forget

Background: During tuberculosis treatment, sometimes, eventualities can arise. To detect these contingencies, we must look for them continuously, to offer proper treatment as soon as possible.

Case Presentation Summary: Our first case is a 12yo girl with pulmonary tuberculosis under a four-drug regimen with isoniazid (H), rifampin (R), pyrazinamide (Z) and ethambutol (E). On day 10, she developed acute liver failure with hepatocellular injury and coagulopathy. Antituberculous treatment was discontinued until liver tests returned to normal. Autoimmune and infectious hepatitis were excluded, so she was finally diagnosed with drug-induced liver injury. R was resumed and well-tolerated. She completed treatment with R and 2 non-hepatotoxic drugs. Lymphocyte transformation test was positive for Z.

Our second case is a 13yo boy with pulmonary tuberculosis with pleural effusion. On day 15 of HRZE, fever and symptoms reappeared. Imaging studies showed pleural thickening. Other comorbidities, including HIV-coinfection, were excluded. He was diagnosed with a paradoxical reaction, so oral prednisone was started, with clinical recovery.

Our third case is a 2yo girl, with bilateral pulmonary tuberculosis under HRZ. Follow-up chest radiographs revealed significant worsening of preexisting lesions without clinical deterioration. A paradoxical reaction was suspected, so a watchful-waiting approach was decided. The lesions resolved completely in the subsequent radiographs.

Learning Points/Discussion: During the follow-up visits of our patients with antituberculous treatment, we should always bear in mind, the possibility of an adverse reaction when they show clinical/radiological worsening. This type of events are not infrequent and should be included in our differential diagnosis as they may have therapeutic implications.
EXTRACORPOREAL MEMBRANE OXYGENATION (ECMO) SUCCESSFULLY RESCUES SEVERE PERTUSSIS IN INFANTS

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Title of Case(s): Extracorporeal membrane oxygenation (ECMO) successfully rescues severe pertussis in infants

Background: Pertussis is a highly contagious disease caused by Bordetella pertussis that can lead to severe respiratory distress, most frequently in preterm infants, with birth weight < 2500 gr, and aged less than 3 months old. In this study, we present the cases of two twins who developed a severe disease from whom ECMO was required for survival.

Case Presentation Summary: Two twins, male and female, born at 34 weeks of gestational age with birth weight of 1600 g (SGA) and 1885 g (AGA) were admitted to Parma's Children Hospital Neonatal Intensive Care Unit at the age of 59 days. They both presented with whooping cough, respiratory distress and poor appetite. Antibiotic therapy with macrolides was promptly started. Polymerase chain reaction for B. pertussis turned positive on nasopharyngeal aspirate. A marked increase of peripheral lymphocytes (up to 27060/μL and 16720/μL respectively) was simultaneous to the worsening of clinical conditions. Over the course of a few hours, severe pulmonary hypertension complicated hyperleukocytosis. The respiratory support was increased from High Flow Nasal Cannula (HFNC) ventilation, to nasal Continuous Positive Airway Pressure (n-CPAP) and then to ECMO. ECMO was performed for 12 days. The male twin developed arterial hypertension and cerebral hemorrhage as complications due to the treatment. The twins were both discharged after 119 days, in good clinical conditions.

Learning Points/Discussion: Pertussis in young infants can cause severe respiratory distress and continuous to cause significant morbidity and mortality in infants, in particular during the first months of life. ECMO appears effective in rescuing infants with severe pertussis. Improving immunization strategies, in particular maternal immunization, is crucial to reduce the incidence of the disease in young infants.
VIRAL INFECTION AS A CAUSE OF ACUTE GASTROENTERITIS IN HOSPITALIZED CHILDREN - SINGLE CENTER STUDY

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Background: Hospital studies showed that 45-75% of children with AGE had a pathogenic enteric organism isolated from their stools. Rotavirus is the most common cause of AGE in children in all European countries. Children with rotavirus infection had significantly higher severity scores, more diarrheal events, and longer-lasting diarrhea than children with adenovirus-induced AGE. Aim of the study: Analysis of the incidence of viral infections among children hospitalized for AGE.

Methods: 1411 medical records of children aged 1 month to 18 years old in the years 2017-2019 hospitalized due to AGE in Gastroenterology Unit Department of Pediatrics in Katowice were subject to retrospective analysis. Depending on the clinical course, all children were tested for rota and adenoviral infection by ELISA method in fresh stool and / or stool culture for Salmonella, Shigella, Pathogenic E. coli, Campylobacter pyroli.

Results:

<table>
<thead>
<tr>
<th>Year</th>
<th>Total AGE</th>
<th>Viral etiology</th>
<th>RV</th>
<th>AV</th>
<th>RV+AV</th>
<th>Bacterial etiology</th>
<th>Unknown etiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>2017</td>
<td>512</td>
<td>286 (56%)</td>
<td>239</td>
<td>28</td>
<td>19</td>
<td>50 (10%)</td>
<td>176 (34%)</td>
</tr>
<tr>
<td>2018</td>
<td>467</td>
<td>237 (51%)</td>
<td>79</td>
<td>85</td>
<td>73</td>
<td>40 (9%)</td>
<td>190 (40%)</td>
</tr>
<tr>
<td>2019</td>
<td>432</td>
<td>243 (56%)</td>
<td>87</td>
<td>95</td>
<td>61</td>
<td>20 (5%)</td>
<td>169 (39%)</td>
</tr>
</tbody>
</table>

Seasonality of occurrence was observed only in the case of RV infection from January to May.

Conclusions: During the observed period, a decrease in the frequency of hospitalization was noted, as well as a decrease in the occurrence of RV infection which may be associated with an increase in RV infant vaccination.
ROLE OF VIRUS AND PNEUMOCOCCAL LOAD IN CHILDREN WITH COMMUNITY ACQUIRED PNEUMONIA

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Background: Community-acquired pneumonia (CAP) causes substantial morbidity and mortality in children worldwide. Determining the etiology of CAP is challenging because children may be colonized with Streptococcus pneumoniae, one of the most common bacterial causes of CAP. The objective of our study was to determine whether the interaction between viruses detected and pneumococcal load measured can differentiate infection and colonization.

Methods: We enrolled children, 3 months to 11 years of age, with CAP and asymptomatic healthy controls in a prospective cohort study. Pneumococcal load was determined based on quantifying the lytA gene fragment from nasopharyngeal specimens. Viruses were identified using the Luminex respiratory panel. The primary outcome was CAP, defined as a provider diagnosis of CAP and a focal opacity on chest radiography. The association between the outcome and independent variables were determined using logistic regression.

Results: There were 409 children with CAP (median age of 3.2 years (interquartile range, 1.5-5.8)) and 168 healthy controls (median age of 4.5 years (interquartile range, 2.1-7.7)). Virus detection was significantly greater in healthy controls (n=110, 66%) than in children with CAP (n=147, 36%). Pneumococcal load was higher across viruses in healthy controls compared with children with CAP (Figure 1). When adjusting for age and pneumococcal load, children with a virus were 3.79 more likely to have CAP than healthy controls (95% CI: 2.32,6.33). Figure 1

Conclusions: Although presence of pneumococcus alone does not indicate infection, there is seems to be an association between viral and pneumococcal presence in predicting children with CAP. Further studies are needed to determine levels of pneumococcal load and viral infection that may be helpful in differentiating true infection from colonization.

Clinical Trial Registration: Not Applicable
Background: The 13-valent pneumococcal conjugate vaccine (PCV13) universal vaccination program was introduced in December 2016 in Andalusia, Spain.

Methods: Ongoing cross-sectional carriage study to evaluate the molecular epidemiology of pneumococcal nasopharyngeal colonization. 353 healthy children aged 6 months to 5 years were recruited from primary healthcare centres in Seville for the period April 2018 through November 2019. MIC interpretative breakpoints were used according to EUCAST. Genomic DNA from Streptococcus pneumoniae isolates were fully sequenced and serotypes were determined by mapping reads to concatenated CPS locus. MLST was determined through a similar approach. Unpublished data from a previous carriage study conducted during 2007-2008 were used for comparison.

Results: 64 (18%) children were colonized with S. pneumoniae during 2018-2019 and there was 154 isolates collected during the pre-PCV13 period. Colonization with vaccine (PCV13) serotypes (VT) declined significantly in 2018-2019 (14% vs 39%, P=0.003). During 2018-2019, serotypes 19F (9%), 3 (2%) and 6B (2%) were the only circulating VT; serotype 19A, most prevalent VT in 2007-2008, was eradicated. Serotypes 15B/C and 11A were the most frequently identified non-PCV13 serotypes in the post-PCV13 period (19%;14%) the later one increased significantly between time periods (P=0.003). Serotype 11A was exclusively associated in 2018-2019 with an ampicillin-resistant (CMI>2 mg/L) variant of the Spain 9v- ST156 clone (ST6521)

Conclusions: There is a limited circulation of PCV13-VT, mainly serotype 19F, in pneumococcal carriage in the early post-PCV13 period. Further studies are warranted to characterize disease causing potential of the emerging ST6521 clone within serotype 11A, which is associated both with high level antibiotic resistance and increased ability to produce biofilm.
INCIDENCE AND OUTCOMES OF MULTI-DRUG AND EXTENSIVELY DRUG-RESISTANT ACINETOBACTER INFECTIONS IN NEONATES

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Background: Drug-resistant Acinetobacter has emerged as a predominant cause of neonatal septicemia. The data regarding its epidemiology are emerging. Acinetobacter is associated with a high incidence of drug resistance and thus is currently a major threat for sick premature neonates. We present 5-year data of Acinetobactor infections in a level-III NICU of an academic research institute in Northern India.

Methods: Data of neonatal admissions including episodes of suspected and proven infections in past 5 years (Jan 2015 - Dec 2019) were extracted from the electronic database and case records. Culture-proven sepsis was defined as isolation of pathogenic bacteria from blood or CSF. Early onset sepsis (EOS) was defined as bacterial growth in first 72 hours of life. Meningitis was diagnosed by >10 cells in CSF along with culture-positive sepsis or bacterial isolation from cerebrospinal fluid (CSF). Multi-drug (MDR) and extensively-drug resistant (XDR) were defined according to standardised terminology by ECDC & CDC.

Results: 484 episodes of culture-proven sepsis were documented among 29,126 live births over 5 years study period. Acinetobacter [n=165 (34%)] was single most common pathogen [EOS 43% (56/131); LOS 31% (109/353) episodes]. Based on susceptibility pattern, seven neonates were treated with ciprofloxacin, 19 with extended-spectrum penicillin or carbapenems and rest with colistin/polymyxin. Fifty-five episodes of culture-proven meningitis were identified, of which Acinetobacter was isolated in 60% (32/55) CSF samples. Seventy-eight of 165 acinetobacter positive neonates died. Acinetobacter neonatal infections had an alarmingly high case fatality rate of 48% (95% CI: 41-56).

Conclusions: Acinetobacter was the most common pathogen contributing to one-third of all episodes of neonatal sepsis. It was responsible for both EOS & LOS. The incidence of drug resistance and case fatality rates was extremely high.
COMPARING THE EFFECTS OF INTRADERMAL VERSUS INTRAMUSCULAR ADMINISTRATION OF A PNEUMOCOCCAL CONJUGATE VACCINE IN MICE

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Background: Streptococcus pneumoniae remains a leading cause of severe infections worldwide. Currently used pneumococcal conjugated vaccines (PCVs) are effectively reducing disease rates but their production costs are high. Several studies have shown that intradermal vaccination leads to improved immunity. Subsequently, lower doses of antigen and adjuvant may be required, which reduces the cost per vaccine dose. To determine whether intradermal delivery could potentially lead to dose sparing for PCV13, we compared the effects of intradermal and intramuscular administration of PCV13 in mice.

Methods: Two groups of ten mice were immunized with PCV13 three times at two-week intervals either intradermally or intramuscularly. Blood was drawn pre-immunisation, the eleventh day post-immunisation and three days post-infection. Three weeks after the last immunisation, all mice were infected intranasally with 100 colony forming units (CFU) of a S. pneumoniae serotype 4 clinical strain. Three days after infection, the mice were euthanized and CFU-counts in the nasal associated lymphoid tissue were determined. Antibody titres against all thirteen polysaccharides included in the PCV13 vaccine were measured in blood and mucosal samples using a Luminex-based multiplex immunoassay.

Results: Antibody titres in both serum and mucosal samples were higher in the intramuscular vaccinated group as compared to the intradermal vaccinated group. CFU counts in the nasal tissue of all mice were higher than the initial infection dose with no significant differences between the control and the immunized groups, indicating that mucosal antibodies did not block the acquisition of colonisation. Whether immunized mice are more effectively clearing S. pneumoniae at later timepoints post-primary infection remains to be determined.

Conclusions: Serotype-specific antibody titres in intramuscular immunized mice were higher than in intradermal immunized mice. However, induced antibody-titres did not prevent S. pneumoniae acquisition and colonization.

Clinical Trial Registration: Not Applicable
BURDEN OF RSV BRONCHIOLITIS IN THE PAEDIATRIC INTENSIVE CARE UNIT -A 13-YEAR NATIONAL REGISTRY STUDY-

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Background: Respiratory syncytial virus (RSV) bronchiolitis is one of the most common respiratory tract infections in children, resulting in substantial global morbidity and mortality. However, we have limited insight in the burden of severe RSV bronchiolitis for which paediatric intensive care unit (PICU) admission is indicated. Our aim was to determine the burden of RSV bronchiolitis for the PICU in the Netherlands. Second, we aimed to define the potential impact of a maternal vaccination strategy on severe RSV bronchiolitis.

Methods: We had access to a unique nationwide PICU registry to study patient characteristics and dynamics in 2161 children <= 24 months with a confirmed RSV infection from 2003 to 2016. We manually subtracted additional clinical data, respiratory support modes and outcome. We defined children born term and <= three months at admission as children who possibly could have benefitted from a maternal vaccination strategy.

Results: The number of PICU admissions increased significantly during the study period (b 4.05, p=0.01). The use of non-invasive respiratory support in the PICU, especially high flow nasal cannula, increased significantly (b 8.86, p< 0.01), whereas the number of children requiring invasive ventilation remained stable. We identified 1152 (53.3%) term children aged <= three months at admission.

Conclusions: The burden of severe RSV bronchiolitis for the PICU in terms of admissions has increased in the Netherlands. Concomitantly, the use of non-invasive mechanical ventilation modalities has also increased. A maternal vaccination strategy may have a high impact on the burden of RSV bronchiolitis for the PICU.
PHYLOGENETIC AND CLINICAL CHARACTERIZATION OF A LOCAL OUTBREAK OF PARECHOVIRUS INFECTIONS

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Background: Parechovirus infections (HPeV) have emerged as a dominant cause of sepsis and encephalitis in newborns and young infants. In the summer of 2018, we experienced a cluster of HPeV infections in two neighboring German hospitals with 25 cases - 19 being admitted during a 6-week period. Here, we present the detailed clinical and phylogenetic workup of the outbreak scenario.

Methods: We sequenced the VP1 genomic region and compared the sequences to clinical isolates from four other German centers. Currently, we are broadening these analyses by whole-genome sequencing of the outbreak isolates in order to better understand the sequence variation and conservation patterns across the entire HPeV genome. From a clinical perspective, we collected detailed information of the clinical disease course of the admitted patients.

Results: Of the 25 HPeV strains detected in Freiburg in 2018, 21 were typed as HPeV-3, 2 were assigned to HPeV-1, and 2 to HPeV-5, respectively. Phylogenetic analysis of the VP1 genomic region demonstrated co-circulation of several sublineages and could therefore rapidly rule out clonal relationship of the isolates. Whole-genome analysis of the strains is under way and will hopefully give deeper insights into sequence variations across the entire HPeV genome. The clinical pattern of HPeV disease showed fever (96%), poor feeding (72%) and irritability (56%) as the leading symptoms. A rash was present in 32% of the cases. Of note, PCR from plasma samples had the highest diagnostic yield (100%) of all specimens and outperformed CSF PCR.

Conclusions: Sequencing of the VP1 region is a reliable tool for rapid phylogenetic analysis in a HPeV outbreak situation. When HPeV disease is suspected, PCR from plasma samples alone could potentially be a promising diagnostic approach, especially if available in a point-of-care-format.

Clinical Trial Registration: The study does not report the results of a controlled trial.
PROLONGED FEVER IN YOUNG INFANT

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Title of Case(s): PROLONGED FEVER IN YOUNG INFANT

Background: Leishmaniasis is caused by Leishmania spp. It is transmitted by sand fly vector (Phlebotomus spp. and Lutzomyia spp.), and its main mammalian reservoir host is the dog. There are four types: cutaneous (focal or diffuse), mucosal and visceral. The visceral (Kala-Azar) is caused by species L.infantum and L.donovani and consists of invasion and replication within host macrophages, evading innate and cell-mediated immune responses. In the absence of treatment is lethal, however with the correct treatment mortality is low.

Case Presentation Summary: Male infant, six months old, previously healthy, with fever lasting for eleven days, and splenomegaly of 9 cm. Blood tests revealed microcytic anemia (Hb 10.2 g/dL), lymphocytosis (73% lymphocytes), without thrombocytopenia, C-reactive protein 16.4 mg/L, sedimentation velocity 33 mm, hypertriglyceridemia (216 mg/dL), without hyperferritinemia or hypofibrinogenemia. Blood smear compatible with viral infection "mononucleosis-like". Negative EBV, CMV, Herpes simplex 1 and 2, Borrelia, Toxoplasmosis, Coxiella, Rickettsia, VIH serology’s. Negative PCR for Parvovirus B19, CMV, Bartonella, VIH. Normal immunoglobulins values. Bone marrow (BM) biopsy compatible with inflammatory or infectious disease, without signs of primary oncology disease or observation of parasites. Soluble CD25 in serum was significantly high (7158 U/ml). On the thirteen day of admission positivity of Leishmania infantum PCR in blood and BM was known, being established visceral leishmaniasis diagnosis and initiated treatment with Amphotericin B liposomal, with apyrexia after 48h. At discharge, he was oriented to Infectious disease external consultation.

Learning Points/Discussion: Being visceral leishmaniasis endemic in Portugal, especially in Alto Douro, Lisbon and Algarve, this should be a differential diagnosis when history of prolonged fever. It is important to implement vector and reservoir control measures. Treatment is highly effective, so it should be started as soon as possible after diagnosis is made.
Background: Currently, causes of death (CoD) in children from low-middle income countries are imputed from sparse and non-specific vital registration and verbal autopsy data. Despite neonates contributing to 45% of under-5 childhood deaths, biological investigation of neonatal CoD is almost non-existent in LMIC. We evaluated CoD using post-mortem MITS in South African neonates enrolled in CHAMPS.

Methods: Deaths (mainly in a secondary-tertiary care hospital) were investigated by MITS within 24-48 hours. Investigations included bacterial culture and multiplex PCR of blood, cerebrospinal fluid and lung samples, and histopathology of lung, liver and brain tissue. Deaths were reviewed by an expert panel, which assigned underlying (predisposing condition), antecedent/comorbid and immediate (final event) CoD per WHO classification.

Results: The leading underlying CoD among 307 investigated neonatal deaths were prematurity complications (n=162; 52.8%), infection (n=51; 16.6%), intrapartum complications (n=44, 14.3%) and congenital malformations (n=37; 12.1%). Where infection was attributed as underlying CoD (n=51), leading aetiologies were Group B streptococcus (GBS; 27.5%), Escherichia coli (11.8%), Listeria monocytogenes (11.8%), and Cytomegalovirus (9.8%). Infections were implicated in the casual pathway in an additional 52% (133/256) of deaths with a non-infectious underlying cause, including 64.2% of those with prematurity complications as underlying cause; among these, leading implicated pathogens were Acinetobacter baumannii (68.4%; 91/133), Klebsiella pneumoniae (39.1%; 52/133), Candida sp. (13.5%; 18/133), Staphylococcus aureus (9.0%; 12/133) and E. coli (7.5%; 10/133). In total, infections were involved in 58% (178/307) of all neonatal deaths, with Acinetobacter baumannii (33.2%), Klebsiella pneumoniae (20.3%), GBS (7.8%), Candida sp. (6.8%) and E. coli (5.9%) most common.

Conclusions: Prevention of systemic infections, implicated in causal pathway of 58% of neonatal deaths, warrant prioritisation to reduce under-5 childhood deaths in setting such as ours.

Clinical Trial Registration: Not applicable
SEVERE DIABETIC KETOACIDOSIS WITH RHINO-CEREBRAL MUCORMYCOSIS WITH SUPERIOR ORBITAL FISSURE SYNDROME

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Title of Case(s): SEVERE DIABETIC KETOACIDOSIS WITH RHINO-CEREBRAL MUCORMYCOSIS WITH SUPERIOR ORBITAL FISSURE SYNDROME

Background: Rhinocerebral mucormycosis is a common manifestation in patients with uncontrolled diabetes. However, angio-invasive fungi can present at the onset of diabetes to cause extensive tissue necrosis. Progression of the infection to central nervous system is heralded by development of poor sensorium and features of raised intracranial tension.

Case Presentation Summary: A 8-year-old female presented with increased frequency of urination for 25 days, increased thirst, fast breathing and lethargy for one day. Examination revealed dehydrated child with acidotic breathing. Admission investigations showed blood sugar 430mg/dL, Blood ketone 5.2 mmol/L, pH 7.01, bicarbonate 5 mmol/L. Child was diagnosed as Severe Diabetic Ketoacidosis and started on intravenous fluids considering 8.5% dehydrations and Insulin infusion at 0.1U/Kg/hr. She was noticed to have right eye proptosis with complete ophthalmoplegia on day 5. Oral cavity revealed a non-tender black necrotic lesion over the hard palate. MRI brain revealed a hypointense lesion in right basofrontal area, right temporal lobe with cavernous sinus invasion. Her further investigations revealed Hb1ac 11.8%, Tissue transglutaminase 78 U/mL, and thyroid stimulating hormone 1.39 µU/mL. Liver function and kidney functions were normal. KOH mount of the palatal tissues showed aseptate broad ribbon like hyphae suggestive of Rhizopus species. Culture reported mucormycosis. Due to worsening sensorium child was intubated and received raised intracranial pressure reducing measures. She received Liposomal Amphotericin B(5 mg/Kg/day) and Low molecular heparin(LMWH). Nasal endoscopy with debridement was done to remove necrotic tissue from bilateral nasal cavities, frontal, ethmoidal and maxillary sinuses. After 10 days the sensorium gradually improved, she was extubated and later discharged.

Learning Points/Discussion: Early diagnosis and treatment of mucormycosis is extremely important due to the aggressive course of the 3 disease. Prompt institution of antifungal therapy, combined with surgical debridement forms the cornerstone of management.
**Background:** Bacteremia-septicemia is a serious condition with a demanding diagnostic and therapeutic approach, during which all paediatric defense mechanisms are affected. Our aim was to record retrospectively all cases of children hospitalised for bacteremia in our department during the last 1-year period and prospectively over a 7-month period.

**Methods:** Through utilization of our electronic database of hospitalised patients, we searched for corresponding medical records and discharge summaries using specific keywords regarding children’s medical condition upon discharge.

**Results:** Retrospectively, 12/1059 (~1.1%) patients suffered from sepsis and pathogenic factors were isolated in 5 of them (42%), namely: Salmonella (2), E. coli (1), Streptococcus pneumoniae (1) and Campylobacter coli (1). Main symptoms were fever (100%), vomiting (50%), pain (33%), diarrhea (25%) and tachypnea (8%). Upon entry, most children sustained leukocytosis ($\bar{x}$: 23.490c/$\mu$l) with polymorphonuclear type ($\bar{x}$: 70.8%) and high CRP levels ($\bar{x}$: 68.9 mg/l). Prospectively, we recorded 7/585 (~1.2%) children with bacteremia and 5 (71%) pathogenic factors, namely: Salmonella (2), Acinetobacter Iwoffii + Klebsiella oxytoxa (1), Enterobacter (1) and Shigella(1).

**Conclusions:** The main symptoms that should alert the paediatricians according to our study were fever, grunting, pain, diarrhea and cough. The medical staff of our Pediatric Department effectively managed all children hospitalised for bacteremia according to global guidelines. Our findings included registering a female predominance that could possibly trigger multi-center studies in larger patient sample populations.
A RETROSPECTIVE CROSS-SECTIONAL STUDY INVESTIGATING MALNUTRITION RATES IN CHILDREN UNDER 5-YEARS ATTENDING MOBILE CLINICS IN RURAL PANAMA.

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Background: Previous studies have estimated that one in every two indigenous children in Panama is malnourished. However there is a paucity of data to support this. The most recent large scale estimates come from a 2007 study using census data, which showed malnutrition rates in indigenous children under five years to be between 40-60%.

Methods: A retrospective cross-sectional analysis was performed on data from the Floating Doctors database. The aim was to assess the burden of malnutrition in children under 5 presenting to Floating Doctors clinics during 2017. Data was analysed using the World Health Organization (WHO) Anthro Analyser Survey, a validated online tool developed by the WHO to analyse child anthropometric data using height-for-age, weight-for-age, weight-for-height and BMI-for-age according to WHO growth charts.

746 eligible children were identified of whom 630 remained after filtering for insufficient data.

Results: The rates of severe wasting (z-score <-3) and moderate and severe wasting (z-score <-2) were 0.7 % and 1.7% respectively. The rate of obesity (z-score >+3) was 5.4% rising to 20.6% for overweight and obese (z-score >+2)
The rates of severely underweight (z-score <-3) and moderate and severely underweight children (z-score <-2) were 2.8% and 7.1% respectively. The rate of severe stunting (z-score <-3) was 22%, rising to 45.2% for moderate and severe stunting (z-score of <-2).

Conclusions: The above results show extremely high rates of stunting in the surveyed population. In addition, there were high rates of overweight and obesity. Children with wasting and who were underweight were also identified, although at much lower rates. Analysis and correlation of these trends with a range of variables is still ongoing. This data will be used to inform Floating Doctors approach to malnutrition interventions in the future. They also highlight the need for public health interventions in this high risk and often neglected group.
Background: Higher plasma concentration of neurofilament light protein (NfL) seems to be associated with CNS injury in HIV-infected adults. To our knowledge this is the first study to report the values of plasma NfL in a PHIV cohort compared to non-HIV (HIV-) controls.

Methods: Cross sectional study. Thirty-three PHIV patients and 28 HIV- controls matched by age were recruited. Moreover, in a subgroup of 43 participants (25 PHIV patients and 17 HIV- peers), brain volumes through magnetic resonance imaging (MRI) and neuropsychological (NP) testing, also was conducted and compared with NfL values. Plasma NfL levels were determined using Single molecule array (Simoa) immunoassay. NP assessment tested Processing Speed by VPZ7.

Results: Fifty-eight participants were included, median age 20.7 years [IQR 17.8-23.4]. PHIV group: 54% women, 73% Caucasians, 42% were CDC C category (21% with stable encephalopathy), median CD4% nadir 274 cel/mm$^3$. At assessment, 100% were under cART, 85% had viral load <50 cp/ml and median CD4 738 cel/mm$^3$. Although no significant differences were found between patients and controls regarding plasma NfL concentrations there was a trend towards higher levels in patients with detectable viral load (dVL) (median 6.64) (p = 0.063). With regard to brain volumes, in the PHIV group, a significative decrease in the total white matter volume (WMV) was associated with higher NfL values (p=0.045).

Conclusions: Most PHIV adolescents under cART, have normal NfL levels in plasma although the infection happened early in the development. As reported in adults, those with dVL showed a trend towards higher values and a lower WMV that may imply an ongoing CNS injury. Plasma NfL could be a feasible biomarker of CNS injury in otherwise asymptomatic PHIV patients, showing good correlation with white matter volume.

Clinical Trial Registration: THIS STUDY IS NOT A CONTROLLED TRIAL, SO IT HAS NOT BEEN REGISTRED
A RARE CASE OF SEPTICEMIA FROM CAMPYLOBACTER-COLI IN A FEMALE-CHILD UNDER ONE YEAR OF AGE, WHO HOSPITALISED IN OUR CLINIC

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Title of Case(s): A RARE CASE OF SEPTICEMIA IN A FEMALE-CHILD UNDER ONE YEAR OF AGE, WHO HOSPITALISED IN OUR CLINIC

Background: The purpose of this paper is to describe a case of Campylobacter coli (C. coli) bacteremia in an 8-month-old infant and analyze Campylobacter infections along with their diagnostic and therapeutic approach. In particular, C. coli is an important cause of acute gastroenteritis worldwide, mainly transmitted by chicken, and mainly affects infants <1 year old.

Case Presentation Summary: An 8-month-old female infant was brought to our hospital, due to an episode of fever convulsions with hemi-diarrhea outbreaks and a family environment of flu. Clinically the infant was alert with good muscle tone and without a clear source of the fever. Although the results of the first laboratory tests were not indicative of bacterial infection, after the first 24 hours there was a worsening of the clinical condition, with a simultaneous increase of the inflammatory markers. The initial pharmaceutical plan was to treat the case as a possible bacteremia with cefotaxime but a few days later despite of not being possible to isolate certain type of bacteria in the stool, C. coli was developed in the blood culture, therefore the medication was modified to Amikacin and Clarithromycin with rapid clinical and laboratory improvement over the next 24 hours.

Learning Points/Discussion: This is one of the rare bibliographic references to C. coli bacteremia in an infant. It is of major importance to mention that the recorded cases of bacteremia from campylobacter are extremely rare and usually occur in patients with an immune system disorder. In conclusion, due to the rarity of the event, a basic examination of the infant's immune adequacy was performed at the end of the present hospitalisation, which did not reveal any abnormalities, so she was discharged with instructions for further investigation, in case of a future similar event.
Background: After pneumococcal conjugate vaccines (PCVs) implementation, most of the published carriage studies were focused on young children and few data on carriage dynamic during childhood.

Methods: Between 2006 and 2019, 77 pediatricians obtained nasopharyngeal swabs from healthy children ≥ 6 months old. Children were excluded from the study in case of antibiotic treatment within 7 days before enrolment.

Results: Among 5,520 healthy children, the carriage rate of S. pneumoniae, H. influenzae, and B. catarrhalis increased from 1 to 6 years old, then decreased sharply. S. aureus carriage was lower for younger children and increased after 4 years old (11.6% and 33.0%, p<0.001). Serotype distribution was different according to the age: serotype 3 was carried most frequently in children ≥ 5 years old (9.5% vs 1%, p<0.001) while serotype 11A (8.8% vs 4%, p=0.049) and 15A (7.7% vs 2.7%, p=0.026) were more frequently carried in younger children.

Conclusions: In our knowledge, this study is the largest including older healthy children in post PCV era. It shows that carriage rate of otopathogens continues to increase until to 4 to 6 years old with an inverse correlation between carriage of otopathogens and S. aureus.
PNEUMOCOCCAL EPIDEMIOLOGY AMONG HIGH-RISK INDIVIDUALS IN DIFFERENT GEOGRAPHICAL REGIONS AND SOCIOECONOMIC SETTINGS AND IMPLICATIONS FOR IMMUNISATION STRATEGIES: ONE SIZE DOES NOT FIT ALL

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Background and Objective: Nearly 30 years since the development of the first pneumococcal vaccine, controversy persists regarding the optimal immunization policy for individuals at high-risk for Invasive Pneumococcal Disease (IPD). Here, we review the supporting data on disease burden in high-risk individuals in high-income (HICs) and low- & middle-income countries (LMICs).

Methods: A search via Pubmed database was conducted using ‘pneumococcal vaccine’; ‘invasive pneumococcal disease’; ‘high-risk’ & ‘immunocompromised’ keywords.

Learning Points/Discussion: The collected data show that: - IPD epidemiological data specifically in high-risk individuals in HICs are limited. The percentage of IPD occurring in immunocompromised individuals varies and it has been reported as 30% in Canada, 17% in Finland, 36% & 37% in Spain and the UK, respectively. - Serotype-specific analyses from Spain, the UK and the US show a rise of PPSV23-only (10A, 11A, 15A/B, 15B, 23A & 33F) and Non-Vaccine serotypes (6C, 15A/C, 23A, 35B) causing IPD in high-risk individuals post-PCV13 implementation. - In LMICs, incidence of IPD and associated mortality are higher compared to HICs. Before the initiation of infant PCV schedule implementation in the region, Africa accounted for 57% of deaths in children <5 years due to IPD worldwide. This is mainly due to low vaccine coverage and higher prevalence of coexisting morbidity, such as HIV, malaria and sickle cell disease. - Data on the evolution of IPD sero-epidemiology among the high-risk patients in LMICs during the current PCV implementation programs is limited. Data from the South Africa surveillance show that IPD rates are 25-fold higher in HIV-infected children than in the HIV-uninfected. In the PCV13 era (2010-2014), a significant reduction of PCV13-type IPD was documented, with 11%, 17% and 64% of cases caused by PCV7-, PCV13-only and non-PCV13 serotypes respectively. Most non-vaccine serotypes currently causing IPD in the HIV-infected population (10A, 15A, 16B and 35B) are not included in the PPSV23.

Epidemiological data show that high-risk individuals in HICs could benefit from a combined PCV13/PPV23 immunization schedule, whereas there is currently no evidence of emerging PPSV23-only IPD in LMICs.
CLINICAL CASE OF ACQUIRED IMMUNODEFICIENCY SYNDROME ASSOCIATED WITH ETHICS IN MEDICINE.

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**Title of Case(s):** Clinical case of acquired immunodeficiency syndrome associated with ethics in medicine

**Background:** AIDS - the general name of the lesions occurring at III-IV clinical stages of infection caused by human immunodeficiency virus. The combination of recurrent infection in pediatrics is a clinical problem that is becoming more urgent due to its prevalence, lack of timely diagnosis and etiotropic treatment under conditions of false medical history. **AIM** of the work was to investigate the objective state of a child with severe recurrent aphthous stomatitis, anemic syndrome and to make a differential diagnosis.

**Case Presentation Summary:** AIM of the work was to investigate the objective state of a child with severe recurrent aphthous stomatitis, anemic syndrome and to make a differential diagnosis. Results. Patient, 4 years old, hospitalized with complaints of mouth rash, decreased appetite and fever, which did not decrease under the action of antipyretic drugs. Ill for 3 weeks, the onset of the disease is associated with rash in the mouth. The result: CD 4 lymphocytes; CD3-43.8%, MCL-712 CD4-0.6%, MCL-10. The peculiarity of this case was that during collection of anamnesis, information about the HIV infection of patient’s father was hidden. In result, appeared the delay with timely diagnosis of the disease and appointment of specific therapy. Conclusions. 1. Prolonged herpetic infection is indicative of an examination for immunodeficiency states. 2. Medical staff should be warned about the growing number of immunocompromised patients. 3. Low trust towards medical personnel lowers the possibilities for timely diagnostics and conduction of etiopropic treatment.

**Learning Points/Discussion:** Conducted microbiological studies of seeding from the oral mucosa revealed C. albicans in diagnostic concentration. Esophageal candidiasis - the most common cause of esophageal lesions in children with severe immunosuppression. The main etiologic factor of primary infection of S. albicans (80-100%) in half of cases.
SHORT-TERM SAFETY OF 4-VALENT HUMAN PAPILLOMAVIRUS VACCINE AMONG MALES IN THE UNITED STATES

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Background: The 4-valent human papillomavirus (HPV) vaccine (4vHPV vaccine), Gardasil®, is indicated for the prevention of several HPV-related diseases. In the US, it was licensed for use in females in 2006 and males in Oct-2009. The 4vHPV vaccine is licensed in many parts of the world. The objective was to report safety results from an observational study of the 4vHPV vaccine in males.

Methods: Using a US health insurance database, males vaccinated with 4vHPV vaccine were followed for clinical outcomes associated with emergency department (ED) visit or hospitalization within the 1-14 day risk period following vaccination (not including the day of vaccination) and a subsequent 14-day self-comparison period. Events were identified by diagnosis codes mapped into clinically meaningful categories developed by the Healthcare Cost Utilization Project (HCUP). For each HCUP category, event incidence in the risk and self-comparison periods was compared by relative rates (RR) and 95% confidence intervals (CI). Analyses were conducted for all vaccine doses combined, first dose only, and new outcomes (i.e., without a similar outcome in the 12 months prior to Dose 1). Safety data were reviewed by an independent Safety Review Committee.

Results: Between Oct-2009 and Dec-2016, 114,035 males initiated 4vHPV vaccination, with 51.3% and 26.4% receiving 2 and 3 doses, respectively, for a total of 202,737 doses. In the Dose 1 analysis, one HCUP category had a significantly elevated RR: skin and subcutaneous tissue infections (RR 2.35, 95% CI 1.15-5.11). This association was likely the result of local injection reactions. No other increase was identified in this 14-day period.

Conclusions: No new safety events were identified for 4vHPV vaccine in the 1-14 days following vaccination. These study results are consistent with the known safety profile of 4vHPV vaccine.

Clinical Trial Registration: This was an observational study and not a clinical trial.
Background: Acinetobacter is a leading cause of neonatal sepsis and is associated with high incidence of mortality and morbidity. Although it can involve any organ system, central nervous system involvement could be associated with worse prognosis. The information about neuro-morbidities associated with neonatal acinetobacter infections is scanty.

Methods: All episodes of culture-proven neonatal sepsis from Jan 2015- Dec 2019 were analyzed. Culture-proven sepsis was defined as isolation of pathogenic bacteria from blood or cerebrospinal fluid (CSF) within 48 hours of incubation. Meningitis was diagnosed by either >10 cells in CSF along with blood-culture positive septicemia or bacterial isolation from CSF. We compared 165 episodes of culture-proven Acinetobacter sepsis identified during 5-year study period with 319 non-Acinetobacter culture proven episodes. Independent predictor of meningitis developing from culture-proven acinetobacter sepsis was studied using logistic regression analysis.

Results: Fifty-three of 165 acinetobacter positive neonates developed meningitis (CSF culture-positive, n=32). Acinetobacter sepsis had higher risk of developing meningitis [RR 2.7 (95% CI 1.6 to 4.4); p-value <0.001] compared to 'non-acinetobacter' sepsis (23/319). Gestation <30weeks [OR 2.5 (95% CI 1.2, 5.1); p=0.01] and Late-onset sepsis [OR 2.6 (95% CI 1.2, 5.7); p=0.02] were independently associated with meningitis. Fifteen neonates developed complicated meningitis (either ventriculitis, brain abscess or subdural empyema) [incidence among all episodes of meningitis 28% (95% CI 17-42%)]. Twenty-six neonates (50%) with meningitis died vs. 49 (47%) without meningitis (p-value 0.85).

Conclusions: Acinetobacter has significantly higher rates of central nervous system infections as compared to other common etiological bacteria causing neonatal sepsis. It is associated with high rates of neurological complications.
INCONSISTENT MANAGEMENT OF NEONATAL HERPES SIMPLEX VIRUS INFECTIONS

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Background: The incidence of neonatal herpes simplex virus (nHSV) infections is monitored periodically in the Netherlands, yet management and outcome is unknown. Comprehensive national guidelines are lacking. We aim to describe management and outcome in the last decade to explore current diagnostic and therapeutic challenges. We aim to identify possible variability in management of patients with a suspected nHSV infection.

Methods: We conducted a retrospective case series of management and outcome of nHSV infections at 2 tertiary care center locations in the Netherlands.

Results: An nHSV infection was diagnosed in 1% (12/1348) of patients in whom polymerase chain reaction for HSV was performed. Of the patients with nHSV infection, 3/12 died, and 4/9 (44%) survivors suffered neurologic sequelae. Neurologic symptoms at presentation were seen in only 2 of 8 patients with encephalitis. A cerebral spinal fluid analysis was performed in 3/6 patients presenting with skin lesions. Only 3/6 patients with neurologic symptoms received suppressive therapy. nHSV infection was diagnosed in 8/189 (4%) patients who were empirically treated.

Table 1. Characteristics, management and outcome of neonatal HSV infection cases

<table>
<thead>
<tr>
<th>Year</th>
<th>HSV class</th>
<th>Co-morbidity</th>
<th>Presenting symptoms</th>
<th>HSV contact</th>
<th>HSV + sample</th>
<th>Age at symptom onset</th>
<th>Age at sample collection</th>
<th>Age at Tx start</th>
<th>Tx length</th>
<th>Outcome</th>
<th>Supp</th>
<th>Sequence after discharge</th>
<th>Recurr</th>
<th>BSID- GMFCS</th>
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<tbody>
<tr>
<td>2017</td>
<td>CNS HSV-2</td>
<td>No</td>
<td>CSF</td>
<td>16</td>
<td>17</td>
<td>17</td>
<td>4</td>
<td>deceased</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<td>CNS HSV-2</td>
<td>Mat, Oth</td>
<td>CSF, plasma</td>
<td>10</td>
<td>18</td>
<td>18</td>
<td>4</td>
<td>recovery</td>
<td>Yes</td>
<td>No</td>
<td>3x SEM</td>
<td>?</td>
<td>?</td>
<td></td>
</tr>
<tr>
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<td>CNS HSV-1</td>
<td>lesions</td>
<td>Mat, Oth</td>
<td>CSF</td>
<td>28</td>
<td>28</td>
<td>21</td>
<td>recovery</td>
<td>No</td>
<td>?</td>
<td>?</td>
<td>?</td>
<td>?</td>
<td></td>
</tr>
<tr>
<td>2017</td>
<td>CNS HSV-1</td>
<td>lesions</td>
<td>Mat, Oth</td>
<td>CSF</td>
<td>?</td>
<td>38</td>
<td>38</td>
<td>21</td>
<td>recovery</td>
<td>No</td>
<td>abnormal moving pattern, on AEDs</td>
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<td>Mat, Oth</td>
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<td>10</td>
<td>12</td>
<td>12</td>
<td>14</td>
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<td>prem 27 wk</td>
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<td>Mat, Oth</td>
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<td>0</td>
<td>3</td>
<td>14</td>
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<td>hemiparesis</td>
<td>3x SEM</td>
<td>BSID 94 GMFCS 1</td>
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<td>SEM</td>
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<td>Mat, Oth</td>
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<td>12</td>
<td>12</td>
<td>21</td>
<td>recovery</td>
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<td>?</td>
<td>?</td>
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<td>-</td>
<td>4</td>
<td>21</td>
<td>recovery</td>
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<td>17</td>
<td>21</td>
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<td>lesions</td>
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</table>
**Conclusions:** Management of nHSV infection, particularly when presented with skin lesions, is inconsistent. Many infants without a HSV infection are exposed to antiviral medication. There is substantial interhospital variation in diagnostic and therapeutic management of a suspected infection. Comprehensive guidelines need to be developed to standardize management of suspected nHSV infection.
PROSPECTIVE EPIDEMIOLOGICAL STUDY DOCUMENTING CHILDREN COMING TO THE EMERGENCY DEPARTMENT OF THE GENERAL HOSPITAL-VOLOS, WITH RESPIRATORY DISEASES FROM 01/03/2019 TO 30/09/2019.

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Background: Respiratory diseases are the main cause of children-admissions to Emergency Department (ED), internationally. Their increased incidence is attributed to several risk factors (active and passive smoking, atmospheric-indoor pollution, occupational exposure to harmful substances-during first years of life, diet-nutrition, genetic-predisposition). Internationally, a large number of studies are recorded in metropolitan cities with severe air pollution problems. In Greece, most studies are focused on large urban centers and few at Volos city.

Methods: We used data from our electronic archive and patient registry of the Pediatric Department. 2,039 children with respiratory diseases out of a total of 5,495 were studied in this period and seasonal variation of the proportion of respiratory diseases versus total morbidity between spring, summer and autumn 2019 was recorded, with September as reference month for autumn 2019, time of arrival, their age groups and gender.

Results: show that children with respiratory diseases is 37.1% of total, date of arrival shows a random distribution, the percentage of admission between 00.00-08.00, 08.00-16.00 and 16.00-00.00 was 32.4%, 22.1% and 45.5% respectively, age groups 0-1, 1-6, 6-12 and 12-16 years was 14.9%, 43.6%, 30.4% and 11.1% respectively and boys/girls ratio 52.4%: 47.6% respectively. Children with respiratory illnesses to all patients admitted at ER ratio in spring, summer and autumn 2019 was 40.4%, 34.1% and 36.2% correspondingly to 41.5% for the month June.

Conclusions: Therefore, respiratory diseases for Volos from March to September 2019 are a significant proportion of overall morbidity and are most common at spring for boys aging from 1-6years coming at ER between 16.00-00.00. These findings are consistent with Greek and international bibliography. Final conclusions about the annual seasonal variation of respiratory diseases are expected with completion of thesis incorporating data from October 2019- February 2020.
THE DIAGNOSTIC CHALLENGES OF AN ATYPICAL PRESENTATION OF CAT SCRATCH DISEASE IN AN IMMUNOCOMPETENT PATIENT

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Title of Case(s): The diagnostic challenges of an atypical presentation of recurrent neck swelling in an immunocompetent patient.

Background: Cat Scratch Disease is caused by Bartonella Henselae. Usually a self-limiting regional lymphadenopathy occurring following contact with cat saliva, disseminated disease can occur. We describe an atypical case of extensive disease in an immunocompetent patient with no reported feline contact.

Case Presentation Summary: An adolescent presented to hospital with a month's history of post-auricular swelling, fevers and 3kg weight loss. He recently returned from a 2 month holiday in Pakistan and had been treated in the community with oral beta-lactamases for 3 weeks. Examination revealed tender right-side swellings measuring 2cm and 1.5cm. He was well, with normal bloods excepting raised CRP 41mg/L and WBC 11x10^9/L. Ultrasound demonstrated abscesses and reactive lymph nodes in the region. Aspiration obtained microbiological samples. Intravenous flucloxacillin and oral clindamycin commenced for the provisional diagnosis: staphylococcal/streptococcal soft tissue infection. Differentials included bacterial, mycobacterial, inflammatory and malignant aetiologies. Two further drainages occurred over 10 days. He was discharged with 2 weeks of oral antibiotics. Bacterial cultures, PCR and TB diagnostics failed to identify any pathogen. 3 weeks later he re-presented with similar symptoms. Further samples went for culture, molecular testing and histology. CT revealed extensive phlegmonous collections within the posterior triangle, extending from the mastoid process to sternocleidomastoid anteriorly and trapezius posteriorly, encompassing the deep cervical chain with multiple suppurative nodes.
Learning Points/Discussion: The extensive nature of disease made this an atypical case. No immunocompromise was identified, with no apparent feline contact. Histology identified distinctive pathology, "granulating infiltration, central necrosis, palisading histiocytes". Serology confirmed Bartonella Henselae infection. Oral rifampicin and doxycycline commenced and the patient is doing well with clinical follow-up planned. This case reminds us of the importance of histological examination of surgical samples, and maintaining an open mind regarding differentials.
PARECHOVIRUS A IN HOSPITALIZED CHILDREN WITH RESPIRATORY TRACT INFECTION. A NINE YEAR LONG PROSPECTIVE SURVEILLANCE STUDY

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Background: Parechovirus A (PeV-A) is frequently found in Pediatric airway samples, but its role is unclear. Is this virus an innocent bystander or can it indeed cause respiratory tract infection (RTI) in children? In this survey, we studied the occurrence and impact of PeV-A over nine years in children referred to hospital with RTI.

Methods: During 9 years (2006-2016), 3689 children from Sør-Trøndelag County, Norway, hospitalized with RTI were prospectively enrolled. 664 healthy controls was recruited among children admitted to elective surgery. Clinical data was recorded and nasopharyngeal swabs were analysed with semi-quantitative polymerase chain reaction tests for 17 airway pathogens. PeV-A positive samples were genotyped.

Results: 8.8% of the patients and 11% of the controls were positive for PeV-A. Genotypes 1, 3, 5 and 6 were detected. In 6% of the patients, only PeV-A was detected whereas 94% showed co-detection of one or more virus. In a logistic regression analysis, PeV-A was not related to RTI, adjusted for relevant confounders and other viruses. Patients with PeV-A and single virus detection more often had upper RTI than those with co-detections (74% vs 27%, p <0.001) and had a higher genomic load (mean cycle threshold-value 30.6 vs 33.0, p = 0.029).

Conclusions: PeV-A occurred frequently in children with RTI and controls. Nearly all had co-detections of other viruses. We found no evidence that PeV-A causes severe RTI in hospitalized children, but PeV-A is a likely cause of mild, upper RTI.
RESPONSE TO HEPATITIS B VACCINATION AMONG HIV-EXPOSED UNINFECTED CHILDREN IN CANADA

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Background: HIV-Exposed Uninfected (HEU) children are at increased risk of morbidity and mortality from infectious diseases, as compared to HIV unexposed uninfected (HUU) children from the same environment. While the cause is potentially multifactorial, a suboptimal immunological response to vaccination is suspected to play a role. The objective of this study was to assess immunological response to Hepatitis B vaccination (HBV) among HEU infants.

Methods: Retrospective study of HEU children enrolled in the Centre Maternel et Infantile sur le SIDA (CMIS) cohort, Montreal, Canada between 1998-2016 (n=760). HBV was administered according to provincial guidelines at 0, 1 and 6 months (1998-2012; early schedule) or 2, 4, and 18 months (2013-2016; delayed schedule). Children who had anti-HBs IgG titers (CMIA architect assay, Abbott) after 3 doses of HBV were included (n=91). A titer of >10mUI/ml was considered protective.

Results: 65 children (71.4%) received their 3 doses according to the early, and 25 (28.6%) according to the delayed schedule. Median time of serological testing after the third dose was 2 years (IQR 1-5) in the early group, and 4 years (IQR 4-5) in the delayed group. Overall, 25% of children were non-responders (NR); 30.7% in the early group vs. 11.5% in the delayed group (p=0.06). There was no difference in the proportion of NR according to maternal viral load or delivery CD4 T cell count.

Conclusions: The overall incidence of non-response to HBV in this cohort of HEU children (25%) is significantly higher than that reported in the general population of HUU children (3.6-5%). Given the estimated 1.5 million HEU children born annually in predominantly resource limited settings, further work needs to be done to understand immune mechanisms, and optimize the dosing schedule for this at-risk population.
SEVERE AND COMPLICATED CASE OF IPD CAUSED BY 19A SEROTYPE IN 8 MONTH BOY.

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**Title of Case(s):** Severe and complicated case of IPD caused by 19A serotype in 8 month boy.

**Background:** Routine vaccination against pneumococci with 10-valent pneumococcal conjugate vaccine was implemented in the Polish vaccination schedule on 1st of January 2017. Part of the population applies the 13 valent vaccine, which is not reimbursed. In the period of 2 years (2017-2018), in the region of Malopolska Province (population of 3.4 million), 90 bacteriologically confirmed cases of IPD were reported including 16 cases aged <14. 4 of them were triggered by 19A serotype. We present one of the cases, caused by multidrug-resistant strain, with an exceptionally severe course, requiring multidisciplinary treatment.

**Case Presentation Summary:** An 8-Month-Old boy, with proper development prior to the illness, wasn’t vaccinated at all, due to convictions of his parents. The course of the disease was unusually dynamic and followed by several months of hospitalisation, including 8 weeks in ICU. The biggest inflammatory changes were found in CNS, together with intracranial bleeding requiring neurosurgical procedure. Symptoms of arterial hypertension unresponsive to treatment occurred. Carbohydrate metabolism disorders demanding intensive insulin therapy arose. As a consequence of renal failure peritoneal dialysis was employed. The control over these disorders was reached, however, for a substantial period, symptoms of eating disorder were present. As a result of the IPD the child is affected with hemiparesis, total hearing loss, significantly delayed psychomotor development and drug-resistant epilepsy.

**Learning Points/Discussion:** Conviction of vaccination negative effects can lead to tragedy, that could be prevented. Questions is: if, in this case, the routine vaccination with 10 valent vaccine would prevent the illness?
IMPORTED MALARIA IN CHILDREN VISITING FRIENDS AND RELATIVES: THE IMPORTANCE OF PREVENTIVE MEDICINE

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Background: Paediatric imported malaria is an emerging infectious disease in Europe due to the increasing population movements of children from and to areas with malaria endemic transmission. The aim of this study was to analyse the associated factors to imported malaria of children visiting friends and relatives (VFR) and to compare them with those patients living and coming from endemic areas (migrants).

Methods: Retrospective case series study of all children younger than 18 years of age diagnosed of imported malaria who were attended at the Paediatric Infectious Diseases Unit in Hospital Universitari Vall d’Hebron and at the International Health Unit Drassanes-Vall d’Hebron in Barcelona (Catalonia, Spain) between January 2009 and December 2019. Epidemiological, clinical, laboratory and microbiological data were collected on a RedCAP® database and analysed with Stata©v15.

Results: Fifty-four children were included into the analysis, median [IQR] age was 9.9[4.7-14.9] years, 63% were male, and 85% acquired malaria in sub-Saharan Africa. Overall 35% were VFR and 65% migrants. Median [IQR] travel duration for VFR was 61 [21-77] days. Two-thirds of VFR children attended a pre-travel health advice but only 41.6% of them adhered to an appropriate chemoprophylaxis. Fourteen patients (26%) had severe malaria being 71.4% of them VFR versus 28.6% migrants (p=0.003). In the multivariable analysis children VFR were associated to severe malaria (p=0.01).

Conclusions: In our case series, VFR children diagnosed with imported malaria showed a low pre-travel visit attendance and an inappropriate adherence to malaria prophylactic regimens. They also had a significantly higher risk for severe malaria compared to other traveller children. Therefore, it is mandatory to implement more adequate preventive measures to improve not only pre-travel but also post-travel advice in VFR children.
MULTIPLE BIRTH AS A RISK FACTOR FOR RESPIRATORY SYNCYTIAL VIRUS HOSPITALISATION (RSVH) IN CHILDREN LESS THAN 2 YEARS OF AGE

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**Background:** Multiple birth has been associated with an increased risk of RSVH in young children. However, published data remain limited and it is unclear how much of this risk is related to preterm delivery. This study provides further information on multiple birth as a risk factor for RSVH using national data from Scotland over a 12-year period.

**Methods:** All live births between 2000-2011 from NHS Scotland Information Services Division databases were followed until 2 years of age and RSVHs (ICD-10 codes J12.1, J20.5 & J21.0) assessed in children born as singletons or multiples and stratified by weeks' gestational age (wGA) at delivery.

**Results:** Of 623,344 children, 18,199 (2.9%) were born as multiples (mean wGA 35.6 vs. 39.3 for singletons). RSVH incidence was significantly higher in multiples (4.1%; 739/18,199) compared to singletons (2.1%; 12,605/605,145; relative risk 1.94, 95% CI 1.81-2.08, p<0.0001). RSVH rates were 45/1,000 vs. 26/1,000, respectively (p<0.0001). RSVH incidence and rates were higher for multiples than singletons for those born <36 wGA (6.5% [435/6,709] vs. 6.0% [1,275/21,278], respectively, p=0.1317; 72 vs. 68/1,000, p=0.1833) and ≥36 wGA (2.6% [304/11,490] vs. 1.9% [11,330/583,867], p<0.0001; 29 vs. 24/1,000, p=0.0006), but significantly so only in the latter. Median age at first admission, ICU requirement and length of stay in hospital and ICU did not significantly differ between multiples and singletons when analysed by those born <36 wGA or ≥36 wGA (p>0.05 for all comparisons in each GA group; see Table).

**Conclusions:** This study provides evidence for multiple birth as a risk factor for RSVH, which warrants further investigation. **Acknowledgements** Matthew Freddi (Stratgen Ltd) – editorial services.

**Systematic Review Registration:**
INHIBITION OF PNEUMOCOCCAL ADHERENCE TO LUNG EPITHELIAL CELLS INDUCED BY HUMAN ANTIBODIES AGAINST IMMUNODOMINANT B-CELL EPITOPES LOCATED WITHIN PNEUMOCOCCAL SURFACE PROTEINS

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Background: Adherence of Streptococcus pneumoniae to human epithelial cells is the first step leading to pneumococcal disease. Recent studies have highlighted a preventive role of antibodies against pneumococcal proteins in lung adherence. This study aimed to determine the role of human antibodies elicited against previously identified, immunodominant, highly-conserved B-cell epitopes within pneumococcal surface proteins in preventing adherence to human lung epithelium.

Methods: Specific antibodies against 4 B-cell epitopes, (CbpD-pep4[aa291-310], PhtD-pep19[aa200-219], PhtE-pep40[aa79-98] and ZmpB-pep125[aa431-450]), purified from sera from children with invasive pneumococcal disease, were incubated with different pneumococcal clinical strains, and were subsequently added to A549 cells. Adherence inhibition was measured as percent of reduction in CFU counts compared to those of the initial inoculum and purified total IgG from an unvaccinated child (negative controls). Antibody-mediated pneumococcal agglutination was also evaluated using electron microscopy.

Results: Mean percent adherence inhibition for anti-PhtDs for serotype 1, 15C and 19A was 79% vs 69% vs 71%, respectively. Similarly for anti-PhtEs it was 69% vs 63% vs 65%, for anti-ZmpBs 70% vs 60% vs 62% and for anti-CbpDs 62% vs 55% vs 59%, respectively. No pneumococcal agglutination was detected using the anti-peptide antibodies, in this context.

Conclusions: Anti-peptide antibodies inhibited adherence of different serotypes to respiratory epithelium, suggesting a role in the prevention of pneumococcal disease. No pneumococcal agglutination was confirmed, in this context, implying a specific adherence inhibition effect. Anti-PhtD-antibodies consistently demonstrated the highest rates of inhibition among different isolates. Interestingly, the corresponding epitope resides within the highly virulence zinc-binding domains of PhtD, further highlighting its potential as vaccine antigen.

Clinical Trial Registration: The present study is not a controlled trial and clinical trial registration is not applicable.
IMPROVING SERIOUS BACTERIAL INFECTION DIAGNOSIS IN A LARGE COHORT (983 PATIENTS) OF YOUNG FEBRILE CHILDREN USING A COMBINATION OF BACTERIAL AND VIRAL BIOMARKERS


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Background: Fever is one of the leading causes of consultation in pediatric emergency department (PED). Differentiate viral versus serious bacterial infection (SBI) is challenging. Our aim was to identify a new biomarkers combination that can differentiate bacterial from viral infection in children younger than 3 years old with higher performance than C-reactive protein (CRP) and procalcitonin.

Methods: We conducted multicenter assay (ANTOINE Study) using Paxgene® tubes, serum and whole blood heparinate tube collected at 3 PED from children aged from 7 days to 36 months attending PED with suspicion of serious bacterial infection (SBI). Different types of infections were adjudicated by an independent committee, blinded from biomarkers results, based on clinical data collected at inclusion and at day 7. Seven biomarkers Lipocalin-2, Mixovirus Resistance Protein 1, IFNg-Induced protein-10, TNF related apoptosis-inducing ligand, C reactive protein, ProCalcitOnine and Interleukine-6 were dosed in a first time (Train Test). The best combinations were secondary tested on a second independent part of the cohort (Test Set).

Results: From June 2017 to June 2019, 983 patients were included and biomarkers have been quantified on 698 patients. Patients from June 2017 to June 2018 and from June 2018 to June 2019 were included respectively in the TRAIN set and the TEST set. We highlighted various combinations that allowed to diagnose SBI with higher performance than CRP and PCT alone. Statistics analysis are still in progress to select the best combination.

Conclusions: New biomarkers combinations are promising and could improve BSI diagnosis and management in young children attending PED and reduce antibiotic misuse. Adding viral to bacterial biomarkers improve SBI diagnosis in febrile children younger than 3 years old. External validation is needed to confirm those results.

Clinical Trial Registration: clinicaltrials.gov (NCT03163628)
Background: Acinetobacter has emerged as a leading cause of neonatal sepsis. It is associated with a high incidence of adverse outcomes. However there is insufficient information about clinical profile and management of acinetobacter ventriculitis and/or brain abscess in neonates.

Methods: Data of neonates developing culture-proven acinetobacter sepsis during 5-year study period was extracted from electronic database and case record files. Meningitis was diagnosed as either >10 cells in CSF along with blood-culture positivity or bacterial isolation from CSF. Out of 53 episodes of meningitis among acinetobacter sepsis over 5 year study period, we compared neonates who developed complicated meningitis [i.e. ventriculitis (n=13), brain abscess (n=2) and subdural empyema (n=1)] with neonates who had uncomplicated meningitis.

Results: Neonates developing complicated and uncomplicated meningitis were comparable at baseline. On regression analysis, only CSF culture positivity independently predicted development of complicated meningitis. Most common presentation were recurrent apnea (66%) and seizures (33%). Intravenous colistin was used in 14 (93%) neonates [one isolate colistin resistant, recovered with tigecycline]. Six neonates (40%) received additional drug as per culture sensitivity. Eight (55%) neonates required intraventricular antibiotics. Shunt was placed in 5 (33%) neonates. Seven (47%) neonates survived, of which 3 recovered with only intravenous colistin.

Conclusions: Acinetobacter ventriculitis and brain abscesses universally require treatment with intravenous colistin. Almost half of the neonates required intraventricular antibiotics as alone intravenous colistin was not effective in all neonates. Case fatality rates are very high and half of survivors required ventriculoperitoneal shunt for management of hydrocephalus.
BACTERIAL PROFILE OF PUS CULTURES IN DISTRICT PUBLIC HEALTH LABORATORY, NAMAKKAL, INDIA, 2018.

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Background: Identification of pathogens from the clinical specimens and performing antibiotic sensitivity test are crucial for effectively treating infections. Pus swabs were received from inpatients of district headquarters hospital, Namakkal district, India, for culture and sensitivity. We analysed the pus culture reports for profiling the bacterial spectrum, prevalent in pus cultures in Namakkal district.

Methods: We did a cross sectional study. We analysed the reports of pus cultures, done in District Public health laboratory between January and December 2018. We abstracted the data from the nominal register by data abstraction form. We computed proportions to calculate the positivity among the samples. We calculated the proportions of microorganisms by gram positive and gram negative organisms.

Results: Samples received during reference period was 539. Growth of microorganism was found in 71% of samples (n=384). Gram negative microorganisms were found in 48% of pus samples (n=184) and gram positive microorganisms were found in 52% of samples (n=200). Among the gram positive microorganisms, majority (51%) were Staphylococcus species (n=118). Coagulase positive Staphylococcus was 42% (n=84) and coagulase negative Staphylococcus was 17% (n=34). Enterococcus contributed to 38% (n=76). Among the gram negative microorganisms, 32% were Proteus (n=59), 30% were E.Coli (n=56), Klebsiella were 12% (n=22), Acenitobacter lowtii were 5% (n=9) and Enterobacter aerogenes were 3% (n=6).

Conclusions: In India, gram negative organisms are common in pus cultures. But in Namakkal, there was predominance of gram positive organisms. However, Staphylococcus being the most prevalent organism among the gram positive organisms in Namakkal, it resembles bacterial profile across India. But the bacterial profile among gram negative organisms in Namakkal are quite different from prevalent gram negative organisms across India. Proteus is predominant in Namakkal district, than the common Pseudomonas species.

Clinical Trial Registration: This is not a clinical trial registration.
PAEDIATRIC ENTERIC FEVER IN BRUSSELS. A RETROSPECTIVE STUDY OVER 14 YEARS

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Background: Enteric fever is a major public health problem and a witness of the global health disparities. It is caused by Salmonella enterica serovar Typhi and Salmonella enterica serovar Paratyphi A,B,C and is estimated to infect 12-26 million persons per year. Paediatric data on enteric fever in Europe are missing. In this context, a case series of enteric fever was analysed to describe the clinical, biological and microbiological characteristics as well as the diagnostic challenges identified in a paediatric population in Brussels.

Methods: We performed a retrospective study of all lab-confirmed cases of enteric fever in children aged 0-15 years at two Brussels teaching hospitals, between January 2005 and December 2018. We looked at variables such as age, gender, travel history, consultations before diagnosis, hospitalisation duration, fever, cough, headache, gastrointestinal symptoms; and biological findings: Haemoglobin, C-Reactive Protein, White Blood Cell, Eosinophil and Platelet counts.

Results: There were 30 positive isolates: 27 patients had bacteriaemia, 1 had positive bone drainage, 2 patients had positive stool culture (one patient had missing data, and was excluded). Females were 17/29. The median age was 3.5 years (range 5 months to 14 years). Half of patients had recently travelled to endemic areas. For 80% of the patients there was a delayed diagnosis. Eosinopenia was present in 93% of the cohort. None of the patients had received any preventive education or vaccination.

Conclusions: Enteric fever poses a diagnostic challenge to clinicians working in non-endemic areas. It must be high on the differentials at the returning traveller. Eosinopenia in a febrile patient coming from the tropics, should raise suspicion of enteric fever. Travellers to endemic areas, should be better educated about enteric fever risks and typhoid fever vaccination should be promoted.
STAPHYLOCOCCUS EPIDERMIDIS IN NEONATES WITH MATERO-NFETAL INFECTION - PITFALLS OF A BACTERIA CONSIDERED OPPORTUNISTIC

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Background: Although *Staph. Epidermidis* is an universal coloniser of healthy human skin and infections involving it are considered nosocomial (medical devices related), we observed during last 4 years that it appears in the blood-cultures (collected at birth) of neonates hospitalized in our NICU for suspicion of infection and/or respiratory distress. Two possibilities - contamination of the blood samples during collection procedure or confirmation of materno-fetal infection with *Staph. Epidermidis* were analysed.

Methods: Starting with January'2019 all blood-cultures results (with detailed antibiograms) were registered separately in the unit, matching "intrauterine infection/sepsis" confirmed diagnostics and *Staph.Epidermidis*+ cultures. In parallel, prescribing behaviors (as length of non-argumented antibacterial treatment overall in the unit, type of antibiotics used) that may influence an opportunistic bacteria to become viruled were noticed.

Results: 65 cases (13,48% from all neonates in 2019) have been diagnosed with "Intrauterine infection/Sepsis", 17 cases of them (26,15%) having blood-cultures positive, and among those cultures - 52,94% (9 cultures) with Staph.Epidermidis hemolytic were confirmed. Only one (11,11%) was sensitive to Ampicilline/Cefepime/Meropenem/Gentamicin. The sensibility to Doxycycline/Tetracycline/Cefatoxim/Ciprofloxacine was high (in 83,3% cultures), followed by sensibility to Clindamicine/Ofloxaceine/Levofloxacine/Ceftriaxone (74%), Cefoxitine/Ciprofloxacine (66,7%), Amikacine/Cloramphenicol/Tobramacine/Claritromicinc (48%), and Azitromicine/Eritromicine (23,6%). Two main prescribing behaviors related to antimicrobial misuse were noticed - the prolonged (>96h, even if no "infection"-related in clinical diagnostic was established) antibacterial treatment especially in premature babies and multiple cases (at least in 27 situation - from interviewing nurses) of switch from Ampicilline to Amoxacilline (and again to Ampicillin in the same babies) when "Ampicilline was out of stoc in the hospital pharmacy".

Conclusions: When properly registered and analysed blood-culture results(&antibiograms) help to determine the high virulence &multiresistance of so "considered" opportunistic bacteria. The absence of antimicrobial stewardship leads to not-evidence-based prescribing &overuse of antibiotics.
FIRST CASE OF TYPHOID FEVER DUE TO EXTENSIVELY DRUG-RESISTANT SALMONELLA ENTERICA SEROVAR TYPHI IN ITALY

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Title of Case(s): FIRST CASE OF TYPHOID FEVER DUE TO EXTENSIVELY DRUG-RESISTANT SALMONELLA ENTERICA SEROVAR TYPHI IN ITALY

Background: Typhoid fever is a potentially severe and occasionally life-threatening bacteremic illness due to Salmonella enterica serovar Typhi (S. Typhi). It is endemic in many developing countries, while it is relatively rare in industrialized ones. In Pakistan an outbreak of extensively drug resistant (XDR) S. Typhi cases was underway since November 2016. In recent years in industrialized countries a sudden increase in the number of typhoid fever diagnoses had occurred, and most of them were due to a XDR S. Typhi strain. These have been demonstrated to be Pakistan-outbreak-related cases.

Case Presentation Summary: We report on a five-year old boy who contracted enteric fever during a travel in Pakistan and was diagnosed after returning to Italy in September 2019. Blood culture isolated Salmonella enterica serovar Typhi which harboured XDR to all first-line antibiotics, including ceftriaxone and fluoroquinolones. Empiric therapy was switched to meropenem and he completed recovery. Whole-genome sequencing showed that this isolate was of haplotype H58. The XDR S. Typhi clone encoded a chromosomally located resistance region and harbored a plasmid encoding additional resistance elements, including the blaCTX-M-15 extended-spectrum β-lactamase, and carrying the qnrS fluoroquinolone resistance gene.

Learning Points/Discussion: This is the first case of typhoid fever due to XDR S. typhi detected in Italy. While new vaccines against typhoid are in development, clinicians should be vigilant of future cases and consider to adapt their empiric approach for patients returning with typhoid symptoms from regions at risk of XDR S. thypi outbreak.
PREVALENCE OF OCCULT HEPATITIS B INFECTION: A SYSTEMATIC REVIEW AND META-ANALYSIS

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**Background:** Chronic hepatitis B virus (HBV) infection is a global problem with more than 360 million carriers worldwide. Maternal transmission is a major source of chronic HBV infection. Occult Hepatitis B infection (OBI) among children born to HBsAg-positive mothers has been associated with Hepatitis B Virus (HBV) immunoprophylaxis failure. This is a systematic review and quantitative analysis of this underestimated phenomenon.

**Methods:** A systematic literature search of published studies on the prevalence of OBI among children born to HBsAg-positive women in Medline, Scopus and Web of Science databases was performed by two independent reviewers and a meta-analysis followed. The search was limited to articles published up to June 2018, written in English language and involving humans. Meta-analyses were undertaken using random-effects models.

**Results:** Overall 25 eligible studies were included. A variable mean follow-up period was observed ranging between 6 and 60 months, whereas four studies reported prevalence rates of OBI only at birth. Factors such as antiviral treatment during pregnancy, compliance to immunoprophylaxis and maternal viral load were associated with the OBI prevalence. In addition, genotypes B,C,D and recombinant genotype C/D were mostly prevalent among OBI cases. At birth, the prevalence rate of OBI was estimated at 7% (95% CI: 4-15%) while at the end of follow-up prevalence was 10% (95% CI: 5-19%).

**Conclusions:** Despite the universal HBV immunoprophylaxis measures, the prevalence of OBI worldwide in neonates born to HBsAg-positive women remains important. OBI possibly is associated with not only virus-associated but also human-associated factors. This first attempt to summarize current findings yields effect estimates and also points to potential underlying factors that could orient researchers to generate and further explore specific etiologic hypotheses.

**Systematic Review Registration:** N/A
Title of Case(s): REFRACTORY LARYNGITIS AND SEVERE PULMONARY DISEASE THAT RESULTED IN AN 8 YEAR OLD PATIENT’S DEATH

Background: Diphtheria was one of the leading causes of childhood death in the pre-vaccine era. Nowadays, physicians in many nations including Greece have never seen a case of diphtheria despite the fact that approximately 5000 cases are reported worldwide each year. 

Case Presentation Summary: An 8-year-old boy with Down syndrome presented at the ER with fever and acute laryngitis that didn’t improve despite corticosteroids and epinephrine, thus resulting in intubation and admission in the Paediatric Intensive Care Unit (PICU). With the suspicion of upper and lower respiratory bacterial infection he was treated with ceftriaxone and vancomycin. The patient was reported fully vaccinated – nevertheless no official documents were provided. Despite mechanical ventilation (Pressure Regulated Volume Control with high parameters), the patient remained hypoxic (max PaO₂: 50mmHg). A complete heart examination (ECG, echo) was conducted without pathological findings 24 hours after the admission. High Frequency Oscillatory Ventilator was also used without sufficient results. Because of persistent hypoxia and hypotension despite the use of noradrenaline, a second cardiac examination was conducted on the 3rd day of hospitalization that showed pulmonary hypertension with minor ventricular septal defect resulting in severe intrapneumonic shunt. Despite intensive support (i.e. milrinone, sildenafil, dopamine and dobutamine), progressive cardiopulmonary failure resulted in the patient’s death within a few hours. 24 hours later Corynebacterium Diphtheriae was detected in the bronchial secretions’ culture.

Learning Points/Discussion: Diphtheritis may be a rare disease but should remain in the differential diagnosis of severe upper respiratory infections and severe pulmonary disease despite reported vaccination history. Furthermore, this case points out that persistent hypoxia can be the cause of pulmonary hypertension even in previously healthy children.
CHALLENGING MANAGEMENT OF FUSARIAL solani INFECTION IN A CHILD WITH ACUTE LYMPHATIC LEUKAEMIA: A CLINICAL CASE

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Title of Case(s): Challenging management of Fusarium solani infection in a child with acute lymphatic leukaemia: a clinical case

Background: Invasive fungal diseases (IFDs) are related to significant morbidity and mortality in paediatric patients with haematological diseases, with 20%-70% overall case-fatality rates. Within mould infections, Fusarium spp. is an emerging pathogen leading to disseminated, skin and pulmonary diseases in severe neutropenic patients.

Case Presentation Summary: A 9-year-old patient with recent diagnosis of B-cell precursor lymphoblastic leukaemia was admitted to Onco-Haematology. Weeks before, he had an accidental trauma with abrasion of left elbow. During the phase of induction (AIEOP Protocol 2017) he presented swelling, erythema and pain at right leg, confirmed at ultrasound scan as an inhomogeneous lesion within the gastrocnemius muscle. He further developed a similar lesion at left leg, an ulceration of the skin and subcutaneous tissues at the left elbow with transient fever during the neutropenic phase. At CT-scan, a 11 cm pulmonary lesion with cavitation at inferior left lobe and hilar lymph node reaction were reported. B-D glucan levels between 356-500 pg/ml were found at repeated measurements, therefore high dose amphotericin B lipid complex (8 mg/kg/day) was started. Fusarium solani was isolated from right leg lesion biopsy, confirming the IFD. Voriconazole was added at 8 mg/kg bid, after loading dose of 9 mg/kg bid, with unsatisfactory plasma levels at repeated therapeutic drug monitoring(TDM) and poor clinical improvement. A daily dose of 10 mg/kg tid was needed to maintain TDM targets of 3-5 mg/L and was not associated with toxicity. Drug optimization and bone marrow recovery led to clinical and radiological improvement, confirmed at 20 weeks of follow-up.

Learning Points/Discussion: Among IFDs, fusariosis remains particularly challenging among immunocompromised patients. High-doses antifungal therapy are often required to achieve a target dose. TDM is mandatory in paediatric patients, as wide pharmacokinetic variability may be observed.
HPV VACCINATION UPTAKE IN BOYS AFTER INTRODUCTION OF GENDER-NEUTRAL HPV VACCINATION IN GERMANY - A RETROSPECTIVE DATABASE ANALYSIS (IMS VACCINE ANALYZER)

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Background: HPV vaccination has been recommended in Germany for girls since 2007. In June 2018 the German Standing Committee on Vaccination (STIKO) published a gender-neutral recommendation for HPV vaccination for girls and boys 9-14 years old (with catch up to 17). Since January 2019 it is part of mandatory funding by health insurers. The aim of this study was to monitor the monthly uptake of HPV vaccination in boys in Germany.

Methods: We did a retrospective database analysis using IMS® Vaccine Analyzer data from January 2018 to October 2019. This database contains vaccination records from a panel of office-based physicians (pediatricians, GPs, gynecologists) and is used to estimate nation-wide counts. The primary outcome of the study was the monthly number of boys receiving their first dose. Secondary outcomes included the number of girls.

Results: The nation-wide number of boys 9-17 years old vaccinated each month before the gender-neutral recommendation (January-May 2018) varied from 98 to 950 per month (first dose). From June-December 2018 that number increased from 832 to 9,670. In January 2019 when reimbursement for boys was fully implemented this number increased sharply to 28,691. By May 2019 that number further increased to 52,092 and until October 2019 the number of boys vaccinated remained between 40,000 and 50,000 per month.

Conclusions: Over only a few months, uptake of first HPV vaccine doses for boys increased after recommendation and reimbursement of gender-neutral vaccination to the level of girls. Further analyses will link the results to population size to estimate HPV vaccination coverage.
VIRAL INFECTIONS IN IMMUNOCOMPROMISED PEDIATRIC PATIENTS

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**Background:** Several viral infections are associated with severe viral complications in immunocompromised hosts. Some of these complications are: hemorrhagic cystitis, pneumonia, retinitis, gastroenteritis, encephalitis, meningitis, post-transplant lymphoproliferative disease, hepatitis, myocarditis, peritonitis, intestinal pneumatosis, severe diarrhea, disseminated infection, etc. Some of them may be fatal for immunocompromised patients.

**Methods:** We studied 917 samples of biological material (blood cells, serum, urine, saliva, biopsy, autopsy, CSF, faeces and also hair and nails) from 87 patients (0 to 19 years old HSC recipients, oncological or onco-hematological patients) for BKV and JCV polyomaviruses, CMV, EBV, HHV-6, HHV-7, AdV A-F, NoV. Biological material was analyzed twice per month. Detection of viral DNA or RNA and genotyping of HHV-6A/HHV-6B was performed by in-house PCR and with commercial kits.

**Results:** Detection frequency of BKV was 56.9% (n=58), JCV – 6.9% (n=58), CMV – 21.8% (n=55), EBV – 30.9% (n=55), HHV-6 – 59.65% (n=57), HHV-7 – 46.6% (n=58), AdV – 27.8% (n=37), NoV – 20% (n=5). Viraemia was detected during BKV- (13.8%), CMV- (14.5%), EBV- (25.5%), HHV-6- (35.1%), HHV-7- (13.8%), AdV-infection (16.7%). In one patient were detected BKV+EBV+AdV in kidney autopsy and EBV in the stomach biopsy. All HHV-6 were identified as HHV-6B (n=20). One patient with germinoma was cIHHV-6B-positive: CSF (4×10² copies/ml), blood (4×10³ copies/ml), hair (8.2×10⁴ copies/10⁵ cells) and nails (7.8×10⁴ copies/10⁵ cells).

**Conclusions:** This data show the high detection frequency of viral infections among pediatric immunocompromised patients and the importance of regular quantitative molecular-biological tests to detect the start of viral infections.
WHICH ARE THE MOST COMMON VIRAL RESPIRATORY COINFECTIONS IN HOSPITALIZED CHILDREN UNDER 5 YEARS OLD?

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Background: It is very common that different respiratory viruses could infect at the same time the respiratory tract of hospitalized patients, especially in very young children. The objective of this study was to analyse respiratory viral coinfections in hospitalized children less than 5 years old (y.o.) from seasons 2011/2012 to 2018/2019 (i.e. study period; usually November-March/April, except September-June/July in 2017/2018 and 2018/2019).

Methods: The Valencia Hospital Network for the Study of Influenza (VAHNSI) conducts annually a prospective, active-surveillance hospital-based study on respiratory viruses. All admissions with a suspicion of respiratory infection fulfilling the inclusion criteria and consenting were swabbed. Samples were tested by RT-PCR for influenza, RSV, rhinovirus, adenovirus, coronavirus, bocavirus, metapneumovirus and parainfluenza. Patient information was obtained from legal tutors and/or from clinical records review.

Results: 5,359 children were tested being 3,040 (57%) PCR-positive; 278 (9%) were coinfections. The commonest coinfections were RSV+rhinovirus (21%) and RSV+coronavirus (20%). 36 coinfections included influenza; A(H3N2)+RSV (25%) was the most frequent. The coinfection hospitalization incidence rates (per 100,000 children-study period) were 173.39, 65.77, 12.35 and 51.44 for children <1, 1, 2-4 and <5 y.o., respectively. Among children <1 y.o., the highest incidence rates were detected in 1 and 2 months of age, 619.27 and 309.64 per 100,000 children-study period and then decreased with age.

Conclusions: In hospitalized children, 9% of PCR-positive results implicated two or more different respiratory viruses. RSV was present in most of the coinfections detected in children <5 y.o., being RSV+rhinovirus and RSV+coronavirus the most frequent. Among mixed infections involving influenza, A(H3N2) was the commonest subtype. Highest coinfection hospitalization incidence rates were found in children <1 y.o., especially in those 1-2 months of age.
Background: Kawasaki disease (KD) is the most frequent cause of acquired heart disease in children in high-income countries because of the coronary artery involvement. Risk factors for coronary lesions can vary in consideration of different genetic background and environmental factors.

Methods: Multicentre retrospective and prospective study including 372 consecutive children (58% boys; mean age 34.3±30.3 months, Caucasian 85%) diagnosed with KD. We divided the Cohort into 2 groups according to the presence of coronary anomalies (CAA). We compared the groups and studied the risk factors for CAA and for aneurysms, the most severe lesion.

Results: Children with CAA were 91/372 (24.46%, aneurysms:20/372, 5.37%). Children with CAA were more likely to have longer duration of fever(p<0.00), later day of treatment(p<0.00), to be IVIG non-responders and late-treated (p<0.00). Age, clinical presentation and seasonality weren't different. They also had significantly higher WBC and neutrophils, lower lymphocytes, Hb and Na during acute stage and slower resolution of inflammation. Age, IVIG-responsiveness and presence of non-coronary cardiac findings were independent risk factors for CAA and for aneurysms, while neutrophils just for CAA. Age under 6 months was a risk factor for aneurysms.

Conclusions: Very young children with non-coronary cardiac findings are at increased risk for a more severe form of KD with aneurysms. These children could benefit from adjunctive therapy beside IVIG, especially if they have higher markers of inflammation, especially neutrophils.
Background: Non-polio enteroviruses (EVs) include over 100 serotypes belonged to species A–D, which can cause various symptoms in children. EVs are the most common viruses causing meningitis and encephalitis. In the Republic of Belarus since 2009 to 2018 the frequency of enteroviral encephalitis varied from 0.18% to 0.97%, meningitis - from 2.24% to 19.42%. The aim of the study was to determine EV types that caused neurological infections in the recent 4 years.

Methods: Cerebrospinal fluid, feces, blood specimens were collected from Belarusian children (N=495) aged 1 month to 17 years with meningitis (37.97%), encephalitis (11.11%), meningoencephalitis (12.32%) and other neurologic disorders (36.36%) between 2016 and 2019. Specimens were tested by reverse transcription qPCR, followed by the molecular typing of EV from positive samples based on the Sanger sequencing of VP1 gene.

Results: Eighty eight children (17.7%) with neurological disorders were positive on EV RNAs, molecular typing was successful for 54 of them (61.3%). The main etiologic agents of meningitis were ECHO6 (24.1%), ECHO 9 (18.5%), ECHO 30 (16.7%), Coxsackievirus B5 (12.96%), ECHO 16 (11.1%), whereas ECHO 14, 15, 19, 25, Coxsackievirus B2 and B4 were diagnosed less often (1.85% of each). In 2016 the predominant causative agent of neurological infection was ECHO9 (53%), in 2017–2018 – ECHO6 (25%, 47%, respectively), in 2019 – ECHO30 (33%).

Conclusions: Altogether 12 types of EV were responsible for neurological diseases in the Republic of Belarus between 2016 and 2019, however the predominant types were ECHO 6, ECHO 9 and ECHO 30 - viruses that are most often connected with meningitis morbidity and outbreaks worldwide. Whereas ECHO 6 and ECHO 30 caused meningitis constantly during recent four years, ECHO 9 was the predominant type in 2016 only.
ANTIMICROBIAL AND ANTI FUNGAL STEWARDSHIP IN A TERTIARY CARE PAEDIATRIC HOSPITAL IN INDIA: OUR EXPERIENCE AND THE WAY AHEAD

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Background: Antimicrobial stewardship (AMS) is a key strategy to prevent emergence of antimicrobial resistance and decrease preventable healthcare-associated infections. Currently, AMS is rare in India but gaining momentum. We describe our experience in implementing an AMS program in a paediatric tertiary care centre in India.

Methods: AMS program was started by Medical Director with team including pharmacist, microbiologists and ID specialist in 207 bedded pediatric hospital. Forms with restricted antibiotics used with dose, date of starting and reason for escalation was to be filled by treating physician. In our first attempt, we had few forms in 2 months. After re-strategizing, forms were handed to nursing leads with instructions to not administer day 2 antibiotics without AMS form. Forms were collected by pharmacist on daily rounds, culture details were entered by microbiologists and reviewed by ID specialist. ID rounds were conducted thrice/week in intensive care areas. We present data from April 2019-December 2019.

Results:

<table>
<thead>
<tr>
<th>Month</th>
<th>Not justified</th>
<th>SICU</th>
<th>PICU</th>
<th>NICU</th>
<th>BMT</th>
<th>Ward</th>
</tr>
</thead>
<tbody>
<tr>
<td>April</td>
<td>6/29</td>
<td>2/3</td>
<td>2/8</td>
<td>1/2</td>
<td>0/7</td>
<td>1/5</td>
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<tr>
<td>May</td>
<td>2/22</td>
<td>0/3</td>
<td>0/3</td>
<td>0/3</td>
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<td>June</td>
<td>3/20</td>
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<td>1/1</td>
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<tr>
<td>July</td>
<td>1/28</td>
<td>1/5</td>
<td>0/7</td>
<td>0/3</td>
<td>0/11</td>
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<td>August</td>
<td>3/27</td>
<td>0/7</td>
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</tr>
<tr>
<td>Sept</td>
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<td>0/3</td>
<td>0/3</td>
<td>0/3</td>
<td>1/5</td>
<td>0/0</td>
</tr>
<tr>
<td>Oct</td>
<td>4/28</td>
<td>0/9</td>
<td>2/9</td>
<td>2/9</td>
<td>0/1</td>
<td>0/0</td>
</tr>
<tr>
<td>Nov</td>
<td>2/16</td>
<td>0/1</td>
<td>1/12</td>
<td>1/6</td>
<td>0/2</td>
<td>0/0</td>
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<tr>
<td>Dec</td>
<td>1/21</td>
<td>0/6</td>
<td>0/5</td>
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</tr>
</tbody>
</table>

205 forms were received in 9 months. Antibiotics + antifungals restricted—vancomycin, teicoplanin, carbapenems, polymyxins, daptomycin, linezolid, clindamycin, voriconazole, posaconazole and echinocandins. Maximum use was restricted to intensive care or step down units. There were 23 inappropriate antibiotic prescriptions with maximum in first month of implementation (6/23). With good coordination between cardiac ICU, microbiologists and ID
specialist, inappropriate prescriptions were lowest in that unit (3/23 - 2 in first month). Commonest reason was not de-escalating in time. We are now attempting to reduce use of colistin to culture proven carbapenem resistant organisms only. For bronchoalveolar lavage positive for MDR organisms, colistin nebulization is used if no evidence of sepsis. All children who received colistin nebulization did well.

**Conclusions:** With appropriate microbiology, ID support, it is possible to restrict use of antibiotics and to use them in best possible way to optimize care.
INFLUENZA VACCINE: DELAYED VACCINATION SCHEDULES AND MISSED OPPORTUNITIES IN CHILDREN UNDER 2 YEARS OLD IN ARGENTINA.

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Background: In Argentina In 2011 influenza vaccination was included as a national strategy for children between 6 and 24 months (two doses schedule). The aim was to determine the proportion of complete schedules, delayed schedules (DS) and missed opportunities (MOV), to assess the characteristics of MOV and to explore the perception of influenza disease and vaccination.

Methods: Analytical observational multicenter cross-sectional study. Structured surveys were carried out to the children’s parents who were between 6 and 24 months of age during the influenza virus vaccination season (April–November 2019). A logistic regression model was built to identify delay predictor variables in the vaccination schedules.

Results: 1,110 surveys were conducted in four centers. We detected 65.9% of complete influenza schedules, 75.9% of DS (all associated with MOV). The independent protective factors associated with a decreases risk of DS were: (a) parents perception of the importance of influenza vaccination (OR=0.10(0.01–0.80); p=0.030) and (b) vaccination schedule parents knowledge (OR=0.69(0.51–0.94); p=0.021), (c) to have received information about flu (OR=0.52(0.33–0.82); p=0.005). The risk factors were: (a) having more than one year of age (OR=2.61(1.91–3.56); p=<0.001) and (b) the health care workers (HCW) vaccination rejection for any reason (OR=1.46(1.09–1.95); p=0.009). There was 50% of MOV in 1st and 50.3% in 2nd dose. The main causes of MOV were to have false contraindication for vaccination (33% in 1st, 30% in 2nd dose) and the unacknowledged of the vaccination schedule (31% in 1st, 30% in 2nd dose). A 4% of hesitancy was detected.

Conclusions: High frequency of delayed vaccination schedules and missed opportunities were detected. All the DS were related with MOV 3. Parent’s education about influenza vaccine protects against DS. Missed opportunities were related with a lack of HCW training.

Clinical Trial Registration: Not applicable
STREPTOCOCCAL TOXIC SHOCK SYNDROME IN CHILDREN: PREVALENCE AND CLINICAL CHARACTERISTICS

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Background: Streptococcal toxic shock syndrome (STSS) is a severe invasive disease with increasing incidence in last few years. This report aimed to describe clinical, epidemiological, diagnostic and therapeutic characteristics of STSS.

Methods: Retrospective study of children <14 years-old with STSS admitted to a tertiary care hospital between 2010-2019. We consider statistical significance a p-value<0.1 due to our small sample size.

Results: Data from 11 children were analyzed (63.6% in 2018-2019). Epidemiological and clinical characteristics are presented in table 1. Most children (72.7%) were initially treated with cefotaxime+clindamycin during a median of 17 days (IQR 14-19 days). Intravenous immunoglobulin (IVIG) was administered in 36.4%. Admission to PICU was required in 81.8% (n=9), 27.3% required mechanical ventilation (MV) and 54.5% vasoactive agents (VA). One patient required ECMO. No factors were related to PICU admission, MV nor VA with statistical significance. Median admission time was 18 days (IQR 13-28 days). Complications appeared in 72.7%, as skin/soft tissue abscess (37.5%), empyema (25%), deep venous thrombosis (25%) and lower limb ischemia (12.5%). Complications were more often in women (100% vs 50.0%; p=0.06), children < 5 years-old (80% vs 0%; p=0.08) and those receiving IVIG (100% vs 50.0%; p=0.09) with statistical significance, and in those with cellulitis (100% vs 57.1%; p=0.12) with differences close to significance. No children died.
Conclusions: - STSS prevalence increased in the last few years, as it has been previously reported. - Female sex, age <5 years-old and skin involvement could be related to higher risk of complications, but more studies are required to confirm these results. - Study design and its inability to detect severity bias in patients receiving IVIG could explain the higher prevalence of complications in this group.
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Background: Candida bloodstream infection in patients with risk factors, is an important cause of hospital morbidity and mortality. Although most candidemia are produced by Candida albicans, an increase in other species has been observed. The objective of this study is to analyse the incidence, characteristics and risk factors associated with candidemia episodes in neonates and paediatric patients of a tertiary hospital.

Methods: We conducted a retrospective observational study in which all cases of candidemia in paediatric patients (<15 years old) belonging to a tertiary hospital were collected between 2010-2018 including Pediatric Intensive Care Unit (PICU) and Neonatal Intensive Care Unit (NICU). Epidemiology, clinical data and candida species, were analysed using IBM SPSS Statistics version 25.0.

Results: A total of 65 candidemia were documented: 52.3% in NICU and 38.5% in PICU. Median age 12 months (IQR 7.5-34.5). Women 55.4%. Predominant risk factors were having central venous catheter (96.9%) and broad-spectrum antibiotherapy (95.4%). Prevalent specie was Candida parapsilosis (52.3%), followed by Candida albicans (26.2%). 29% of PICU and 52% of NICU patients received antifungal prophylaxis. Regarding treatment, liposomal amphotericin B predominated (54.8%) followed by combined therapy (24.2%). Global mortality was 20%, being higher in PICU (40%, p<0.05). An incidence rate of 0.5% in NICU and 0.8% in PICU was estimated.

Conclusions: An increase in the incidence of candidemia due to Candida parapsilosis has been observed in recent years, especially in intensive care units. This change of candida specie although seems to be multifactorial, could be also linked to the use of antifungal prophylaxis. Higher combined treatments and prophylaxis rates in PICU are probably due the previous lack of antimicrobial stewardship programs at this hospital.
SYSTEMATIC REVIEW OF NURSING CARE AND PARENT EDUCATION IN KAWASAKI DISEASE

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Background: Kawasaki (KD) is an inflammation of the blood vessels throughout the body with an unknown cause. KD is also one of the main non-communicable heart diseases in children. Nursing care and parent’s education may decrease disease trigger and progress.

Methods: This study is a systematic review on nursing care and parent education in Kawasaki patients by searching in several search engines such as Pub Med and Medline, Elsevier Cochrane controlled trials registry (2010 to November 2020) using key concepts of Children, Kawasaki, Nursing, Care, Education, Parent.

Results: Nursing Care

Training for parents
Signs and symptoms that may be presented in children up to two months after the first sign: Child’s discomfort. Painfulness of hands and feet. Coldness and low temperature and muscle cramps. After waking up. Joint pain persists for several weeks. Inform your doctor as soon as possible: If your children have a fever above 38 degrees. If symptoms of poisoning of aspirin include: tinnitus, headache, dizziness, bruising, bleeding nose, blood sputum, hematemesis, and bloody stool. Heartache, chest cramps, cold and pale limbs, abdominal pain, nausea, vomiting, restlessness, and severe crying. Avoid vaccination with live virus vaccines up to 11 months after receiving intravenous immunoglobulin.

Conclusions: Kawasaki is a dangerous disease that treat children under five years therefore, rising knowledge of health care provider and parent is necessary to early diagnosis and manage KD to decrease children mortality and morbidity of KD.

Systematic Review Registration:
Background: Respiratory syncytial virus (RSV) a leading cause of respiratory tract infection in hospitalised children. However, data on its clinical burden of disease and medical resource utilisation (MRU) in Europe are limited. This retrospective, non-interventional study included children ≤5 years old, hospitalised for >24 hours with PCR-confirmed RSV at a German tertiary care University Hospital during three consecutive seasons (2015–2018).

Methods: MRU was assessed via overall hospital length of stay (LoS), intensive care unit (ICU) admission/LoS, supplemental oxygen need/method, and medication use. Diagnoses, re-hospitalisations and mortality were also recorded. 312 children had PCR-confirmed RSV (median age 11.5 months, IQR 3–23.5; 0–<6 months [n=108], 6–<12 months [n=48], 1–<2 years [n=78], ≥2 years [n=78]). 51 children (16.3%; 95% CI: 12.4%–20.9%) had pre-defined comorbidities and 26 (8.3%; 95% CI: 5.5%–12%) had pre-term birth status. Bronchiolitis (n=196; 62.8%), pneumonia (n=92; 29.5%) and otitis media (n=23; 7.4%) were the most frequent diagnoses.

Results: Median hospital LoS was 5.0 days (IQR 4.0–7.0). 16 (5.1%) infants were admitted to ICU, 10 of which were <6 months old. Median ICU LoS was 5.0 days (IQR 2.0–8.0). Supplemental oxygen was administered in 180 (57.7%) patients, mainly by nasal cannula (n=176; 56.4%, median duration 2 days [IQR 1–4]). Mechanical/high-flow ventilation was provided for 11 (3.5%) and invasive ventilation (intubation) for 6 (1.9%) patients. While in hospital, 228 (73.1%) children received short-acting beta-agonists, 189 (60.6%) antipyretics, and 136 (43.6%) antibiotics. 14 patients (4.5%) were re-hospitalised with no RSV-associated deaths.

Conclusions: RSV infection in hospitalised children aged ≤5 years, caused significant clinical burden and MRU particularly ICU admission in those <6 months old.
Background: Although most of the urinary tract infections are caused by Escherichia coli, other bacteria like Proteus, Klebsiella, Enterococcus, and Staphylococcus may also cause severe infections. Urine samples were received from inpatients of district headquarters hospital, Namakkal for culture and sensitivity. We analysed the urine culture reports for the bacterial profile.

Methods: We did a cross sectional study. We analysed the reports of urine cultures, done in District Public health laboratory between January and December 2018. We abstracted the data from the nominal register by data abstraction form. We computed proportions to calculate the positivity among the samples. We calculated the proportions of microorganisms by gram positive and gram negative organisms.

Results: We received 542 samples between January and December 2018. 99 samples were positive for culture (18%). Among the culture positive samples, 81 were gram negative microorganisms (82%) and 17 were gram positive microorganisms (17%) and 1 was yeast (1%). Escherichia coli was the predominant organism among the gram negative organisms, contributing to 72% (n=58). Klebsiella species were second predominant organisms (n=10), contributing to 12%. Klebsiella oxytoca were most common among Klebsiella species (Klebsiella oxytoca=8, Klebsiella planticola=1 and Klebsiella pneumoniae=1). Pseudomonas aeruginosa species were third most common microorganism (7%, n=6) among gram negative bacteria. Among the gram positive organisms, Enterococcus was predominant (76%, n=13). Other microorganisms were Staphylococcus (n=2), coagulase negative Staphylococcus (n=1) and Streptococcus (n=1).

Conclusions: Gram negative bacteria profile in Namakkal was similar to the bacteria isolated from urine cultures across India. But the predominant isolates among the gram positive organisms differ from the distribution across India. Instead of Staphylococcus predominance, Enterococcus were much more predominant in our study.

Clinical Trial Registration: This is not a clinical registration trial.
RECURRENT RESPIRATORY PAPILLOMATOSIS: SUCCESSFUL RESPONSE TO SYSTEMIC BEVACIZUMAB

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Title of Case(s): RECURRENT RESPIRATORY PAPILLOMATOSIS: SUCCESSFUL RESPONSE TO SYSTEMIC BEVACIZUMAB

Background: Recurrent respiratory papillomatosis (RRP) is determined by HPV type 6 and 11 that cause the proliferation of the mucosae leading to an obstruction of upper and lower respiratory ways. The first-choice therapy is the laser surgery while there is no consensus regarding the adjuvant therapy.

Case Presentation Summary: We describe the case of a boy affected by RRP by HPV genotype 6, diagnosed in Benin when he was 3 years old. Because of the recurrent laryngeal obstructions, he had needed frequent laser surgeries and tracheostomy. Medical therapy with alfa-interferon, ribavirin and indole was started at the age of 5 years. At 6 years of age, therapy with intralesional cidofovir was added with following reduction of the frequency of surgeries. Cidofovir was replaced after 2 years with systemic therapy with PEG interferon, with clinical stability but needing of laser surgeries every 1-2 months. He came to our attention at 9 years of age. HPV 9-valent vaccine was administered, and PEG interferon was stopped because of the acute onset of lymphopenia and thrombocytopenia. After this suspension, he presented a rapid worsening of laryngeal papillomatosis, a progression to the trachea and to the lung with a decline in respiratory function that needed intensive support. A systemic therapy with the humanized anti-VEGF monoclonal antibody Bevacizumab was started at the dosage of 10 mg/kg every 3 weeks with stringent monitoring of platelets count, systemic pressure and renal function. A rapid clinical and endoscopic improvement was observed without any adverse events. Therefore, it was possible to stop ribavirin and to reduce Bevacizumab infusion frequency (8 weeks).

Learning Points/Discussion: Systemic adjuvant therapy with Bevacizumab may be a promising and safe option in the treatment of children with RRP with multiple localization.
Background: Respiratory tract infections contribute a huge burden of morbidity and mortality among children. Viral causes though common, have been less well studied in low and middle income (LMIC) settings. Here we describe the distribution of virus detected from throat swabs of febrile children presenting to hospital.

Methods: Between Dec 2016 and Sep 2018, children with fever (≥38°C) or suspected infection 0-18 years of age were recruited. We collected throat swabs using eNAT® from 495/500 children. The swabs were processed using Luminex® NxTAG® Respiratory Pathogen Panel assay for detection of viruses.

Results: Sixty percent of the swabs were positive for one or more virus. Influenza A was the most common virus detected in 20% of the children. Influenza B was present in 16.7%, Respiratory Syncytial virus (RSV) in 6.5%, Adenovirus in 5.7% and Parainfluenza 3 in 1.6%. The common viruses showed a seasonal variation, see Figure. Seventy-seven of the children (15.6%) of the children were clinically diagnosed with pneumonia and 13 (2.6%) as undefined lower respiratory tract infection.

Figure: Frequency distribution showing Influenza A, Influenza B and Respiratory Syncytial virus
Conclusions: Viruses were commonly detected among febrile children in the Gambia, however clinical diagnosis of respiratory tract infections was made in only a fifth of the children. There were no controls in this study to better understand the clinical relevance of the viruses present. Acknowledgements PERFORM; Personalised Risk assessment in Febrile illness to Optimise Real-life Management across the European Union, Consortium MRCG at LSHTM, Serekunda General Hospital This project has received funding from the European Union’s Horizon 2020 research and innovation programme under grant agreement No. 668303
ANTIMICROBIAL STEWARDSHIP IN DONOSTIA UNIVERSITY HOSPITAL: PROGRAMS FOR OPTIMIZING THE USE OF ANTIBIOTICS (PROA)


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Background: Antimicrobial stewardship (AMS) activities are intended for the optimization of antimicrobial use in the clinical setting. Inappropriate or suboptimal utilization of antibiotics can lead to increased length of stay, multidrug-resistant infections, and mortality. This study assessed the impact of an ASP team implantation.

Methods: Prospective intervention study from January 2013-December 2018 in children aged ≤14 years admitted to Donostia University Hospital. Everyday the ASP multidisciplinary team evaluated the presence of bacteriemia, broad-spectrum antibiotics and antifungal consumption, and the length of antibiotic-therapy. Regular peer-to-peer interventions between advisors and prescribers were performed to reinforce the appropriate use of antibiotics. Some indicators were monitored to measure prescribing quality, antimicrobial consumption (defined daily doses per 1000 occupied bed-days), length-stay and economic impact. The Mann-Whitney U test and χ² tests were utilized to analyze continuous and categorical data, respectively.

Results: A total of 180 interventions of 988 patients were performed. The prescriber accepted 84% of suggestions (60% in carbapenem). The consumption of antimicrobials reviewed was reduced -34.8% DDD/100-stays. A significant change in trend was observed for antifungal consumption, with a sustained reduction of -20%. The average cost was reduced from €50.418 to €27.268 (-45.9%). There were no significant differences in length of stay or mortality.

Conclusions: The ASP has succeeded in optimizing the use of antimicrobials without adversely affecting the evolution of the patients.
Background: Countries which have good rubella surveillance, report around 10,000 to 20,000 rubella cases annually. In India, not many cases of rubella are reported. Hebballi agasi ward in Karnataka state, India reported rubella cases on last week of January, 2015. We investigated to describe the outbreak by time, place, person and clinical symptoms.

Methods: We did cross-sectional study. We defined a case as any resident of Heballi agasi, who had fever and rash, with or without lymphadenopathy, arthralgia, conjunctivitis, coryza and cough, after 15th of December, 2014 to March 2015. We collected details on socio-demography, clinical symptoms and rubella vaccination. We tested 5 serum samples for measles and rubella antibodies. We computed mean age of cases. We calculated proportions for attack rates and clinical presentation.

Results: Population of Heballi agasi was 1458. We identified 15 rubella cases (9 females and 6 males). Outbreak lasted between 10th December, 2014 to 21st February 2015. Overall attack rate was 1% (15/1458). Mean age of cases was 6 years (Range:1 year to 23 years). Attack rate was high (7.7%) among age group between 1 year to 6 years (11/143). Attack rate among age group greater than 6 years was 0.3% (4/1315). In addition to fever and rash, 93% of cases (7/15) had coryza, 47% had cough (7/15) and 40% had conjunctivitis (6/15). Lymphadenopathy was present in only one case (1/15) and arthralgia was absent among all 15 cases. There was no death among cases. All five serum were positive for rubella and negative for measles. Routine rubella vaccination was not in immunisation programme.

Conclusions: There was rubella outbreak in Heballi agasi ward. Children aged 1 to 6 years were most affected. We recommend routine rubella vaccination.

Clinical Trial Registration: This is not a clinical trial.
COMPLICATED PYOMYOSITIS OF OBTURATOR MUSCLES: A THERAPEUTIC CHALLENGE

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Title of Case(s): Complicated pyomyositis of obturator muscles: a therapeutic challenge

Background: Pyomyositis of the obturator muscles is a rare condition that usually presents with hip pain and high fever, requiring differential diagnosis from septic arthritis. Depending on size and depth of the infection, treatment consists of intravenous antibiotics alone or associated with abscess drainage.

Case Presentation Summary: A 13-year-old boy comes to the Emergency Department with high fever (40 °C) and a painful left hip with inability to bear weight. 3 days before, while doing some physical exercise, he felt an acute pain to the left thigh, quickly disappeared. On physical examination he shows an hyperemic pharynx and presents pain to passive movements of left hip. Initial laboratory exams reveal a normal white blood cell count, but CRP 10.5 and PCT 2.1 mg/dL. Plain radiograph and ultrasound of the hip are negative. The patient is admitted and IV antibiotic therapy with Clindamycin and Oxacillin is started. Blood culture grows Methicillin-Sensitive Staphylococcus Aureus, consequently Clindamycin is suspended. The MRI shows pyomyositis of left external obturator muscle with a fluid collection of 2x0.7cm and initial involvement of ilio-pubic bone. After two weeks a second MRI demonstrates a slight improvement of muscular abscess, but unchanged bone involvement; the IV antibiotic therapy is therefore continued, for a total duration of 6 weeks. During the hospital stay the pain gradually decreases, with a complete recovery of hip movements. The patient is dismissed but will continue antibiotic therapy orally with Clindamycin for other 4 weeks. Later he will be monitored clinically and radiologically for other 8 months.

Learning Points/Discussion: Early diagnosis and rapid start of intravenous antibiotics often allow to successfully treat in a conservative way pyomyositis, even if already complicated by osteomyelitis, with no need for more invasive treatments.
IMPORTANCE OF THE AGE AND THE MONTH OF BIRTH IN THE HOSPITALIZATIONS WITH RSV IN A. Mira-Iglesias¹, A. Orrico-Sanchez¹, C. Demont², F.X. López-Labrador³, J. García-Rubio¹, M. López-Lacort¹, M. Tortajada-Girbés⁴, J. Mollar-Maseres⁵, M. Carballido-Fernández⁶, G. Schwarz-Chávarri⁷, J. Puig-Barberà¹, J. Diez-Domingo¹
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Background: RSV is the most common cause of severe respiratory illness in the first year of life. Birth month might be an important risk factor for RSV infection and subsequently, hospitalization. To help direct targeted interventions and future RSV vaccine programs, we examined risk of RSV-related hospitalization by infant age and birth month in hospitalized <1-year-old children in the VAHNSI network.

Methods: A prospective active-surveillance hospital-based (4 to 10 hospitals) study in the Valencian Region (Spain) was conducted from 2014/2015 to 2017/2018 seasons. All consenting admissions of patients fulfilling the inclusion criteria were swabbed. RSV+ (RT-PCR)-hospitalization rates by season and month of age were studied. RSV status was compared according to month of birth. A negative binomial regression was performed to adjust RSV hospitalization rates by months of age.

Results: 2,184 children were screened and 1,494 (68.41%) were included in the analysis. Of those, 1,056 (70.68%) were PCR-positive and, 631 (42.24%) were RSV+. Around 70-75% of RSV infections were in infants born in August-December. RSV result differed according to the month of birth in all seasons (p-values <0.005). The highest RSV hospitalization rates were found in children 1 month-of-age (~200x100,000 children-week). The adjusted risk of RSV decreased by 78% (RR=0.22, 95% CI=(0.17-0.29)) in children >3 vs. ≤3 months of age.

Conclusions: Most of RSV-associated hospitalizations in children less than 1 year of age occurred during their first 2 months of life. Children born just before or at the beginning of the season presented higher risk of developing an RSV infection. Due to the immature response of the immune system in very young children, the combination of prevention strategies will be probably needed.
CLINICAL OUTCOMES IN PERINATALLY HIV-INFECTED PATIENTS TRANSFERRED FROM PEDIATRIC TO ADULT CARE IN SPAIN: A NATIONAL MULTICENTER STUDY


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Background: The transition of HIV-infected patients from paediatric to adult care is a risky moment. The aim of this study was to describe clinical outcomes of perinatally HIV-infected patients after transition to adult care.

Methods: Multicenter retrospective, observational study. Perinatally HIV-infected patients followed-up in the Spanish paediatric HIV cohort (CoRISpe) transferred to adult care during 1997-2016 were included. Immuno-virologic data were collected at baseline (12 years of age), transition (last visit in paediatrics), one and three years after transition, and at the last follow-up moment. Mixed-effect models analysed changes in CD4 count and viral suppression; multivariate analysis evaluated risk factors for virologic failure and CD4 count at 3 years post-transition.
332 patients were transferred. After transition 11 patients (3.3%) died. Viral suppression (≤200 copies/mL) of patients followed-up ≥3 years post-transition (n=258) were: 42.8%, 59.7%, 69.7% and 71.3%, at baseline, transition, one- and three-years post-transition, respectively (p<0.001). No differences (p=0.716) in the trend of CD4 comparing pre- vs post-transition (Figure 1). Risk factors for virologic failure 3 years post-transition were: female gender, foreign birth and virologic failure at transition; factors associated with lower CD4 3 years post-transition were gipsy ethnicity, lower age and CD4 count at transition, and lower CD4 nadir.

Conclusions: Virologic suppression among perinatally HIV-infected patients in the evaluated cohort improved after transition to adult care, which could be related to integrase-inhibitor treatment. However, immunological status remains similar. Identifying patients with risk factors for worse outcomes may aid during transition.
Background: *Influenza virus* is still a worldwide problem, increasing hospital admissions during the epidemic period. The aim of this study was to describe the characteristics of children admitted due to *Influenza*, as well as the factors associated with admission in pediatric intensive care unit (PICU).

Methods: Prospective study of children <14 years-old admitted in a tertiary care hospital during 2015-2019. Influenza was diagnosed by PCR. A logistic regression analysis was used to establish the possible factors of PICU admission.

Results: 116 patients were analyzed during four seasonal epidemics (SE). 2015-2016 and 2017-2018 were the SE with more admissions (42 admissions each one). 57% were males, mean age 24 months (IQR 20-2). 50% had any chronic disease, being respiratory (43%) and neurologic (15%) the most prevalent. About this group, only 25% had been vaccinated during the SE. 74% were secondary to *Influenza A*. 32% had a viral coinfection, being RSV the most prevalent (32%) followed by adenovirus (16%). Oxygen therapy was necessary in 53%, along a mean of 7.4 days (SD ±8.24 días), and 40% needed systemic steroids. Oseltamivir was indicated in 23%. Thirteen patients (11%) needed PICU admission, mean length stay of 10.46 days (SD 8.23 days). Having respiratory distress (OR 5.4; IC 1.3-22.9) and viral coinfection (OR 4.2; IC 1.1-16.3), were related to a higher ICU admission with statistical significance. Those with fever at the admission had lower admission in ICU (OR 0.16; IC 0.02-0.92). There were no deaths.

Conclusions: - Half of the patients had a chronic disease, 75% of whom had not been vaccinated. - Having developed respiratory distress or had viral coinfection, could be risk factors of PICU admission, being necessary more studies to confirm these.

Clinical Trial Registration: No Clinical Trial Registration
VALIDATION OF SIX RNA BLOOD BIOMARKERS USING QPCR TO DISCRIMINATE BETWEEN BACTERIAL AND VIRAL INFECTIONS IN FEBRILE CHILDREN

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Background: Diagnostic approaches for infectious disease focus mainly on pathogen detection and identification. Current host biomarkers are neither sensitive nor specific enough. In recent years, host blood gene expression biomarkers have been described for their ability to distinguish between bacterial and viral infections. Several discovery gene expression studies in acute infections have been published using sophisticated techniques, like microarrays or RNA-Seq.

Methods: We evaluated an RT-q PCR assay for six host-transcripts (FAM89A, ADGRE1 and EBI3 overexpressed in bacterial infections, IF44L, IFI27 and OASL overexpressed in viral infections and two housekeeping genes) inferred from microarray data and included in the 38-transcript signature published in Herberg et al. JAMA 2016. These six transcripts’ expression was measured in a cohort of 51 children evaluated for fever in the ED of our hospital¹-²5 had confirmed bacterial and 26 confirmed viral infection(Table).
Results:

All six genes were significantly differentially expressed between confirmed bacterial and confirmed viral infections (IFI27 P-value = 2.9 × 10−7, IFI44L P-value = 3.6 × 10−6, OASL P-value = 1.2 × 10−4, FAM89A P-value = 2.7 × 10−3, ADGRE1 P-value = 0.011, EBI3 P-value = 0.016). When evaluated as single markers, the highest AUC was achieved by IFI27 87.2% CI 95 (76.8-97.5), while all the viral markers outperformed the bacterial ones. The best combination of two marker genes was IFI27 + FAM89A, which achieved AUC of 93.8%(87.7-100), sensitivity of 92.3%(76.9-100) and specificity of 88%(72-100). Only two patients with confirmed bacterial infection were misclassified (both with UTIs) none with invasive infection.

Conclusions: Host-expression signatures are shown to be robust across different detection platforms. In the future, a fast, highly accurate and relatively inexpensive RT-q PCR assay could be used in clinical settings to facilitate the discrimination between viral and bacterial infections. For this purpose, a reliable combination of both viral and bacterial marker genes can be used to identify viral and bacterial co-infections.
INVASIVE INFECTIONS WITH SEPTIC SHOCK: WHO’S TO BLAME?

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Title of Case(s): INVASIVE INFECTIONS WITH SEPTIC SHOCK: WHO’S TO BLAME?

Background: *Staphylococcus aureus* (SA), a leading agent of invasive infections in children, can cause septic shock (SS). Panton-Valentine leukocidin (PVL) is a virulence factor associated with more severe local disease, greater systemic inflammatory response and rapidly progressive bone and joint infections.

Case Presentation Summary: The authors describe 3 previously healthy children with SA-SS. A 10-year-old female, with recent right wrist fracture, admitted with a 3-day history of fever, headaches, vomits and right-hand inflammatory signs. Hand ultrasound revealed middle-carpal joint arthritis. Echocardiography performed for a newly detected systolic murmur, revealed aortic valve endocarditis. Clinical deterioration within 3 days with SS. She underwent surgical joint cleaning and aortic valve replacement. Brain-CT revealed multiple abscesses, without surgical intervention required. Methicillin-susceptible SA (MSSA) isolated in blood cultures, joint and cardiac samples. PVL detection not performed. A 12-year-old female, admitted with a 2-day history of right hip pain, claudication and fever. MRI revealed buttocok's abscess with psoas extension and abdominal wall cellulitis. Clinical deterioration within 48 hours with SS, respiratory, liver and renal failure. She underwent surgical cleaning, with PVL-positive MSSA isolation. Negative blood cultures. A 14-year-old boy admitted with a 3-day history of fever and right-knee inflammatory signs after minor trauma. MRI revealed tibial osteomyelitis and pyomyositis. He underwent surgical cleaning and fasciectomy with clinical deterioration 24 hours later, SS and respiratory failure. He needed multiple debridements and surgical cleanings. PVL-positive methicillin-resistant SA isolated in blood cultures and surgical samples. Protein synthesis inhibitor antibiotic added in all cases by toxin inhibitory adjuvant effect.

Learning Points/Discussion: From the presented cases, we highlight the rapid clinical deterioration, with serious presentations and multiorgan failure on previously healthy children as clues to PVL-positive SA strains. We alert to its early recognition to optimize therapy.
IMPACT OF VARICELLA VACCINE INTRODUCTION ON THE SEROPREVALENCE IN PEOPLE BETWEEN 1-40 YEARS.

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Background: Argentina introduced in 2015 varicella vaccine (1 dose - 15 months). The aim of this study was to determine the seroprevalence of varicella (VZV) in a healthy population of 1-40 years (4 years after the vaccine introduction).

Methods: Cross-sectional study including healthy people between 1-40 years stratified in nine age groups, attending the outpatient clinic at Ricardo Gutiérrez Children’s Hospital in Buenos Aires, between June-December 2019. Exclusion criteria: fever in the last 2 days or immunosuppression. Anti-VZV IgG levels were detected by the fluorescent antibody to membrane antigen (FAMA) assay. Data was analyzed using Epi Info 7.

Results: We included 599 samples. Overall seropositivity was 70.8% (95%CI=67-74.3%) and increased with age:1-15 months 12.2%(5/41); 15-23 months 53.6%(52/97); 2-5 yo 64.6%(62/96); 6-11 yo 65.4%(53/81); 12-15 yo 90.5%(67/74); 16-20 yo 86.8%(59/68); 21-25 yo 88.5%(46/52); 26-30 yo 87.2%(34/39); 31-40 yo 90.2%(46/51). Seropositivity according vaccination or chickenpox history is showed in figure 1. In 16.5% (32/192) of children <5 years had non-detectable anti-VZV IgG tests after varicella vaccine. The association of positive Anti-VZV IgG in cases with history of illness (OR: 10.4; 95%CI:6.4-16.8);p<0.001) or contact with household members with chickenpox (OR: 4.8; 95%CI:3.1-7.6);p<0.001) was high. Vaccination in children <5 years was a protective factor of having chickenpox (OR: 0.25; 95%CI:0.09-0.68);p=0.004).

Figure 1: Seropositivity by age groups according vaccination and chickenpox history* (n=424).
Cases without history of having chickenpox or vaccination were excluded from this figure.

**Conclusions:** The prevalence of Anti-VZV IgG was high in all age groups except in the 12-15 month group because of not being included in the national strategy. Seropositivity in younger groups (15m to 5 years) were due to vaccination while in the older groups (from 6 years old) it was due to the disease. **Clinical Trial Registration:** Not Applicable
AXILLARY MASS IN A 7.5 MONTH-OLD BOY

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Title of Case(s): Axillary mass in a 7.5 month old boy: An innocent lesion after Bacillus Calmette-Guérin vaccine?

Background: Bacillus Calmette Guerin (BCG) vaccine is administered to all children aged 2 months in Turkey. It is important for pediatricians and all physicians to be aware of BCG-related complications, which may be the first sign of an underlying immunodeficiency.

Case Presentation Summary: A 7.5 month-old boy was referred to our clinic with an axillary mass which is noticed one week ago. Physical examination showed fever, 2x3 cm left axillary lymph node on BCG side and enlarged liver and spleen. He had neonatal sepsis, diagnosed with perianal abscess, had fever, urticarial rash, perianal dermatitis, moniliasis and anemia on his previous hospitalizations. Significant leukocytosis (WBC:25500/mm³) and elevated liver enzymes were detected. ESR (21 mm/h) and CRP (22 mg/L) were increased. Immunoglobulin levels and lymphocyte subset panel were normal. Serologic tests for hepatitis, toxoplasma, rubella, CMV and EBV did not show acute infection. HIV Ag/Ab was negative. Chest and humerus X-rays were normal. Abdomen ultrasonography showed hepatosplenomegaly but no lymph nodes. TST was 20x20 mm. Three specimens of gastric aspirate turned out negative for AFB. Lymph node excision was performed and M. tuberculosis complex DNA-PCR was positive. Further analysis in the national laboratories indicated M. bovis BCG strain. Standard antituberculosis therapy could not be initiated due to elevated liver enzymes. Ethambutol, streptomycin and ciprofloxacin were administered until liver enzymes were in normal limits. Then, the regimen was changed into streptomycin, isoniazid, ethambutol and rifampicin. Dihydrorhodamine-123 test pointed out chronic granulomatous disease. The patient received trimethoprim/sulfamethoxazole and itraconazole for prophylaxis and interferon-gamma. After 7 months of therapy, the patient was transferred to another facility for hematopoietic stem cell transplantation.
Key Learning Points: BCG complications could indicate primary immunodeficiencies and could be difficult to treat. It is important to differentiate between disseminated BCG and disseminated tuberculosis. HSCT could be the only way to reconstitute the immune functions and to overcome the infection.
EXPLORATION OF MYCOPLASMA PNEUMONIAE AND CHLAMYDIAE PNEUMONIAE INFECTIONS IN ATYPICAL ACQUIRED PNEUMONIA IN MOROCCAN CHILDHOOD COMMUNITY WITH ASSESSMENT OF ASSOCIATED SOCIO-ECONOMIC AND ENVIRONMENTAL RISK FACTORS

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Background: Pneumonia is widely recognized as the leading cause of morbidity and mortality among children less than five years. According to the World Health Organization, it represents 15% of deaths in that age. Our purpose is to explore the role of Mycoplasma pneumoniae and Chlamydiae pneumoniae atypical infections in childhood Community-Acquired Pneumonia in Morocco and evaluate the associated risk factors.

Methods: Children less than 15 years old, consulting for pneumonia in pediatric department of CHU Casablanca were enrolled, after informed consent obtained from parents or gradients, clinical information were recorded and samples were collected to investigate the presence of the above agents.

Results: Since 29 May 2019, 35 patients were recruited. Collected data analysis showed an age less than 5 years in 88.6% and 57.1% are male gender. Most of the participants (91.4%) have a mediate economic status and 68.6% have had mixed feeding. Among them, 28.6% were exposed to tobacco and 80% were living with fraternity. The clinical information analysis revealed that 5.7% had cyanosis and 71.4% had a high fever (>37° C) and majority (87.5%) showed breathing difficulties. The results revealed that 77.1% of patients are exposed to air pollution since they are urban. However, 5.7% are living near to public dumps or factories. Our data also revealed that 31.4% were exposed to humidity and 20% have contact with domestic animals.

Conclusions: These preliminary results showed that environmental factors and living conditions burdens are important; they can be a cause of childhood pneumonia. The molecular detection and characterization of Mycoplasma pneumoniae and Chlamydiae pneumoniae atypical infection is in process, the results can provide explanation to the childhood Community-Acquired Pneumonia in the studied population.

Clinical Trial Registration: there are no clinical trials number
Background: In 2019 approximately 400,000 measles cases were reported around the world by the WHO. In Brazil, more than 16,000 cases and 15 deaths were registered. Therefore the country lost its virus elimination certificate, previously achieved in 2016. Facing this epidemiologic situation, we evaluated the clinical and laboratorial profile of patients with measles in a high complexity tertiary care reference hospital in São Paulo.

Methods: All patients that met measles clinical criteria from June to December 2019 were included. Demographic data, underlying disease, clinical manifestations and vaccine status were recorded for 31 children. Blood, urine and saliva samples were collected for serology and viral-PCR at disease onset. After 14 days patients were re-evaluated and new samples were collected for paired serology when the first result was non-conclusive.

Results: Thirty-one suspected measles cases were identified. Fourteen were confirmed by PCR or serology. Eight children (57%) had comorbidities (HIV n=1; Liver transplant n=2; malignancies n=3; immunosuppression therapy n=2) and one was HIV-exposed uninfected. Main symptoms were cough/coryza (100%), skin-rash (92.8%), fever (92.8%) and conjunctivitis (71%). Only 2 patients had a complete measles immunization schedule. Empirical antibiotics were prescribed in ten patients but only seven (50%) had confirmed bacterial infections (pneumonia n=5; otitis media n=3; both n=2). Hospitalization rate was 82% (n=12) with two ICU admissions. There were no deaths.

Conclusions: We described measles cases in pediatric patients with comorbidities. Eight of our patients were immunosuppressed. This could be a contraindication for vaccination and also a risk for more severe disease. Our patients presented more complications, hospitalizations and antibiotic usage but favorable outcomes and no deaths. Therefore thorough support is needed in immunosuppressed children during an infectious disease outbreak.
ST AND HIV AMONG ADOLESCENTS IN SPAIN: ARE WE READY TO FACE IT?

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Background: The incidence of sexually transmitted infections (STI) in Spanish adolescents is growing rapidly. From 2018, the Spanish Society of Infectious Diseases and Microbiology offered a course focused on the management of STIs and HIV in adolescents for health workers. The course was subsequently available online during 6 months. We summarize baseline knowledge at pre-course assessment.

Methods: Before course enrollment, in both classroom and online versions, participants completed an anonymous questionnaire with 16 questions covering different aspects of sexuality among adolescents. Demographic characteristics of participants were collected and average baseline knowledge analyzed in those who completed the questionnaire.

Results: From 338 students completing full training sessions, 171 pre-course questionnaires were available. 78% were women with median age of 36 years [IQR 29-44.5]. All were health-related professionals: doctors (57%), residents (26%), nurses (5%), pharmacists (5%) and other (7%). Half of professionals worked primarily with children. 13% felt confident with their training in managing STIs and sexuality. Regarding HIV transmission, 60% ignored (undetectable=untransmissible). Half of doctors (52%) chose the incorrect empiric treatment for non-gonococcal urethritis and 28.7% would not empirically treat genital Herpes Simplex primary infection. No differences were found comparing professionals with different backgrounds (ie. Pediatricians vs other)

Conclusions: Most health care professionals lacked confidence in their training and were uncomfortable discussing sexuality and managing STIs with adolescents. There is a need for specific training among healthcare professionals and new technologies can be helpful. A multidisciplinary team is required in order to face the epidemics among adolescents.
TARGETED REVIEW TO UNDERSTAND THE EVOLUTION OF NATIONAL MENINGOCOCCAL VACCINATION RECOMMENDATIONS IN FOUR COUNTRIES

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Background and Objective: In the past few decades, cost-effectiveness analyses (CEA) of vaccination programs have been part of the decision-making process. However, results of a standard CEA may be less favorable for vaccines that provide protection against rare diseases with potentially catastrophic outcomes. An example are vaccines to protect against Invasive Meningococcal Disease (IMD). In order to understand the impact of IMD incidence, CEA and disease on policy decisions about IMD vaccination programs, we describe the evolution and the factors driving this evolution in four countries: the UK, US, the Netherlands, and Canada.

Methods: A targeted literature review was conducted of publications and internet sources for the four countries relating to IMD vaccination. The review focused on the impact of CEA results on vaccine policy decisions and how other factors influenced policy decisions.

Learning Points/Discussion: Summary: Three types of meningococcal vaccines are available to protect against serogroup(s) B, C or ACWY. The Figure 1 illustrates the evolutions of the recommendation in relation to epidemiology in 4 countries. The review indicated that the recommendations have considered CEA results and these have impacted the specific age groups targeted. However, when outbreaks of IMD occurred, pressure from parents, physicians, and the media and support from public health authorities have also influenced the recommendations. In addition, vaccine availability, changes in the incidence of different IMD serogroups over time, and the catastrophic nature of the disease that is exacerbated by the difficulty in achieving early diagnosis and by its rapid development have been considered in the decision-making process. Conclusion: IMD vaccination programs in four countries with formal processes for their evaluation were based on IMD incidence, the frequently catastrophic nature of the disease and CEA results.
Figure 1. IMD Epidemiology and Routine Vaccination Recommendations Over Time

- MenC program evolution summary: In 1999, temporary recommendation for 3 doses MenC in infants and catch-up campaign at 11 years and younger. In 2002, this program became permanent for infants. In 2007, program changed to 2 doses in infants with booster at 12 months. In 2013, program changed to 1 initial dose, booster at 12 months and booster at 14 years. In 2013 dropped infant dose, in 2013 dropped adolescent dose.
- Measles program evolution summary: In 2013, recommendation for 3 doses in infants.


- MenACWY program evolution summary: In 2017, recommendation for 3 doses in infants.
- Measles program evolution summary: In 2017, recommendation for 3 doses in infants.


Epi source: Incidence prior to 2013 was Advisory Committee on Immunization (ACI) National Advisory Committee on Immunization (NACI), Update on Quadrivalent Menopneumococcal Vaccines effective in Canada (April 2013), Incidence 2012-2013: Canadian Immunization Conference (2013).


COULD THE DIAGNOSE OF RASHES CHANGE WITH GLOBAL WARMING?

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Background: Climate change is a reality with a significant impact in warm latitudes. The seasonal distribution of exanthematous infections sometimes leans our clinical approach. Nowadays we ignore if environmental changes could have an impact in this issue. The aim of the study was to compare the epidemiological profile of the rash cases in our area with the literature review, to identify in a preliminary way possible changes related to the global warming.

Methods: Descriptive observational study in a Hospital of the Mediterranean coast. We reviewed the medical records of children between 0-14 years with a clinical diagnosis of some predominant rashes in our environment (chickenpox, Hand-foot-and-mouth disease -HFMD-, scarlet fever, roseola, fifth disease) between September 2017-January 2020. The variables age, sex, and month at the diagnose were collected to compare the seasonal distribution of cases in our area with the reported ones.

Results: 562 patients were registered. The distribution is showed in figure 1. The most frequent diagnosis (208 cases) was chickenpox, with a median age of 36m (RIQ 12-72). Followed by HFMD (173 cases) with a median age of 12m (RIQ 12-24). Scarlet fever was also recorded frequently (136 cases), with a median age of 36m (RIQ 24-60). Other diseases less frequent were roseola (30 cases), and fifth disease (15 cases).
Conclusions: In our sample distribution of chickenpox was predominant in late spring-summer (typical late winter-spring). Cases of HFMD collected were distributed mainly in autumn-winter (described spring-summer). Roseola mainly appeared in summer months (unlike the literature). We matched the literature for scarlet fever and fifth disease. The changes we observed in some entities could be consequence of global warming. Future studies are needed to lead changes in our practice.
Human herpesvirus type 6 (HHV-6) is a DNA virus considered as a member of Herpesviridae family. HHV-6 is acquired early in life, when it may cause roseola infantum and nonspecific febrile illnesses which is usually a self-limiting disease before the age of 2 years. The primary HHV-6 encephalitis and Acute necrotizing encephalopathy (ANE) are a rare disease to occur in immunocompetent children.

Case Presentation Summary: A previously healthy, 13-month-old male, who presented with three days history of nonspecific febrile illness, 2 days later, he started to have drowsiness, decrease level of consciousness and generalized tonic seizures. The diagnosis of HHV-6 encephalitis is confirmed by positive HHV-6 DNA in the cerebrospinal fluids (CSF) with a quantitative PCR of 3559 copies/ML. Brain MRI showed restriction diffusion in multiple areas that represent HHV-6 encephalitis, and Acute necrotizing encephalopathy of childhood (ANEC). The immunological workup were all normal. The patient was treated with ganciclovir and foscarnet. There was a significant neurological improvement at the follow up after completing 4 weeks of intravenous antivirals and 3 months of valganciclovir.

Learning Points/Discussion: Although the incidence of primary HHV-6 encephalitis is rare in immunocompetent children, HHV-6 encephalitis associated with acute necrotizing encephalopathy is a devastating disease, highly fatal and neurologically damaging disease, therefore early testing and diagnosis are crucial as well as effective management of encephalitis with antiviral therapy is highly recommended.
DIGEORGE SYNDROME: NO LONGER AN ORPHAN DISEASE

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Title of Case(s): It’s Time We Address the Elephant in the Room

Background: DiGeorge Syndrome (DGS) or 22q11.2 deletion syndrome affects an estimated 1 in 4,000 children. The features in this syndrome varies widely from conotruncal heart defects, impaired immunity and distinctive facial features. The nature and degree of involvement in different organs determines the prognosis of children with this syndrome. The impaired immune system primarily T-cell defect, children with DGS are prone to severe and recurrent infections usually present in children older than three months.

Case Presentation Summary: We present the case of a five-month-old infant in a district hospital with recurrent infection. This infant was born full term via spontaneous vertex delivery with respiratory distress, cyanosis and stridor at birth. She was diagnosed with Tetralogy of Fallot, severe pulmonary stenosis with MAPCAs (Major Aortopulmonary collateral arteries). Her ionized calcium at birth was 1.37. Since birth she developed multiple bouts of sepsis, severe infected perianal excoriation following intolerance to Medium chain triglycerides oil and frequent episodes of ophthalmia neonatarum. She was treated for presumptive methicillin resistant staphylococcus Aureus (MRSA)sepsis as all cultures for were found to be negative apart from persistent nasal coloniser of MRSA. In view of her recurrent infections, hypocalcaemia and cardiac lesion, she was investigated for DGS. She was confirmed to have DGS at the age of five-months old when her FISH study revealed 46XX.ish del(22)(q11.1q11.2).

Learning Points/Discussion: A clinical diagnosis of DGS was made in this patient due to her varied clinical features with the presence of hypocalcaemia at birth. Primary immunodefiency should no longer be perceived as a rare disease. This is especially important in developing countries where cytogenetic services may not be readily available which requires a high index of suspicion among treating clinicians.
ENCEPHALOMYELITIS AS AN UNUSUAL PRESENTATION OF BORRELIOSIS IN CHILDHOOD

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Title of Case(s): Encephalomyelitis as an unusual presentation of borreliosis in childhood

Background: Lyme borreliosis is a multisystemic disease with a wide range of clinical manifestations. Neurologic involvement occurs in 5-10% of patients, affecting either the peripheral or central nervous system. Lyme transverse myelitis is a severe and uncommon presentation in children.

Case Presentation Summary: A previously healthy 16-year-old girl was admitted with fever and bilateral lower limb pain with paraesthesia, abdominal pain and vomiting. Three days after, she evolved with symmetrical paraparesia, diminished facial mimicry, hypoesthesia of D10-12 dermatomes, decreased proprioception of the lower extremities and an urinary retention episode. Brain and spinal cord (SC) magnetic resonance imaging revealed multiple T2 hyperintense lesions on the brain but also an extended involvement of the SC affecting the grey matter in all its length and the white matter from C5-C7. This was suggestive of encephalomyelitis with a severe transverse myelitis. The cerebrospinal fluid (CSF) revealed pleocytosis (160 cells/mm³, lymphocytes) normal protein level (57.9mg/dL) and normal glycochachia (54mg/dL). The serum Borrelia burgdorferi s.l (BB) specific antibodies were inconclusive by ELISA (serion) but positive by immunoblot (anti-Borrelia Euroline RN-AT, Euroimmun) with serum-specific bands on IgM (OspC Bg, OspC Bb and OspCBa) and IgG (VlsE Ba, VlsE Bb, VlsE Bg and p41). Intrathecal index confirmed blood-brain barrier disruption (=33.04 g/L, >2). The patient was treated with intravenous ceftriaxone for 3 weeks, immunoglobulin for two days and methylprednisolone for 5 days, with clinical recovery within the first month.

Learning Points/Discussion: Borreliosis diagnosis is often difficult in low prevalence areas, such as Portugal. The presence of serum-specific bands on IgM and IgG by immunoblot suggests the diagnosis. In children, although Lyme encephalomyelitis is rare, it must be considered on differential diagnosis of transverse myelitis.
PROSPECTIVE EVALUATION OF MANAGEMENT OF >5,000 PAEDIATRIC PATIENTS IN THE EMERGENCY DEPARTMENTS ACROSS EUROPE (PERFORM PROJECT)

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Background: Fever in children causes considerable anxiety, both amongst family and professionals, since it can represent both a mild process and a potentially serious condition. The aim was to describe the diagnosis, diagnostic approaches, management and outcomes of paediatric patients assessed in different Emergency departments (ED) across Europe.

Methods: Children<18 years with suspected infection or fever attending ED and who had blood samples taken, at 24 hospitals in the European PERFORM network (www.perform2020.org), were recruited prospectively between 2016 and 2019.

Results: 5,740 children (53% male, 15% <1 year). 1813/5740 (31.6%) looked ill upon arrival at ED. 2561/5740 (50.5%) attended ED in first 72 hours of symptoms, 611/5740 (10.6%) had been previously evaluated for same illness and 761/5740 (13.3%) required new evaluation after their first assessment. 1902/5740 (33.1%) had a chest-ray (991/1902 (52.1%) abnormal), 2535/5740 (44.2%) a urinalysis (635/2535 (25.0%) abnormal), 474/5740 (8.3%) a lumbar puncture (139/474 (29.3%) pathological) and 1494/5740 (26.0%) a rapid microbiological test (325/1494 (21.8%) positive). 3655/5740 (63.7%) received antibiotic therapy. Bacterial infection was confirmed in 645/5740 (11.2%) and 171/5740 (3%) suffered sepsis/severe sepsis/septic shock. 3348/5740 (58.3%) were hospitalized, 660/5740 (11.5%) required intensive care and 58 (1%) died.

Conclusions: 58% of the patients attending ED for suspected infection or fever were considered unwell enough to require blood tests and required admission (11.5% at intensive care). Complementary tests other than bloods, are used in the management of febrile patients in at least 25% of cases, main diagnostic test used being the urinalysis (44%). Less than 15% of patients have a confirmed bacterial infection and less than 5% a serious bacterial infection. This project has received funding from the European Union’s Horizon 2020 research and innovation programme under grant agreement No.668303.
INVASIVE GROUP A STREPTOCOCCAL DISEASE IN CHILDREN AND ASSOCIATION WITH VARICELLA-ZOSTER VIRUS INFECTION

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Title of Case(s): Invasive Group A Streptococcal Disease in children and association with varicella-zoster virus infection

Background: Childhood invasive Group A Streptococcal (GAS) is a serious lifethreatening disease. Chickenpox infection is the most important risk factor identified for the acquisition of invasive GAS infection in children. The mortality is about 30-50% and it can rise up to 80% in the presence of necrotizing fasciitis.

Case Presentation Summary: A 3-year-old boy, presented with a generalized pruritic rash and high fever. He was diagnosed with varicella and medicated with aciclovir. In 2 days, he was hypotensive, tachycardic, with severe dehydration, abdominal pain, inflammation signs of the right inguinal region, and pain on the left lower limb. Blood tests identified leucopenia (3350/uL leucocytes) and C-reactive protein value of 286,8mg/L. He showed acute respiratory distress syndrome, acute renal failure, liver involvement, coagulopathy, acute myocardial infarction, pancreatitis, so toxic shock syndrome was diagnosed. He started vancomycin, clindamycin and immunoglobulin. Streptococcus pyogenes growth was observed in blood culture. He was ventilated for fifteen days, with inotropic support in the first eight days. It was identified fasciitis of the left lower limb with osteomyelitis of the femur. In the context of vasopressor dependent shock, it happened ischemia of the last three fingers in both feet, that ended up with bilateral amputation of 3° and 5° fingers. After four months of physical rehabilitation, leg strength has improved even though with some walking difficulties.

Learning Points/Discussion: Treatment of toxic shock syndrome includes surgery, supportive therapy, immunotherapy as well as appropriate antibiotic use. Clindamycin is more effective as it inhibits SPE-A and SPE-B synthesis and it’s suggested as standard treatment. Early diagnosis, and appropriate therapy initiation are the most important prognostic determinants.
SIGNIFICANCE OF BLOOD CULTURE IN IMMUNO COMPROMISED PATIENTS FOR ISOLATION OF UNUSUAL NON FASTIDIOUS PATHOGENS.

SRCC Children's hospital managed by Narayana health, Microbiology/pathology Laboratory, Haji Ali, Mumbai, India

Title of Case(s): SIGNIFICANCE OF BLOOD CULTURE IN IMMUNO COMPROMISED PATIENTS FOR ISOLATION OF UNUSUAL NON FASTIDIOUS PATHOGENS

Background: Mycobacteria are mainly divided into 2 major groups for the purpose of diagnosis and treatment: Mycobacterium tuberculosis complex, which comprises M. tuberculosis, and the second group nontuberculous mycobacteria (NTM). NTM can cause pulmonary disease resembling tuberculosis, skin and soft tissue infections (SSTIs), central nervous system infections, bacteremia, and ocular and other infections.

Case Presentation Summary: An 8 year old boy with Ph +ve Acute Lymphoblastic leukemia presented with febrile neutropenia post chemotherapy. Blood cultures were negative with persistence of fever beyond 72 hours. He was evaluated with chest CT scan, USG abdomen and viral PCRs which were negative. As fever persisted beyond 10 days with no focus, PICC line removal was planned as the likely source. Three blood cultures were done at 72 hr intervals, by the BACTEC FX 40 system TM (Becton, Dickinson and Company. Franklin Lakes, NJ). The first culture was prior to the first dose of antibiotics. Two cultures had shown Acid fast bacilli in the ZN Stain and grew Mycobacterium abscessus on culture after 8 days. These were identified by MALDI TOF as M. abscessus. The PICC line was removed and culture from the PICC line tip also showed the same growth of M. abscessus. After four weeks of treatment with Levofloxacin and Azithromycin the patient got admitted with fever, mucositis and Right middle finger tenosynovitis.

Learning Points/Discussion: Mycobacterium abscessus, have the ability to survive and proliferate in habitats that they share with humans, such as drinking water, soil, dust and are associated with infections after cosmetic/plastic surgery, invasive medical procedures, contaminated equipment, and in immunocompromised, transplant patients. Mycobacterium abscessus infections are challenging to treat because of the multi drug resistance which necessitates prolonged IV therapy.
A RARE CAUSE OF PANUVEITIS IN CHILDREN - A CASE REPORT

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Title of Case(s): A Rare Cause of Panuveitis in Children - a Case Report

Background: Panuveitis is the global inflammation of the uveal tract and has numerous etiologies, including viral infections. This case shows a rare cause of panuveitis in children hence its importance.

Case Presentation Summary: A 6 years old boy was referred to the Emergency Department for frontal headache and red right eye with 1 day of evolution, associated with itchy eyes, photophobia and decreased visual acuity. He had no other symptoms and denied feverish complications, recent immunizations or trips. Objectively, he had right conjunctival hyperemia of ciliary predominance. Ocular biomicroscopy revealed diffuse hyperemia of the right eye, panuveitis with hypopyon in the anterior chamber and vitritis. Blood tests results were: hemoglobin 14.4 g / dl, leukocytes 14900 / uL (neutrophils 72.8%, lymphocytes 20%), C- reactive protein 6.88 mg / dL, Epstein Barr Virus (EBV) viral capsid antigen (VCA) IgG positive (731 U / ml), with no other changes. He was admitted for etiological investigation and underwent diagnostic vitrectomy, with collection of vitreous humor for cytological, bacteriological and virological analysis. The Polymerase Chain Reaction of the vitreous humor was positive for EBV. A Real Time- Polymerase Chain Reaction in the plasma was performed to confirm the diagnosis. The child completed a total of 28 days of Acyclovir and 35 days of oral steroids. During hospitalization, there was the occurrence of retinal detachment having undergone a new therapeutic vitrectomy. After discharge, he was referred to pediatric and ophthalmology consultation for follow-up and subsequent treatment of sequel cataract.
**Learning Points/Discussion:** Infectious panuveitis occurs mostly due to bacterial or viral infections. This case is of particular interest because it shows a rare etiology of uveitis about which there are very few cases reported in the literature.
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EPIDEMIOLOGY OF RESPIRATORY SYNCYTIAL VIRUS IN BRONCHIOLITIS IN CHILDREN IN SPAIN (2012-2017)

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Background: Bronchiolitis represents a heavy burden of disease in children below 2 years of age in our society, due to the high infectivity of the Respiratory Syncytial Virus [RSV] and the vulnerability of the youngest children. The purpose of this study is to gather epidemiological data about the cases of bronchiolitis that required hospitalization in Spain during a 6 year period (from 2012 to 2017).

Methods: The Spanish national information system for hospitalary data (CMBD) was accessed to gather retrospective cases with diagnoses of bronchiolitis (due to RSV or due to other agents) in children below 2 years of age hospitalized from 1 January 2012 to 31 December 2017. All gathered data was sorted out for statistical analysis in regard to average length of stay, gender, age, year, hospitalization rates, mortality and case-fatality rates.

Results: A total of 101,903 discharges for bronchiolitis were reported in Spain from 2012 to 2017. 42.1% of them were girls, and 57.9% were boys. The mean age was 3.64 months, and the mean duration of the hospitalization was 5.47 days. Most hospitalizations happened in the first 3 months of age. The Hospitalization rate in our study was 3,910 per 100,000 children during the first year of age. Regarding mortality, there were 85 deaths due to bronchiolitis during this past 6 years.

Conclusions: Bronchiolitis due to RSV requiring hospitalization in Spain represents a heavy burden of disease for children until 2 years of age. Future public health measures as vaccination and/or the administration of monoclonal antibodies against RSV to children in their first year of age during the epidemic months of the RSV could help to reduce the disease burden.
ESTIMATES FOR QUALITY OF LIFE LOSS DUE TO RESPIRATORY SYNCYTIAL VIRUS

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Background: Decisions regarding the future RSV-prevention strategies will be informed by their impact and cost-utility (morbidity, mortality and health-related quality of life (HRQoL)). There is a lack of validated instruments to estimate HRQoL in very young children. This study aims to assess the loss of HRQoL in children <2 years old infected with RSV and their families in Spain and the risk factors associated with RSV.

Methods: Observational, prospective and multicentre study. Children infected with RSV were enrolled in 8 primary care centres and 1 hospital during one season. Impact of infection on HRQoL was assessed using a new 38 items-questionnaire developed Ad hoc. Parents of infected children completed 4 questionnaires in four moments (day 0, 7, 14 and 30). HRQoL score was compared using a log-normal model. Risk of smoking at home and age was also assessed.

Results: Of the 117 children screened, 86 (76%) were RSV-positive. Of those, 87% and 61% were under 1 year and 6 months, respectively. Children exposed to smoke at home increased their risk of RSV by 3 times (OR= 3.01 (1.16-8.95)). Risk of RSV in youngest children (<1 year of age) was higher (OR=3.12 (1.09, 9.05)). Compared to the total recovery (30 days after infection), HRQoL score was 39% (IC95%:34%-43%), 29% (IC95%:24%-33%) and 8% (IC95%:3%-13%) lower in days 0, 7 and 14 since the diagnosis of the disease, respectively.

Conclusions: RSV infection decreases the quality of life of around 40% in children <2 years and their families. Children <1 year of age and the ones who are exposed to smoke at home have three-fold higher probability of being infected by RSV. These data are necessary to carry out cost-utility analyses of the future RSV vaccination programmes

Clinical Trial Registration: It is a prospective study. Not a Clinical trial

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Background: Listeriosis is a potentially fatal disease mainly transmitted through the consumption of contaminated food. It is a rare disease, but its prevalence and severity are higher in risk groups such as newborns and immunocompromised children. Neonatal listeriosis is vertically transmitted and frequently manifests as bacteremia or meningitis. We aim to describe neonatal listeriosis cases in the Community of Madrid in the last 20 years.

Methods: Multicentre retrospective longitudinal study. We reviewed medical charts of neonatal listeriosis cases identified between 2000-2019 in 8 hospitals from the Community of Madrid. We included all of the confirmed cases (positive blood or CSF culture for Listeria monocytogenes) and probable cases (diagnosis of neonatal sepsis/meningitis and a positive L. monocytogenes culture from maternal blood, neonatal body surface, placenta or amniotic fluid).

Results: 52 cases were identified (36 confirmed, 16 probable). Incidence remained stable throughout the study period. 36 patients (71%) were premature with median (IQR) GA of 33(29-37) weeks. Chorioamnionitis was diagnosed in 27 cases (52%). Symptoms started within first 24h in 42 neonates (80%) including respiratory distress (63%), shock (35%), hypotonia/hypoactivity (35%), rash (19%) and fever (15%). Blood culture was positive in 31/51 (61%) and CSF culture in 11/41 (27%). Ampicillin plus gentamicin were prescribed for a median duration of 14(11-20) days. 23 neonates (44%) suffered neurological complications and 6(12%) died.

Conclusions: Neonatal listeriosis is a rare disease but it must be suspected in premature newborns with early-onset sepsis. Preterm birth induced by chorioamnionitis is common in these patients. Definitive diagnosis may be challenging due to a relatively low yield of blood culture and a very low yield of CSF culture. Morbimortality rates are high despite early initiation of appropriate antibiotic therapy.
SERVICE EVALUATION OF THE MANAGEMENT OF OSTEOARTICULAR INFECTION OVER 13 YEARS IN A SINGLE UK CENTRE

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Background: Despite new data on non-inferiority of oral vs intravenous (IV) antibiotics in adults, there is no consensus on the management of Paediatric osteoarticular infection (OAI) in the United Kingdom. Practice varies widely, with differences in duration of antibiotic treatment, switch time from intravenous (IV) to oral antibiotics, and requirements for peripherally inserted central venous catheters (PICC). Furthermore, data about recurrence and complication rates are scant. We aimed to evaluate local management practices and to determine any complications.

Methods: Cases of OAI in children aged 0-17 years, presenting to one UK hospital, from 09/2006 - 01/2020 were identified through hospital coding, and clinician records. OAI included septic arthritis, osteoarthritis and discitis. Cases were anonymised and information collected on a secure hospital system in accordance with data protection. The records were analysed in Microsoft Excel and SPSS.

Results: 297 cases were identified, 183 confirmed with notes for analysis. 55% male, 45% female, Median age 4.5 years. 63.8% had OM, 31.6% SA, 3.3% mixed OM/SA and 0.5% discitis, The femur was the most commonly affected bone (18.8%). An organism was isolated in 34.4% of cases, most commonly S.aureus (22.7%). Median total duration of antibiotics was 36 days (7-301) with 14 days (0-91) IV. Complications included two with back stiffness, one DRESS syndrome and three PICC line blockages.

Conclusions: Cases analysed confirm variation in management, partly due to the diversity in age, presentation, and organism. As antimicrobial resistance increases it is appropriate to follow guidelines to reduce total antibiotic use for OAI, providing there is no increase in the complication rate. Reduced use of PICC lines and iv antibiotics also reduces associated complications and cost. An RCT of oral vs IV antibiotics in the UK would be welcomed.
VENTILATOR-ASSOCIATED AND COMMUNITY-ACQUIRED PNEUMONIA IN A PAEDIATRIC INTENSIVE CARE UNIT

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Background: Around 12-20% of patients with community-acquired pneumonia (CAP) require critical care. Additionally, ventilator-associated pneumonia (VAP) is the second cause of nosocomial infection in Paediatric Intensive Care Units (PICU). The aim of the study was to compare clinical and microbiological characteristics of patients with CAP and VAP admitted to the PICU.

Methods: Retrospective and descriptive study, including patients diagnosed of VAP and CAP, with a positive respiratory culture and under mechanical ventilation, admitted to the PICU from 2015 to 2019.

Results: 220 patients were included; 71(32.2%) had VAP and 149(67.7%) had CAP. In comparison with CAP, patients with VAP had more length of stay (24days vs.13days; \( p < 0.001 \)), more days of antibiotic (10days vs.7days; \( p < 0.001 \)), and more days under mechanical ventilation (14days vs.7days; \( p < 0.001 \)). They needed more days of inotropics (8days vs.3days; \( p < 0.001 \)), ECMO [8patients(11.3%) vs.2patients(1.3%); \( p = 0.001 \)] and had higher mortality [9patients(12.7%) vs.4patients(2.7%); \( p = 0.003 \)]. Most frequent microorganisms in VAP were enterobacteriae (36patients,55.7%) and in CAP were gram negatives (83patients,55.7%) and gram positives (58patients,38.9%); \( p < 0.001 \). From all resistant bacterial infections, multidrug-resistance tended to be more frequent in VAP [5patients(27.8%) vs.3patients(8.6%); \( p = 0.147 \)].

Conclusions: Patients with VAP needed more days of antibiotic treatment, mechanical ventilation, inotropic and ECMO support, had longer length of stay and had an increased mortality, in comparison with patients with CAP. Moreover, the microorganisms were different depending on the origin; for VAP mainly enterobacteriae with higher multiresistances and, for CAP, other gram negatives and gram positives.
Background: After the introduction of pneumococcal vaccination, the incidence of community-acquired pneumonia (CAP) by Streptococcus pneumoniae in children has decreased. However, changes in the prevalence of other bacterial etiologies has been poorly evaluated in our environment. The aim of this study was to analyze the epidemiological changes in bacterial CAP in children in the Community of Madrid.

Methods: Multicenter, retrospective study. Patients <16 years-old diagnosed with bacterial CAP (S. pneumoniae, Streptococcus pyogenes or Staphylococcus aureus) microbiologically confirmed in 5 tertiary hospitals of the Community of Madrid from 2010 to 2018 were included. Epidemiological changes were evaluated by logistic regression.

Results: 214 bacterial CAP were diagnosed, the most frequent was S. pneumoniae (68.7%), followed by S. pyogenes (17.3%) and S. aureus (14.0%). Increase in the prevalence of S. pyogenes: annual increase of 2% (OR: 1.19 [95% CI: 1.04-1.38], p=0.011), from 11.8% in 2010 to 26.9% in 2018. Annual decrease of 2.5% in CAP by S. pneumoniae (OR: 0.87 [95% CI: 0.78 -0.97], p=0.016), from 76.5% in 2010 to 65.4% in 2018. The prevalence of bacterial CAP has remained stable (average of 10.1 cases/10,000 admissions/year), with an increase in the prevalence of S. pyogenes (p=0.004).

Conclusions: During the last 9 years we have seen a change in the epidemiology of bacterial CAP in our environment, with a decrease in the prevalence of pneumococcal pneumonia and an increase in that produced by S. pyogenes. This increase coincides with that observed in other nearby countries.
PREVALENCE AND ANTIBIOTIC SUSCEPTIBILITY PATTERN OF ISOLATES FROM PEDIATRIC PATIENTS IN KARACHI WITH URINARY TRACT INFECTIONS

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**Background:** Urinary tract infections (UTIs) are a major health-care problem in developing countries. With the increased use of antibiotics, UTIs have become more difficult to treat. This study is designed to find out the occurrence of different isolates in UTI pediatric patients from Karachi.

**Methods:** 157 pediatric patients were recruited in a private diagnostic and research laboratory of Karachi and their early morning mid-stream urine samples were collected. Out of which, 93 (59.2%) were positive samples for UTI, with 125 (79.6%) females (Mean Age: 8.9 ± 4.9 years) and 32 (20.4%) males (Mean Age: 13.6 ± 4.4 years). Urine samples exhibited ≥10^3 colony forming units (cfu)/ml of uropathogens in pure culture or ≥10^5 cfu/ml as predominant growth were reported being scanty to heavy positive bacterial count, which defined significant bacteriuria. Kirby-Bauer disk diffusion susceptibility test was also carried out to observe antibiotic susceptibility pattern of isolated uropathogens towards different antibiotics.

**Results:** Female children were found to be more effected than male children. Statistically significant association was found out between gender and UTI (P<0.01, OR=4.16 (3.26-5.32) and the most prevalent organism and UTI (P<0.01). The most frequent isolates were *E. coli* (24.7%), *Klebsiella spp.* (14.52%), and CNGS (*Coagulase Negative Staphylococcus*) (7.1%). Piperacillin-Tazobactam was observed as the most effective drug as 46.18% isolates were sensitive towards it. Similarly, Doxycycline was found to be the least effective as 47.25% isolates were resistant. The most effective antibiotic regime against the most prevalent organism i.e. *E. coli* was Imipenim (95.68% sensitive), Amikacin (94.01%) and Fosfomycin (93.68%).

**Conclusions:** Females are at high risk of developing UTIs. These results also give clues about increasing antibiotic resistance in uropathogens which is the cause of high prevalence of UTIs in pediatric patients of Karachi.

**Clinical Trial Registration:** Not applicable
Background: Fever is one of the most common symptoms in pediatrics and accounts for one third of emergency consultations. The aim was to describe the clinical and microbiological characteristics of children attending the emergency department (ED) with suspected infection or fever in Europe.

Methods: Children with suspected infection or fever <18 years attending the ED of any of the European PERFORM network hospitals (www.perform2020.org) were recruited prospectively between 2016-2019 and had blood samples taken. Demographic, clinical and microbiological data were collected.

Results: 5,740 children included (53.7% male). Average age 5.99 years. Most frequent diagnosis were upper respiratory tract infections 1147/5740 (20%) followed by lower respiratory tract infections 1052/5740 (18.3%) and undifferentiated fever 819/5740 (14.3%). 645/5740 (11.2%) were confirmed bacterial infections, mainly due: E.coli 225/645 (34.9%), S.aureus 73/645 (11.3%) and S.pneumoniae 50/645 (7.8%). 735/5740 (12.8%) were confirmed viral infections, mainly due: Influenza A/B 272/735 (37.0%), respiratory syncytial virus 99/735 (13.5%) and adenovirus 91/735 (12.4%). A causative organism wasn’t detected in 63.0%. Antibiotics were initiated in 3655/5740 (63.7%). 1191/2570 (46.3%) received antibiotics even though bacterial infection could not be confirmed by the time of discharge.

Conclusions: Most commonly diagnosed clinical syndrome were upper and lower respiratory tract infections. Antibiotic use remains globally high despite a definitive bacterial infection being confirmed in less than 15% of acute infections in children/ emergency fever consultations. Despite applying optimal microbiological diagnostic techniques, a causative microorganism was identified in <40% of patients. This project has received funding from the European Union’s Horizon 2020 research and innovation programme under grant agreement No. 668303.
INVASIVE MENINGOCOCCAL DISEASE IN SLOVENIAN CHILDREN – A 13 YEAR EXPERIENCE FROM A UNIVERSITY HOSPITAL

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Background: The aim of the present study was to assess epidemiological, clinical and laboratory features as well as response to treatment in children with invasive meningococcal disease (MD) treated at the Department of Infectious Diseases, University Medical Centre Ljubljana.

Methods: A retrospective analysis of children with IMD treated at our institution between June 2006 and June 2019 was performed.

Results: In 53/82 (65%) IMD was microbiologically confirmed. 39.6% presented with bacteraemia, 20.7% with meningitis and 32.3% with both. Severe meningococcal septicaemia developed in 7.4%. Median age was 17 months, 54% were girls. Mean duration of fever was 14.5 hours, 19% of children were transferred to the PICU, 3.7% had severe necrosis and 3.7% have died. Neisseria meningitidis was isolated from blood cultures in 56.6% and from CSF cultures in 45.3%. 41.5% of isolates were susceptible to Penicillin G. Serogroup B was the most common (76.5%), followed by serogroup C (17.6%) and serogroup Y (5.9%).

Conclusions: IMD remains a significant cause of morbidity and mortality in children, with serogroup B (MenB) being the most common in our country and throughout Europe. With implementation of MenB vaccinations in 2019 we hope to subsequently reduce the burden of this disease.
Title of Case(s): From Gastroenteritis to ARDS and to antibiotic resistant bacteria

Background: Antimicrobial resistance in Romania is a serious concern.

Case Presentation Summary: We present a case report of a three-month-old boy, who presented to the Emergency Department for diarrhea and vomiting. He was discharged 2 days prior from our hospital setting, where he was admitted for Adenovirus-enterocolitis. During the hospitalization he was a measles contact. His personal background: at 23 days of age he was admitted to our clinic for bronchiolitis and is coming from a poor/low social economic family. The clinical exam revealed: sunken eyes and fontanelle, prolonged capillary refill time, slow skin turgor, otherwise clinically normal. Paraclinical: elevated white blood cells count, normal CRP. Rotavirus rapid antigen test was positive. His gastrointestinal symptoms improved under symptomatic treatment, but after 5 days following admittance he developed symptoms of respiratory distress. The X-Ray showed diffuse ground glass lungs. Cefazidime, Cortisone and iv Ig were added to the treatment. After a few days he was transferred to the ICU, due to the need for ventilatory support. He was intubated and antibiotic treatment was changed to Meropenem and Teicoplanin. During this whole time blood-, urine-, nasal-, throat cultures were all negative. He developed hepatic- ALT-120U/l (NV: 0-45 U/l); AST-790 U/l (NV: 0-35U/l), renal- urea: 113.9 mg/dl (NV:15-50); creatinine: 1.4mg/dl (NV:0.70-1.30) and metabolic impairment-serum proteins-4.3g/dl (NV: 6.20-8g/dl), presented generalized edema. These were reversible under specific treatment, but the respiratory dysfunction remained persistent. After 24 days of hospitalization, culture of tracheal secretions was positive for Pseudomonas aeruginosa sensitive only to Colistin. He developed a spontaneous pneumothorax, which needed drainage, maintaining low O2 saturations afterwards. Shortly after that he got into cardiac arrest with no response to CPR. The autopsy showed confluent bronchopneumonia with subpleural micro-abcesses.
Key Learning Points: This is a case of a Pseudomonas aeruginosa antibiotic resistant VAP, in an infant with ARDS, due to a viral infection.
Background: Post-marketing surveillance of adverse events following immunization (AEFIs) is routinely carried out by a passive system, based on the spontaneous notification by Health Care Workers and patients: this model is badly affected by the risk of underreporting. In Apulia region a systematic surveillance program has been implemented to evaluate safety and effectiveness of anti-meningococcal B vaccine in pediatric, adolescent and adult patients: it was available since 2013 and actively and free offered to all newborns since 2014, with different schedules depending on the age at the first dose administration.

Methods: From regional immunization database number of meningococcal B vaccine doses administered was obtained from 2014 to 2018 while from National Pharmacovigilance Network meningococcal B AEFIs were selected. For every subject who have reported AEFIs a specific form was built including patient information, date of the vaccine administration, other vaccines administered in the same visit and information about AEFIs. For serious AEFIs causality assessment was carried out.

Results: From 2014 to 2018 652,793 doses of Men B vaccine have been administered and 179 AEFIs were notified with a reporting rate (RR) of 27.4x100,000 doses. 127/179 (71,0%) not serious AEFIs were reported (RR=19.5x100,000 doses), while 41/179 (22.9%) were serious AEFIs (RR=6.3x100,000 doses); 11/179 (6.1%) were undefined.

Performing causality assessment 18/41 (43.9%) serious AEFIs have a causal relationship with vaccine's administration (reporting rate = 2.8x100,000 doses). Fever and hyperpyrexia (15/18, 83%) and hypotonic-hyporeponsive episode (2/18) resulted the signs and symptoms detected in consistent AEFIs, that resulted completely resolved at the follow-up.

Conclusions: The post-marketing safety profile in our study is consistent with pre-licensure data: it should be consolidated to reinforce data of vaccine safety profile and increase people adherence to public health global strategy about vaccinations programs.
Background: There are no epidemiologic studies of Chlamydia trachomatis (CT) eye infections in infants in the United States of America (USA) that evaluate the effect of universal screening and treatment (UST) of pregnant women, as recommended by the CDC in 1993. It is unknown how the burden of eye disease caused by CT has changed in relationship to this intervention.

Methods: This is a retrospective observational study of all CT eye cultures submitted to the Chlamydia Research Laboratory at SUNY Downstate Medical Center, Brooklyn, NY. All culture reports from 1986-2002 were reviewed and analyzed according to calendar year and time period (pre-UST era = 1986-1993; post-UST era = 1994-2002).

Results: During the study period a total of 880 samples were tested by Chlamydia culture. Of these 103 were positive (11.7%). The number of submitted samples and positive cultures both declined over time. The culture positivity rate declined from 15.6% during pre-UST (1986-1993) era to 1.8% during post-UST era (1994-1998) (p<0.001).

Conclusions: The healthcare burden of infant conjunctivitis caused by CT decreased significantly in the study population since the implementation of routine CT screening and treatment of pregnant women. Our results confirm the effectiveness of this important public health intervention in the USA.
EXTENDED-SPECTRUM B-LACTAMASE-PRODUCING ENTEROBACTERIACEAE AMONG CHILDREN FROM PORTUGUESE-SPEAKING AFRICAN COUNTRIES

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Background: The production of extended-spectrum β-lactamase (ESBL) is one of the main mechanisms of Enterobacteriaceae antibiotic resistance. Resistance responsible genes are encoded into plasmids that can rearrange between themselves, making these gram-negative bacteria challenging to treat. We aim to characterize incoming patients from PSAC colonized by ESBL-producing Enterobacteriaceae in a tertiary paediatric hospital.

Methods: Descriptive analysis of patients incoming from portuguese-speaking african countries (PSAC) with culture-based detection of ESBL bacteria on colonization studies, between 2013 and 2019.

Results: In a total of 183 samples were reported 61/124 colonized patients from PSAC. Diagnosis included infectious diseases (n=23), central nervous system pathology (n=14) and tumor (n=9). The more frequent risk factors were previous antibiotic treatment (36%) and previous hospitalization (46%). Other risk factors were previous surgery/invasive procedure (36%), chronic wound (21%), immunodepression (10%) and dialysis (2%). We also identified MRSA (n=1) and carbapenemase-producing (n=1) bacteria. Moreover, 6 cases of ESBL disease were reported out of 61 colonized patients. The length of stay of colonized patients was medium 27 days.

Conclusions: Almost half of incoming patients from PSAC are colonized by ESBL bacteria that could potentially be associated with long term hospitalizations and demanding antibiotic treatment strategies.
A Rare Cause of Acute Liver Failure in an Immunocompetent Child – A Case Report

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Title of Case(s): A Rare Cause of Acute Liver Failure in an Immunocompetent Child - a Case Report

Background: In previously healthy children, acquired Cytomegalovirus (CMV) infection is usually asymptomatic. However, in 10% of the cases it may presents as a mononucleosis–like syndrome.

Case Presentation Summary: A previously healthy 7-year-old girl presented with a seven-day history of fever, prostration and abdominal distension. Six days before, she was treated with amoxicillin for a tonsillitis. Physical examination showed poor general appearance, fever, tachypnea, tachycardia, jaundice, macular rash, abdominal distension, diffuse abdominal pain and hepatosplenomegaly. Laboratory tests results: Hemoglobin 10.8 g/dL; Platelets 144,000/µL; WBC count 13,260/µL; CRP 24.3 mg/dL; AST/ALT/ALP: 177/166/334 UI/L; Total bilirubin/conjugated bilirubin 7.9/5.37 mg/dL; PT 14.7 sec; INR 1.35. Renal function was normal. Serologies (leptospira, rickettsia) and viral markers for hepatitis A, B, C and HSV were negative; EBV IgM/IgG 7.06/37.44 U/ml with EBNA 5.31 U/ml; CMV IgM/IgG 38.09/44.90 UA/ml. Abdominal ultrasound: hepatosplenomegaly, small volume ascites, right pleural effusion. During admission, she presented clinical and analytical deterioration: cholestatic hepatitis, coagulopathy (maximum INR 1.8); anemia and thrombocytopenia (Hemoglobin 10 g/dL; Platelets 27,000 /uL); hypoalbuminemia (albumin 2g/dL). The diagnosis of primary CMV infection was made by positive IgM/IgG and a highly positive PCR for CMV and she was treated with intravenous gancyclovir and ursodeoxycholic acid. After discharge, she completed a 10-week course and a 6-week-course of valgancyclovir and ursodeoxycholic acid, respectively. At two months evaluation, the patient was asymptomatic with total resolution of the anemia, thrombocytopenia, hepatitis, coagulopathy and hypoalbuminemia. CMV DNA load was undetectable.
Learning Points/Discussion: In immunocompetent children, severe complicated primary CMV infection is rare and antiviral therapy is usually not indicated. However, the present case shows a severe presentation of the disease, with hepatic involvement.
EFFECT OF PROPHYLACTIC ADMINISTRATION OF ANTIPYRETTICS IN IMMUNE RESPONSE OF ROUTINE IMMUNIZATION: SYSTEMATIC REVIEW

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Background and Objective: Prophylactic antipyretic administration at the time of immunization seems to decrease the adverse effect of vaccination. The aim of this systematic review is to assess the existing literature concerning the effect of prophylactic use of antipyretics on immune response following vaccination.

Methods: A systematic review of literature concerning the immune response to vaccines after antipyretic administration was performed. A broad search of literature until June 2019 was conducted in electronic databases of Pubmed and Scopus, as well as in clinical trials database. Randomized controlled trials that refer to children ≤18 years old were included in the study.

Learning Points/Discussion: Published studies that met the eligibility criteria concerned the following vaccines: Pneumococcus (n=5), Diphtheria-Tetanus-Pertussis-Polio-Haemophilus influenzae type b (DTaP-IPV-Hib) (n=5), Hepatitis B (n=4), Rotavirus (n=1), Meningococcus type B (4CMenB) (n=1). The prophylactic administration of paracetamol caused a significant decrease in the immune response to certain pneumococcal serotypes in 5/5 studies, pertussis toxin in 1/5 studies and tetanus (1/5). The use of ibuprofen had a negative effect on pertussis (FHA, PT) in 1/2 studies and Hepatitis B (1/2). Despite the reduction, the antibody titers remained above protective levels.
PREVENTION OF PERINATAL HEPATITIS B VIRUS TRANSMISSION: ARE WE MISSING SOMETHING?

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Background: Prevention of perinatal Hepatitis B virus (HBV) is crucial to reach WHO’s goal to eliminate viral hepatitis as a public health threat by 2030. A retrospective analysis of policies and practices to prevent HBV vertical transmission was carried out in the Italian hospital with the highest number of deliveries, after running into two infants infected despite correct perinatal immunoprophylaxis. The high viral load of their mothers was not considered in time for antiviral prophylaxis.

Methods: Paired maternal-infant medical records between 2017 and 2019 from AOU Città della Salute e della Scienza di Torino were reviewed. Data included maternal HBsAg status, HIV/HCV coinfection and the administration of prophylaxis in newborns at risk.

Results: A total of 133 newborns from HBsAg positive mothers (21.8% Italian) were identified among 21,143 newborns. In 96.2% prenatal HBsAg status was known. No other serologic markers of HBV maternal infection were reported in most cases. 130 (98%) were tested for HIV (one positive) and 60 (45.1%) for HCV (all negative). All newborns received immunoprophylaxis: 119 (89.5%) within 24 hours (63% within 12 hours), 12 (9%) between 24-36 hours and 2 (1.6%) after 36 hours.

Conclusions: Although current policies foresee immunoprophylaxis for all newborns at risk, the lack of earlier and extensive maternal serologic screening in HBsAg positive cases and late vaccination may contribute to perinatal HBV infection. Next steps: to establish a postnatal serologic check-up to exclude transmissions; to implement multidisciplinary clinical pathways for the prompt identification of HBV positive mothers; to provide timely immunoprophylaxis, up to a very early vaccination. Our proposal: a multicenter survey to provide a snapshot of the European reality to improve international guideline’s full application. Will you join us?
ACUTE GLOMERULONEPHRITIS SECONDARY TO STREPTOCOCCUS EQUI IN HORSE RIDER PATIENT

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Title of Case(s): Acute glomerulonephritis in horse rider patient

Background: St. equi is an opportunistic group C streptococcus in equine livestock. Outbreaks are uncommon and have been described in humans due to meat consumption, unprocessed milk and contact with horses. Clinically, it presents as a severe bacterial infection, commonly producing an acute glomerulonephritis (GN). Here, we describe a GN case by St. equi with good clinical evolution.

Case Presentation Summary: A healthy 12-year-old female child presenting fever and emesis of 2 weeks duration. Bilateral eyelid and lower limb edema were relevant, accompanied by dark normal volume urines. She frequently rides horses, with no history of contact with other animals and no ingestion of unpasteurized products. She presents high blood pressure (HBP) with analytical findings compatible with AGN and bilateral pleural effusion detected in pulmonary ultrasound. Rapid antigen detection test (RADT) was positive and St. equis sensitive to penicillin was isolated in pharyngo-tonsillar sample cultures. Treatment was established with hydrosaline restriction, furosemide, amlodipine and benzathine penicillin. Clinical outcome was favorable, with full renal function recovery (Table) and remission of HBP within the following 3 months.

<table>
<thead>
<tr>
<th>Date</th>
<th>Blood test</th>
<th>Urinalysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>On admission</td>
<td>Urea 84 mg/dl, Creatinine 1 mg/dl, GFR 63ml/min/1.73m²; ACR 551 mg/g. Normal ion levels. C3 11 mg/dl, C4 30 mg/dl.</td>
<td>Proteinuria 70 mg/dl; Haematuria 300 mg/dl, FENa 2.8 % ACR 551 mg/g</td>
</tr>
<tr>
<td>1 week</td>
<td>Urea 91mg/dl, Creatinine 0.9 mg/dl.</td>
<td>Proteinuria 0 mg/dl Haematuria 66 mg/dl ACR 13.2 mg/g</td>
</tr>
<tr>
<td>2 weeks</td>
<td>Urea 26 mg/dl, Creatinine 0.6 mg/dl, GFR 105ml/min/1.73m²</td>
<td>Proteinuria, Haematuria 0mg/dl.</td>
</tr>
<tr>
<td>12 weeks</td>
<td>Urea 34 mg/dl, Creatinine 0.71 mg/dl, GFR 90ml/min/1.73m²</td>
<td>Proteinuria, Haematuria 0 mg/dl ACR 7.3 mg/g</td>
</tr>
</tbody>
</table>

Learning Points/Discussion: We should consider St.equi in GN cases after exposure to horses. Unlike St. pyogenes GN, St. equi is more frequently associated with HBP and chronic renal failure.
CONGENITAL RUBELLA SYNDROME IN INFANT WITH CONGENITAL CATARACT: A 6 YEARS EXPERIENCES IN A TERTIARY HOSPITAL OF INDONESIA

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Background: Rubella infection in-utero may caused the congenital rubella syndrome (CRS) with congenital cataract as the most common ocular sign. CRS may affects ocular structures, either in isolation or in combination with other defects. This study aimed to identify laboratory confirmed CRS among infants with congenital cataract in a tertiary hospital of Indonesia.

Methods: This study was part of national surveillance of CRS in Indonesia. Infants with suspect CRS according to WHO criteria were collected from 2014-2019 in Dr. Soetomo Academic General Hospital, Surabaya, and data of congenital cataract and laboratory confirmed CRS were evaluated. Congenital cataract was diagnosed by ophthalmologist. Laboratory confirmed CRS defined as rubella IgM antibody detected for infants <6 months, while for infants 6-12 months of age, rubella IgM and IgG antibody detected, or a sustained rubella IgG antibody level on at least two occasions.

Results: We collected the data of 556 infants with suspect CRS, there were 108 (19%) diagnosed as congenital cataract. Among them, 57% were male, 74% were less than 6 months of age, and 31% were preterm. Laboratory confirmed CRS was found in 49/108 (45%) infants with congenital cataract. Two congenital anomaly were found in 43% infants, whereas 31% infants had at least three congenital anomaly.

Conclusions: Almost half of Infant with congenital cataract were due laboratory confirmed CRS, most cases had more than two congenital anomaly.
LEPTOSPIROSIS OUTBREAK IN A HILL DUE TO WATER FROM AN UNPROTECTED WELL, KEERAKADU VILLAGE, KOLLIHILLS, NAMAKKAL, TAMILNADU, INDIA, 2017.

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Background: Annually, an estimated 1.03 million leptospirosis cases lead to 2.9 million disability adjusted life years. Cluster of fever cases were reported from Keerakadu village, Kollihills in Namakkal district of Tamilnadu state, India, on 28th of April, 2017. We investigated to control the outbreak.

Methods: We did cross sectional survey. We defined a case of fever as any resident of Keerakadu with fever for more than two days, with or without headache or myalgia, between 15th of April and 1st of May, 2017. We did active surveillance. We reviewed medical records. We computed proportions to calculate attack rate. We collected 11 serum samples and tested for dengue, scrub typhus, Hepatitis A and Leptospirosis by IgM ELISA method. We did Widal slide agglutination test. We interviewed for water sources and did dengue larval survey. We collected 5 water samples - one from unprotected well, one from overhead tank and three from houses. We tested water samples for faecal coliforms.

Results: Population was 540. We identified 11 cases. Attack rate was 2% (11/540). Hospitalisation rate of cases was 81%(9/11). Median age was 45 years. Three out of eleven samples were positive for leptospirosis. All were negative for dengue, scrub typhus, Hepatitis A and typhoid. Water from an unprotected well was the only water source. There was no breeding of dengue larva. All five water samples were positive for faecal coliforms. Water was not chlorinated regularly. All patients were isolated and treated in primary health center. Prophylactic antibiotics were given to the whole community.

Conclusions: There was leptospirosis outbreak in Keerakadu, probably due to unprotected well water. We recommend to chlorinate the well water regularly and protect the well. We also recommend continued surveillance and rodent survey.

Clinical Trial Registration: This is not clinical trial study.
EPSTEIN-BARR VIRUS INDUCED MEDULLOMYELORADICULITIS

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Title of Case(s): EPSTEIN-BARR VIRUS INDUCED MEDULLOMYELORADICULITIS

Background: Neurologic complications of Epstein-Barr virus (EBV) infection in previously healthy individuals are rare but very heterogeneous - meningitis, encephalitis, cerebellitis, myelitis, cranial nerve palsies, radiculopathies, Guillain-Barré syndrome, sleep and behavioral abnormalities.

Case Presentation Summary: A previously healthy two-year-old girl was admitted to intensive care unit in Angola with progressive respiratory difficulty, somnolence and fever. Neurological examination revealed aphonia, hypotonic and hyporeflexic tetraparesis (predominantly right), and lower limb dysesthesia. CSF analysis showed pleocytosis and elevated protein and one cycle of intravenous immunoglobulin (IVIg) was done. After two weeks, she was transferred to our centre in order to perform additional investigation. Electromyography was compatible with an acute motor polyneuropathy. Brain and spine MRI revealed an extensive T2-hyperintense lesion in the posterior region of medulla oblongata and myeloradiculitis (T2-hyperintensity from C3-C4 to conus medullaris, with enhancement in cervical and conus medullaris segments), with remarkable anterior horns involvement from C3-C7 to D10-D12, as well as enhancing ventral roots of the cauda equina. CSF and serum PCR analyses revealed EBV DNA (2100 and 270000 copies/mL, respectively). Other active infections, neoplastic diseases and autoimmune causes were ruled out. Two additional IVIg cycles and corticotherapy were performed and treatment included a 35-day course of acyclovir. Tracheostomy was performed, due to respiratory insufficiency progression. Nevertheless, there was global clinical improvement; intensive physical rehabilitation provided an important recovery of function and muscle strength. Currently, serum EBV is 11000 copies/mL.

Learning Points/Discussion: The pathogenesis of EBV nervous system infection is not fully understood but probably involves direct viral invasion and indirect immune effects, which can have therapeutic implications. Although there is no therapy targeted to EBV with established efficacy, our patient improved after IVIg and acyclovir in line with some cases reported in literature.
Impact of BioFire® FilmArray® Meningitis/Encephalitis in Aseptic Meningitis in Children

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Background: Cerebrospinal fluid culture and viral PCR are the current standard of care to diagnose bacterial and viral meningitis/encephalitis. These methods need 3 days to provide a result. BioFire® FilmArray® Meningitis/Encephalitis, instead, identifies the pathogen precisely in about an hour; early diagnosis and correct therapy improve the outcome.

Methods: We analyse the length of hospitalization and duration of antiviral therapy in children with aseptic meningitis, in pediatric infectious disease department (Policlinico Umberto I, Rome) through a retrospective cohort study. We focused on children hospitalized from 1st January 2014 to 31th December 2017 (when only herpetic virus PCR was available) and from 1st January 2018 to 31th December 2019 (when FilmArray® was available). A total of 38 children with aseptic meningitis included: 16 in the first period, 22 in the second. Non parametric Mann-Whitney test was used.

Results: In the first group, there was no isolated pathogen using PCR and 15 of these received aciclovir for 3 days each, waiting for PCR results (total: 45 days). In the second group, when FilmArray® was available, there was pathogen isolation in 86% of cases (16 enterovirus, 3 HHV-6). Four received aciclovir, for a total of 16 days. The duration of therapy is different between two groups (p<0.0001). Furthermore, the length of hospitalization was different in two groups (p<0.0001): median in the first was 9.5 days (range 6-16 days); median in the second was 6 (5-12 days).

Conclusions: This analysis suggests that BioFire® FilmArray® allows patients to discharge faster than using traditional diagnostic methods and to administer correct therapy immediately, bringing benefits to patients and saving in healthcare costs.
Differences in Length of Inpatient Stay in Children with Sepsis-Like Syndrome Between European Countries – Results from the PED-Mermaids Prospective Cohort Study

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Background: Sepsis-like syndrome (SLS) in infants is of diverse aetiology and causes considerable morbidity. Comparative studies on management and aetiology applying the same protocols across European countries are rare.

Methods: The EU-funded Paediatric Multi-centre EuRopean study of MAjor Infectious Disease Syndromes (PED-MERMAIDS) enrolled infants below the age of 6 months hospitalised for SLS across 11 EU countries. Information on symptoms, course of disease and management was collected prospectively. Admission day nasopharyngeal swabs, CSF and blood samples were analysed for viral and bacterial pathogens by multiplex PCR.

Results: 121 SLS infants, median age 0.13 years (interquartile range, IQR 0.07-0.24) were enrolled over 2½ years. 97 infants (88.8%) infants presented on the first day of symptoms. On admission, 33 (27.3%) presented with fever >39°C, 72 (59.5%) with poor feeding, 21 (17.4%) with tachypnea and 29 (24.0%) with prolonged capillary refill time. 105 (86.8%) received antibiotics, 11 (9.1%) required supplemental oxygen, 55 (45.5%) received intravenous fluids and 8 (6.6%) were managed on ICU. A lumbar puncture was done in 76 (62.8%). One child (0.8%) in the study died after admission for SLS. Length of stay (LOS) in hospital ranged between <1 and 47 days (median 3, IQR 2-6) and was different by country of admission (see table, p<0.001). A potential pathogen was detected on respiratory swabs in 76 children (62.8%), most frequently detected were human rhinovirus in 29 (17%), RSV in 9 (7.4%) and enterovirus in 8 (6.6%). CSF and blood sample analyses are in progress.

<table>
<thead>
<tr>
<th>Patient n</th>
<th>Spain</th>
<th>Greece</th>
<th>UK</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (IQR)</td>
<td>0.11 (0.06-0.17)</td>
<td>0.11 (0.08-0.23)</td>
<td>0.16 (0.07-0.27)</td>
<td>0.13 (0.07-0.24)</td>
</tr>
<tr>
<td>Poor feeding</td>
<td>11 (42.3%)</td>
<td>11 (52.4%)</td>
<td>46 (71.9%)</td>
<td>72 (59.5%)</td>
</tr>
<tr>
<td>Tachypnea</td>
<td>4 (15.4%)</td>
<td>6 (29.6%)</td>
<td>11 (17.2%)</td>
<td>21 (17.4%)</td>
</tr>
<tr>
<td>Supp. oxygen</td>
<td>3 (11.5%)</td>
<td>0 (0.0%)</td>
<td>7 (10.9%)</td>
<td>11 (9.1%)</td>
</tr>
<tr>
<td>IVF</td>
<td>11 (42.3%)</td>
<td>14 (66.7%)</td>
<td>22 (34.4%)</td>
<td>55 (45.5%)</td>
</tr>
<tr>
<td>ICU</td>
<td>6 (23.1%)</td>
<td>0 (0.0%)</td>
<td>1 (1.6%)</td>
<td>8 (6.6%)</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>18 (69.2%)</td>
<td>18 (85.7%)</td>
<td>61 (95.3%)</td>
<td>105 (86.8%)</td>
</tr>
<tr>
<td>LP performed</td>
<td>15 (57.7%)</td>
<td>8 (38.1%)</td>
<td>51 (79.7%)</td>
<td>76 (62.8%)</td>
</tr>
<tr>
<td>LOS (IQR)</td>
<td>3.5 (3-7.5)</td>
<td>5 (3.5-6.5)</td>
<td>2 (2-3)</td>
<td>3 (2-6)</td>
</tr>
</tbody>
</table>

10 children were enrolled across 7 other participating countries and are not shown in the table except in the “total” column.

IQR: interquartile range, IVF: intravenous fluids, ICU: intensive care unit, LP: lumbar puncture, LOS: length of inpatient stay
Conclusions: Characteristics of presentation and management in children with SLS differ between European countries but outcome is generally good. The difference in LOS is unadjusted for aetiology and severity of disease at presentation, a multivariate analysis is in progress.

Clinical Trial Registration: observational, not registered
Title of Case(s): Murphy's law: One patient, many diagnosis

Background: Complications can develop when patients with prolonged chronic diseases have been subjected to inadequate, or even unknown, treatment. This can make patient management even more challenging. Osteomyelitis is an example of a disease whose diagnosis is complex. The treatment is difficult to achieve, requiring long term antibiotic therapy. Nonetheless, it has a high morbidity rate, especially if not properly treated.

Case Presentation Summary: Fifteen years-old male from Angola, newly arrived to Portugal, with a history of tuberculosis (TB) allegedly treated. He presented draining fistulas and edema in his left thigh. He also complained of weight loss and a cervical mass. Facial edema and high blood pressure were presented and complementary exams revealed nephrotic-range proteinuria, microcytic hypochromic anaemia, thrombocytosis, high sedimentation rate (92mm/h), C-reactive protein (61.1mg/dL) and high serum creatinine levels (1.04 mg/dL). The lower limb CT showed chronic femur osteomyelitis. Due to MRSA isolation, he was treated with linezolid, debridement and antibiotic impregnated femoral intramedullary nail. Additionally, IGRA was positive and the thorax CT showed a right hilar adenopathy with calcifications. Since the previous treatment was unknown, TB was assumed and started anti-TB therapy. The renal ultrasound revealed an increased echogenicity of the kidney parenchyma and reduced corticomedullary differentiation, in favour of nephropathy. Afterwards, the renal biopsy clarified the presence of amyloid deposits, secondary to a chronic inflammation process.

Learning Points/Discussion: Amyloidosis results from the accumulation of pathogenic amyloids in different tissues. Although rare, amyloidosis can occur, and is usually caused by chronic inflammation. In the presented case, it is likely that chronic osteomyelitis and untreated TB might have played a role. This highlights the importance of connecting all data to reach a diagnosis and the best treatment for each patient.
Background: Due to the large number of cases of measles diagnosed in the last years, due to the continuous poor vaccination coverage, Romania was at the center of public attention. The objectives were to identify demographic and epidemiologic characteristics, the clinical evolution and to assess the frequency of complications of children diagnosed with measles in an infectious disease hospital, during the outbreak.

Methods: We performed a retrospective study, on a group of children with measles, admitted to ``Dr. Victor Babes'' Infectious and Tropical Diseases Clinical Hospital, from Bucharest, Romania, between January 2016 and March 2019. Epidemiological data, clinical characteristics and the results of the biological samples were obtained from the patient's medical records.

Results: Out of the 1041 patients, 555 (53.31%) were males. Most of them (39.19%) were children, between 1 and 4 year-old, while 301 (28.91%) were infants. More than half of the children (52.54%) were unvaccinated. 795 (76.36%) were diagnosed with interstitial pneumonia. Bacterial pneumonia was diagnosed in 13.83% patients out of which 20.12% were also associated with respiratory failure, requiring oxygen therapy, corticotherapy and antibiotics. 8 patients required transfer to the pediatric intensive care unit for respiratory support, and 2 died. Other complications were enterocolitis (60.51%), laryngitis (13.35%), otitis (13.35%), liver cytolysis (16.33%) and thrombocytopenia (32.56%).

Conclusions: The number of children diagnosed with measles registered an alarming increase, especially in children under 4 year-old, with a high number of complications with favorable evolution. We consider it mandatory to apply the vaccination program to ensure an optimal vaccine coverage, useful both in stopping the current outbreak and in preventing future outbreaks.
Background: Adverse event following immunization (AEFI) might be a cause for hesitancy and immunization delay.

Methods: Children up to 10 years who developed an AEFI and were referred to our immunization center from November/2018 to June/2019 were invited to participate in the study. At enrolment, a photo of the child’s immunization records was taken. After four months, parents received a phone call, were asked to answer a questionnaire and a photo of the child's vaccination records. Another phone call was made to parents of children whose record were not up-to-date at the second assessment and a third photo of the child's vaccination records was asked.

Results: Thirty-seven children were included (median age: 10 mo; range 2-51). AEFI were assigned into 4 groups: BCG; whole pertussis vaccine, immunoallergic events and MMR(Table). At enrolment, 24/37 (64.9%) children were up-to-date with vaccine records; at the first call, 17/37 (45.9%) children were up-to-date. There were 6 cases of vaccine hesitancy, 3 of them reversed with counseling. In most cases, however, vaccine delay was associated with necessity to dismember Pentavalent vaccine components (DTwP+Hib+Hepatitis B) due to unavailability of combined vaccine with acellular pertussis component at the immunization center or the need to administer vaccine antigens on different days in immunoallergic phenomena.
Conclusions: Vaccination delay is frequent after AEFI but usually not due to vaccine hesitancy; children who develop them should be closely followed-up by professionals trained in the management of these situations.
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Title of Case(s): Toddler presenting with emesis and oedema

Background: Protein loosing gastroenteropathy (PLE), known also as Menetrier’s disease, is uncommon for children and the etiology is uncertain. It has been rarely described. The childhood forms, have benign and transient course and require only supportive treatment. Cytomegalovirus (CMV) is the most common pathogen among children. We report a case of a 13 month old boy with episodes of vomiting and edema.

Case Presentation Summary: The boy had fever and rhinitis for three days and the next day presented with episodes of vomiting, periorbital and lower limbs edema. The rest physical examination was unremarkable. From blood examinations Na and total Ca were low, but the K, urea, creatinine, transaminases, CRP, total blood count and cholesterol were normal. Total protein was 3.3g/dl (3.7-7.5) and Albumin 1.4g/dl (1.9-5.0). Urine test was normal. Stool test was positive for blood. As liver and renal disease were excluded, the patient proceeded gastroscopy and colonoscopy. Mucosal biopsy findings were typical of PLE (Menetrier’s disease). Immunohystochemic procedures of the mucosa were negative for CMV and Helicobacter Pylori. CMV immunoglobulin G and M were detected in the serum. The child was treated with Intravenous Human Albumin once. Then he was under high protein diet and Omeprazole. After one month edema and hypoalbuminemia had subsided.

Learning Points/Discussion: PLE in children has been correlated with CMV infections and they are considered as the most common cause. Detection of the virus in the mucosa immunohistochemically, or by PCR can confirm its causative role. In our case CMV infection was serologically proved and clinically supported by the preceded febrile infection. Causative relationship was not justified. However, since no other cause was suspected, we could consider CMV infection as the cause of PLE.
HIGH PREVALENCE OF COMMUNITY-ACQUIRED METHICillin-RESISTANT STAPHYLOCCUS AUREUS BACTEREMIA IN A PEDIATRIC POPULATION

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Background: Several studies have shown an increasing incidence of Community-Acquired Methicillin-Resistant Staphylococcus Aureus (CA-MRSA) infections in adult and pediatric populations since 1990. Prevalence of CA-MRSA infections worldwide is highly variable, ranging from zero to 70% in some regions. Few studies have investigated the prevalence of CA-MRSA in children, especially in Brazil. Our study aimed to determine the frequency of CA-MRSA bacteremia in pediatric patients at a tertiary hospital in São Paulo, Brazil.

Methods: Retrospective study of positive blood cultures for S. aureus isolates of pediatric patients at Santa Casa de São Paulo Hospital, from 2014 to 2017. We defined CA-MRSA according to antibiotic susceptibility: resistant to oxacillin and < 4 antibiotic class. Bacteremia was considered healthcare associated if the patient had a positive blood culture after 48 hours of hospitalization, and any of the following: hospitalization, surgery, comorbidities or indwelling percutaneous devices or catheters in the last year.

Results: Of 106 episodes of S. aureus bacteremia, 38.6% were MRSA, 75.6% considered CA-MRSA. According patient epidemiology, only 16 episodes were considered community, with 18.8% MRSA, all CA-MRSA; and 90 were healthcare associated infections, with 42.3% MRSA, 73.7% CA-MRSA.

Conclusions: We observed a high prevalence of MRSA both in community and in healthcare associated infections. It is interesting that most episodes of healthcare associated infections were caused by CA-MRSA. These data are very important when considering empirical antibiotic therapy.
EPIDEMIOLOGY AND MANAGEMENT OF SEXUALLY TRANSMITTED INFECTIONS IN CHILDREN AND ADOLESCENTS IN A HEALTH AREA IN MADRID (SPAIN)

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**Background:** Sexually transmitted infections (STI) are increasing over the last years, probably due to changes in sexual behaviour and a lower use of condoms. The aim of our study is to describe the characteristics and management of STI in children and adolescents in our health area in Southern Madrid, Spain.

**Methods:** Swabs for microbiological STI evaluation (PCR for Chlamydia trachomatis, Neisseria gonorrhoeae, Mycoplasma genitalium or HSV) during a 6-month period (June-November 2019) from patients <20 years were selected. Patient's data, microbiological results and management were analysed.

**Results:** The 155 enrolled patients formed 3 groups: adolescents with symptoms/risk behaviour (86.4%;median age 18 years), newborns with oftalmia-neonatorum (8.9%;median age 11.5 days) and children with sexual abuse (4.5%;median age 5 years). Samples came from emergency-room(38.6%), primary care(32,5%) and gynaecological consultations(13,2%). 48.2% of patients with symptoms were treated empirically, mainly with ceftriaxone+azithromycin. Microbiological result was positive in 66 samples (42,5%,figure1). 31,8% infections were mixed. 24.2% of confirmed infections were never treated. STI serologies were performed in 40,4% of patients and pregnancy tests in 16,6% of indicated cases.

<table>
<thead>
<tr>
<th>Positive results</th>
<th>66 (42.5%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlamydia trachomatis</td>
<td>62.1%</td>
</tr>
<tr>
<td>Neisseria gonorrhoeae</td>
<td>34.8%</td>
</tr>
<tr>
<td>Mycoplasma genitalium</td>
<td>22.7%</td>
</tr>
<tr>
<td>HSV</td>
<td>18%</td>
</tr>
</tbody>
</table>

**Conclusions:** Management of STI in adolescents in our health area needs improvement. Empirical treatment and complementary studies should be empathized in this vulnerable population.
A TRICKY DIAGNOSIS OF MYCOPLASMA PNEUMONIAE-INDUCED RASH AND MUCOSITIS (MIRM)

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Title of Case(s): A Tricky Diagnosis Of Mycoplasma Pneumoniae-Induced Rash and Mucositis (MIRM)

Background: Mycoplasma pneumoniae is a common cause of respiratory tract infections. Although the majority of infections are mild, 25% of patients experience extrapulmonary complications, including severe mucocutaneous blistering complications. MIRM was first described as a distinct clinical entity in 2015 (Canavan and colleagues). MIRM should be considered in children who present with oral (94%), ocular (82%) or urogenital lesions (63%) with few scattered skin lesions.

Case Presentation Summary: We report the case of a previously healthy 11-year-old boy who presented with a seven-day history of progressive conjunctivitis and diffuse erosions of the tongue, oropharynx, and lips, with superimposed crusting followed by rare erythematous papulovesicular on the forehead, foot and abdomen. The boy presented worsening cough five days earlier and he was treated with clarithromycin because clinical evaluation and Chest X-ray demonstrated possible Mycoplasma Pneumoniae infection. Laboratory examination revealed a markedly positive Mycoplasma pneumoniae IgM titer and high seropositivity of IgG titer one month later. The patient was diagnosed with Mycoplasma pneumoniae-induced rash and mucositis (MIRM) and he was treated with supportive care leading to a complete clinical remission within a week.

Learning Points/Discussion: Distinguishing between infection-triggered MIRM and drug etiologies of SJS may be clinically useful for evidence based treatment strategies. Drug-induced Stevens–Johnson syndrome (SJS) is associated with significant morbidity and mortality. In contrast, MIRM's morbidity is less alarming and supportive care less complex.
TIMING OF OSELTAMIVIR IMPLEMENTATION DOES NOT INFLUENCE OUTCOME OF INFLUENZA-RELATED PNEUMONIA IN HOSPITALIZED CHILDREN

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Background: Earlier oseltamivir implementation reduces risk of influenza complications, especially in adults. Here, we aimed to assess how the period between fever duration and oseltamivir implementation influences effects of treatment in children hospitalized due to influenza-related pneumonia.

Methods: We retrospectively analyzed children hospitalized in 2015/2016 to 2018/2019 influenza seasons due to pneumonia and confirmed influenza. We verified if earlier (i.e. up to 48, 72, 96 and 120 hours from the start of fever) oseltamivir implementation would decrease risk of antibiotic treatment, intensive care unit (ICU) transfer, time for defeverscence or length of stay (LOS).

Results: Eighty-four children aged 18 days-17 years were eligible for the analysis. Earlier oseltamivir implementation did not decrease the risk of ICU transfer, nor time for defeverscence in a multiple regression model. Interestily, patients with later treatment implementation were at lower risk of antibiotic treatment (OR=0.17, 95%CI: 0.04-0.69, p=0.013; OR=0.24, 95%CI: 0.06-0.98, p=0.047; OR=0.014, 95%CI: 0.03-0.57, p=0.006; and OR=0.23, 95%CI: 0.07-0.76, p=0.016 for consecutive timing groups). Similarly, there was an inverse correlation between treatment timing and LOS (r=-0.39).

Conclusions: Earlier oseltamivir implementation in children with pneumonia does not influence disease outcome as expected. Thus, oseltamivir treatment should be considered irrespective of duration of fever.
MYCOPLASMA INDUCED MUCOSITIS: A CHALLENGING DIAGNOSIS

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Title of Case(s): AN ATYPICAL STEVENS-JOHNSON SYNDROME, IT IS NOT WHAT IT SEEMS

Background: Mycoplasma pneumoniae Induced Rash and Mucositis (MIRM) is a recently described clinical entity mimicking Stevens Johnson Syndrome (SJS). Two mucosal sites affected, minimal skin involvement with scattered atypical targets and an underlying Mycoplasma pneumoniae infection are the mainstays for this rare diagnosis. MIRM carries a favorable prognosis with low recurrence and mortality.

Case Presentation Summary: A 7 years-old boy was admitted to our Pediatric Emergency Department for high fever since eight days, vomit and painful stomatitis resistant to beta-lactam and antiviral administration. Inspection highlighted oral and ocular mucositis with hemorrhagic crusts on the cheeks and genital area. Blood examinations showed leukocytosis (19,400/µL) and elevated C reactive protein (10.84 mg/L). Differential diagnosis included SJS, Kawasaki Disease and Herpes infection. Chest X-rays documented an interstitial involvement. Echocardiography was normal and the mucosal swab resulted negative for Herpes virus infection. Serology for a wide panel of viral infections and immunological investigations were negative but nasopharyngeal aspirate pointed out M.pneumoniae infection, allowing the diagnosis of MIRM. First line treatment with clarithromycin, systemic steroids and supportive care (intravenous hydration and analgesia) did not result in a significative improvement of mucositis. Seven days later, we administered intravenous immunoglobulins (IVIG) and started topical laser therapy with positive clinical response. The patient was discharged after 10 days from admission in good conditions.

Learning Points/Discussion: Prompt recognition of MIRM is critical to start adequate therapy and to avoid painful and disabling complications such as synechiae. Moreover, response to IVIG instead of specific antimicrobial treatment raises suspicion on an autoinflammatory pathogenesis. Since there still no clear indications concerning MIRM in literature, more data are needed to better characterize this condition and to identify the ideal therapeutic approach.
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E-POSTER VIEWING - ALL OTHER TOPICS
10-28-2020 8:00 AM - 7:00 PM

PREDICTIVE VALUE OF RENAL ANGINA INDEX FOR ACUTE KIDNEY INJURY IN HOSPITALIZED CHILDREN WITH INFECTIONS

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Background: Identification of acute kidney injury (AKI) in patients early-on helps in timely initiation of appropriate treatment. Based on serum creatinine alone, 67.2\% cases of AKI with low urine output were missed. Renal Angina Index (RAI) is a clinical scoring method for risk stratification of patients for the development of severe AKI. We aimed to study the diagnostic accuracy of RAI calculated on day 0, to predict the development of AKI on day 3, among children admitted in pediatric emergency (PE)/ PICU with infections.

Methods: Consecutive children (2 months –14 years) with hospital stay > 6 hours were prospectively enrolled over one year. Demographic and clinical data was collected for all eligible children till discharge or death. Day0 RAI was calculated to predict Day3 AKI (defined as per KDIGO criteria). RAI is the product of risk of AKI and signs of renal injury. The score varied from 1-40 and a score > 8 was interpreted as positive for RAI. AUROC curves were constructed to calculate the discriminative ability of day0 RAI to predict day3 AKI.

Results: Of a total of 220 children who were admitted to PE/PICU and observed for development of AKI, 81 (36.8\%) children suffered from infections. Tropical infections were predominant (36\%), followed by acute respiratory illness and acute gastroenteritis (16\% each), sepsis and acute CNS infections (15\% each) and Urinary tract infections (2.5\%). Median age of the children was 42 months (IQR 8,96). Eleven children (13.5\%) developed AKI. AUROC for day0 RAI to predict day3 AKI was 0.49 (95\%CI:0.31-0.68).

Conclusions: Day 0 RAI did not predict development of day 3 AKI amongst hospitalised children with infectious illnesses.
UNUSUAL PERITONITIS: A CASE OF OMENTAL TUBERCULOSIS IN A HIV-NEGATIVE CHILD

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Title of Case(s): Unusual peritonitis: a case of omental tuberculosis in a HIV-negative child

Background: In 2018 WHO estimated TB incidence in Europe in 28 cases per 100000 and in 7 per 100000 in Italy. Peritoneal TB accounts for about 0.1%-0.7% of all cases of TB.

Case Presentation Summary: A 12-years-old boy was admitted to the hospital with a 4-days history of high fever and diarrhoea. History revealed a recent travel to Morocco. Vital signs were within the normal ranges, body temperature up to 39°C. Physical examination revealed ascites. Complete blood count, renal and hepatic tests were normal. C-reactive protein was 22.59 mg /dl and procalcitonin 2.1 ng/mL. Chest X-ray report was negative. Abdominal ultrasonography confirmed huge ascites all troughout abdomen and pelvis without any other abnormal finding. Blood cultures resulted negative, as well as microbiological tests on blood, stool, urine and sputum. Ceftriaxone plus metronidazole were given for 7 days and thereafter azithromycin and piperacillin/tazobactam, without improvement. The child lost weight, developed anemia and hypoalbuminemia. Paracentesis was performed: ascitic fluid resulted rich in lymphocytes, with 4.7 gr/dL protein content but negative for acid-fast bacilli as well as for M. tuberculosis Protein-Chain-Reaction. Mantoux tuberculin skin test turned 14 mm large and Quantiferon TB-PLUS positive. Therefore chest and abdominal CT displayed colliquated hilar lymphadenopathy (18 mm) and subpleural consolidation (15 mm) in the right lung, huge omental thickening with increased vascular enhancement, peritoneal hyperemia without nodular lesions, no abnormalities of bowel loops and large amount of diffuse ascites. Omental biopsy was decided and confirmed the diagnosis of TB. Subsequently M. tuberculosis grew from ascitic fluid and peritoneal biopsy. No antitubercular drugs resistance was found.

Learning Points/Discussion: When omental TB is highly suspected, biopsy could be a safe and fast diagnostic test to confirm the diagnosis and suddenly start antitubercular therapy.
**Background:** Clinical trials (CT) performed with home self-collected nasal swabs for the detection of acute respiratory infections (ARI) in young children have not been published in Spain. Demonstrating the ability of parents to take the nasal swabs is very important to decide to perform remote decentralized trials. We conducted a pilot study to assess the feasibility of nasal swabs collected by parents in children aged 12-35 months.

**Methods:** During the influenza season 2019-2020, parents recorded the presence/absence of 7 respiratory symptoms in a daily-diary using an ad hoc App. Based on the introduced data, the App detected an ARI episode and requested to take a nasal swab either at home or at Primary Care Centre. Swabs were subsequently analysed (PCR) for the presence of 8 respiratory viruses. Home self-collected nasal swabs and their validity (enough DNA sample for it detection) was analysed.

**Results:** A total of 48 subjects were enrolled in the study and fulfilling the app. Of them, 38 ARI episodes were detected and 38 swabs were analysed. 34 (89%) of the analysed swabs were home self-collected and 30 of them (78%) were valid. 4 swabs (10%) were taken in the Primary Care Centre. The results will be updated at the end of the current influenza season.

**Conclusions:** Home self-collected nasal swabs taken in young children by parents has demonstrated to be an effective methodology for the development of CT. This strategy provides a novel approach for clinical diagnostics and surveillance of respiratory virus infection in remote decentralized CT. The development of remote decentralized CT could reduce substantially the number of surveillance visits and, therefore, improve the adherence in CT.

**Clinical Trial Registration:** Nº EUDRACT: 2019-001186-33
DIRECT-ACTING ANTIVIRALS FOR CHILDREN WITH CHRONIC HEPATITIS C: A BRAZILIAN SINGLE CENTER EXPERIENCE

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Background: Hepatitis C virus (HCV) chronic infection affects approximately 3.5 million children under 15 years globally. Until recently there was no direct-acting antiviral (DAA) regimen approved for children. In 2018, Brazil’s Ministry of Health approved DAA for children older than 12 years or weighing more than 35Kg. The aim of this study was to describe clinical profile and treatment with DAAs in Brazilian pediatric patients.

Methods: We conducted an observational prospective cohort at Pediatric Hepatology outpatient service in a Brazilian tertiary care center. HCV chronically infected patients were included. Eligible candidates to DAA treatment received ledipasvir-sofosbuvir fixed-dose combination tablet (90mg-400mg) once daily for 12 weeks for genotype 1 and sofosbuvir 400mg plus ribavirin 1g daily for 24 weeks for genotype 3. We analyzed clinical profile, side-effects and treatment response.

Results: Forty HCV infected children were evaluated: mean age 12y [4-18], 50% females, 2 HIV co-infected (5%), vertical transmission (97.5%), genotype 1 (95%), genotype 3 (5%), no known cirrhosis. Currently only 25 patients are eligible for DAAs, 60% treatment-experienced. DAA has been initiated for 10 patients, 4 still ongoing. Side-effects were transient and non-severe: headache (60%), nausea (30%), fatigue (20%) and diarrhea (10%). HCV-RNA was negative in week-12 for all patients that completed treatment. HCV-RNA in week-24 will be performed to confirm sustained virologic response (SVR).

Conclusions: DAAs approval for pediatric population in Brazil represents the beginning of a new era in treatment options of chronically HCV infected children. In our study, we observed high tolerability and excellent response to DAAs, with rapid HCV-RNA decline. We enlighten the importance of children and adolescents to be targeted for Hepatitis C treatment as part of the global strategies for the elimination of this disease.
 WHEN A DIAGNOSTIC DELAY PRODUCE A WATERFALL OF IMMUNOLOGICAL EVENTS AND INFECTIOUS RESOLUTION

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Title of Case(s): When a diagnostic delay produce a waterfall of immunological events and infectious resolution

**Background:** Mother-to-child transmission (MTCT) rates for women diagnosed with HIV infection have fallen to around 1–2% in recent years in developed countries. Nevertheless, the world-wide rate of MTCT of HIV is still far from reaching the zero transmission target, even in countries with consolidated screening programmes and standardized protocols of HIV management during pregnancy.

**Case Presentation Summary:** Peter is an 11-month caucasian baby. He was born with normal delivery. His mother had rare medical checks during pregnancy giving in anamnesis an episode of persistent lymphadenopathy. The child’s infective episode have started prematurely with a slow resolution. The suspects were of milk intolerance. At the age of 5 months the baby was admitted in hospital for a breath distress treated with mechanical ventilation. The blood test showed high platelet count, Hypergammaglobulinemia and hypertransaminasaemia. The Chest X Ray showed Interstitial Pneumoniae. CMV culture positive was treated. He delayed neuromotor development and hypoacusia was diagnosed. At 11 m. of age in a recovering for a resistant pneumonia blood test showed anaemia and lymphopenia with a very low value of CD4+. Finally, HIV RNA was detected (> 10.000.000 copie/ml) Lopinavir/Ritonavir, Raltegravir and Lamivudina was started. The follow up of opportunistic infection showed Cryptococcus Neoformans. For the worsening of the breathing dynamic a cortisonic therapy was started improving the clinical breath condition but producing a Cushing Syndrome with persistent hypertension. TDM (Therapeutic Drug Monitoring) balanced the entire therapy.

**Learning Points/Discussion:** Pietro was dismissed after a 4 month recovering presenting actual good clinical conditions. The late diagnosis has generated strong clinical manifestations (neurological delay, LIP, immune deficit and infections) and has exposed the baby to the serious danger of a Drug-Drug interaction. Therapeutic Drug Monitoring has allowed the checking and the containing of a possible therapeutic failure.
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SUCCESSFUL OUTCOME OF EXTENSIVELY-DRUG RESISTANT PSEUDOMONAS AERUGINOSA VENTILATOR ASSOCIATED PNEUMONIA TREATMENT WITH CEFTOLOZANE-TAZOBACTAM IN AN INFANT

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Title of Case(s): SUCCESSFUL OUTCOME OF EXTENSIVELY DRUG RESISTANT (XDR) PSEUDOMONAS AERUGINOSA INFECTION WITH CEFTOLOZANE-TAZOBACTAM IN AN INFANT

Background: Emergence of extensively drug resistant (XDR) Gram negative bacteria is a major public threat. Therapeutic treatment options for these bacteria are extremely limited to ≤2 antimicrobial agents (including colistin) for which few or no efficacy/safety data exist. The aim of this study is to describe the successful treatment outcome of an XDR Pseudomonas aeruginosa Ventilator-associated pneumonia (VAP) in a 10-month old boy using ceftolozane - tazobactam, a newly developed antibiotic with activity against XDR P. aeruginosa.

Case Presentation Summary: A 10-month old boy was admitted to Pediatric Intensive Care Unit (PICU) after surgical oesophageal atresia repair. He was intubated and had a central venous catheter (CVC) in place. On day 34 of hospitalization he suffered from surgical site infection due to P. aeruginosa showing resistance to all antimicrobials except colistin and intermediate resistance to piperacillin/tazobactam. Colistin and piperacillin/tazobactam were used for treatment. On day 46 of hospitalization the patient developed Ventilator-associated pneumonia (VAP) due to XDR P. aeruginosa with similar antimicrobial susceptibility testing. The patient presented with high fever and C-reactive protein (max 135mg/l). Due to clinical deterioration, ceftolozane-tazobactam was added to the antimicrobial regimen at a high dose of 50mg/kg per dose every 8hours in a 60 min infusion, whereas piperacillin-tazobactam was discontinued. The isolate was fully susceptible to ceftolozane-tazobactam. Colistin was discontinued and patient showed significant improvement.

Learning Points/Discussion: Treatment of infections caused by XDR-Gram negative bacteria in children is challenging. Administration of ceftolozane-tazobactam in a higher than recommended dose (30mg/kg/dose every 8h) could be efficacious against VAP caused by in vitro susceptible XDR-P. aeruginosa without any significant adverse effects.
INFLUENZA VIRUS INFECTION IN CHILDREN ADMITTED TO A PAEDIATRIC INTENSIVE CARE UNIT

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Background: Influenza virus infection is common in children. Severe cases requiring intensive care are poorly characterized. The objective of this study was to describe all children with influenza infection admitted to a paediatric intensive care unit (PICU).

Methods: Exploratory study with retrospective data collection of all paediatric patients with a respiratory specimen positive for seasonal influenza A or B virus, admitted to PICU between 2009 and 2019. Demographical and clinical data and outcomes were collected. We performed comparisons between data from patients with and without multiple organ failure (MOF). Statistical analysis was performed using the SPSS 26.0 software.

Results: Over an 11-year period, 31 children with influenza infection required PICU admission. The median age was 3.5 years old. From November to March occurred 90% of cases. The rate of acute respiratory distress syndrome was 19% and 13% encephalitis. 55% had comorbidities. Influenza A was the most common type in 87%. Coinfection was detected in 45%. 61% needed mechanical ventilation with a median duration of 7 days. 94% received antiviral therapy, 36% steroids and 29% vasoactive drugs. Three children died. Patients with MOF had significantly higher C-reactive protein levels at admission and maximum procalcitonin (p<0.05).

Conclusions: The majority of children had comorbidities but despite this fact the mortality rate was lower than reported in literature. Factors related to MOF have previously been assessed in other studies. In our study raised inflammatory markers were associated with MOF.
A PROSPECTIVE COHORT STUDY TO ASSESS WHETHER PRETERM INFANTS CAN BE PROTECTED BY A DELAYED 2+1 VACCINATION SCHEDULE FOLLOWING SECOND TRIMESTER MATERNAL PERTUSSIS IMMUNIZATION.

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Background: Late 2019, the Netherlands implemented maternal Tdap vaccination to protect newborns against pertussis. Maternal vaccination replaces the first infant vaccination who may then be vaccinated according to a 2+1 DTaP-IPV-Hib-HBV schedule at 3-5-11-months, instead of a 3+1 schedule at 2-3-5-11-months. This was based on a randomized controlled trial with maternal Tdap immunization between 30-32w GA, including term infants. We now study whether preterm neonates are sufficiently protected based on anti-pertussis toxin (PT) antibody concentrations after maternal Tdap between 20-24w GA. The study 1. Aims to assess determinants of acceptance of second trimester maternal vaccination. 2. Assesses antibody levels in cord blood and at 2m.

Methods: For the first study part, 6750 pregnant women need to fill in a questionnaire on determinants of acceptance of second trimester maternal vaccination. Midwives/gynaecologists offer Tdap vaccination between 20-24w GA and ask participation in the second part. Herein we aim to compare anti-PT-antibody concentrations in 60 preterms (<35w GA) and 60 terms (≥37w GA). Maternal- and infant blood is collected directly after delivery and at 2m, before the first vaccination.

Results: The study is ongoing. On January 27th 2020, 548 women participated, with >97% acceptance of vaccination. Fifteen women gave birth. For one infant, being preterm, blood at 2m has been collected.

Conclusions: The Netherlands is the first country with a personalized infant vaccination schedule. After maternal Tdap a reduced schedule is offered to term infants if 1. the mother isn’t a hepatitis-B-carrier and 2. the interval between maternal vaccination and birth is ≥2w. Comparing anti-PT between children from mothers vaccinated at 20-24w with those vaccinated around 30w may inform us if such a reduced vaccination schedule is also feasible in preterms.

Clinical Trial Registration: not applicable
Background: Gastroenteritis is a common acute infectious disease and the viral etiology represents a significant cause of hospitalization in infants and young children. **Aim of the study:** The analysis of the demographic, clinical, microbiological characteristics and burden of viral or non-viral childhood gastroenteritis in a 2 year period in our clinic.

**Methods:** A prospective study was conducted between December 2017 - January 2020. Stool samples from patients with acute gastroenteritis who were treated at the Brașov Clinical Children’s Hospital were analyzed using a rapid immunochromatographic test. They were divided into three groups and it included 340 patients (103 cases Rotavirus, 100 Cases Adenovirus and 170 cases of negative stool samples). The demographic data of Rotavirus gastroenteritis were collected from the electronic records retrospectively and were compared with those of children with Adenovirus and children with negative stool samples.

**Results:** The median age of children with Adenovirus infections was lower than for Rotavirus, as well as those with negative viral gastroenteritis (7 vs 13.5 vs 11 months). The average hospitalization lasted 3 days and 54% of the population study received antibiotics. Rotavirus infections associated with medical care were more frequent (24%) than Adenovirus infections. Coinfections were also present - Rotavirus and Adenovirus (13 cases), Rotavirus and Verotoxins (7 cases) and Adenovirus and Verotoxins (9 cases). 98% of the children that were hospitalized were accompanied by a parent.

**Conclusions:** Rotavirus infections remain the most frequent cause of hospitalization in gastroenteritis. In our study Adenovirus infections represent the second cause of hospitalization for infants.
REVIEW OF CLINICAL STUDIES COMPARING SEROGRUP C IMMUNE RESPONSES INDUCED BY MENACWY-TT AND MONOVALENT MENC VACCINES

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Background: European countries are increasingly recommending vaccination with quadrivalent meningococcal conjugate (MenACWY) vaccines to replace monovalent serogroup C (MenC) conjugate vaccines. One such MenACWY vaccine, MenACWY-TT, is currently licensed in the European Union and 49 other countries and administered as a 2+1 (age 6 weeks–<6 months), 1+1 (6–<12 months), or single dose (≥12 months) schedule.

Methods: Key European clinical studies comparing MenC immune responses induced by MenACWY-TT and monovalent MenC vaccines were reviewed to potentially support the switch to MenACWY vaccines. Immune responses in these studies were evaluated in serum bactericidal activity assays with human (hSBA) or rabbit complement (rSBA).

Results: Nearly all infants aged 6–12 weeks who were administered a 2+1 schedule of MenACWY-TT, MenC-CRM197 conjugate vaccine, or MenC-TT conjugate vaccine (n=516–527) had MenC rSBA titers ≥1:8 following primary and booster vaccination (Figure); hSBA titers ≥1:4 were similar. MenACWY-TT induced robust increases in geometric mean titers (GMTs), which were generally lower than for the monovalent MenC-vaccinated groups. In 2 studies in toddlers aged 12–23 months administered a single MenACWY-TT or MenC-CRM₁₉₇ dose (n=75–374), nearly all subjects had rSBA titers ≥1:8 at 1 month/42 days postvaccination; percentages with hSBA titers ≥1:4 or ≥1:8 and GMTs were higher following MenACWY-TT. Persistence evaluations for 1 toddler study indicated that generally high percentages of subjects across groups retained protective titers through 10 years postvaccination. In another study (n=81–91 across 3 age groups), toddlers primed with MenC-TT retained protective rSBA responses through 1 year following an adolescent MenACWY-TT or MenC-TT booster dose.
Conclusions: MenC immune responses induced by MenACWY-TT are robust and generally comparable/superior to monovalent MenC conjugate vaccines, supporting changes from monovalent MenC to MenACWY vaccination recommendations. Funded by Pfizer.

Clinical Trial Registration: ClinicalTrials.gov NCT01144663, NCT00474266, NCT00427908, NCT01962207; EudraCT 2013-001823-38.
Title of Case(s): EPIDEMIOLOGICAL AND CLINICAL CHARACTERISTICS OF SUSPECTED LISTERIOSIS CASES IN CHILDREN AND PREGNANT WOMEN DURING 2019 SUMMER OUTBREAK IN CADIZ, SPAIN

Background: Listeriosis is a food-borne disease. High-risk groups for infection include newborns, immunocompromised and pregnant women (PW). Vertical transmission can lead to miscarriage, stillbirth, chorioamnionitis and preterm delivery. On August 16th 2019, Spanish Authorities notified a listeriosis outbreak in Andalusia. It was associated with cold pork roast and other deli meats manufactured by Magrudis Company Limited, under the brand “La Mechá”. We here report the suspected cases in PW and children detected in Cádiz, an Andalusian province.

Case Presentation Summary: 35 cases were reported: 26 PW and 9 children, one of them, a newborn. None other immunocompromised. Blood culture (BC) was obtained in 23/26 (92%) PW and 6/9 (75%) children; stool culture and BC in 1/26 (4%) PW and 1/9 (12.5%) child and BC and CSF culture in 1/9 (12.5%) child. No confirmed cases were notified; all children and 13/26 (55.5%) PW were probable cases and the remaining, suspected cases. Among PW exposed, one late stillbirth and one chorioamnionitis were reported as complications, without microbiologic confirmation (Table 1).

| Table 1. Epidemiological characteristics of listeriosis outbreak in Cádiz |
|---------------------------------|----------------|----------------|
| **Age** (median; years)         | PW             | Children       |
| 33.5 (25-40)                    |                | 7.8 (0.04-15)  |
| **Products n(%) Cold pork Other** | 19 (73%) 7(27%) | 7 (77.7%) 2(22%) |
| **Incubation period** (median;days) | 30.5 (1-80) | 26.6 (6-90) |
| **Symptoms n(%)** Fever Vomit Diarrhea Abdominal pain Headache | 23(88.4%) 7 (23.92%) 10 (38.4%) 2 (7.69) 8 (30.7%) | 9 (100%) 1 (11.1%) 3 (33.3%) 4 (44.4%) 5 (55.5%) |
| **Treatment n(%)** Amoxicillin Ampicillin and gentamicin | 24 (92.31%) - | 8 (88.8%) 1 (11.1%) |
| **Period of illness** (median;days) | 7.1 (5-10) | 7.7 (7-10) |

Learning Points/Discussion: Although this was the largest listeriosis outbreak reported in Spain to date, no confirmed cases were detected in Cádiz. Epidemiological and microbiological investigation was
essential to prevent severe clinical outcomes and potential deaths in high-risk groups.
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CENTRAL VENOUS CATHETER-RELATED BLOODSTREAM INFECTIONS FROM A PAEDIATRIC HAEMATOLOGY-ONCOLOGY UNIT IN A TERTIARY HOSPITAL FROM 2007 TO 2017.


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Background: Central venous catheters (CVCs) are essential in haematology-oncology patients. One of their main drawbacks is catheter-related bloodstream infections (CRBSI). CRBSI are complex to treat; moreover, it is not unusual the need for CVCs removal as a result of CRBSI. Our objective was to describe CRBSI from the last 11 years and evaluate the outcomes of treatment.

Methods: A retrospective study of CRBSI paediatric cases among a referral Spanish Haematology-Oncology unit from 2007-2017 was conducted. We collected the following data: demographics, main underlying disease, symptoms, diagnostic tools, microbiologic isolates, treatment and outcomes.

Results: 39 CRBSI were diagnosed; 72.9% males, median age: 3.4 years (IQR: 1.8-6.9 years). Underlying diseases were: 51.7% leukaemia/lymphoma, 32.7% solid-tumours, 15.5% no -malignancies. Most common microorganisms were gram-positive cocci (60.3%), gram-negative bacilli (27.6%), polymicrobial infections (8.6%) and fungal infections (3.4%). Among gram-positive cocci, coagulase-negative Staphylococci (CNS) were the most frequent (41.4%). We treated 41/58 (71%) cases with antibiotic lock-therapy (ALT). A total of 12/17 (71%) of CVCs treated with no ALT were removed versus 13/41 (32%) treated with ALT [OR 5.2 [CI 95%: 1.5-17.7], p=0.006]. Reasons to remove CVCs in CRBSI-ALT group were: pocket site infection (25%), persistent symptoms (25%) and relapses (25%). No ALT adverse effects were notified.

Conclusions: In our series, CNS was the most frequent aetiology in CRBSI. In our study, CRBSI treated with ALT as adjunctive therapy was an effective approach to maintain the CVCs in place, with no added adverse effects.
SKIN INFECTION IN CAPE VERDE CHILDREN

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Background: Skin infections are prevalent in children from developing countries, mostly due to hot climate, low socio-economic status and poor hygiene. These infections can be potentially serious if not diagnosed and treated correctly. This study has the aim to describe the epidemiology of children with skin infections, diagnosed during an internship in a primary care health center of Santiago Island, in Cape Verde.

Methods: Retrospective, descriptive study with analysis of epidemiological variables such as age, gender, type of infection and treatment, of children with skin infections diagnosed in a primary care health center during October 2019.

Results:
A total of 279 children were observed. Of these, 42% were diagnosed with a skin infection. The great majority (53%) had bacterial etiology; 31% presented impetigo or bullous impetigo. These conditions were treated with topical fusidic acid, oral amoxicillin/clavulanic acid or flucloxacillin, depending on the progression of the disease and the availability of the medication. Fungal infections were the second most prevalent skin infection (29%), mostly *Tinea capiti* and *Tinea corporis*. These infections were treated with topical ketoconazole. A total of 9 children were referred to a Dermatology specialist consultation.

**Conclusions:** Most of the cutaneous infections diagnosed in this setting share a similar etiology to the ones in Portuguese clinical practice. The main difference seems to be the timing of diagnosis, since patients attend to health care services at an advanced stage of disease. This is possibly due to economic difficulties and poor access to healthcare services. This study emphasizes the need of improving the diagnosis and treatment of dermatologic conditions in developing countries. Furthermore, it highlights the demand to increase the awareness of the population to this kind of diseases.
CARBAPENEM RESISTANT GRAM NEGATIVE BACILLI IN GUT AND CORRELATION WITH BLOOD BACTERAEMIA IN A PAEDIATRIC STEM CELL TRANSPLANT UNIT IN INDIA

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Background: Hematopoietic stem cell transplant (HSCT) is used to cure a wide range of malignant, non-malignant and immunodeficiency conditions. Blood stream infections (BSI) are a major source of morbidity and mortality during transplant. CDC introduced the definition of Mucosal Barrier Injury—Laboratory Confirmed Blood Stream Infection (MBI-LCBI) in 2013 in keeping with the concept that BSI in oncology-transplant patients can occur through mechanisms like translocation of gut bacteria through non intact mucosa.

Methods: We conducted a retrospective study from June to December 2019 of all children admitted in the stem cell transplant unit in pediatric tertiary care centre. Rectal swabs or stool cultures were processed on admission and weekly thereafter. Once a Carbapenem Resistant Enterobacteriaceae (CRE) was confirmed as per disc diffusion zones, the isolate was subjected to identification and MIC testing by Phoenix BD system. First line antibiotics were planned as per stool culture sensitivities and isolation precautions were implemented.

Results: 17 patients were reviewed over 7 months duration. 7 culture positive bacteraemia were documented. 4/7 episodes of Enterobacteriaceae bacteraemia were noted with same sensitivities/genotype as stool isolates. 3 patients had CRE bacteraemia with similar gram negative organism isolated from stool prior to the febrile episode. Both isolates (stool, blood) had same antibiotic sensitivities and 2 had the same genotype (OXA 48). One patient had translocation of ESBL E. coli with similar sensitivities as his previous stool isolate. Incidence of bacteraemia was higher in stool CRE positive (37.5%) than negative (16%) cases.

Conclusions: Data from European centres suggest mortality rate of around 60% in patients with CRE in allogenic HSCT with sparse data from India. Delay in appropriate therapy might be a significant contributory factor as these bacteria are resistant to most first line antibiotics. Early initiation of appropriate therapy and prevention of spread of bacteria by appropriate infection control measures are important to reduce mortality secondary to CRE.
Title of Case(s): An atypical abdominal pain

Background: Mediastinal tuberculous lymphadenitis is mostly seen in primary tuberculosis in children. It usually presents with the systemic symptoms of tuberculosis but can rarely involve vagus nerve compression, resulting in abdominal pain. These patients can easily be misdiagnosed and get delayed or faulty treatments.

Case Presentation Summary: A 16-years-old girl, presented to our hospital with complaints of abdominal pain, headache and nausea in May 2019. At the Emergency Department US showed splenomegaly and she was admitted to the Pediatric Gastroenterology ward. Medical history and physical examination revealed left upper quadrant pain radiated to omolateral shoulder associated with headache and nausea but no vomiting combined. She reported low-grade fever three months earlier and a 3 kg weight loss within three weeks, she denied any travel abroad. We repeated US, chest-X ray and blood tests, all presenting nothing remarkable. Faecal calprotectin, celiac disease screening tests, Widal-Wright test, serum antibodies for CMV, EBV, HIV, Echoviruses, Adenoviruses, M. pneumoniae, C. pneumoniae, and Leishmaniasis, as well as echocardiography, OGD and brain MRI, tested negative or within normal range. Abdominal MRI confirmed hepatosplenomegaly, while Mantoux tuberculin skin and IGRA-QFT tested positive. Subsequently, we performed Chest CT Scan that detected mediastinal and right-hilar lymphadenopathy, with no sign of calcification nor colliquation. Cultural and bacterioscopic examination of urine and sputum were negative. The patient was later transferred to Infectious Diseases ward where she started standard dose RIF+INH+EMB+PZA therapy and B6 vitamin supplement. Clinical condition improved, symptoms resolved and Chest CT-Scan performed after six months of drug administration showed downgrading of the lymphadenitis.

Learning Points/Discussion: The purpose of this paper is to highlight the varied presentation of mediastinal tuberculous lymphadenitis, in children and identify diagnostic clues which may help in the early diagnosis of MTL.
CLINICAL FORMS OF CLOSTRIDIUM DIFFICILE INFECTION ON CHILDREN – DURING JANUARY 2019 – JANUARY 2020 - INBI “ PROF. DR. MATEI BALS”, ROMANIA

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Background: Clostridium difficile infection is widespread worldwide, including in Romania, with an increased incidence over the past few years. This pathogen became more virulent and with high resistance to the usual antibiotics and can cause more aggressive clinical forms that can be refractory to the standard therapy.

Methods: We performed a retrospective study on cases of Clostridium Difficile infection in children who were hospitalized in the 9th Pediatric Department of the INBI “Prof. Dr. Matei Bals”, Bucharest, Romania, during January 2019 – January 2020. The diagnostic was built upon clinical, epidemiological and laboratory data. In all patients, we detected the presence of toxins and nucleic acid for genes associated with toxin production. In those patients, we analyzed background if they received antibiotic treatment before if they were immunocompromised patients, age, sex, clinical forms and complications of the illness.

Results: During the studied period, we registered 20 cases of Clostridium difficile infection on children with a female predominance (65%). The most affected age group was 2 - 4 years (65%) and all patients received antibiotics during the last 8 weeks. The majority of clinical forms were mild (70%) followed by severe forms (20 %) that requiring rescue therapy, four cases were immunocompromised patients ( two of them with acute lymphocytic leukemia, another with non-Hodgkin's and another with a brain tumor) undergoing chemotherapy. No deaths were registered.

Conclusions: The distribution of cases with Clostridium difficile infection according to the risk factor prove once again that we must further limit the administration of antibiotics. To reduce the incidence of severe cases and death from Clostridium difficile infection in immunocompromised patients through chemotherapeutic treatment, a weekly screening protocol would be ideal.
ESCHERICHIA COLI RATE OF RESISTANCE ON CHILDREN'S URINE CULTURES IN AN ITALIAN METROPOLITAN AREA

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**Background:** Extended spectrum beta-lactamase producing Escherichia coli are increasing worldwide. Besides, recent studies reported an increasing resistance rate of *E.coli* to amoxicillin/clavulanic acid (AMC). Our aim was to investigate the resistance rate of *E.coli* to the commonly prescribed antibiotics for urinary tract infections (UTIs).

**Methods:** Data from children's urine cultures (UCs) collected from 2016 to 2019 in a metropolitan area located in Northern Italy, covering about 1 million people and 3 hospitals, were analysed. We did not consider only febrile UTIs, but we included all positive UC. UCs positive for *E. coli* and their antibiograms were evaluated. Resistance rate was compared between 2016 and 2019 with a Chi square test.

**Results:** In the study period, 957 positive UCs were collected and 520 (54%) were positive for *E. coli*. The AMC resistance rate has significantly worsened from 21% to 42% (p<0.001). The rate of resistance to cotrimoxazole, cefotaxime, ceftazidime and ciprofloxacin remained stable, changing respectively from 20% to 26% (p=0.36), from 9% to 7% (p=0.64), from 9% to 6% (p=0.49) and 13% to 7% (p=0.14).

<table>
<thead>
<tr>
<th>Period of study</th>
<th>2016 (n=105)</th>
<th>2017 (n=107)</th>
<th>2018 (n=163)</th>
<th>2019 (n=145)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMC</td>
<td>22 (21%)</td>
<td>27 (25%)</td>
<td>57 (35%)</td>
<td>61 (42%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cotrimoxazole</td>
<td>27 (26%)</td>
<td>39 (36%)</td>
<td>47 (29%)</td>
<td>29 (20%)</td>
<td>0.36</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>9 (9%)</td>
<td>10 (9%)</td>
<td>18 (11%)</td>
<td>9 (7%)</td>
<td>0.64</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>9 (9%)</td>
<td>6 (6%)</td>
<td>17 (10%)</td>
<td>8 (6%)</td>
<td>0.49</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>14 (13%)</td>
<td>11 (11%)</td>
<td>21 (13%)</td>
<td>10 (7%)</td>
<td>0.14</td>
</tr>
</tbody>
</table>

**Conclusions:** AMC is indicated as first-line treatment in febrile UTIs by recent Italian guidelines. Despite that, in our metropolitan area, this choice is no longer feasible at the moment. This acquired resistance can be reversible, but this worrying data requires a prompt intervention to improve antibiotic consumption and prescription.
ASSOCIATIONS BETWEEN EDUCATION OF THE PARENTS AND THEIR HESITANCY TO VACCINATION IN CAPITAL OF UKRAINE

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Background: World Health Organization admitted vaccine hesitancy (VH) among ten threats to global health in 2019. This complex problem include context specific varying across time and place. VH individuals are heterogeneous group of community with different background. One of the main and largest group is parents with their fears. Identification of the sources of negative information that they receive may vary from place to place. That is why important to have information not only at the country level, but also more specific in the regions.

Methods: Cross-sectional study with direct interview of 797 parents using relevant questionnaire

Results: The results show that 81.5% of parents with university degree agree that vaccination of their child is important for the health of others in the community, whereas people who graduate from school only 67% (p≤0.05) supported this view. The only reason to vaccinate their child is so they can enter daycare or school were supported only 4.5% of parents with university education background and 15.3% of people who graduate from school (p≤0.05).

Conclusions: Parents with university degree are more likely to immunize their children than parents without higher education. However, the problem of refusing vaccination remains relevant to different population across Ukraine, so a set of measures to prevent its development should be developed and put into practice.
ASSESSMENT OF PAEDIATRIC THERAPY IN THE INTENSIVE CARE UNIT AT A PRIVATE HEALTHCARE FACILITY

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Background: In developing countries, infants constitute large proportion of the population. Establishing safe and effective therapeutic regimen for children is a big challenge. The infant mortality has declined from 57 to 34 per 1000 from 2006-2016. This study was an attempt to assess the pharmacotherapy in the neonatal intensive care unit (NICU) at a private paediatric healthcare facility with special reference to the use of antimicrobials.

Methods: A cross-sectional record based study was conducted at a private healthcare facility catering to the paediatric segment. Patients who had received at least one antimicrobial and were admitted in the ICU for at least 24 hours were included. The prescribing pattern for 142 patients was analyzed.

Results: 89 male and 53 female neonates were studied. The average age of patients was found to be 2.70±0.33 days.

The most common diagnosis was sepsis followed by neonatal jaundice and respiratory distress. The average number of antimicrobials prescribed was 2.82±0.10; and, the average duration of this treatment was 6.48±0.23 days.

Cefotaxime and amikacin were the most commonly prescribed antimicrobial followed by vancomycin, meropenem, gentamicin and ampicillin.

A number of gram positive and gram-negative bacteria exhibited resistance to clinically useful antimicrobials. Gram-negative isolates showed a high level of resistance to all cephalosporins.

Conclusions: The results of this small study reinforce that utmost caution needs to be exercised while using antimicrobials in the neonates.
CUTANEOUS MUCORMYCOSIS IN A TODDLER WITH MATURE B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA

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Title of Case(s): Cutaneous mucormycosis in a toddler with mature B-cell acute lymphoblastic leukemia

Background: Infections caused by Mucorales can be fatal for immunocompromised patients (especially those with hematologic malignancies). Cutaneous mucormycosis is caused by inoculation of the spores of the fungus into the dermis. The rapid expansion of the infection reflects the formation of tissue infarcts, caused by infiltration of the microvasculature by the hyphae of the fungus.

Case Presentation Summary: A 2.5 year-old female toddler with mature (Burkitt cell) B-cell ALL [Immunophenotypic profile: CD45+,CD19+,cCd79a+,CD10+,κ-clonal-karyotype:47,XX,+i(1)(q10),t(8;14)(q24;32)], on day 14 of hospitalization, after completion of COP (cytoreductive) and COPADM1 (first induction) cycles, developed a≈15mm diameter circular lesion with a slightly protruded, flattened red base and a central dark-coloured depression (“ecthyma-like lesion”), on the middle third of the extensor surface of her left forearm. On day 15, a central necrotic eschar with a peripheral reddish halo and a mild induration was noted. On day 18, in view of the clinical presentation, the lesion's rapid growth and the patient's severe immunosuppression, mucormycosis was suspected and IV administration of high-dose liposomal amphotericin-B (7mg/kg/d) was decided. Considering the severe underlying neutropenia and the presumed healing disorder, due to the primary disease, simple drainage was performed, instead of extensive surgical debridement and a wound culture specimen was obtained. Two days later, Mucorales was isolated from the culture. On day 23, the necrotic eschar was completely detached, leaving a crater, with a highly vascularized and clean wound bed. Culture of the detached material again revealed Mucorales (genus: Rhizopus, species: arrhizus)(MIC→Amphotericin B:0.5mg/L,Posaconazole:1mg/L). The wound was eventually healed by second intention.
**Learning Points/Discussion:** The complete resolution of the infection reflects the importance of vigilance in the prompt diagnosis and the critical role of liposomal amphotericin B in the treatment of cutaneous mucormycosis, in pediatric immunocompromised patients with underlying hematologic malignancy.
CONGENITAL SYPHILIS: PUBLIC HEALTH PROBLEM

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Title of Case(s): TWO CASES: PRETERM INFANTS WITH EDEMA AND HEPATOSPLENOMEGALY

Background: Gestational and congenital syphilis remains a major public health problem with serious consequences for the fetus, although surveillance systems are optimized for this the incidence of syphilis continues to increase and the prevention of cases such as those presented should be a priority to continue your vigilance.

Case Presentation Summary: 1 case: 34 weeks premature, male, product of the first pregnancy of adolescent mother with diagnosis of late gestational syphilis due to not performing controls early, with multiple social factors, psycho active substance use, non-adherence to full treatment. Spontaneous delivery with good adaptation, but with generalized edema and persistence of significant respiratory distress, leading to respiratory failure and rapidly entering into multi-organ failure, dies within 4 days 2 case: Premature of 30 weeks, mother performs 2 controls only, refers to the beginning of controls at 10 weeks, but abandonment because it is an unwanted pregnancy, when arriving at the institution febrile patient, fetal tachycardia, urinary infection and rapid and confirmatory test for syphilis positive, mother with a history of chickenpox during this gestation at 20 weeks. At birth, induced adaptation, respiratory distress, requiring positive pressure ventilation. Generalized edema, hepatosplenomegaly, is associated with enterocolitis and intestinal perforation.

Learning Points/Discussion: Congenital syphilis is an infection caused by T. pallidum, its surveillance during pregnancy is of great importance, due to the serious consequences that can be left in our newborns when not receiving treatment, in addition associated problems such as those seen in our patients should be addressed in prenatal control programs as priorities.
RESPIRATORY VIRAL INFECTIONS CAUSED BY RHINOVIRUS DURING EPISODES OF FEVER IN CHILDREN UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT)

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Background: Children undergoing HSCT can present respiratory viral infections (RVI) during fever episodes. There are few data about clinical outcomes in RVI caused by rhinovirus in this population. Our aim was to determine clinical outcome of RVI caused by rhinovirus in children with HSCT.

Methods: Prospective study, children ≤18 years with cancer and HSCT admitted with fever at National Bone-Marrow-Transplant Center, Chile (April 2016 to May 2019). Clinical examination, laboratory tests, blood cultures, nasopharyngeal-sample for multiplex-PCR (20 respiratory pathogens), viral quantification and cytokine panel (Luminex). The following outcomes were evaluated: upper/lower respiratory tract disease (RTD), admission to PICU/mechanical ventilation, mortality and antimicrobial withdrawal.

Results: From 56 episodes of fever, 25(45%) were rhinovirus(+); 2(8%) had co-infection with another respiratory virus. Median rhinovirus viral-load was 29.450/mL (IQR:250-3.152.375); cytokine study showed increased level of GRO,IL-8 and IP10. Median age was 8 years(IQR:12-192), 72% male gender and median days after HSCT was 64(IQR:6-372). At admission, 76% of fever episodes had respiratory symptoms, median of absolute-lymphocyte count was 422/mm³(IQR:0-4540), median absolute-neutrophil count was 2382/mm³(IQR:0-8316) and median C-reactive protein was 17.5mg/L(IQR:5-166). At discharge 22/25(88%) presented upper/lower-RTD; 15/25(60%) lower-RTD. PICU admission was 8% and 4% required mechanical ventilation. No mortality was observed, and antimicrobial withdrawal was 20%.

Conclusions: Rhinovirus was frequently detected in fever episodes after HSCT, with 88% of upper/lower-RTD and no mortality. Its detection might help to rationalize the use of antimicrobials in this population (FONDECYT GRANT#1171795).
Title of Case(s): Cape Verde – The reality of a traineeship

Background: Cape Verde is an insular developing country in Northwest Africa where children under 14 years account for 35% of the population. Poverty, cultural aspects and climactic conditions potentially contribute to a high burden of infectious diseases. A group of pediatric residents has done 1 month traineeship in a primary healthcare unit at Praia, Santiago Island. This study pretends to analyze the reality of pediatric infectious diseases management with limited medical resources.

Case Presentation Summary: A total of 310 pediatric consultations were performed, mostly to females (53%) and to children under 1 year old. A total of 379 diagnoses were reached, 78% with infectious etiology. Out of all diagnoses, respiratory system diseases accounted for 33% (with upper respiratory tract disease being the most common), disorders of skin and subcutaneous tissues for 31% (with 53% being bacterial infections and 29% fungal) and digestive disorders for 8% (where, unsurprisingly, acute gastroenteritis was the most frequent). Regarding treatment, most bacterial respiratory infections were treated with oral amoxicillin, bacterial skin infections with oral amoxicillin/clavulanic acid (4:1) and/or topical fusidic acid and fungal skin infections with topical ketoconazole. Some patients have shown restrictions on acquiring medication which may have delayed clinical recovery. Referral was required in 42 cases, most frequently to the emergency care unit or dermatology specialty.

Learning Points/Discussion: This study confirmed a high prevalence of infectious diseases, probably enhanced by living conditions. Providing medical care with limited resources can be a challenge for both diagnosis and treatment and our purpose is to underline and reflect on the difficulties to achieve adequate healthcare in developing countries.
Background: Several studies have shown an increasing incidence of community-acquired methicillin-resistant Staphylococcus aureus (CA-MRSA) infections in adult and pediatric populations since 1990. Its prevalence is highly variable, ranging from zero to 70% in some regions. It is a matter of concern that CA-MRSA is resistant to almost all beta-lactam agents, which are the most widely prescribed drugs for the empirical treatment of typical S. aureus infections. Our study aimed to determine the frequency of clindamycin-resistant CA-MRSA bacteremia in pediatric patients at a tertiary hospital in São Paulo, Brazil.

Methods: We evaluated antibiotic susceptibility for all S. aureus strains that grew in blood cultures from 2014 to 2017 at Santa Casa de São Paulo. We defined CA-MRSA according to antibiotic susceptibility: resistant to oxacillin and < 4 antibiotic class. Bacteremia was considered healthcare-associated if the patient had a positive blood culture after 48 hours of hospitalization, and any of the following: hospitalization, surgery, comorbidities or indwelling percutaneous devices or catheters in the last year.

Results: Of 106 episodes of S. aureus bacteremia, 38.6% were MRSA and 44.6% resistant to clindamycin. According to patient epidemiology, only 16 episodes were considered community-acquired, with 18.8% MRSA and 37.5% resistant to clindamycin (38.5% in MSSA and 33.3% in MRSA); 90 were healthcare-associated infections, with 42.3% MRSA, 44.5% resistant to clindamycin (34.6% in MSSA, 46.4% in CA-MRSA, 90% in HA-MRSA).

Conclusions: We observed a high prevalence of clindamycin resistance in MSSA and MRSA, both in the community and in healthcare-associated infections. Our data suggest that clindamycin should not be used as a first-line empirical antimicrobial treatment at our center.
ANTIBIOTIC STEWARDSHIP INTERVENTIONS AT ICU: CONTROLLING EMERGENCE OF MULTI-DRUG RESISTANT ORGANISMS

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Background: Antibiotic therapy is frequently prescribed in the intensive care unit (ICU). Stewardship is particularly relevant in this setting because it provides the framework necessary to improve antimicrobial use such as to reduce unnecessary antibiotic use and to limit the appearance of multidrug-resistant organisms (MDROs).

Methods: Retrospective data of antibiotics use at ICU Fatmawati General Hospital and antimicrobial resistance patterns of the common pathogen were obtained from January to December 2019. The quantity evaluation of antibiotic use were reported by using the Defined Daily Dose (DDD) method.

Results: The highest use of antibiotics from was ceftriaxone injection which was 58.25 DDD (100 patients - days) rather than meropenem injection as one of third-line antibiotics with an average value of 27.96 DDD (100 patients - days). The MDRO dominantly ESBL rather than MRSA. The use of meropenem has decreased compared to the results on 2018 which has a value of 55.0 DDD (100 patients - days). After ARCP interventions, prescribing antibiotics among clinician at ICU were more selective, indicate rational use of antibiotics has increased. Unfortunately, the increasing of Ceftriaxone use, had increase ESBL rather than MRSA.

Conclusions: The intervention antibiotics use at ICU has succesfully carried out with the recommendation of ARCP so that can control the emergence of MDRO pathogens.
TRANSITION OF ADOLESCENTS WITH HIV INFECTION TO ADULT CARE: REALITY OF A TERTIARY HOSPITAL

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Background: Transition of adolescents with HIV infection to adult care is a necessary but difficult process. With improved survival rates, the number of adolescents with HIV infection transitioning to adult care is increasing. A structured and gradual transition program can improve disease acceptance and clinical follow-up compliance, therefore improving individual and global health outcomes. The aim of this study is to characterize HIV-infected patients that transitioned from pediatric to adult care between 2012 and 2018, at a tertiary hospital; analysis of the transition program with the goal of further improvement.

Methods: Retrospective, observational and descriptive study. Literature review and sample characterization by consulting electronic health records with descriptive statistical analysis of the data.

Results: Of the 49 HIV infected cases reviewed, 41% transitioned to adult care, 60% at the age of 18. Mother-to-child transmission occurred in 90%. Antiretroviral therapy was started before 5-year-old in 50% of individuals. Virologic failure was observed in 45%. Adverse effects of antiretroviral therapy were reported in 60%, dyslipidemia in 53%. During transition, 80% had undetectable viral load, 90% had CD4 counts above 500/mm³. Currently 70% have undetectable viral load, 80% have CD4 counts above 500/mm³. Current mean age is 22 years. All patients maintain clinical follow-up in adult care.

Conclusions: We were successful in preventing loss to follow-up in the transitioned population. However, a higher proportion of patients have detectable viral load since transition and lower CD4 cell counts. Further improvement in our transition program regarding adherence must be implemented.
COMPLICATED ACUTE TONSILLITIS OR SOMETHING ELSE?

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Title of Case(s): Complicated acute tonsillitis or something else?

Background: Kawasaki disease (KD) is one of the most common vasculitis in childhood and may cause serious complications, such as coronary artery aneurisms (CAA). A prompt diagnosis and treatment are critical to reduce cardiovascular sequelae.

Case Presentation Summary: A previously healthy 4-year-old female presented with a 4-day history of fever, left cervical swelling and torticollis, having received 2 days of oral amoxicillin for acute tonsillitis. Laboratory tests revealed leukocytosis and elevated C-reactive protein (CRP) (>200mg/L). Cervical CT suggested a mild retropharyngeal abscess and the child was admitted with intravenous ceftriaxone and clindamycin. Within 24 hours left peritonsillar and parapharyngeal puncture was performed, without exudate drainage. On day 3, for sustained fever and worsened CRP, she repeated cervical CT which was similar, and surgical reintervention was decided. Peritonsillar and parapharyngeal drainage was again negative. On day 6 of admission, day 10 of fever, a non-specific generalized rash and hand edema was noted. Incomplete KD was suspected and echocardiogram revealed CAA. She was treated with intravenous immunoglobulin (IVIG), corticosteroids and ASA, with apyrexia in <24 hours and clinical improvement. Only 1 week later, a coronary artery z-score reduction was noticeable (from 3.2 and 5.4 to 2.04 and 2.2, in the left anterior descending and left circumflex, respectively). The child completed 4 weeks of corticosteroids and 6 weeks after discharge she presented mild desquamation, normal laboratory findings and echocardiogram.

Learning Points/Discussion: In suspected cases of complicated acute tonsillitis, which does not respond to adequate treatment, KD suspicion should remain high. 2-3 clinical criteria with supplemental laboratory criteria or positive echocardiogram makes the diagnosis of Incomplete KD. Early coronary involvement should be treated aggressively with IVIG and corticosteroids. In this case, small and medium CAA disappeared rapidly with treatment.
SEVERITY AND COMPLICATIONS OF 49 CHILDREN WITH STAPHYLOCOCCUS AUREUS (35 MSSA/ 14 MRSA) ASSOCIATED PARAPNEUMONIC PLEURAL EFFUSION/EMPYEMA - RESULTS FROM A NATIONWIDE SURVEILLANCE STUDY (GERMANY 2010-2018)

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**Background:** *Staphylococcus aureus* (SA) is a pathogen frequently associated with community-acquired pneumonia complicated by pleural effusion/empyema (PPE/PE) in children. In the frame of nationwide pediatric hospital surveillance study, we analyzed clinical characteristics and management of children with PPE/PE and methicillin-sensitive (MSSA) or methicillin-resistant SA (MRSA).

**Methods:** From 10/2010-06/2018, children <18 years of age hospitalized with PPE/PE persisting >7 days or requiring pleural drainage were reported to the German Surveillance Unit for rare Diseases in Childhood. All children with PPE/PE and detection of bacterial pathogens in blood culture (BC), pleural fluid culture (PC) or pleural fluid PCR (PPCR) were included in the analysis.

**Results:** In 596 of 1724 cases reported, a pathogen was detected including 49 children with SA (8%, 35 MSSA, 14 MRSA). Increase of the annual proportion of MRSA on all SA (0-14% until 2013/14, 27-43% since 2014/15). Lower median age (2.0 vs. 4.1 years, p<0.001), longer hospital stay (23 vs.19 days, p=0.003) and longer intravenous antibiotic treatment (21 vs. 17 days, p=0.007) of SA compared to other pathogens detected. No difference in need of intensive care treatment, mechanical ventilation, use of invasive procedures, complication rate or potential sequelae.

**Conclusions:** Although SA associated PPE/PE occurred in younger children and required longer hospital stay, we found no difference in severity and complications compared to other bacterial pathogens. There was no clinical differences between MSSA and MRSA. The increase in MRSA requires further surveillance.
INFLUENZA IN CHILDREN PRESENTED IN EMERGENCY DEPARTMENT

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Background: Influenza generates significant morbidity and mortality rate among risk groups, including children below 5 years. Unfortunatelly influenza vaccine costs for children immunisation are not reimbursed in our country and flu vaccine is not actively recomended in this age group, by GP’s. In 2019 we had an increased circulation of influenza in our region, with a notable mortality rate in children [8 cases - 4.23% of total deceased people nationwide].

Methods: We conducted a prospective study of influenza in children diagnosed within the Emergency Department of a tertiary hospital in Bucharest, Romania, between January and April 2019. Testing for influenza was performed using rapid detection tests PreventID® Influenza A plus B, Bensheim, Germany. Parents of positive patients had to complete a questionnaire regarding immunisation status and medical history.

Results: 422 children with ILI [influenza-like illness] were tested. 36.7% positive tests, with type A predominance (n = 152, 98.1%). Median age of influenza patients (3.4 years) was significantly higher than of negative ones (2.8 years), p = 0.030, r = 0.11. Dominant clinical features were fever (96.7%) and cough (75.0%). The overall flu vaccination rate for the whole group was 2.6%, and among those positive for influenza 1.3% (n = 2 cases). A total of 16 (10.3%) patients with influenza required hospitalization, none of whom were vaccinated for influenza.

Conclusions: We identified an increased rate of influenza positivity among children who presented to Emergency Department with the predominance of influenza A viruses. A significant low vaccination rate among the pediatric population was documented, reflecting particular national aspects of vaccine hesitancy. New approaches, in Social Media communication era, are required in order to raise parents’ awareness of influenza infection impact on disease burden.
Title of Case(s): CATS: A REAL PAIN IN THE LOWER BACK

Background: Cat-scratch disease (CSD), caused by Bartonella henselae, usually manifests as cutaneous reaction at scratch site followed by lymphadenitis. However, in a small percentage of cases, atypical manifestations can occur, one of the rarest being bone involvement.

Case Presentation Summary: A previously healthy 10-year-old girl came to the hospital with a two-week history of right lumbar paravertebral pain, that awakened her during the night, following minor trauma of that same area. Eleven days after onset of pain, she developed fever. She denied other symptoms, as well as recent contact with sick people or animals, nor international travelling. On examination, she did not report spontaneous pain nor upon palpation, but did mention pain when flexing her torso, that limited this movement; there were no inflammatory signs or palpable masses on the lumbar region, nor palpable lymph nodes; the remainder of the physical examination was unremarkable. Blood tests showed an elevation of inflammatory markers, with maximal leukocytosis of 16180/uL and CRP of 73.7mg/L; MRI was performed, showing a right psoas’ abscess and L2 osteomyelitis. Empirical antibiotics were started, but due to persistence of symptoms and high CRP, two CT-guided biopsies were performed, showing, in the second biopsy specimen, granulomas on histological analysis, with identification of Bartonella spp. by PCR. Upon knowing this result, the family recalled contact with a young cat six months before; PCR for Bartonella spp. in the first biopsy specimen was requested and it also became positive. She was started on Doxycycline and Rifampicin, with clinical and analytical improvement.

Learning Points/Discussion: This case shows how Bartonella spp. must be an agent to consider in children with osteomyelitis and contact with cats, although the diagnosis may be challenging in the absence of typical features of CSD.
EPIDEMIOLOGICAL CHARACTERISTICS OF INVASIVE CANDIDIASIS DURING THE LAST TEN YEARS IN A TERTIARY-LEVEL HOSPITAL IN MADRID

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Background: Invasive candidiasis is widely recognized as a major cause of morbidity and mortality in the healthcare environment. The epidemiology of Candida species has changed in the last years and antifungal resistance has become a problem in some settings. The aim of this study is to describe epidemiology of invasive candidiasis in paediatrics population in hospital 12 de Octubre.

Methods: Retrospective observational study. Positive haemocultures for Candida species from patients under 18 years were selected from 2010-2019. Clinical data and susceptibility to antifungals were collected from the medical history.

Results: There were 43 invasive candidiasis. Mean age: 21.3 months. 39.5% were women. 55.8% were admitted in paediatrics-ICU, 13.9% in neonatal-ICU, 6.9% in oncological guard and 20.9% in other guards. Most patients had a medical condition: cardiac surgery (30.2%), abdominal surgery (16.3%), preterms (16.3%), neurosurgery (9.3%), immunosuppression (7%) and organ transplant (7%). About risk factors: 86% had a central catheter, 81.4% had received previous antibiotics and 46.5% were receiving parenteral nutrition. 6 patients were receiving antifungal prophylaxis. The preferred initial treatment was amphotericin B (62.8%). 16.3% reached a poor outcome.

<table>
<thead>
<tr>
<th>Candida species</th>
<th>%</th>
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<tbody>
<tr>
<td>C. albicans</td>
<td>46.5</td>
</tr>
<tr>
<td>C. parapsilosis</td>
<td>27.9</td>
</tr>
<tr>
<td>C. glabrata</td>
<td>6.9</td>
</tr>
<tr>
<td>C. tropicalis</td>
<td>6.9</td>
</tr>
<tr>
<td>C. lusitaniae</td>
<td>2.3</td>
</tr>
<tr>
<td>C. guillermondii</td>
<td>2.3</td>
</tr>
<tr>
<td>C. orthopsilosis</td>
<td>2.3</td>
</tr>
</tbody>
</table>

Conclusions: Candida albicans is the major cause of invasive candidiasis in our hospital. Antifungal resistance is unusual (97.7% of the isolated Candida were sensible to amphotericin B, 93.1% to voriconazole, 92.7% to fluconazole, 82.7% to micafungin, 75.9% to caspofungin, and 75.9% to anidulafungin).
Title of Case(s): Opsoclonus-myoclonus syndrome associated with *Mycoplasma pneumoniae* infection

**Background:** Opsoclonus-myoclonus syndrome (OMS) is a rare neurological disorder characterized by chaotic uncontrolled movements of the eyes, myoclonus and ataxia. In childhood, paraneoplastic causes, specifically neuroblastoma, are more common. From the second decade of life, post-infectious causes have greater expression.

**Case Presentation Summary:** A 10 years-old boy with an uneventful past medical history presented with abnormal eye movements and unsteady gait for two days. He had pneumonia in the previous 2 weeks. On admission, he had intermittent, multidirectional, chaotic eye movements, associated with myoclonic jerks of the proximal extremities and signs of cerebellar ataxia. Blood testing, brain CT and cerebrospinal fluid analysis were normal. He was admitted to the department of paediatrics with the diagnosis of OMS. Brain MRI showed no abnormalities. Extensive etiological investigation was able to rule out paraneoplastic, post-infectious, metabolic and autoimmune causes. The only positive finding was a serum IgM+ for *Mycoplasma pneumoniae*. Treatment with prednisolone was performed for 2 months. There was gradual clinical improvement, with full recovery after 6 weeks. No relapses occurred for a follow-up of 10 months.

**Learning Points/Discussion:** *Mycoplasma pneumoniae* has been implicated in some immune-mediated neurologic diseases. Although the number of cases of OMS associated with *Mycoplasma pneumoniae* reported in the literature is very small so far, it seems that the disease has a monophasic course and favourable outcome.
NEW DIAGNOSIS APPROACHES FOR PULMONARY TUBERCULOSIS IN BRAZILIAN CHILDREN AND ADOLESCENTS

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Background: The WHO estimates 69% and 40% of under-diagnosis and under-reporting in children <5 years and between 5-14 years, respectively. Brazilian ministry of Health hypothesizes that the reported Tuberculosis in those <15 years is just part of the real picture. The purpose of the survey is to investigate pulmonary TB in hospitalized patients diagnosed with lower respiratory tract infection in Brazilian cities with a higher incidence of tuberculosis, ≥50 cases/100,000 inh/year).

Methods: Multicenter cross-sectional study performed based on the evaluation of children and adolescents hospitalized by lower respiratory tract infection. Inclusion criteria: admission due to lower tract respiratory infection (WHO criteria of pneumonia), <15 years, to have a chest X-Ray at admission. All included patients will perform the following exams: Xpert MTB Rif/ Ultra (two induced sputum and one tongue swab), MTB liquid culture (induced sputum), tuberculin skin test, and QUANTIFERON. Calculated sample size is 1118 patients. This study is approved by Hospital Moinhos de Vento ethics committe (CAAE: 24730819.7.1001.5330), and available on-line at Plataforma Brasil.

Results: The study are going to evaluate: -The applicability of induced sputum collection in hospitalized patients; -The accuracy of MTB Rif/ Ultra in oral swab (tongue) and sputum; -Accuracy of the Brazilian tuberculosis clinical score to patients with negative microscopy and culture -Latent tuberculosis infection (LTI). -The current Brazilian clinical score (tuberculin skin test and questionnaire) versus IGRA and questionnaire.

Conclusions: Children are long term reservoir of TB and they have a highest chance to progress to more severe disease forms. It is hypothesized that the introduction of the induced sputum in as strategy to obtain respiratory samples will improve the diagnosis of tuberculosis in the Brazilian pediatric population. In Brazil, it is unknown the real impact of tuberculosis in those <15 years, mainly in children <5 years.
Title of Case(s): Late presentation of a feverish child, managed in a low resource setting in Zambia

Background: This unfortunate case illustrates late clinical features of severe falciparum malaria and the pitfalls of using intravenous quinine to treat this, as well as challenges accompanying working in low resource environments.

Case Presentation Summary: A 6-month-old boy AZ presented to a first-level hospital in Lusaka, Zambia with 7 days of non-productive cough, 4 days of fevers and difficulty breathing and 1 day of poor feeding. AZ was normally fit and well, fully immunised, not malnourished, had no previous HIV exposure nor any unwell contacts. On examination, AZ looked ill. He was febrile at 39°C, lethargic, tachypnoeic and tachycardic (heart and respiratory rates not documented), had bilateral chest crepitations and was pale. Heart sounds were normal and there was no organomegaly. As Lusaka was not endemic for malaria, AZ was appropriately treated as a presumed severe bacterial pneumonia. There was no cardiorespiratory monitoring, chest x-ray, blood tests nor culture facilities available; and malaria rapid diagnostic tests have run out. Blood films were sent to exclude malaria. Low flow oxygen and maintenance IV fluids were started. By the morning, the boy's condition was unchanged, and blood films showed high falciparum parasitaemia (3+). Intravenous quinine was started but discontinued 2 hours later when AZ was found to have a blood sugar of 1.2. After receiving 2 dextrose boluses, the blood sugar only improved to 2.7. When AZ was reassessed, he had features of pulmonary oedema, acidotic breathing, capillary refill time 3 seconds, peripheries were cold and oedematous. During the assessment, AZ had a generalised seizure which terminated with diazepam (blood sugar was 4.5). AZ then became apnoeic and bradycardic, and resuscitation was unsuccessful.

Key Learning Points: Pulmonary oedema, acidosis, convulsions, hypoglycaemia, shock and anaemia are classic signs of severe malaria and carries a poor prognosis. Intravenous quinine is associated with hypoglycaemia and arrhythmias thus should be used with frequent monitoring.
ENTERIC FEVER: 4 CASES IN AN ITALIAN PEDIATRIC WARD

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Title of Case(s): Enteric Fever: 4 cases in an Italian pediatric ward
Background: Enteric fever (EF) is rare in Italy (123 cases in 2016), occurring mainly among travellers returning from endemic areas. Clinical features are non-specific therefore differential diagnosis is broad. If not promptly treated it may lead to acute complications and septic shock.
Case Presentation Summary: 4 cases of EF due to S. enterica serovar Typhi were identified in children aged 4 – 11 years (3M, 1F) returning from a prolonged stay in endemic areas (2 India, 2 Pakistan) 7 -14 days before the onset of symptoms. Patients had high, long-lasting fever and diarrhea (4/4), abdominal pain (3/4) and vomiting (1/4). On physical examination sunken eyes, dry mouth, abdominal distension (4/4); splenomegaly (1/4) and relative bradycardia (1/4) were found. Blood tests showed anemia, eosinophilopenia and mild elevation of transaminases and CRP. Abdomen-US detected lymphoadenopaties (4/4), free fluid in the peritoneal cavity (4/4), gallbladder wall thickening (1/4).
Diagnosis was made by isolating S.Typhi from blood culture (3/4) or presumptively on the basis of Widal test positivity (1/4). One strain was resistant to ciprofloxacin and one to ciprofloxacin, ampicillin and trimethoprim-sulfamethoxazole. All were treated with systemic third-generation cephalosporins (ceftriaxone, cefotaxime) for at least 12 days, first administered i.v. and then orally. In addition, patients needed ciprofloxacin (1/4) and azithromycin (2/4). Time to apyrexia after the onset of treatment varied between 7-20 days. Relapse (1/4) and prolonged illness (1/4) occurred in children infected by a resistant strain of S.Typhi.
Learning Points/Discussion: In a febrile child with gastrointestinal symptoms it is important to ask about recent travel abroad. In high suspicion of EF, empiric antimicrobial therapy should be promptly administered after blood sampling for culture. Increase of drug-resistant typhoidal organisms makes susceptibility tests essential to choose definitive antimicrobial therapy.
RETRO- AND/OR PARAPHARYNGEAL ABSCESSSES IN CHILDREN, HOSPITALIZED AT PAEDIATRIC DEPARTMENT OF INFECTIOUS DISEASES, LJUBLJANA, SLOVENIA FROM 2006 TO 2019

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Background: Retro- and parapharyngeal abscesses in children can present a challenge for paediatricians due to their uncommon presentation. Prompt diagnosis and treatment is imperative to prevent complications.

Methods: We conducted a retrospective analysis of children with retro- and/or parapharyngeal abscesses, hospitalized at our department from 2006 to 2019.

Results: We treated 11 children with retro- and/or parapharyngeal abscesses; 64% girls and 36% boys, with median age of 40 months. Patients presented with torticollis (81%), neck swelling (72%), posterior pharynx wall protrusion or unilateral tonsil medialization (63%) and fever (54%). 72% needed surgical drainage. Streptococcus pyogenes was isolated in 5/11 (45%), oral microbiota in 2/11 (18%) and Staphylococcus aureus in 2/11 (18%). 45% developed complications: obstruction of great neck veins (4/5) and mediastinitis (2/5). In 7/11 (64%) deep neck abscess was suspected due to clinical worsening despite ongoing antibiotic treatment.

Conclusions: Retro- and/or parapharyngeal abscesses should be considered in all children presenting with fever, neck swelling and impaired neck movement. Detailed examination of the pharynx can direct us to further diagnostics. Failure of empirical antibiotic treatment for bacterial lymphadenitis should raise suspicion for retro- and/or parapharyngeal abscess.
INFANT WITH GROUP B STREPTOCOCCUS BACTEREMIA PRESENTING WITH PAROTITIS

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Title of Case(s): INFANT WITH GROUP B STREPTOCOCCUS BACTEREMIA PRESENTING WITH PAROTITIS

Background: Acute bacterial parotitis is a very rare infectious disease in infants under 3 months and the most common causing pathogen is *Staphylococcus aureus*. We present previously healthy 50-day-old full term infant with group B Streptococcus (GBS) bacteremia with acute bacterial parotitis.

Case Presentation Summary: A 50-day-old full term infant was brought to Emergency Department with a few hour history of poor feeding, irritability and a febrile temperature once till 39° C. The patient was breast-fed, and prenatal, postnatal medical history was without any significant complaints. On admission the baby was with tachycardia, irritable, but general examination was without any significant changes. Laboratory tests showed white blood count - 12 660/mm³, hemoglobin - 9.5 g/dL, platelet count - 421 000/mm³, C-reactive protein - 9.62 mg/L (maximal CRP 94.12 mg/L) and II-6 - 4972 pg/mL. During the stay in the Emergency Department the infant developed swelling in left parotis region with hyperaemia and sharp margins of hyperaemia, drainage of pus into the oral cavity was observed. The baby was holding his head in forced position. However, serum amylase levels were normal. Ultrasonography showed enlarged left parotid gland with edematous tissue and significantly increased blood flow. The blood cultures were obtained and Ceftriaxone and Clindamycine antibacterial treatment was started. On the second day of intravenous antibacterial treatment hyperaemia was no longer observed and the child had normal body temperature. *Streptococcus agalactiae* (GBS) was detected in the blood cultures. Antibacterial therapy was continued for 9 days and the infant was discharged from hospital with no complaints.

Learning Points/Discussion: 1. Acute bacterial parotitis is a really rare condition in infants but should be considered in infants with increased inflammatory markers and swelling in the preauricular region. 2. With appropriate antibacterial treatment regime complete recovery can be achieved.
NEURODEVELOPMENTAL OUTCOMES OF INFANTS WITH BACTERIAL MENINGITIS AND GROUP B STREPTOCOCCAL BACTERAEMIA IN ENGLAND

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Background: Neonatal infection is an important cause of morbidity and mortality. Demonstrating the long-term consequences of bacterial infections is a crucial part of disease surveillance. Knowledge of the burden of post-infection morbidity is important when developing interventions to prevent infection or reduce infection rates. It also aids financial and service provision planning, and parental counselling. The primary aim of the study was to assess the neurodevelopmental outcomes of neonatal Group B Streptococcus infection survivors.

Methods: Participants were identified from a previous bacterial meningitis healthcare delivery study and Group B streptococcus (GBS) infections in the Public Health England database. The children’s cognitive, language, and motor development were assessed using the Bayley Scales of Infant Development (BSID-III). Information on neurological status, sensory, behavioural, and somatic problems was also collected. Parents were invited to complete a Paediatric Quality of Life Inventory (PEDsQL) to assess the health status of their child by proxy, and an EQ-5D-5L questionnaire to assess their own health status.

Results: 119 infants were recruited - 40 GBS meningitis, 68 GBS bacteraemia, 11 non-GBS meningitis. Sequelae were identified in 13/40 children with GBS meningitis, 13/68 of those with GBS bacteraemia, and 2/11 with non-GBS meningitis. Four children have a hearing impairment. 30 children have some communication difficulties. Mean PedsQL scores are lower in children with identified problems.

Conclusions: Fewer severe complications were identified than in earlier work however long-term sequelae were still captured. Long-term problems in children who had suffered from GBS bacteraemia were identified (raising questions about both optimal follow-up and meningitis identification). The amount of language/communication/behavioural problems were noted; previous focus tended to be on motor/cognitive problems. The importance of follow-up was highlighted both by the outcomes identified but also parental feedback.
A SERIOUS HEPATIC DISEASE IN A REFUGEE CHILD WITH PICA

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Title of Case(s): A serious hepatic disease in a refugee child with PICA

Background: Hepatic capillariasis is a serious hepatic disease caused by the nematode Capillaria hepatica, a parasite of mammalian liver primarily rodents who accidentally infects humans.

Case Presentation Summary: A 3-year-old girl living in a refugee centre was referred for persistent high fever, weakness, PICA, abdominal pain, vomiting and hepatomegaly. The blood test revealed microcytic anaemia, eosinophilia, hyperglobulinemia and elevated levels of ALT and AST. Serologic tests were positive for Fasciola Hepatica and Toxocara canis. This result ended up being a false-positive due to a cross-reaction. Liver biopsy was done and revealed adult worms and characteristic eggs of Capillaria hepatica. The diagnosis was confirmed by PCR on the liver tissue. Our patient has been treated for 100 days by albendazole and is currently receiving degressive doses of corticosteroids with positive clinical and biological response. The clinical manifestations of hepatic capillariasis are nonspecific. The typical triad is fever, painful hepatomegaly and eosinophilia. The parasite and his eggs are undetectable in faeces. The larvae mature, mate and lay her eggs in the liver parenchyma and they cannot be excreted. Currently, there is no valid immunodiagnostic method for the diagnosis of hepatic capillariasis. Moreover, serological cross-reactivity lead to misdiagnosis. Therefore, liver biopsy remains the cornerstone of diagnosis. The deposition of eggs in the liver parenchyma causes granulomas and liver necrosis, which can lead to potentially fatal liver dysfunction. Thereby, prompt diagnostic and treatment are crucial.

Learning Points/Discussion: Hepatic capillariasis is a rare condition that should be taken into consideration in a child presenting with persistent fever, hepatomegaly and eosinophilia. Liver biopsy is the gold standard for the diagnosis. Evidence-based treatment, optimal duration of albendazole and corticosteroids, is lacking.
SAFETY AND IMMUNOGENICITY OF A QUADRIVALENT MENINGOCOCCAL CONJUGATE VACCINE (MENACYW-TT) ADMINISTERED IN HEALTHY MENINGOCOCCAL VACCINE NAÏVE TODDLERS (12-23 MONTHS) CONCOMITANTLY WITH DTAP-IPV-HB-HIB CONJUGATE PEDIATRIC VACCINE

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Background: MenACYW-TT is an investigational quadrivalent meningococcal conjugate vaccine intended for use in individuals 6 weeks of age and older. We evaluated the safety and immunogenicity of MenACYW-TT when co-administered with routine pediatric vaccines.

Methods: A total of 1183 toddlers participated in a Phase III, randomized study to receive a single dose of MenACYW-TT administered alone or concomitantly with other pediatric vaccine(s) in South Korea, and Thailand (measles-mumps-rubella [MMR] vaccine + varicella [V] vaccine), Mexico (diphtheria, tetanus, acellular pertussis, hepatitis B, poliomyelitis and Haemophilus influenzae type-b conjugate [DTaP-IPV-HB-Hib] vaccine), and the Russian Federation (pneumococcal conjugate vaccine [PCV13]). Safety data were collected up to 30 days post-vaccination. Here we present results of only co-administration with DTaP-IPV-HB-Hib conjugate vaccine.

Results: Immune response induced by MenACYW-TT administered alone was comparable to when administered concomitantly with DTaP-IPV-HB-Hib conjugate vaccine. The percentages of subjects with hSBA titers ≥ 1:8 (ranging from 89.9% to 100%) or rSBA titers ≥ 1:128 (ranging from 96.8% to 100%) were comparable in all the groups and for all serogroups. Immunogenicity profile of DTaP-IPV-HB-Hib conjugate vaccine administered alone was comparable to when administered concomitantly with MenACYW-TT. The post-vaccination GMTs and response rates for DTaP-IPV-HB-Hib conjugate vaccine were comparable in all the groups. The safety profiles of MenACYW-TT administered alone or concomitantly with DTaP-IPV-HB-Hib conjugate vaccine, and that of the DTaP-IPV-HB-Hib conjugate vaccine when administered alone or concomitantly with MenACYW-TT, were generally comparable.

Conclusions: MenACYW-TT and DTaP-IPV-HB-Hib conjugate vaccine were found to be well tolerated and immunogenic among meningococcal-vaccine naïve toddlers 12 to 23 months of age, when administered alone or concomitantly. This provides the evidence for concomitant administration of MenACYW-TT vaccine with hexavalent combination vaccines and achieve high coverage rates.

Clinical Trial Registration: EudraCT# 2018-001472-38
CLINICAL-EPIDEMIOLOGICAL ANALYSIS OF THE INFLUENCE OF MATERNAL PREDISPOSITION FACTORS ON THE NEONATAL SEPSIS IN THE CONDITIONS OF ENVIRONMENTAL PRESSING.

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Background: To improve the results of diagnosis and treatment of neonatal sepsis, to study the peculiarities of maternal predisposition factors to its development in contrast to the ecological characteristics of the regions of residence of pregnant women.

Methods: Clinical and epidemiological analysis of the influence of maternal predisposition factors on the formation of neonatal sepsis in 260 newborns, has been conducted, which depends on the environmental characteristics of the places of residence of pregnant women.

Results: It has been shown that in case of the absence of significant differences in the indicators of reproductive health, as well as somatic pathology and obstetric and gynecological history, the dwelling of pregnant women in unfavorable conditions is accompanied by the increased risk of miscarriage and the birth of children in the gestation period to 35 weeks (HS = 2.04; 95% CI 1.2-3.7), children with extremely low body weight (HS = 2.9; 95% CI 1.1-7.3), as well as probably lower Apgar score on the 5th minute (VS = 5.12, 95% D 2.1-12.6).

Conclusions: The change can be regarded as a consequence of chronic contact of pregnant women with the pollution areas of their residence.
Title of Case(s): Pleural nodules in healthy 13 years old boy: Tuberculosis (TB) or not TB?

Background: Pleural nodules can be associated with a variety of conditions from infectious diseases, including tuberculosis, to inflammatory syndromes and tumors. Histological analysis is often needed to obtain a certain diagnosis. This case highlights the diagnostic challenges of a child presenting with multiple pleural nodules and who was found to have an inflammatory myofibroblastic tumor.

Case Presentation Summary: A previously healthy 13-year old boy referred to our hospital for multiple pleural nodules. He presented with a 7 months history of fatigue, weight loss, pallor, dry cough, evening fever and sharp pain on the right chest wall. Blood tests showed elevated inflammatory markers and microcytic anaemia. Chest x-ray suggested pneumonia with right pleural effusion. He performed multiple antibiotic therapy with no clinical improvement. All microbiology tests were negative, including respiratory viruses, Mycoplasma, Chlamydia, Legionella, Haemophilus, Streptococcus pneumoniae and Bordetella pertussis. CT chest showed right pleural effusion and multiple pleural nodules located on the costal, diaphragmatic, mediastinal and scissural right pleura, with central necrotic areas and calcific spots and a specific tuberculous process has been hypothesized. Skin Mantoux test, Interferon Gamma Release Assay and sputum analysis were all negative. Bronchoalveolar lavage showed inflammatory cells, especially macrophages. A biopsy of the lesions was performed and proved an inflammatory myofibroblastic tumor with TGF-ROS rearrangement. Treatment with Crizotinib was subsequently started.

Learning Points/Discussion: Pleural nodules are a rare finding in children and represent a challenge for the clinician. Infectious diseases (tuberculosis), inflammatory syndromes and tumors must be ruled out. Inflammatory myofibroblastic tumor is a rare benign neoplasia, which occurs more often in children and young adults. Symptoms mimic chronic infectious diseases, which may delay diagnosis. Histological analysis is needed to obtain a certain diagnosis with prompt therapy.
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Title of Case(s): Zika Virus Infection

Background: Zika virus (ZIKV) is an emerging arthropod-borne virus that belongs to the genus Flavivirus, and transmitted primarily by Aedes spp. mosquitoes. In May 2015, the Ministry of Health of Brazil confirmed autochthonous transmission of ZIKV associated with an outbreak of “dengue-like syndrome” cases. Congenital ZIKV-infection may present with a spectrum of clinical and neuroradiographic findings. There is an urgent need to assess neurodevelopment in ZIKV-exposed infants. Our aim was to describe the first preliminary clinical/serological outcomes of ZIKV-exposed children followed-up of a non-endemic country.

Case Presentation Summary: Prospective observational cohort study of ZIKV-exposed mother-child pair (January 2019- December 2019). Children were recruited at birth and laboratory/clinical data from mothers obtained from microbiology department. ZIKV-infected mothers were defined as confirmed, probable or undetermined following national guidelines. Epidemiological, clinical and laboratory data were registered on a database. Statistical analysis was carried out through SPSS. Ethical approval was obtained. 7 children (51.4% male) were included; Mean gestational age at birth was 40.2±1.02 weeks. ZIKV-pregnant women were from South-America 28.6%(2/7), North-America 14.3%(1/7), Central-America 42.8%(3/7), and 1 from Nigeria (14.3%). At birth, ZIKV-RNA performed on blood and urine and ZIKV-IgM were negative in all children. ZIKV-IgG seroreversion was achieved at a mean of 6.5±1.8 months. All children had a normal neurological evaluation at birth (clinical and radiological) as well as they succeed in hearing screening. Congenital cytomegalovirus infection was ruled out at birth. 1 of 7 infants (14.28%) without initial evidence had lately repetitive seizures showing intraparenchymatous bleeding in the cerebral ultrasound. The follow-up was performed every 3-5 months after birth.

Learning Points/Discussion: ZIKV infection remains still uncertain. Although a large proportion of ZIKV-exposed infants without microcephaly and with seroreversion develop normally, many do not. These infants need a multidisciplinary follow-up almost until 18 months of age.
OUTCOMES OF INFANTS BORN TO MOTHERS WITH MATERNAL SYPHILIS. A CASE SERIES

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Title of Case(s): OUTCOMES OF INFANTS BORN TO MOTHERS WITH MATERNAL SYPHILIS. A CASE SERIES

Background: Syphilis remains a great concern, pregnant women especially at risk. Maternal screening and treatment constitute effective prevention strategies to reduce disease burden. Possible outcomes of mother-to-child transmission include spontaneous abortion, stillbirth, prematurity, clinical manifestations of congenital syphilis, infant death, and late sequelae. Outcomes of infants born to serologically positive syphilis mothers will be presented, along with an illustration of a 18 month-follow-up.

Case Presentation Summary: At birth, except for reactive serology for syphilis, all babies had no clinical/laboratory abnormalities, considered as congenital syphilis, received a full 10-day-course procaine penicillin. Case1, female, caesarean section. First pregnancy resulted stillbirth, diagnosed as syphilis since 4th month, VDRL (1:32), TPHA (1:640), treated with Benzathine Penicillin-G, 1 and 3 months later VDRL was (1:2). She had multi sex partners. Birthweight was 2900 grams, VDRL non-reactive. Darkfield test from placenta, umbilical cord, amniotic fluid, revealed spiral-shaped organisms. VDRL test 1, 3, 7, 18 months revealed non-reactive. Case2, male caesarean section, birthweight 2500 grams. Mother, diagnosed as syphilis since 28th gestational age received benzathine penicillin-G. Mother's VDRL was (1:16), TPHA (1:2560); baby’s VDRL (1:2), TPHA (1:1280). Case3, male, vaccume extraction, mother’s VDRL (1:32), diagnosed since 6th month, given benzathine penicillin-G. Birthweight 3910 grams, VDRL 1:16, reactive TPHA.. Case4. female, caesarean section, referred at 46 days. Mother had multi sex partners, married twice, diagnosed as syphilis since 8-month-pregnancy, treated with doxycycline. She experienced abortion twice. Mother’s VDRL and TPHA were reactive, birthweight 3910 grams, VDRL 1:16, TPHA 1:2560.

Learning Points/Discussion: Outcomes were abortion, stillbirth, Proven and Possible Congenital Syphilis. Case 1 deserved no further evaluation/treatment, case 2-4 should receive follow-up examinations and serologic testing. Inadequately treated mother, multi sex partners, history of abortion being risk factors.
CULTURAL METHOD IN THE STUDY OF GUT MICROBIOTA IN CHILDREN WITH AUTISM SPECTRUM DISORDER (ASD)

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Background: Autism spectrum disorder (ASD) is characterized by poor social skills, stereotypical behavior, anxiety and cognitive inflexibility manifesting in early childhood. Multiple studies describe the association of imbalanced gut microbiota in ASD development. The aim of the study is using of high-throughput cultural methods to investigate the features of the gut microbiota in children with ASD in comparison with a control group.

Methods: We studied faecal microbiota of 67 children at the age of 1.5–10 years old including 41 autistic ones. The strain isolation was made by seeding serial dilutions of the material on 11 nutrient media. The MALDI-TOF MS and 16S rRNA gene sequencing were used for the identification of microorganisms. We applied the logistic regression approach for statistical analysis of microorganisms occurrence on species, genera and families levels using groups and age of the patients as predictors. Family-wise error rate was controlled using Holm-Bonferroni correction. The analysis of the total number of representatives of taxonomic groups was performed using ANCOVA with the same predictors that described above.

Results: Totally we isolated 5513 strains belonging to 203 species. The identification of 348 bacteria was derived by sequence of 16S rRNA gene. We found that the gut microbiota of children with ASD was considered to have the lower diversity on species ($p=0.00036$), genera ($p=0.001$) and families ($p=0.022$) levels. The occurrence of Ruminococcaceae family representatives was lower in children with ASD ($p=0.024$).

Conclusions: Obtained data demonstrate the qualitative and quantitative differences in the intestinal microbiota of autistic children in comparison to the control group that can be a consequence of the specific eating habits or the involvement of gut commensals in ASD pathogenesis.

Clinical Trial Registration: ClinicalTrials.N/A
A RARE PRESENTATION OF A COMMON ENEMY

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Title of Case(s): A rare presentation of a common enemy

Background: Hemophagocytic lymphohistiocytosis (HLH) is a potentially fatal hyperinflammatory condition caused by a highly stimulated but ineffective immune response. The incidence is estimated to be approximately 1.2 cases/ million/year, but this is almost certainly an underestimate. EBV infection consists the most common viral factor causing stimulation, generation and uncontrolled secretion of T- and NK- cells and IL-2, INF-α and IL-6, molecules.

Case Presentation Summary: A previously healthy 3-year-old girl was admitted due to fever and generalized skin rash. She had skin necrosis at about 60% of body surface (toxic epidermal necrosis/TEN) and ulceration at mucous membranes (mouth, eyelids). Physical examination suggested EBV infection (cervical lymphadenopathy, splenomegaly) that was confirmed by serological tests. At day 2, respiratory impairment led to tracheal intubation and blood tests showed pancytopenia, elevated levels of ferritin, fibrinogen, triglyceride, LDH and hyponatremia. Laboratory findings suggested HLH, diagnosis that was confirmed by bone marrow biopsy. She received dexamethasone and etoposide according to HLH-2004 and broad-spectrum antibiotics. Due to persistent leukopenia, she received filgrastim with progressive amelioration. At day 30, the already established mucosal damage caused obstruction of upper respiratory tract from necrotic membranes leading to cardiopulmonary arrest. She underwent urgent tracheotomy and a second arrest took place with positive outcome. On following days, she became hemodynamically unstable requiring antihypertensive drugs. The chemotherapeutic treatment was successful (undetectable EBV DNA copies) and bone marrow transplantation was avoided. She was discharged on day 94 of staying with severe neurological sequelae.

Learning Points/Discussion: Clinicians involved in the diagnosis and management of TEN must be alert to the possibility of coexisting HLH, particularly in cases with severe multi-organ system involvement. As fatal cases of TEN might present symptoms associated with HLH, treating appropriately could be vital for patient outcome.
VACCINATION COVERAGE FOR CHILDREN AND ADOLESCENTS WITH CHRONIC DISEASES IN CRETE GREECE

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Background: The national immunization program includes special recommendations for high-risk children and adolescents with chronic medical conditions. Suboptimal vaccination coverage has been previously reported for high-risk populations. The aim of this retrospective study was to assess vaccination coverage for high-risk children and adolescents with chronic diseases.

Methods: Immunization records of children and adolescents with asthma, type I diabetes mellitus, neurological diseases, nephrotic syndrome and chronic renal diseases and cystic fibrosis, examined at the Department of Paediatrics, University Hospital of Heraklion, Crete during a six-months' period, were assessed.

Results: Three hundred and five children and adolescents participated in the study. Twenty-one percent of the participants were immunized for influenza in the precedent influenza period and only 5% had a three-year in a row influenza vaccine. One dose over one year of age of a conjugated pneumococcal vaccine had received 96% of children with asthma, 77.8% with cystic fibrosis, 87.1% with type I diabetes mellitus, 83.3% with renal diseases and all the children with neurological diseases. The 23-valent polysaccharide pneumococcal vaccine were administered to 4% of the study population.

Conclusions: Suboptimal vaccination coverage for high risk populations, especially for influenza, were recorded. This finding highlights the need for emphasizing on the special recommendations for high-risk children and adolescents in everyday practise and better reminding techniques.
CHARACTERIZATION OF NASOPHARYNGEAL MICROBIOTA DURING EPISODES OF FEVER CAUSED BY RESPIRATORY VIRAL INFECTIONS AND BACTERIAL INFECTIONS IN CHILDREN WITH CANCER UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT)

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Background: Children with cancer undergoing HSCT may develop fever episodes caused by respiratory viral infections (RVI). In them, the role of the nasopharyngeal microbiota as a determinant of predisposition or severity is unknown. The aim of our study was to characterize the nasopharyngeal microbiota during episodes of fever caused by RVI, bacterial infections (BI) or unknown cause in children with cancer undergoing HSCT.

Methods: Composition of nasopharyngeal-microbial communities was determined by amplification of 16S-ribosomal subunit gene, with 27F/1492R universal primers, and sequencing using PacBio Sequel platform (MRDNA Lab,TX,USA). Four different groups analyzed included healthy controls (HC,n=7) and children with fever caused by RVI(n=19), BI (n=9), or unknown causes (UC,n=6). Reads were passed through quality control, trimming and alignment to public 16S-gene databases to establish operative taxonomic units(OTUs). Composition of microbial communities between different groups of samples was compared by performing redundancy analyses (RDA) and by comparing the abundance of taxonomic groups.

Results: According to RDA, composition of nasopharyngeal microbiota from children who presented fever episodes was significantly different from the HC(p<0.001). Comparison between the three groups only also indicated significant differences in microbiota composition among them(p=0.027). A significantly higher proportion of Firmicutes was found in RVI,BI and UC compared to HC (p<0.0001). Representative genera among these phyla included Salinicoccus in BI and Lachnobacterium in RVI. In contrast, a significantly higher proportion of Proteobacteria was found in HC compared to BI(p=0.031) and UC(p=0.0008). Representative genera for the HC group included Terrahaemophilus, Aggregatibacter and Saccharibacter.

Conclusions: The study of the nasopharyngeal microbiota could be useful in understanding the interaction between respiratory viruses and bacteria. Eventually, this interaction could be relevant in the predisposition and/or severity of the RVI in children with HSCT (FONDECYT-GRANT#1171795).
EFFECTIVENESS OF INFLUENZA VACCINE IN CHILDREN WORLDWIDE: A SYSTEMATIC REVIEW

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Background: Influenza is common cause of mortality and morbidity in children worldwide. We aimed to investigate the effectiveness (VE %) of the flu vaccine in children aged 0-17 years on all continents.

Methods: A systematic search (2009-2019) was conducted in PubMed, Scopus, Cochrane databases. Reference lists of selected articles were screened to identify additional studies. Cohort studies, patient / control studies, cross-sectional studies, and systematic reviews were eligible for inclusion. Data were selected for the following criteria: age 0-17 years, vaccine effectiveness (VE%). Study quality was evaluated using the Critical Appraisal Skills Programme Tool (CASP) and the Specialist Unit for Review Evidence (SURE). Study selection and quality assessment were conducted by 2 independent researchers. Fixed- or random-effect models, as appropriate, were used to synthesize data.

Results: Vaccine effectiveness data were available from 48 eligible studies. Vaccine effectiveness ranged between 3% - 93.5%, with 31 studies ending up in efficacy rates >50% and 2 studies finding negative result. Analyzed studies come from Asia (39.9%), USA (35.4%), Europe (18.8%) and Oceania (6.3%). Vaccines effectiveness (VE%) through the decade 2009-2019 was in: Asia: 46.7%(95%CI:33,2-58,4%), USA: 56.7%(95%CI:50,6-62,7%), Europe: 46.2%(95%CI:33,2-59,1%)(P-value:0.094). VE% in 3 chronological periods was: (2009-2012): 66.8%(95%CI:57,9-75,6%), (2013-2016) 43,3%(95%CI:34,9-51,7% and (2017-2019):51,5%(95%CI:45,3-57,8%),(P-value:0.003).

Conclusions: Influenza vaccine effectiveness in children and adolescents, although not very high, varied depending on the geographical area and chronological period. During 2009-2012 was found the best vaccine effectiveness throughout the decade.

Systematic Review Registration: N/A
Background: Bacteraemia is one of the main causes of childhood mortality worldwide. Blood cultures (BC) are crucial for bacterial identification but contamination of blood culture vials (BCV) leads to misinterpretation of the results. We aimed to describe the clinical, laboratory and microbiological features of children with a positive BC, and determine the factors associated with contamination.

Methods: Children aged <18 years old attending to our paediatric emergency department or admitted between November 2017 and July 2019, with a positive BC, were retrospectively included. Results of the BC were extracted from the microbiological laboratory records. For each positive BC, data of the patients were anonymised and collected.

Results: Among 1849 BCV, 127 (6.9%) were positive in 111 children. BC yielded a pathogen in 29/127 (22.8%) vials, and a contaminant in 98 (77.2%). 22/111 (19.8%) children had a clinically relevant bacteraemia, mainly related to pyelonephritis (n=6; 27.3%) and febrile neutropenia (n=5; 22.7%). Predominant pathogens were Escherichia coli (n=7), Staphylococcus aureus (n=3), and Streptococcus pneumoniae (n=2). Predominant contaminants were Staphylococcus epidermidis (n=37), Staphylococcus hominis (n=15) and Micrococcus luteus (n=9).

Patients with bacteraemia were older and had more underlying diseases, higher temperature, and higher CRP level than those with contaminants (p<0.05).

Conclusions: Bacteraemia are rare in our centre and E. coli was predominant. Our results are consistent with the current epidemiology in high-income countries after implementation of the pneumococcal conjugate vaccine. Identification of factors associated with contamination of BCV may help to improve sampling process.
DALBAVANCIN AS COMBINATION THERAPY FOR THE TREATMENT OF A MULTIFOCAL OSTEOMYELITIS IN A CHILD

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Title of Case(s): Dalbavancin as combination therapy for the treatment of a multifocal osteomyelitis in a child

Background: Staphylococcus aureus is the most common microorganism causing acute osteomyelitis in children. The increasing incidence of infections caused by methicillin-resistant Staphylococcus aureus (MRSA) complicates therapy. Dalbavancin is a long-acting lipoglycopeptide antibiotic with strong activity against gram-positive pathogens. Unfortunately, pediatric safety and dosages have not been established yet. Here we report the first case of paediatric osteomyelitis successfully treated with dalbavancin as combination therapy.

Case Presentation Summary: A 8-years female patient, affected by hypogammaglobulinemia and autoimmune enteropathy due to LRBA deficiency, on treatment with abatacept and sirolimus, was admitted to the Pediatric ward on December 2017 for catheter induced-MRSA septic shock. Teicoplanin was started and the central venous catheter was removed. After one month, she developed an arthritis of the left knee with a tibial and femoral osteomyelitis. Bacterial cultures from arthrocentesis confirmed MRSA, so a regimen with amikacin and linezolid was initiated. For persistent fever and elevated levels of CRP, she underwent a MRI which detected bilateral femoral and tibial septic osteomyelitis. She was treated with other combination therapies: teicoplanin/daptomycin/levofloxacin followed by daptomycin/ceftaroline/rifampicin and finally trimetophrim/sulfamethoxazole and levofloxacin. Repeated surgical treatments of curettage and drainage were also performed. After 12 weeks of antibiotics, fever still persisted; dalbavancin at the dosage of 18mg/Kg was administered on day 1 and day 8, and repeated in association with fosfomycin after three and six weeks. The patient's clinical conditions gradually improved and she underwent allogeneic hematopoietic cell transplantation. At a 10 months follow up she was asymptomatic and MRI was negative.

Learning Points/Discussion: Dalbavancin may provide an alternative option for children, in order to avoid prolonged hospitalization and central venous access.
MULTIDRUG-RESISTANT GRAMNEGATIVE BACTERIAL INFECTIONS IN PREVIOUSLY COLONIZED CHILDREN: A 1-YEAR STUDY FROM A TERTIARY SPANISH HOSPITAL

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Background: Multidrug-resistant gramnegative bacteria (MDRGNB) are a major global public health threat. In our hospital, ESBL and VIM-type carbapenemase have been the predominant mechanism of resistance in recent years. We have previously reported that 13% of VIM-type colonized patients had an infection during follow-up. Our aim is to describe the carbapenemase-type frequency in 2019 and to analyze the percentage of colonized patients who subsequently had an infection.

Methods: Retrospective study from a Spanish tertiary hospital in 2019. A systematically rectal colonization was performed (at admission and weekly) in the following departments: Transplantation units, Hemato-oncology ward, Resuscitation area, Pediatric intensive care unit, Medically complex children’s ward and Neonatal intensive care unit. Patients who were colonized with MDRGNB were followed-up, and positive culture results from patients who developed infections were collected.

Results: 93 MDRGNB colonized patients were detected. ESBL and OXA-48 were the main mechanisms of resistance. Of these 93 patients, 29% had a subsequent infection (Table 1). Median time between colonization and infection was 42 days. Bloodstream infection was the most frequent (10/29), followed by intrabdominal (7/29) and lung infection (7/29).

<table>
<thead>
<tr>
<th>Caracteristic</th>
<th>Colonization</th>
<th>Infection</th>
<th>Colonized patients who develop infection (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESBL</td>
<td>35</td>
<td>8</td>
<td>22,8</td>
</tr>
<tr>
<td>OXA-48</td>
<td>33</td>
<td>12</td>
<td>36,4</td>
</tr>
<tr>
<td>VIM</td>
<td>19</td>
<td>3</td>
<td>15,8</td>
</tr>
<tr>
<td>KPC</td>
<td>2</td>
<td>2</td>
<td>100</td>
</tr>
<tr>
<td>NMD</td>
<td>1</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>MR Pseudomonas</td>
<td>3</td>
<td>2</td>
<td>66,7</td>
</tr>
<tr>
<td>TOTAL</td>
<td>93</td>
<td>27</td>
<td>29</td>
</tr>
</tbody>
</table>

Conclusions: In 2019, a significant burden of OXA-48 carbapenemase-producing bacteria was observed in our hospital, replacing VIM-type carbapenemase which was the most prevalent in previous years. Infection by MDRGNB in previously colonized children is frequent (29%), reaching 36% in OXA-48
carbapenemase colonized patients. It is essential to establish a PROA program, to continue training of health professionals, and to maintain active surveillance by routine colonization cultures.

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Background: Limited data is published on local Romanian rotavirus gastroenteritis epidemiology. Moreover, the rotavirus vaccine is not mandatory in Romania. Due to this, we decided to analyze the socio-demographic aspects, determine any correlations with the hospitalization time, economic burden for children found with rotavirus positive stools at the emergency room or admitted at Children's Clinical Hospital Brasov, Romania. The second objective was to observe the burden of nosocomial rotaviral infection.

Methods: Observational, descriptive, retrospective study from 01.01.2011 through 31.08.2019 with a total of 2116 enrolled children. Demographic data, clinical manifestations and economic data were studied.

Results: 97% were under 5 years of age, 41.67% being girls. From the 82.2% of admitted children, 17% had nosocomial infection, mostly Rromas (p<0.012). The median hospitalization was 5 days, the Rromas being admitted longer (p<0.005). The longer the admittance the bigger the chances of receiving also an antibiotic treatment p<0.005. Caucasians were 74.6% compared with Rroma 26.4% with a typical distribution from January to March and October-November, 4.79% received antibiotics before admission. Direct costs of hospitalization/day are high, with a median of 1/4 of one month Romanian minimal income.

Conclusions: The seasonality of the disease was according to the published data. Most affected children were from urban area, nosocomial infections were more prevalent at the rroma population. Due to the high burden of rotavirus disease, and high costs of hospitalization there is a need for implementation of the vaccine.
SALMONELLA MENINGITIS IN AN INFANT: A CASE REPORT

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Title of Case(s): SEIZURE WITH HIGH FEVER, IRRITABLE AND DIARRHEA IN AN INFANT

Background: Salmonella meningitis is a rare form of meningitis and also an unusual manifestation of salmonellosis. However, it relatively common in developing countries, although rarely seen in developed ones. The prognosis is poor, as patients are more likely to die from Salmonella meningitis than from meningitis due to the other major bacterial pathogens and in survived cases, recurrence/ complication occurs in almost 30% of cases.

Case Presentation Summary: A 7 month infant presented with seizures, high fever, irritable and diarrhea for 2 days. There were no significant medical problems before, growth and development were appropriate. From laboratory examination, the baby had anemia, leukocytosis and very high CRP. CNS tap cultures revealed Salmonella Paratyphi B, sensitive to first line therapy. Head CT scan showed leptomeningeal and gyral enhancement on bilateral temporoparietal lobe supporting of meningoenchepalitis. Third generations cephalosporin were given for one week, but fever persisted. After changed to ampicillin and chloramphenicol fever decreased, and treatment continued for another week. Three months follow up in outpatient clinic revealed no recurrence nor complication

Learning Points/Discussion: The treatment protocol for Salmonella meningitis can be modified depending upon the sensitivity pattern of the organism and the clinical response to the antibiotic in use. In our case, the infant responded well with intravenous ampicillin and chloramphenicol. Salmonella meningitis tends to cause a high percentage of neurological abnormalities, hence neuroimaging is recommended in all patients. Ventriculitis, subdural empyema, hydrocephalus and chronic neurological abnormalities may found in as many as 43% cases and a 64% relapse rate, thus follow up are needed.
ACUTE GASTROENTERITIS IN ICELANDIC CHILDREN – IS IT TIME FOR IMMUNISATION AGAINST ROTAVIRUS?

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Background: Rotavirus commonly causes acute gastroenteritis (AGE) in young children. Where introduced, vaccinations against rotavirus have led to fewer hospital visits and admissions due to rotavirus gastroenteritis. This prospective study explores the burden of rotavirus disease and potential advantages of introduction of rotavirus vaccine in Iceland.

Methods: Children ≤5 years of age presenting with AGE to the Children's Hospital Iceland emergency department (ED) during 2017-2018 were offered participation. Information was collected on age, sex, day-care attendance, recent antibiotic use, Vesikari score, need for treatment and/or admission and stool PCR results. Within 14 days from ED visit, information on duration of illness, days missed from day-care/work and number of other infected family members was collected.

Results: 325 (40% of eligible) children were enrolled. The median age was 16 months (range 1-71). A pathogen was identified in 79% of cases (258/325), usually one (n=195 cases) or two (n=55). Rotavirus was most commonly identified; in 142 (44%) cases, followed by adenovirus, norovirus and enterovirus (50, 47 and 39 cases respectively). Children with rotavirus infections had a median age of 18 months (range 1-69), Vesikari score 13 (range 4-18), duration of illness of 6 days (range 1-18), missed 5 days from day-care (range 0-13) and parental absence from work was 4 days (range 0-14). They were older, had higher Vesikari scores, more need for IV fluids and had shorter duration of illness, compared to non-rotavirus AGE. The rotavirus epidemic was larger in 2018 than in 2017 (106 vs. 36 cases).

Conclusions: Rotavirus is the most common cause of AGE in young Icelandic children leading to ED visits. Vaccination against rotavirus is likely to reduce burden of disease from AGE and may be cost-saving for Icelandic society.

Clinical Trial Registration: not applicable
SALIVA AS A POTENTIAL MATRIX FOR THERAPEUTIC DRUG MONITORING OF GENTAMICIN IN NEONATES

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Background: Plasma sampling for therapeutic drug monitoring (TDM) in neonates is associated with pain and unwanted blood loss. Due to these disadvantages, salivary sampling is a potential alternative. The aim of this study was to investigate the feasibility of determining gentamicin in saliva of neonates and to possibly develop a pharmacokinetic saliva/plasma model.

Methods: All neonates receiving gentamicin treatment were eligible for the study. Up to 8 saliva samples, 2 plasma TDM samples and demographic characteristics were obtained for each subject. Saliva samples were analyzed using tandem liquid chromatography mass spectrometry (LC-MS/MS), with an lower limit of quantification (LLOQ) of 0.057 mg/L. A population pharmacokinetic model was developed using the saliva samples and a database of routine plasma concentrations of neonates.

Results:

116 saliva samples of 24 newborns were collected for the interim analysis. In total 73 samples had gentamicin concentrations above the LLOQ. 44 plasma samples were collected as part of standard of care. A plasma model was developed with 686 gentamicin plasma concentrations from 384 subjects. The plasma concentrations were best described by an allometric two-compartment model with postmenstrual age as covariate on clearance. For the saliva concentrations, a third compartment was incorporated in the model with gestational age as covariate on the elimination rate of gentamicin in saliva. This model estimated an elimination rate \( K_{30} \) of 0.609 h\(^{-1}\) with an inter-individual variability (IIV) of 25.8% and an absorption rate \( K_{13} \) of 0.0458 h\(^{-1}\).
Conclusions: The interim analysis demonstrated that gentamicin can be determined in saliva at very low concentrations. The current data are encouraging enough to continue this study and develop a final model.

Clinical Trial Registration: Clinical trial registration: NL66410.018.18, Trial NL7211 (NTR7410)
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Background: The aim of the present study was to assess clinical and laboratory features of gastrointestinal and hepatic involvement in children with Kawasaki disease (KD) treated at the Department of Infectious Diseases, University Medical Centre Ljubljana.

Methods: A retrospective analysis of children with KD treated at our institution between June, 2006 and December, 2009 was performed.

Results: Of 169 children with KD 29/169 (17.2%) presented with gastrointestinal manifestations: 8.3% with diarrhea, 7.7% with vomiting and 5.9% with abdominal pain. Ultrasound showed signs of mesenterial lymphadenitis in 9/169 (5.3%) and peritoneal effusion in 11/169 (6.5%). The mean laboratory values of hepatic enzymes were 1.3 µkat/L for AST, 1.5 µkat/L for ALT and 1.2 µkat/L for GGT. Gallbladder hydrops was diagnosed in 20/169 (11.8%), 10/169 (35.9%) had signs of hepatomegaly and 2/169 (1.2%) had cholecystitis. Our results showed higher percentage of gallbladder hydrops in patients that developed CAA (20% vs. 11%).

Conclusions: Gastrointestinal involvement has often been associated with KD but does not belong to the classic diagnostic criteria. Literature shows that the majority of the intra-abdominal and gastrointestinal manifestations resolve with adequate treatment of KD. Our results show that clinical abdominal manifestations at the onset of KD could be a risk factor for coronary involvement, probably due to more severe and diffuse vasculitis involving the digestive tract. The question that remains to be answered is the significance of gallbladder hydrops in risk stratification of cardiac artery abnormalities (CAA).
INFLUENZA TYPE B VIRAL INFECTION COMPLICATED WITH COMPARTMENT SYNDROME AND ACUTE RENAL INJURY SECONDARY TO RHABDOMYOLYSIS

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Title of Case(s): INFLUENZA TYPE B VIRAL INFECTION COMPLICATED WITH COMPARTMENT SYNDROME AND ACUTE RENAL INJURY SECONDARY TO RHABDOMYOLYSIS

Background: Myositis consists a rare but potentially fatal complication of influenza infection leading to rhabdomyolysis and acute renal injury.

Case Presentation Summary: A previously healthy 8-year-old girl, presented with fever, myalgias and vomiting over the past 8 days. Due to altered mental status (lethargic) and hemodynamic instability, she was admitted to PICU with the presumptive diagnosis of viral infection with severe dehydration, and received intravenous fluids and inotropic drugs. On day 1, her course complicated with seizures and she was intubated. She was treated with IV cefuroxime and oseltamivir, whereas laboratory tests revealed elevated levels of creatine phosphokinase (CPK>15000IU/l) with normal renal function. Plasmapheresis was commenced since hydration and urine alkalization did not manage to reduce CPK levels. As tenseness was noted at both lower extremities, compartment syndrome was suspected and confirmed by measuring intramuscular pressure. Long incisions through the skin and immediate fasciotomy were performed in both calves releasing excessive pressure. Antibiotic treatment changed to IV clindamycin and piperacillin/tazobactam. On day 3, she presented acute renal injury treated with continuous venovenous haemodiafiltration and progressive amelioration of renal function was noted. She, also, presented, capillary leak syndrome with ascites, pericardial effusion and remarkable pleural effusion managed with several paracenteses. On day 7 she was extubated and her course was uncomplicated until discharge on day 17. The final diagnosis was influenza infection as influenza type B antigen was detected complicated with compartment syndrome and acute renal injury secondary to rhabdomyolysis.

Learning Points/Discussion: Despite that the most common influenza complications concern respiratory system, rhabdomyolysis should be kept in mind. Clinical suspicion, immediate management, treatment with oseltamivir and, of course, influenza vaccine can reduce illness severity and mortality.
WHEN TUBERCULOSIS TRAVELS BEYOND THE LUNG: A RETROSPECTIVE CASE SERIES ANALYSIS

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Title of Case(s): TRAVELLING AWAY FROM THE LUNG: A RETROSPECTIVE CASE SERIES ANALYSIS

Background: Tuberculosis is an infection that can affect almost any organ in the body and children are at least twice as likely to have extrapulmonary tuberculosis (EPTb) as adults. The incidence rates of tuberculosis (Tb) have decreased in Europe, and Portugal has been no exception. Accordingly, in 2016, BCG began to be administered only to children belonging to risk groups.

Case Presentation Summary: We present a series of 6 cases of EPTb admitted to our hospital from 2014-2019: 3 meningeal (2 with miliary tuberculosis), 2 peritoneal, and 1 vertebral and hepatic. Five were girls, and half the cases occurred in the first 2 years of life while the other half occurred after the age of 9; five children were previously healthy. Only one case occurred in a child native from another country, and only two had previous known contact with Tb. Four children had been vaccinated with BCG. Regarding exams, the highest values of CRP and ESR recorded were 110.8mg/L and 86mm/h, respectively, in one of the peritoneal tuberculosis cases. All children were started on quadruple antituberculous therapy empirically, one needing parenteral therapy for a limited period; adjunctive corticosteroids were administered in meningeal cases. All meningeal cases and the vertebral case developed sequelae, something that did not happen in the peritoneal cases. The identification of Mycobacterium tuberculosis was obtained in all cases (3 by PCR and 6 in culture).

Learning Points/Discussion: In the absence of typical pulmonary features, the diagnosis of EPTb remains challenging, and a high clinical suspicion is crucial to it, because the disease is easily overlooked. Moreover, extrapulmonary lesions are paucibacillary, and samplings, in most cases, difficult to obtain. Antituberculous therapy can minimize morbidity and mortality but may need to be initiated empirically.
**MYCOBACTERIUM BOVIS INFECTION OF THE HIP – A RARE CAUSE OF HIP PAIN**

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**Title of Case(s):** Mycobacterium bovis infection of the hip – a rare cause of hip pain  

**Background:** Tuberculosis (TB) of the hip is becoming increasingly rare. Early diagnosis and treatment are crucial to prevent the development of chronic pain, loss of movement and progressive development of deformity. Mycobacterium bovis is a rare agent of TB disease, and patients with identification of this agent should be screened for immunodeficiency.

**Case Presentation Summary:** A previously healthy 6-year-old boy, presented in our emergency department with right inguinal pain. He had the recommended routine immunization scheme, including BCG vaccine after birth. On admission, he showed severe pain and external rotation and flexion of the thigh. The hip x-ray was normal. Ultrasound showed a small effusion. Septic arthritis was suspected, and flucloxacillin and gentamycin were started. During hospital stay, the patient initiated fever and the ESR rose to 99 mm/h. Microbiologic study of fluid collected in two arthrocenteses was negative. Biochemical study of the fluid from the latter showed 2335 cells (68% polymorphonuclear cells). The patient maintained pain and progressive loss of range of motion. The MRI showed arthritis, myositis and osteomyelitis of the right femur. An open arthrotomy was performed. A purulent drainage was collected and acid-alcohol fast bacilli were identified by direct examination and PCR. Culture was positive for Mycobacterium bovis. An immunologic study was conducted (HIV, immunoglobulins, lymphocyte subsets, oxidative burst and IL12/23 axis) all normal. Systemic involvement was excluded. The patient completed 1 year of antituberculous drug regimen. A cutaneous fistula developed, resolving after 5 months. No sequelae were observed.

**Learning Points/Discussion:** This case highlights the importance of maintaining a high suspicion for TB disease. In this particular case, the diagnosis was only possible through biopsy obtained by open arthrotomy. Additionally, a very unusual microorganism was found, in an apparently immunocompetent child.
Background: Kawasaki disease (KD) is an acute systemic vasculitis of medium size vessels and yet remains the leading cause of acquired heart disease in childhood.

Methods: This is a retrospective analysis of the medical data from children with KD, admitted to a tertiary pediatric hospital in Athens, from January 2011 to December 2018. The KD diagnosis and the definitions for cardiovascular complications was based on the American Heart Association criteria.

Results: 61 children younger than 14 years were diagnosed with KD, 31 children (50.8%) were considered as typical KD, while 30 children (49.2%) were atypical cases. The presentation of cases showed a distribution in early winter (December-11.5%, March-16.4%, May-11.55%). An elevated SGPT concentration during hospitalization was associated with cardiovascular complications (P=0.027) and was more common in typical KD than in atypical (P=0.019). From the atypical KD children 46.7% were diagnosed with cardiovascular complications in contrast to 38.7% of typical, with no statistical difference (P=0.54).

Conclusions: An increased percentage of atypical KD cases comparing with other studies was diagnosed during the study period. Cardiovascular complications were more prevalent in the atypical than the typical KD cases.
Background: The diagnostic criteria for Kawasaki disease (KD) consist of the clinical features that are shared by other childhood febrile illnesses. In many cases bacterial infection is suspected leading to different antibiotic treatment. The aim of the present study was to assess antibiotic use in children diagnosed with Kawasaki disease (KD) at the Department of Infectious Diseases, University Medical Centre Ljubljana.

Methods: A retrospective analysis of children with KD treated at our institution between June 2006 and December 2019 was performed. We reviewed the medical records for antibiotic use before and after hospital admission.

Results: In a cohort of 163 children diagnosed with KD, 53.4 % (87/163) received an antibiotic treatment in the outpatient clinic before referral to a hospital care. Most widely used antibiotics were penicillin V and amoxicillin clavulanate counting for 40% and 24% respectively. 12.6 % of patients received more than one antibiotic. In a hospital setting, antibiotic treatment was initiated in 44 % (72/163) of KD patients. Flucloxacillin and amoxicillin clavulanate counted for 22% and 18% respectively as a monotherapy and one third (31.9%) of patients received more than one antibiotic.

Conclusions: This analysis showed that a relatively high proportion of children diagnosed with KD receive antibiotics. Given the clinical features and the choice of antibiotic, bacterial skin infections (streptococcal and staphylococcal) such as scarlet fever take the first place in differential diagnosis in both outpatient and hospital setting in our cohort, which is no surprise. However, one of the questions that remain to be answered is coexisting of a bacterial infection with KD.
Background: Children under 5 years of age represent a high risk category of developing complications of influenza, which increase the rate of hospitalization.

Methods: We present the characteristics of children under 5 years of age hospitalized for influenza in a tertiary care hospital for infectious diseases in Bucharest, Romania, in the 2018/19 season, as part of the DRIVE study.
We included 469 children under 5 years with influenza-like illness. A percentage of 27.5% (n=186) of the were positive for influenza by RT-PCR: 48 infants (under 1 year), 82 toddlers (1-2 years) and 56 preschoolers (3-5 years). Only one case of influenza B was identified, the rest being positive for influenza A: 65.9%A/H1, 28.6%A/H3 and 5.4% unsubtyped influenza A.

Results: The clinical presentation was dominated by fever (98.4%) and cough (94.1%). The median duration of hospitalization was 4 days (IQR: 3.5), but was significantly higher when the child had at least one chronic condition (29 patients) [5 days (IQR: 4.7) vs. 4 days (IQR: 3.5), p=0.031, r=0.20], or when a co-infection with RSV (9 cases) was associated [6 days (IQR: 4.9) vs. 4 days (IQR: 3.5), p=0.009, r=0.16]. A number of 5 children required hospitalization in the ICU. Only 9 children had been vaccinated for influenza, of which only one tested positive for influenza. The evolution was favorable in all cases, with no deaths recorded.

Conclusions: We identified an important circulation of influenza viruses and low rate of influenza vaccination among children under 5 years. Measures to increase the vaccination rate are needed.
SAFETY AND IMMUNOGENICITY OF A QUADRIVALENT MENINGOCOCCAL CONJUGATE VACCINE (MENACYW-TT) ADMINISTERED IN HEALTHY MENINGOCOCCAL VACCINE NAÏVE TODDLERS (12-23 MONTHS) CONCOMITANTLY WITH MMR+V PEDIATRIC VACCINES


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Background: MenACYW-TT is an investigational quadrivalent meningococcal conjugate vaccine intended for use in individuals 6 weeks of age and older. We evaluated the safety and immunogenicity of MenACYW-TT when co-administered with routine pediatric vaccines.

Methods: A total of 1183 toddlers participated in a Phase III, randomized study to receive a single dose of MenACYW-TT administered alone or concomitantly with other pediatric vaccine(s) in South Korea, and Thailand (measles-mumps-rubella [MMR] vaccine + varicella [V] vaccine), Mexico (diphtheria, tetanus, acellular pertussis, hepatitis B, poliomyelitis and Haemophilus influenzae type-b conjugate [DTaP-IPV-HB-Hib] vaccine), and the Russian Federation (pneumococcal conjugate vaccine [PCV13]). Safety data were collected up to 30 days post-vaccination. Here we present results of only co-administration with MMR+V vaccines (n=378).

Results: Immune response induced by MenACYW-TT administered alone was comparable to when administered concomitantly with MMR+V vaccines. The percentages of subjects with hSBA titers ≥ 1:8 (ranging from 92.0% to 100%) or rSBA titers ≥ 1:128 (ranging from 97.6% to 100%) were comparable in all the groups and for all serogroups. Immunogenicity profile of MMR+V vaccines administered alone was comparable to when administered concomitantly with MenACYW-TT. The post-vaccination GMTs and response rates were comparable in all the groups. The GMTs ranged from 1998 to 2923 for anti-measles Abs; 80.4 to 108 for anti-mumps Abs; 73.4 to 111 for anti-rubella Abs; and from 11.5 to 19.0 for anti-varicella Abs. The safety profiles of MenACYW-TT administered alone or concomitantly with MMR+V vaccines, and that of the MMR+V vaccines when administered alone or concomitantly with MenACYW-TT, were generally comparable.

Conclusions: MenACYW-TT vaccine can be administered with the MMR+V vaccines between 12 to 23 months of age without affecting the immunogenicity or safety profiles of either vaccine.

Clinical Trial Registration: EudraCT# 2018-001472-38
Background: Adolescents and young people represent a growing share of people living with HIV worldwide. In 2018 alone, 510,000 young people were newly infected with HIV, of whom 190,000 were adolescents between the ages of 10 and 19. Their emotional status represent an important parameter to consider when talking about health as well as a determinant for ART compliance. Emotional frailty in a young people leaving with HIV is constantly sustained by fear of discrimination and isolation. Recent local experiences in other chronical diseases showed also the importance to invest in peer supporter strategies. The aim of our study is promote HIV knowledge, ART compliance and reflection about perceived stigma using the support from patients of the same study cohort who have their own experiences.

Methods: Cohort: 49 perinatally infected HIV patients ages 14-29 - Geographical origins: 50% Italy, 15% East-Europe, 30% Africa, 4% South-America, 1% Asia. - Caregivers experience: 40% Childhood traumas related to the loss of parents; 15% Adoptions; 35% Foster Family experience. a-met immunology and the psychology every two/three months during the follow-up. b-psychological assessment assessment: Emotive status, cognitive level and adaptive behavior with specific psychological tests c-22 patients decided to meet other patients to get to know them d- Organizet a meeting: structure an educational intervention on general well-being and HIV treatment and research innovation studies. e- Emotions about the meeting and ideas about the need to meet peers again have been collected

Results: Some patients who attended the meetings later met outside the hospital and became friends. others wanted to meet together in the same room during the follow up. The problems they would most like to deal with together are the unveiling of the pathology to the partners

Conclusions: Human relationship seems to be one of the best therapies

Clinical Trial Registration: no unique identifying number
Background: Since the introduction of meningococcal C vaccine in 2002, invasive meningococcal disease has become rare in Iceland. Changes in the epidemiology of meningococcal serotypes have been seen in Europe in recent years as well as increase in invasive disease. Meningococcal carriage has never been studied in Iceland. The purpose of this study is to assess meningococcal carriage prevalence and duration in Iceland, study serotype distribution and evaluate if changes are needed in the Icelandic immunisation programme.

Methods: Nasopharyngeal swabs were taken from 1-6 year old children attending day-care centres. Oropharyngeal swabs were taken from adolescents aged 15-16 years and young adults aged 18-20 years attending secondary schools. Swabs were cultured and mass-spectrometry was used for detection of \textit{N. meningitidis}. Follow-up swabs were taken from carriers 6-12 weeks after first swab and again 21-26 weeks after the first swab.

Results: 460 swabs were taken from the youngest age group, 197 swabs from adolescents and 523 swabs from young adults. No carriers were found among the 1-6 year olds (0/460), 1.5% carried meningococci among 15-16 year olds (3/197) and 6.5% (34/523) among 18-20 year olds. After 6-12 weeks, 76% (22/29) of tested carriers still carried \textit{N. meningitidis} and at 21-26 weeks, 62.5% (10/16) were still colonised.

Conclusions: As expected, prevalence of meningococcal carriage increases during adolescence and young adulthood but is very rare in young children. Most carriers remain colonised for months. Serotype distribution of the isolates is pending as well as whole genome analysis(WGS) of meningococci from persistent carriers and the information may aid policy-makers regarding changes in meningococcal vaccine programmes. The WGS may help shed light on long term carriage in adolescents and young adults.

Clinical Trial Registration: not applicable
UNUSUAL COINFECTION IN MENINGOENCEPHALITIS: A CASE REPORT.

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Title of Case(s): Unusual coinfection in meningoencephalitis: a case report.

Background: Central nervous system infections include from meningitis to encephalitis, but also meningoencephalitis (when both are affected). Mainly caused by viruses, bacterial origin should be ruled out because of its worse prognostic. We present an unusual case of coinfection, with important key points to learn more about these diseases.

Case Presentation Summary: 13-year-old adolescent without past history of interest, who complained of fever, psychomotor agitation and altered level of consciousness of sudden onset. He was febrile with pathological neurological examination: Glasgow 10/15 and positive meningeal signs. Petechial lesions were observed in the right hemithorax. Lab test and blood culture were collected (CRP 2.6mg/dL, Procalcitonin 10.95ng/dL), and cefotaxime and vancomycin were started. After CT scan ruling out intracranial hypertension, lumbar puncture was performed: cloudy CSF, hyperproteinorrachia, hypoglycorrhachia and leukocytosis 1015/l; gram staining negative. After that dexamethasone, acyclovir and ampicillin were added to the treatment. Medical study was completed: rapid influenza test and PCR for respiratory viruses: negative; and EEG normal. After 24 hours Meningococcus isolation in blood culture was reported. According to this, cefotaxime and acyclovir were maintained but others antibiotics were stopped. 24 hours later, the detection of HHV-6 in CSF was also reported, and because our patient still referred severe headache and neurological symptoms, acyclovir was modified to ganciclovir. Treatment was completed with progressive improvement of the neurological symptoms. Serotype Y of meningococcus was informed. Final diagnosis: sepsis and meningococcal Y meningitis and HHV-6 encephalitis. Follow up: fully recovery, without complications.

Learning Points/Discussion: - Even when bacterial and virus coinfection is not a common finding in CNS infections, it can happen. - In order to establish microbiological diagnosis, appropriate samples should be taken. - It is also important to remark that treatment should be adjusted after microbiological results.
A RARE COMPLICATION OF A COMMON DISEASE

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Title of Case(s): A RARE COMPLICATION OF A COMMON DISEASE
Background: Lemierre’s syndrome (LS) is a rare and serious complication of an oropharyngeal infection which often affects school-aged children and healthy young adults. It is defined by septicemia and internal jugular vein thrombosis followed by septic emboli. The most common pathogen implicated is Fusobacterium necrophorum. We present a case of atypical clinical presentation of LS in order to draw attention to this condition.

Case Presentation Summary: A previously healthy 17-year old female presented with fever and sore throat. Physical examination revealed tonsillar exudate and bilateral cervical masses. Rapid strep test was negative, but given her complaints of acute pain and malaise, a blood panel and a cervical computerized tomography (CT) scan were performed, revealing heterogeneous right tonsil and infra-centimetric lymph nodes. Serum CRP and leucocyte count were elevated. Given the possibility of complicated tonsillitis, ceftriaxone was prescribed, but the patient remained febrile during the next 5 days and began complaining of cough, dyspnoea and anterior right thoracic pain. She presented no changes on physical examination, except for a remaining painful cervical right mass. Cervical ultrasound revealed right facial vein thrombophlebitis and blood panel showed elevated D-dimers. LS was then suspected and the patient was started on clindamycin. Cervical, cerebral and thoracic angio-CT scans were performed and several septic emboli were found throughout the pulmonary parenchyma. In total, the patient underwent a cycle of 22 days of ceftriaxone and clindamycin.

Learning Points/Discussion: Due to its low incidence and absence of pathognomonic symptoms, the early recognition and prompt treatment of this disease remains a challenge. With this case report the authors aim to alert the paediatric community to the importance of an early diagnosis and a high index of suspicion.
VACCINATION COVERAGE FOR ADOLESCENTS IN A RURAL AREA OF CRETE

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**Background:** Vaccines for adolescents are essential for an optimal vaccination coverage through adulthood. The aim of this study was to retrospectively record vaccination coverage for all recommended vaccines for children and adolescents according to the National Immunization Program in a rural area of Crete with good health services.

**Methods:** Immunization records from high school students of the specific area were assessed.

**Results:** Records form 441 students were analyzed. High coverage rates were reported for hepatitis B (99.3%), MMR (98.6%), MenC (90.5%), while for varicella and pneumococcal vaccine 77.6% and 66% of students respectively were found vaccinated. Suboptimal vaccination rates were found for tetanus-diphtheria-acellular pertussis vaccine for adolescents (80%) and 4-valent conjugated meningococcal vaccine (78.2%), both recommended at the age of 11-12 years of age according to the National Immunization Program. Fully vaccinated for human papilloma virus was the 59.3% of the female students of the study.

**Conclusions:** This study highlights the need for emphasis on post childhood immunization in order to achieve optimal vaccination coverage rates.
BRONCHIOLITIS REQUIRING INVASIVE MECHANICAL VENTILATION – 15 YEARS EXPERIENCE OF A SINGLE CENTER

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Background: Bronchiolitis is the leading cause of respiratory failure requiring invasive mechanical ventilation (IMV) in young children. Bacterial co-infections may prolong pediatric intensive care unit (PICU) stay. The aim was to characterize the bronchiolitis requiring IMV.

Methods: Exploratory study with retrospective data collections of all children <2 years with bronchiolitis requiring IMV, admitted to PICU, between 2004-2019.

Results: There were 231 bronchiolitis admitted during the study period, 38 (16%) required IMV. The median age was 3.9 months (IQR 1.1; 4.3), and 24 (63%) were boys. Seven patients had an underlying medical condition (18%) and 22 (58%) were preterm. Multiplex PCR was performed in respiratory specimen of 37 and it was positive for ≥1 virus in 35 (92%); RSV was detected in 28 (74%). Bacterial co-infection was considered in 35 (92%): according to clinical/analytical features (40%), clinical/radiologic findings (34%), positive bronchoalveolar lavage (BAL) culture (26%). Amoxicillin clavulanate was the most frequent antibiotic used. In six patients antibiotics were started prior to PICU admission. From 20 patients in whom BAL was performed, 10 were positive (8 in the first 48h from admission); H.influenza (30%), S.pneumoniae (20%), M.catarrhalis (20%) were the most common pathogens.

The length of stay was higher in the group with a positive BAL (10.5 days vs 5.50 days; p=0.054). There were no differences regarding IMV mean time or maximum FiO₂.

The median PICU length of stay was 6.5 days, and the ventilation mean time was 3.2 days. There were no deaths.

Conclusions: The rate of IMV in patients admitted with bronchiolitis was 16%, all with good outcome. Bacterial co-infection diagnosis was mainly based on clinical features. BAL was only performed in 52% of cases. It’s essential to obtain cultures before antibiotic therapy to better guide prescription.
AWARENESS AND ATTITUDE OF PEDIATRICS RESIDENTS’ AND PEDIATRICS SPECIALISTS’ TOWARDS MENINGOCOCCAL INFECTIONS AND MENINGOCOCCAL VACCINES

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Background: Invasive meningococcal disease (IMD) is a life-threatening illness caused by the bacterium Neisseria meningitidis. Serogroups B and W are the most common causes of IMD. The purpose of this study is to understand and measure the level of awareness of pediatrics residents and pediatrics specialists relating to meningococcal infections, nasopharyngeal carriage, and available vaccines in Turkey.

Methods: A cross-sectional survey of 16 questions investigating meningococcal infection types, major serogroups, risk factors, incidence, most affected age groups, rates of development of sequelae, and vaccine types was conducted among doctors in the pediatrics department at Bezmialem Vakif University Hospital. Practices and attitude of doctors for inclusion of vaccines into national immunization program were also evaluated.

Results: A total of 45 responses were received: 24 from pediatrics residents and 21 from specialists. The average age of respondents was 35 years. 80% of doctors knew all the major clinical presentations of meningococcal infections. 22% underestimated the incidence of IMD. 90% of specialists agreed that there was a risk of infection with carriers. 47% of specialists believed that IMD was most commonly seen below the age of 1 year. 82% believed that the meningococcal vaccine should be included in the national vaccination program.

Conclusions: One third of survey respondents had practiced care of patients with meningococcal infections which shows that the disease is not rare in Turkey. Majority believed that previously healthy kids are usually affected emphasizing the importance of inclusion of vaccines into national immunization program. It is recommended that our university and pediatrics departments take strides to educate and inform doctors about the importance of IMD and the ease of protection from IMD.
SAFETY AND IMMUNOGENICITY OF A QUADRIVALENT MENINGOCOCCAL CONJUGATE VACCINE (MENACYW-TT) ADMINISTERED IN HEALTHY MENINGOCOCCAL VACCINE NAÏVE TODDLERS (12-23 MONTHS) CONCOMITANTLY WITH PCV13 PEDIATRIC VACCINE

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Background: MenACYW-TT is an investigational quadrivalent meningococcal conjugate vaccine intended for use in individuals 6 weeks of age and older. We evaluated the safety and immunogenicity of MenACYW-TT when co-administered with routine pediatric vaccines.

Methods: A total of 1183 toddlers participated in a Phase III, open label, randomized study to receive a single dose of MenACYW-TT administered alone or concomitantly with other pediatric vaccine(s) in South Korea, and Thailand (measles-mumps-rubella [MMR] vaccine + varicella [V] vaccine), Mexico (diphtheria, tetanus, acellular pertussis, hepatitis B, poliomyelitis and Haemophilus influenzae type-b conjugate [DTaP-IPV-HB-Hib] vaccine), and the Russian Federation (pneumococcal conjugate vaccine [PCV13]). Safety data were collected up to 30 days post-vaccination. Here we present results of only co-administration with PCV13 vaccine (n=399).

Results: Immune response induced by MenACYW-TT administered alone was comparable to when administered concomitantly with PCV13 vaccine. The percentages of subjects with hSBA titers ≥ 1:8 (ranging from 83.7% to 99%) or rSBA titers ≥ 1:128 (ranging from 95.7% to 100%) were comparable in all the groups and for all serogroups. Immunogenicity profile of PCV13 vaccine administered alone was comparable to when administered concomitantly with MenACYW-TT. The post-vaccination GMTs and response rates were comparable in all the groups. The GMTs ranged from 0.802 [serotype 3] to 7.62 [serotype 14] (co-administered group) and from 0.773 [serotype 3] to 6.30 [serotype 14] (administered alone). The safety profiles of MenACYW-TT administered alone or concomitantly with PCV13 vaccine, and that of the PCV13 vaccine when administered alone or concomitantly with MenACYW-TT, were generally comparable.

Conclusions: MenACYW-TT conjugate vaccine can be administered with the PCV13 vaccine between 12 to 23 months of age without affecting the immunogenicity or safety profiles of either vaccine.

Clinical Trial Registration: EudraCT# 2018-001472-38
CHANGE OF CRP IN TIME AND CLINICAL AND PREDICTIVE MEANING. STUDY IN A REPRESENTATIVE SAMPLE OF CHILDREN AND ADOLESCENTS IN CENTRAL GREECE

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Title of Case(s): CHANGE OF CRP IN TIME AND CLINICAL AND PREDICTIVE MEANING. STUDY IN A REPRESENTATIVE SAMPLE OF CHILDREN AND ADOLESCENTS IN CENTRAL GREECE

Background: C-Reactive Protein is among the most useful and sensitive acute phase markers. Several conclusions can be drawn regarding the etiology (bacterial, viral, etc.) and severity of an infection or other inflammatory process through the evaluation of initial CRP value as well as its shift in time, leading to appropriate diagnostic management and treatment.

Case Presentation Summary: The medical files of all children admitted to our Pediatric Clinic with febrile infection (regardless of site) were studied in retrospective. Analysis of CRP values and their shift in time surfaced notable conclusions regarding the suspected etiology of infection, which seem to be essential for the practitioner in order to initiate or discontinue antibiotic therapy. The median admission CRP was remarkably higher in bacterial infections and the difference was statistically significant in relation to the viral ones (p:0.014). The difference between admission CRP and the CRP at time of discharge was also statistically significant in bacterial infections in relation to the viral ones (p:0.030), whereas there was no correlation between the CRP level changes and gender. According to t-test, there is a statistically significant correlation between the elevated CRP levels and the duration of hospitalization (p:0.002), as well as the administration of antibiotics (p:0.004).

Learning Points/Discussion: CRP is an acute phase protein of our immune system with direct and indirect effect. The change of its levels in time, leads to important conclusions for the kind of infection or inflammation, findings that are very important for the management and treatment of all those severe situations, infections and inflammations.
Background: This is an audit of children hospitalised at Department of Infectious Diseases Ljubljana in 5 year period who presented with clinical picture of orbital cellulitis. I think the topic is very relevant, because this diagnosis is rare in children and can be easily overlooked. If you do not pay attention the consequences can be devastating.

Methods: A retrospective study of children with orbital cellulitis who were hospitalised at our institution from 2014 to 2019. Inclusion criteria were painful bulgomatic and MRI conformation.

Results: In 5 years we’ve treated 6 patients, 3 girls (50%) and 3 boys (50%). All presented with local swelling and redness. 5/6 (83%) children had fever and 3/6 (50%) proptosis. The diagnosis was confirmed by magnetic resonance imaging in 4/6 (67%) and computer tomography in 2/6 (33%). Isolation of causative agent from operative swab was successful in 4/6 (66%) – 2/6 S. intermedius, 1/6 S. aureus and 1/6 S. pyogenes. All of the patients were treated with antibiotics intravenously. 5/6 (83%) needed surgical intervention. Complications were seen in all cases with subperiosteal abscess in 83% and optic neuritis in 17%.

Conclusions: All of our patients presented redness and swelling of the eyelid, painful or limited eye movement, discharge and fever. Early diagnosis of orbital cellulitis is urgent and the most alarming symptom is painful bulgomatic. CT scan and MRI of the orbits are two imaging modalities that are commonly used to aid in the diagnosis. Immediate treatment is very important, and it typically involves intravenous (IV) antibiotics and surgical intervention. Although orbital cellulitis is considered an ophthalmic emergency, the prognosis is good if prompt medical treatment is received.
Title of Case(s): STREPTOCOCCAL TOXIC SHOCK SYNDROME CAUSED BY STREPTOCOCCUS PYOGENES DURING AN INFLUENZA A VIRUS INFECTION

Background: Influenza A virus infection can promote secondary invasive bacterial infections, including Streptococcus pyogenes (GAS). The authors present a clinical report of a child with an invasive GAS infection concurrent with H1N1 influenza virus.

Case Presentation Summary: A previously healthy 13-month-old boy was admitted to the emergency department with a 4-days history of fever, cough, diarrhea and vomiting. On admission, he presented severe prostration, generalized micropapular rash and clinical signs of shock. Influenza A (H1N1) virus was detected in the nasopharyngeal swab. Laboratory tests revealed both leukopenia (1930/uL) and increased inflammatory markers (C-reactive protein 25mg/dL, procalcitonin 100ng/mL). Chest x-ray showed a diffuse consolidation in the left lung. Medical management was started with intravenous fluid therapy, antibiotic therapy (ceftriaxone) and oseltamivir. On the first hours clinical signs of deterioration were noticed, requiring admission to PICU; invasive ventilation and cardiovascular support were started. GAS was isolated in blood culture and Streptococcal Toxic Shock Syndrome (STSS) was confirmed. Antibiotic therapy was adjusted and intravenous immunoglobulin was administered in the first 48hours. Acute compartment syndrome and necrosis of extremities developed, requiring emergent decompressive fasciotomies, leading to finger amputations. On D12 was diagnosed a left-sided necrotizing pneumonia with large multiloculated pleural effusion requiring thoracic drainage, with a favourable outcome. The patient was discharged after 85 days of hospitalization and is currently being followed by a multidisciplinary team.

Learning Points/Discussion: Influenza virus may prone to severe bacterial infection, namely GAS infection. STSS caused by GAS can be a severe syndrome with rapid clinical progression associated with a high mortality rate. Should be kept a high level of suspicion and aggressive treatment should be initiated promptly.
SPLENIC INFRACT: A RARE MANIFESTATION OF RICKETTSIAL INFECTION

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Title of Case(s): ABDOMINAL PAIN IN AN ADOLESCENT BOY

Background: Murine typhus manifests with fever, chills, headache whereas the clinical triad of rash-fever-headache is found in less than half of patients. Commensal rats serve as the primary zoonotic reservoirs and rat flea, Xenopsylla cheopis, as the classic vector.

Case Presentation Summary: A 14-year-old boy was submitted to our hospital due to upper left quadrant (ULQ) pain, splenomegaly and anemia. He had an unremarkable personal history and lived in a farm. Two weeks before submission he reported fever (39°C) and cough lasting one week. He was not examined during that febrile episode, and no antibiotics were prescribed. Two days after the recession of fever he started complaining for pain in the ULQ. On admission, he was afebrile, pale, with no palpable lymph nodes, no rash or site of bite. He had low inflammatory markers (WBC 6200/μL, CRP 6.1mg/L, ESR 25mm) and hypochromic microcytic anemia. All biochemical parameters were within normal ranges. Ultrasonography revealed two splenic infarcts (4.5x3.2 cm and 3.2x1.3 cm). The investigation of anemia revealed low ferritin and ferrum, negative sickling test and direct coombs test. D-dimer were negative.

Blood cultures were negative and cardiac ECHO was normal. We observed diagnostic titers for R. typhi in subsequent testing (days 17 and 27) and positive IgM antibodies for R. conori serologically by IFA.

Patient remained stable, with improvement of his clinical signs and symptomatic management.

Learning Points/Discussion: Rickettsial infections are known to cause hemostatic changes that lead to coagulopathies and thrombotic events. Only a few case reports associate splenic infarction and endemic typhus, especially in children. This case highlights the importance of considering rickettsial infection in the differential diagnosis of infectious etiologies of splenic infarcts according to history and regional endemic data.
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**Background:** To individualize diagnostic approaches in neonatal sepsis, to investigate the features of the content of its serologic markers in newborns from childbirth, who are in chronic contact with small doses of heavy metal salts that pollute the soil in the habitats.

**Methods:** To achieve the goal, using the simple random sample method, 260 neonates. The unfavorable influence of environmental factors on the body of pregnant women and their newborns, patients with sepsis, were studied taking into account the geochemical nature joints include family residence. In the complex of a comprehensive examination of patients, informed consent of the parents of the child, studied the serum content of interleukins-6, -8, -10, procalcitonin, C-reactive protein and presepsin.

**Results:** Specific markers of environmental disadvantage of the environment in which mothers of patients with neonatal sepsis of children are, the content of interleukin-6 is greater than 40.0 pg / ml (specificity – 83.88%). The concentration of procalcitonin in the blood serum of premature babies with neonatal sepsis who did not exceed or equal to 0,1 ng / ml is highly susceptible (90,9% sensitivity) to the biomarker of the ecological well-being of their mothers' habitat.

**Conclusions:** The risk of unfavorable geochemical characteristics of the place of residence is increased during the next thresholds of serologic markers of neonatal sepsis in their newborn babies: the content of procalcitonin is greater than 0,2 ng / ml in 6 times (95% CI 2,8-12,9); for the content of C-reactive protein less than 1,0 mg / l in 6,5 times (95% CI 2,7-15,6); Presepsin content over 5000 ng / ml in 272,2 times (95% CI 32,7-226,8).
**Background:** Invasive *Staphylococcus aureus* (SA) infection is associated with increased morbidity. Methicillin-resistant SA (MRSA) is well established in the healthcare setting and in the community. Invasive methicillin-sensitive SA (MSSA) infection is associated with the expression of virulence genes. This study aims to describe the epidemiology and the clinical characteristics of invasive SA infection.

**Methods:** Retrospective and descriptive study of invasive SA infection in children admitted to the paediatric department of a level II hospital, between 2014 and 2018 (5 years). Demographic, clinical and laboratory parameters were analysed using SPSS® 25.0.

**Results:** 19 cases, 14 (73.7%) MSSA and 5 (26.3%) MRSA. The mean duration of hospital stay was 36.8 days. The most common related risk factors were previous hospitalization, recent antibiotic use and chronic disease. The most common clinical presentation was bacteraemia (78.9%), followed by musculoskeletal infection, deep tissue abscess and pneumonia. 52.6% had two or more infection sites. Hospital readmission was significantly associated with MRSA infection (p = 0.007). MRSA more frequently caused multi-site infections, bacteraemia and admission to ICU. No significant differences in presenting symptoms and laboratory examination were found.

**Conclusions:** Invasive MRSA infections had more serious clinical presentation, longer hospital stay and more frequent readmission than MSSA. In order to better understand the impact of the expression of known virulence genes on clinical manifestations and disease severity, molecular characterization of SA strains is crucial.
CONGENITAL SYphilIS, THE GREAT IMITATOR – CASE REPORT AND REVIEW

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Title of Case(s): A severe case of a 3-month-old boy with skin abnormalities, portal hypertension and anemia

Background: Transmission of T. Pallidum can still occur in countries with a high coverage of antenatal screening. As the mother was tested negative for syphilis at 16 weeks gestation, congenital syphilis was initially not considered. The broad spectrum of clinical manifestations hampers early recognition. In this era of decreasing antibiotic use, possibly increasing the chances of transmission, recognition of a potential syphilis infection is crucial in unexplained infectious disease cases.

Case Presentation Summary: A three-month-old boy presented with a rash, progressive abdominal distension with spider naevi and peripheral edema. The neonatal period was uneventful, syphilis screening was negative at 16 weeks gestation. Both the mother and the patient reported skin lesions. Blood count showed severe anemia (2.6 mmol/l) and thrombocytopenia (13 x10⁹/l) with elevated leucocytes (43.8 x10⁹/l) without lymphoblasts, coagulation parameters and liver enzymes were grossly disturbed. The patient was transferred to an intensive care unit due to increasing respiratory, renal and liver failure. The bacterial cultures and polymerase chain reaction for viruses including HIV, hepatitis, herpes simplex, Epstein Barr, immunodeficiency and metabolic screening were negative. The patient recovered without a diagnosis. When the father reported the same skin lesions, blood testing showed positive treponemal tests with elevated rapid plasma reagin (RPR) titers. Retrospective testing of the patient confirmed the diagnosis of congenital syphilis with a T. pallidum IgM immunoblot.

Learning Points/Discussion: This life-threatening case demonstrates the potential morbidity of a “forgotten disease” which was not included in the differential diagnosis by many physicians involved, besides the difficulty in recognizing syphilis by its nonspecific skin lesions in both parents and their child. Moreover, a negative syphilis test during pregnancy does not rule out congenital syphilis, as intercurrent transmission can still occur between testing and labor.
E-POSTER VIEWING
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10-28-2020 8:00 AM - 7:00 PM

A NEW INTEGRATED TOOL TO HELP IN DIAGNOSIS OF FEVER WITHOUT SOURCE IN CHILDREN AT PEDIATRIC EMERGENCY DEPARTMENT

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Background: Management of fever without source (FWS) in infants and children in the emergency department is challenging. The primary goal is to identify patients at high risk of bacterial infection, requiring antimicrobial therapy and/or hospitalization. Recent data indicate that host transcript biomarkers can accurately discriminate bacterial from viral infection. We have adapted the Filmarray® platform to rapidly measure host response transcripts, within 1 hour from venepuncture.

Methods: PAXgene blood samples were prospectively collected from two independent cohorts, 100 patients with proven infections, aged from 1 month to 17 years from across Europe (EUCLIDS study) and 478 French patients with FWS (ANTOINE study, NCT03163628), aged 7 days to 36 months. A multivariate model was developed to predict bacterial infection from the 12 transcripts (7 bacterial and 5 viral markers) measured in the Filmarray® pouch. A TRAIN-set allowed to determine the best signature was applied to a TEST-set to assess the clinical performance.

Results: Using 12 genes, we constructed a classifier for bacterial infection on both cohorts. In EUCLIDS, 46 of 50 bacterial patients were accurately identified; whilst in ANTOINE, it was 144 of 152 patients. The 12-transcript model was more specific (33%) than CRP (19%, calculated from the ANTOINE cohort), whilst sensitivity values were similar. Other parameters like age, fever, ill-appearance and clinical data can be also informative to increase the performance.

Conclusions: Filmarray® represents a promising technology for a new generation of rapid diagnostic tests, based on the host response. Our initial data exploring discrimination of bacterial and viral infection in children demonstrated superior accuracy for 12 transcripts, as compared to CRP. The performance of the signature will be validated on a larger pediatric cohort collected in the PERFORM study.

Clinical Trial Registration: ClinicalTrials.gov Identifier: NCT03163628
UNCOMMON CAUSE OF ACUTE KIDNEY DYSFUNCTION

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Title of Case(s): Uncommon cause of acute kidney dysfunction

Background: Among the rare causes of acute kidney dysfunction is Hantavirus. This RNA-virus is transmitted by rodents. Humans get infected through aerosols with antigens. It can cause a pulmonary or renal syndrome, whose severity depends on the viral serotype involved. The prevalence of Hantavirus infection is underestimated in the Netherlands, Puumalavirus is the most common serotype. Abnormalities seen in urine analysis include proteinuria or hematuria. Blood tests show elevated creatinine and urea. Ultrasound of the kidneys can show echogenic aspect of the renal parenchyma. Usually symptoms resolve spontaneously without permanent damage.

Case Presentation Summary: A 16 year-old boy presented at our Emergency Room with several days of malaise, high fever, headache, stomach pain and vomiting. Physical examination revealed besides fever, no other abnormalities. Vital signs were normal. Blood tests showed a slightly elevated CRP, normal WBC and raised creatinine and urea levels. Urine analysis showed proteinuria, hematuria and an elevated total protein/creatinine ratio. Serological tests, blood cultures and RT-PCR examination showed beside a Rhinovirus no abnormalities. Because of the clinical presentation and test results we performed additional Hantavirus serology. This repeatedly resulted positive for the serotype Puumalavirus. Both the clinical symptoms and renal dysfunction of our patient completely resolved spontaneously.

Learning Points/Discussion: Hantavirus is an underdiagnosed viral infection that can kidney and pulmonary dysfunction. It should be considered in the differentials of acute renal or pulmonary dysfunction.
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**Background:** Survey Inappropriate antibiotic prescribing is an important patient safety and quality matter. Many studies have characterised the quantity of antibiotic prescribing but few have addressed appropriateness. Our objective was to describe the appropriateness of prescribing using the US Sharing Antimicrobial Reports for Pediatric Stewardship methodology and AWaRe WHO antibiotic classification.

**Methods:** A point prevalence survey (PPS) was conducted in all inpatient areas in September 2019. Antibiotic choice, AWaRe category (target 55% or more in the "Access" category), indication, appropriateness, patient location and paediatric infectious diseases (PID) team involvement were recorded. Appropriateness was determined by consensus between an AMS pharmacist and consultant taking local treatment guidelines into account. The primary outcome was the proportion of antibiotics defined as inappropriate.

**Results:** Eighty-nine of 198 (45%) hospitalised patients were receiving an antibiotic. Of these prescriptions, 33 (37%) belonged to the "Access" category, 47 (53%) "Watch" and 9 (10%) "Reserve". A PID consultation was obtained in 34% of cases. There were no relevant guidelines for 9/89 (10%) of cases. Thirteen antibiotic prescriptions (15%) were considered inappropriate due to suboptimal activity spectrum, duplicate bacterial coverage and lack of evidence for choice. No "Reserve" antibiotics were prescribed inappropriately. Meropenem (78%) and Colistin (22%) were the only "Reserve" antibiotics used, in 78% of these cases PID was involved.

**Conclusions:** This PPS indicates a high proportion of inappropriate antibiotic prescribing. A large proportion of these were for surgical prophylaxis, suggesting a specific opportunity for improvement. The target of 55% antibiotics in the "Access" category wasn’t achieved, perhaps due to the high use of amoxicillin-clavulanate and cephalosporins ("Watch" category antibiotics) in local guidelines for the treatment of paediatric infections. Revising the use of "Watch/Reserve" antibiotics in guidelines may increase the prescribing of "Access" antibiotics and encourage the use of more narrow-spectrum agents.
EPIEMIOLOGICAL STUDY LOOKING AT PATIENTS SCREENED FOR MALARIA IN RETURNING TRAVELLERS PRESENTING TO A TERTIARY PAEDIATRIC CENTRE IN THE UK

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Background: This epidemiological study looked at where patients have returned from with a positive diagnosis of malaria and which species were isolated. We present data on where our patients are returning from most frequently and exploring the wide diagnostic differential that should be considered in these patients.

Methods: Non-concurrent database analysis was undertaken of children suspected of malaria disease at a tertiary paediatric hospital in the UK over a 5-year period (2014-19). All included children had at least one Rapid Detection Test (RDT), blood film and Full blood count. The gold standard was discharge diagnosis of malaria by clinical and diagnostic testing. Data on where the patient had returned from and what the discharge diagnosis was collected.

Results: 195 investigated children were included. There were 17 confirmed cases of malaria with 3 cases having positive RDT’s but negative blood films. For the other 14 positive results there was one case of plasmodium vivax from Eritrea and the rest were plasmodium falciparum. All confirmed cases were returned travellers from Africa apart from one from Pakistan. The majority (7 out of the 17 cases) were from Nigeria. There was one child less than one year of age and the rest ranged between 4 and 15 years old.

Conclusions: All cases of malaria were from returning travellers from Africa apart from 1 patient who returned from Pakistan. Africa was also the continent with the highest number of returned travellers. Out of the total number screened for malaria 8.71% were positive on blood film combined with RDT. This could help evaluate the diagnostic workup for patients with suspected malaria including whether a single RDT is sufficient to rule out malaria in children returning from African countries.
**Background:** *Streptococcus pyogenes* (Group A *Streptococcus*, GAS) is associated with common throat and skin infections, but periodic upsurges of severe invasive disease (iGAS) have been reported. This study performed a clinical, epidemiological and molecular characterization of pediatric iGAS in Portugal.

**Methods:** A national surveillance of pediatric iGAS infections during 2014-2018 in Portugal recorded demographic and clinical features of cases. The *emm* type and the presence of superantigen (SAg) genes was determined.

**Results:** We identified 129 children with iGAS, with an average annual incidence of 1.45/100,000. Clinical information was available for 118 cases, 65% males, median age of 3.8 years (IQR 1-5 years); The most frequent diagnosis was bacteremia without focus (38%), osteoarticular infection (21%) and skin/soft tissue infection (20%). The case-fatality rate was 5% (23% among STSS patients, \(p=0.004\)). Risk factors for mortality were diarrhea \((p=0.042)\), elevated cardiac rate at presentation \((p=0.027)\), and STSS \((p=0.040)\). Three *emm* types accounted for 66% of the isolates, namely *emm1* (37%), *emm3* (19%), and *emm6* (10%).

**Conclusions:** The incidence of pediatric iGAS is slightly lower than reported in other European countries, but with a similar associated mortality and STSS. The *emm* type distribution was different from that recorded among the general population in Portugal up to 2015, but further studies are necessary to evaluate these epidemiologic changes.
THE USE OF SERIAL RAPID DIAGNOSTIC TESTING AND BLOOD FILMS IN ORDER TO RULE MALARIA IN OR OUT IN RETURNING TRAVELLERS WITH A FEVER: A RETROSPECTIVE STUDY OF CHILDREN PRESENTING TO SHEFFIELD CHILDREN'S HOSPITAL

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**Background:** Guidance recommends three serial blood films to rule out malaria when investigating fever in returning travellers. At Sheffield Children's Hospital this is accompanied by the use of HRP2/pLDH (Pan) Rapid Detection Test (RDT) to aid diagnosis. We wanted to explore the use of serial RDT and blood films and look at how many tests were requested in practice prior to a diagnosis being reached. We wanted to use this data to see if it was possible to generate any hypotheses around the use of fewer investigations as a way of safely improving practice.

**Methods:** Non-concurrent database analysis was undertaken of children returning from travel abroad or new to the UK who had malaria as a differential diagnosis when presenting to a tertiary paediatric hospital in the UK. Data was analysed from a 5-year period (2014-19). All included children had at least one RDT and blood film. The outcomes were final malaria diagnosis v any other diagnosis. We analysed the result of RDT tests and both locally reported and reference lab reported films.

**Results:** Table highlighting the reliance on RDT and the use of local and reference centre blood films.

<table>
<thead>
<tr>
<th>Malaria</th>
<th>Non-Malaria</th>
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<tbody>
<tr>
<td>RDT +ve</td>
<td>RDT -ve</td>
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<tr>
<td>Local film</td>
<td>Local film</td>
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<tr>
<td>+ve</td>
<td>+ve</td>
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<td>12</td>
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<td>Reference lab film</td>
<td>Local Film (1-4 x per pt)</td>
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<td>+ve</td>
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| Non-malaria diagnoses were made after one (n=97), two (n=30), three (n=48) or four (n=3) serial blood films. 16 cases of Malaria were P. Falciparum and one qas P. Vivax. The possible reasons for blood films being negative in RDT positive cases will be discussed.

**Conclusions:** In returning travellers from Africa, who had not been treated for a recent episode of malaria the Sensitivity (95% CI) of RDT combined with a single blood film was 100%. We hypothesis that, to diagnose malaria in these cases, one blood test could be diagnostic. To rule out malaria, serial blood films would still be required.
MULTIPLE OSTEOARTICULAR INFECTIONS, WHAT’S HIDDEN BEHIND?

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Title of Case(s): Multiple osteoarticular infections, what’s hidden behind?  
Background: Hereditary sensory and autonomic neuropathy type IV (HSAN-IV) is a very rare autosomal recessive disease, with only a few hundred cases reported. It is characterized by recurrent episodes of unexplained fever, anhidrosis, thermoregulation disorders, total insensitivity to pain and developmental delay due to a mutation in the NTRK1 gene. The most frequent complications of this disease are multiple fractures, joint deformities, recurrent osteomyelitis and crippling self-injuries.

Case Presentation Summary: 17-year-old teenager diagnosed at eight months of age with HSAN-IV. Hyperthermia in the first months of life, absence of crying in the administration of the first vaccines and lesions in the oral mucosa and tongue with the appearance of the first teeth allowed an early diagnosis. Insensitivity to pain was suspected, he performed an electromyography that confirmed loss of sympathetic skin response. He manifested developmental delay and recurrent episodes of fever in the first years of life. Since the age of four, he had several infectious complications with osteoarticular involvement, septic arthritis of the shoulder and ankle, recurrent osteomyelitis and tenosynovitis. It was found that in five of these episodes, Staphylococcus aureus was the isolated agent.

Learning Points/Discussion: The high incidence of infections in patients with HSAN-IV is the greatest challenge in their orientation. Deep skin and bone infections are the most frequent and are commonly caused by Staphylococcus aureus, as in the case described. Recently, the absence of TRKA signaling has been shown to increase the susceptibility of these patients to infections and to this agent. Resistance to antibiotics becomes a frequent limitation in the treatment of these patients. The choice of appropriate therapy, duration of treatment and surgical debridement in cases of infection are essential.
WEIGHT GAIN AMONG ADOLESCENTS ON INTEGRASE INHIBITORS

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Background: Integrase Inhibitors (INI) are now the first-line treatment for people living with HIV, including children and adolescents. Clinical trials among adults have risen concerns regarding weight gain in patients starting or switching to INI. Adolescents are usually not included in clinical trials and thus, the evidence is scarce regarding weight gain in this special population characterized by important changes in body composition. We analyze the anthropometric evolution of children and adolescents on INI.

Methods: Within the Spanish Cohort of Pediatric HIV (CoRISpe), all patients below 24 years of age that had switched to an INI based regimen or started treatment with a regimen including INI up to December 2018 were included in the study. Anthropometric measurements were collected yearly and analyzed using paired signed-rank tests.

Results: 122 were included, with a median age of 15y [12 - 17], 57.4% women, 65% Caucasian, 60% were treatment switch (all had VL<50 c/ml). Median CD4 T cell count was 696 [506 - 1085]. Treatment regimen includedRaltegravir 56.6%, Dolutegravir 24.6% and Elvitegravir/c 18.9%. Weight z-score and BMI increased overtime during the first year of follow-up (all p<0.001) with a plateau for BMI over the second-year. No differences were found in anthropometric parameters among treatment groups and no effect of gender, ethnicity or age was identified on BMI z-score evolution.

Conclusions: In this study, no relation between exposure to INI and weight gain was found. However, few patients were on a Dolutegravir based regimen. Larger and longitudinal studies are needed in order to address the long-term effect of INI on weight among the unique population of adolescents, in which changes in body composition may impact long term cardiovascular and metabolic risk.
CASE REPORT: WHEN LUMBAR PAIN COMPLICATES

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Title of Case(s): CASE REPORT: WHEN LUMBAR PAIN COMPLICATES

Background: Vertebral epidural empyema is a rare disease, particularly in children, with few cases described. Opposite to adult population, pediatric patients are less likely to have predisposing conditions - contiguous infections, such as vertebral osteomyelitis are one of the possible risk factors. The dissemination is mostly hematogenic; however, the focus of infection cannot be identified in 20-40% of cases.

Case Presentation Summary: 6-year-old female, artistic gymnast, previously healthy, admitted to the Emergency Room with fever, hip pain and sore throat, following a bicycle fall two days earlier with trauma to the right thigh and gluteal region. She presented with right paramedian lumbosacrate tenderness (aggravated by walking), lateral right thigh bruises and superior gluteal tumefaction. No skin lesions or neurological impairment. Laboratory workout showed an increased CRP (140mg/L). Thigh soft tissue ultrasound was normal but CT and MRI showed a posterolateral L5-S1 epidural empyema and osteomyelitis foci in the sacral right alar plate, adjacent to the right S1-S2 ventral foramen and in the S2 right lamina. The patient was submitted to surgical drainage and was started on empiric antibiotics with ceftriaxone. After identification of a Methicillin-sensitive Staphylococcus aureus specimen on the pus, the antibiotherapy was downgraded to flucloxacilin. Blood cultures were negative. A positive clinical and imaging response was obtained and the patient was discharged with oral antibiotics and recommendations to complete 12 weeks of antibiotherapy. At time of discharge, she had no neurological impairment.

Learning Points/Discussion: The authors present a case of vertebral osteomyelitis complicated with epidural empyema, a rare disease in children. Surgical drainage and long-term antibiotherapy are recommended. Prognosis depends mainly on the neurological function at the time of diagnosis. Early diagnosis and intervention are essential, in order to avoid severe neurological impairment.
Title of Case(s): An atypical clinical presentation of *Mycobacterium tuberculosis* as mumps

**Background:** Tuberculous parotitis is an extrapulmonary manifestation of tuberculosis. It’s a rare disease in children, especially in the Western hemisphere. *Mycobacterium tuberculosis* (*MTB*) infection of the parotid gland occurs in two ways: dissemination from the oral cavity to the ducts of the parotid gland in the same way in which cervical lymph nodes get infected and via hematogenous dissemination from a primary infection focus in the lungs to the parotid gland. Tuberculous parotitis is often misdiagnosed. After starting treatment with anti-TB medicines, it shows full recovery if there’s no resistance against the medicines.

**Case Presentation Summary:** A 17 year old boy from Somalia presented at the paediatric out-patient department with a two-weeks painful swelling in the left cervical and peri-auricular regions. He also had a milder swelling on the right side. Beside the above-mentioned symptoms he had episodes of fever and had 5 kg weightloss in the last month. There was no sign of coughing of night sweating. On physical examination showed a swelling of his left neck and peri-auricular region and on the right side. Except for a slightly elevated CRP his blood results, including WBC were normal. Ultrasound showed an irregular swelling of especially the left parotid gland and cervical lymphadenopathy. IGRA was positive and RT-PCR of fine needle aspiration biopsy of the swollen parotic gland confirmed MTB infection. Treatment with anti-TB medicines, Isoniazide (INH), Rifampicine, Pyrazinamide and Ethambutol was started and resulted in full recovery.

**Learning Points/Discussion:** MTB infection should be excluded in a migrant child with swelling of the parotid glands.
HUMORAL IMMUNITY IN PATIENTS WITH NEONATAL SEPARATE DEPENDING ON ECOLOGICAL CHARACTERISTICS OF THEIR PARENTS ‘ACCOMMODATION.

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Background: The problem of an unfavorable impact of environmental factors on the population’s health is becoming significantly important every year and is being actively discussed by leading experts around the world. The aim of the study was to determine the indices of humoral immunity in children with neonatal sepsis.

Methods: Being treated in Chernivtsi and Khmelnitsky regions, 260 patients with neonatal sepsis were under observation. Newborns were divided into two groups: the I group of children (141) was from parents who permanently lived in polluted areas; the II one (119)- newborns whose parents lived in clean areas.

Results: Among patients with neonatal sepsis, there was a large proportion of prematurely born children who lived in conditionally contaminated areas. The level of Ig A in the blood serum of newborns of I group was 1.53±0.13 g/l versus 1.89±0.12 g/l (p<0.05) of the comparison group. The level of Ig G in the blood serum of newborns whose parents lived in polluted areas 7.68±0.5 g/l versus 9.72±0.47 g/l (p<0.05) of the comparison group. The decrease in Ig M was 0.74±0.04 g/l in group I versus 1.06±0.07 g/l (p<0.05) in group II.

Conclusions: Patients with neonatal sepsis, whose parents lived in conditionally contaminated areas of the city, had significantly lower levels of immunoglobulins in the blood serum than children whose parents lived in rural areas.
FEVER IN A PRIVATE AMBULATORY HEALTH CARE: CHARACTERIZATION OF 5296 FEBRILE EPISODES FROM 1997-2019

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Background: Fever is a common complaint in children, accounting for as many as 20–30% of clinical paediatric visits. Aim: characterize all paediatric febrile episodes (FE) observed in private ambulatory health care with computerized database since January 1997.

Methods: Observational retrospective study that included all febrile children with >3 months old from January 1997 to December 2019. We considered fever as an axillary temperature ≥37.5°C or rectal temperature ≥38°C. FE were classified in four groups: very serious acute infectious disease (VSAID) as having life risk; serious acute infectious disease (SAID) as having a potential complication; acute bacterial benign infectious diseases (ABBID) if there was necessary an antibiotic; and the auto-limited acute benign infectious disease (AL-ABID), with spontaneous resolution, that include the auto-limited without focus febrile syndromes (AL-WFFS).

Results: Were observed 5296 cases: 3212 (60.6%) AL-ABID that included 1955 AL-WFFS, 1672 (31.6%) ABBID, 407 (7.7%) SAID and 5 (0.09%) VSAID. Of the 412 SAID and VSAID, the majority corresponded to pneumonia/bronchopneumonia (n = 326, 79.1%) and pyelonephritis (n = 47, 11.4%). The 5 VSAID cases occurred in 1997 to 2005 period were: 2 sepsis by Neisseria meningitidis, 1 pneumonia caused by Streptococcus pneumoniae and 2 clinical sepsis without germs identification.

Conclusions: The majority of FE observed in ambulatory health care were benign, mostly auto limited. Only one third made antibiotic therapy. We highlight the low rate of SAID and VSAID, the last without any cases in the recent 14 years. However, we consider that the percentage of them are excessive for a private ambulatory health care but justified because the assistant pediatrician works also in the Intensive Unit Care.
CORRELATION BETWEEN STOOL BACTERIAL COLONIZATION AND EMPIRIC ANTIBIOTIC THERAPY IN ONCOLOGY PATIENTS WITH CONFIRMED BACTERAEMIA.

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**Background:** Infections are a major cause of morbidity and mortality in Paediatric oncology patients. Routine surveillance cultures is standard practice in most oncology units in an attempt to guide empiric antibiotic therapy in an infection episode. This practice becomes more valuable when antibiotic resistant pathogens are isolated. The aim of this study is to link surveillance culture results with the empiric antibiotic therapy given to patients with proved bacteraemia.

**Methods:** Bacterial isolates from oncology patients with proven bacteraemia at two paediatric oncology departments in Athens-Greece, Aglaia Kyriakou and MITERA Children’s Hospital, from January 2015 to December 2018 were collected. Each bacteraemia case was matched to corresponding stool surveillance data. Isolate characteristics, such as sensitivities to first line antibiotics, time between surveillance cultures and bacteraemia were documented in a multivariate analysis in order to identify risk factors linking colonization with bacteraemia.

**Results:** 129 bloodstream infections from 84 patients with cancer were recorded the majority of which were gram (-) (53%). Colonization data were available in 97 cases and complete match between colonization and bacteraemia isolate was documented in 22 cases (22.7%). Neutropenia as well as disease type was not found to be correlated with a BSI by an identical pathogen. Multivariate analysis shows that, shorter time interval from surveillance culture(<20 days) and recent use of antibiotics was strongly correlated with a match between colonisation and BSI isolate. MDR colonization was also a major risk factor (p 0.021).

**Conclusions:** Study findings indicate a weak correlation between routine colonization surveillance pathogens and bacteraemia isolates in paediatric oncology patients. Risk factors identified in a multivariate analysis include recent use of antibiotics and colonization with MDR pathogens. These are preliminary results of an ongoing study that we hope to produce more evidence in decision-making when empiric antibiotic therapy is administered to oncology children.

**Clinical Trial Registration:** No controlled trial
Background: Preventative therapy (IPT) with isonazide (INH) is recommended in children under the age of five exposed to infectious tuberculosis even in absence of immunological evidence of infection (LTBI). Without directly observed therapy (DOTS), however, compliance is often an issue and leads to increased rates of LTBI. In this study we wanted to investigate the effect of more detailed information for the families of the affected children.

Methods: Children exposed to infectious tuberculosis in the kindergarten were evaluated with tuberculin skin test (tst) and interferon gamma release assay (IGRA) as part of contact investigations. Compliance rates and reason for non-compliance as well as LTBI rates at the end of the incubation period were recorded.

Results: In two contact investigations 44 respectively 46 children between one and five years of age were investigated for LTBI. In the group of children with no specific information on IPT treatment was administered regularly in 25/46 (54%), in the group with specific information in 39/44 (89%). In the first group 4/46 (8.6%) developed LTBI whereas no child in the second group got infected.

Conclusions: Good information policy increases compliance rates of IPT in children exposed to tuberculosis and therefore reduces the risk of LTBI in those children.
Title of Case(s): NOROVIRUS-ASSOCIATED EPILEPTIC ENCEPHALOPATHY AND ATAXIA

Background: Norovirus (NoV) is one of the most common, self-limiting etiological agent of acute gastroenteritis. Rarely extra-intestinal complications with central nervous system involvement are observed, such as seizures, and ever more rarely encephalopathy or encephalitis.

Case Presentation Summary: Boy, 1 y. 9 m. old, hospitalized in Emergency Department with complaints about two generalized tonic-clonic seizure attacks about 30 seconds long which spontaneously stopped. Body temperature was 36.8 °C. Two days before seizure episodes boy had repeated episodes of vomiting and diarrhea. In the hospital during initial neurologist consultation a recurring seizure episode were observed, treatment with Valproic acid were started. On the second day of hospitalization seizures recurred 5x. To exclude CNS infections lumbar puncture (LP) were performed - cytosis 2, head CT - without pathological finding. On the third day of hospitalization 2 more seizure episodes were observed. In the next days boy became inhibited, with altered gait, shaking hands, unable to hold his head. LP were repeated: Enterovirus RNA, EBV, CMV, VZV, HSV 1,2 DNA were negative; amino acids of metabolic diseases were non specific spectrum; antiGAD antibodies for limbic encephalitis - negative. POSITIVE NoV antigen in feces was found. Pulse therapy with Methylprednisolone 20 mg/kg was initiated due to encephalitis. MRI of head and spine - without pathological finding, EEG - multifocal epileptiform activity. During the pulse therapy for a total of 5 days boy’s condition improved significantly - disappeared movement and coordination disorders and seizures did not repeat. NoV antigen were positive (2x) in feces before discharge.

Learning Points/Discussion: 1. Norovirus could cause extra-intestinal complications with CNS involvement. 2. Laboratory validation of the Norovirus genome in the CSF and serum (RT-PCR) is required to identify possible Norovirus-associated epileptic encephalopathy and ataxia.
FEVER: DOES IT HAVE TO BE INFECTIOUS?

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Title of Case(s): Fever: Does it have to be infectious?

Background: Fever of unknown origin is a diagnostic challenge in daily practice. Such patients require a thorough clinical review and a careful and comprehensive approach to diagnosis. Although most underlying causes are common, such as infections, when atypical manifestations are present and the investigation doesn't lead to an obvious diagnosis, infrequent causes should be considered.

Case Presentation Summary: We present a case of a 17 years old female with three months of recurrent fever, refractory anaemia, weight loss (8Kg in 6 months), asthenia, coughing and headache. She also presented skin pallor and an abdominal murmur along the area of the abdominal aorta. The blood tests carried out revealed microcytic hypochromic anaemia (Hb 9.7x10g/L), high sedimentation rate (120 mm/h) and CRP (85 mg/L). IGRA and HIV, HBV, HCV, EBV and Cytomegalovirus serologies were negative. The chest x-ray showed a mediastinal round hypotransparency and the thoraco-abdominopelvic CT revealed a parietal aortic thickening, probably due to a large vessel vasculitis. Magnetic resonance angiography confirmed the parietal aortic thickening associated with mild stenosis of the left renal artery, likely due to a large vessel vasculitis such as Takayasu arteritis. She was then checked by Cardiology that concluded there was no heart involvement. She started acetyl salicylic acid, corticoids and methotrexate with a good clinical response: the fever stopped, she gained weight and her hemoglobin level increased.

Learning Points/Discussion: Although there are two categories of large vessel vasculitis, only Takayasu Arteritis occurs in paediatric age, but it is extremely rare. Takayasu Arteritis is a chronic, progressive, inflammatory and occlusive disease of the aorta, its branches and pulmonary artery. Since the clinical manifestations and laboratory examinations are non-specific, accurate diagnosis depends on a high degree of suspicion and appropriate imaging studies.
MENINGITIS OF UNKNOWN ETIOLOGY IN A FIFTEEN-YEAR-OLD GIRL WITH LONG HOSPITALISATION. THE ALGORITHM OF THE DIAGNOSTIC/THERAPEUTIC PROCEDURE AND COMMENTS ON THE CASE.

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Title of Case(s): MENINGITIS OF UNKNOWN ETIOLOGY IN A FIFTEEN-YEAR-OLD GIRL WITH LONG HOSPITALISATION. THE ALGORITHM OF THE DIAGNOSTIC/THERAPEUTIC PROCEDURE AND COMMENTS ON THE CASE.

Background: It’s quite rare in a bacterial or viral meningitis, to be unable to diagnose the pathogenic factor, despite the abilities of the laboratory.

Case Presentation Summary: Fifteen-year-old girl presented to the paediatric ED of our hospital because of fever (started five days ago). The last 24 hours the fever got higher, the girl also had headaches and pain in the neck gradually deteriorating. She was under treatment 4 days ago, with cefuroxime, due to red tonsils and red patches in the throat. Furthermore, she had café-au-lait spots due to neurofibromatosis. CSF tests: 800c/mm³ (N:89%, L:11%), Glu:52mg/dl, Proteins:80.3mg/dl, LDH:19IU/l. Taking into consideration that she had already taken antibiotics orally, as well as the results of the CSF, and having the suspicion of partially treated meningitis, she was treated with parenteral ceftriaxone-vancomycin and dexamethasone. Subsequently, after the negative PCR results for bacterial CNS infection, and considering that she had recent infection from herpesvirus according to the blood tests, dexamethasone was stopped and Zovirax was added to the treatment. It was decided to be transferred to the nearest 3rd grade hospital, because 12 hours after the dexamethasone was stopped, she started to have fever again. There, the imaging and the laboratory and CSF tests, couldn’t lead to diagnosis.

Learning Points/Discussion: Taking the whole case into consideration, along with the laboratory tests-clinical symptoms of her, we can assume that the pathogenic factor was herpesvirus HSV ½, which most likely, followed an EBV-infection. HSV-infection, at the first stages, can cause meningitis(25%) and myelitis, clinical picture compatible with our patient. It is common knowledge, that the virus’ DNA cannot be found in the cerebrospinal-fluid of seropositive people, who do not suffer from any neurological disease.
Background: Acute haematogenous osteomyelitis (AHO) still remains a challenge with significant worldwide morbidity. Treatment protocols are changing, towards less aggressive regimens. We aim to analyse trends in OAI aetiology and management to identify risk factors associated with complications.

Methods: Longitudinal observational data analysis of children (< 18 years old) with AHO admitted to a tertiary care paediatric hospital, from 2008 to 2018. Clinical, microbiological, imagiological data, treatment and evolution were obtained.

Results: 71 children, median age 3 years, 55% males. A microbiologic aetiology was determined in 35%, mostly MSSA (56%). The median duration of total antibiotic treatment was 5 weeks and 42.3% underwent at least one surgical procedure. Complications were identified in 45% and sequelae in 2.8%. Children from recent years had more often septic arthritis and were more often treated for less than 4 weeks with similar sequelae rates. Risk factors for complications were age higher than 3 years, positive culture, pyomyositis and surgery. Risk factors for sequelae were surgery and complications.

Conclusions: The present study although single centre confirms that MSSA continues to be the most common causative organism of AHO. We still have a conservative AHO approach, with high surgery rates and prolonged antibiotic courses, although there was a trend for decreasing antibiotic duration in recent years. Identifying risk factors for complications is important for management.
SAFE RULE-OUT OF SEPSIS USING PROCALCITONIN AND A BAYESIAN MODEL: PRELIMINARY RESULTS OF A PROSPECTIVE OBSERVATIONAL STUDY

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Background: According to the current paediatric definition, sepsis is the systemic inflammatory response (SIRS) to infection. The low specificity of such definition often leads to misdiagnosis and antibiotic overuse, possibly causing patient harm, unnecessary costs and increasing antibiotic resistance. Inflammatory biomarkers can guide antibiotic initiation, de-escalation and discontinuation. We evaluated the accuracy of procalcitonin (PCT) and C-reactive protein (CRP) in identifying children with SIRS at no or very low risk for bacterial infection, to suggest the implementation of antibiotic sparing strategies in routine practice.

Methods: Patients aged ≤12 years admitted for suspected sepsis were considered for inclusion, according to age-specific criteria. Samples for serum biomarkers and microbiological testing were collected at presentation. Two investigators – blinded to biomarkers values and through independent retrospective chart review - categorized patients in: microbiologically confirmed, clinically confirmed, possible and excluded sepsis.

Results: Sixteen subjects met the criteria for inclusion. PCT at presentation <0.5 ng/mL performed better than CRP <0.5 mg/dL in detecting patients in which diagnosis of bacterial sepsis was excluded (Accuracy 93.8% vs. 68.8%). Bayes’ Theorem can be useful to show the utility of PCT: a cut-off at 0.5 ng/mL can safely rule-out sepsis in 25% of children (Negative Predictive Value:100%, False negative 0%). Figure 1. Diagnostic Algorithm using PCT at 0.5 ng/mL cut-off value and Bayes’ Theorem.
Conclusions: All the patients received intravenous antibiotics until discharge, regardless of microbiological evidence, clinical course, biomarker values and discharge diagnosis. Bayes’ model shows that patients whose PCT at presentation is < 0.5 ng/mL could be rule-out for bacterial sepsis and benefit from a wait-and-see approach or antibiotic discontinuation. These results, if confirmed, could be used for implementing strategies for containment of antibiotic overuse and resistance.
SEXUALLY TRANSMITTED INFECTIONS IN CHILDREN AND ADOLESCENTS

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Background: Sexually transmitted infections are a public health problem. A worrying increase in the number of cases has been described, including in pediatric age. The analysis of the current situation is essential to change this reality, including forms of prevention.

Methods: Retrospective and descriptive study of cases of infection by Neisseria gonorrhoeae, Mycoplasma genitalium and Chlamydia trachomatis in children and adolescents up to 18 years old, between January 1, 2015 and December 31, 2019. The identification of cases was made by cultural method and/or molecular biology.

Results: Thirty cases were identified; 20 were male. Twenty-one cases occurred in the last 3 years. Median age was 17.4 years. Three cases already had a history of sexually transmitted infection. Three were men who have sex with men. Six reported recent or new sexual partner and 2 cases had multiple sexual partners. Nineteen admitted not using any contraceptive method routinely. The most frequent clinical presentation was urethritis. There was isolation of Chlamydia trachomatis (18) and Neisseria gonorrhoeae (19). In three there was recurrence of symptoms/new sexually transmitted infections.

Conclusions: The authors highlight the increase in the number of sexually transmitted infections among adolescents in recent years. Clinical suspicion, early diagnosis and treatment of the patient and partners are essential. It is also emphasized that sexuality education should be a priority.
LATE-ONSET NEONATAL SEPSIS CAUSED BY KLEBSIELLA PNEUMONIAE IN PRETERM INFANT

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Title of Case(s): LATE-ONSET NEONATAL SEPSIS CAUSED BY KLEBSIELLA PNEUMONIAE IN PRETERM INFANT

Background: Neonatal sepsis (NS) is a life-threatening urgent condition, which can lead to multi-organ failure and death. Late-onset NS is a common problem of Neonatal Intensive Care Units (NICU) because baby who already has severe condition due to another disease / diseases can be easily contaminated and infected with hospital microorganisms such as Klebsiella pneumoniae. The risk is much greater in preterm infants because of immaturity background.

Case Presentation Summary: Newborn boy was admitted to the NICU after birth with primary diagnosis: “Respiratory distress syndrome”. Baby is from 6th pregnancy, 5th delivery in 29 weeks of gestation via C-section. Birth weight – 1480 g. Apgar score assessment – 6/7. Downes score assessment – 4/6. Respiratory support in CPAP mode and administration of exogenous surfactant were prescribed. Condition of the baby was stabilized. On the 7th day of life poor feeding and vomiting appear. CBC: leukocytosis. CRP: positive. Blood culture: Klebsiella pneumoniae was identified. Clinical diagnosis: “Late-onset NS (Klebsiella pneumoniae)”. Antibacterial treatment: Cefoperazone, Gentamicine Outcome: boy was discharged on 38th day of life with satisfactory general condition, body weight – 2515 g. Pediatric and neurological follow up was recommended.

Learning Points/Discussion: NS is still one of the major causes of morbidity and mortality among infants. Premature newborns can have not so clear clinical presentation of the sepsis. It makes us to pay more attention for any, even the least, change in their condition to diagnose and manage sepsis as soon as possible cause delay with the treatment can lead to severe complications and death.
Background: Fever is the main recommendation to perform a blood culture (BC). In many studies, the percentage of positive BC for pathogens does not exceed 2%. Although, there are few studies that correlate the positivity of BC with the day of fever. The aim of this study was to determine the time lag between the onset of the fever and the BC positivity.

Methods: Retrospective opportunistic study including bacterial pathogens isolated in BC from febrile children observed in a pediatric department between 1985 and 2018 (34 years). We considered fever as an axillary temperature ≥37.5°C or rectal temperature ≥38°C. The positive BC were grouped at 24 hour intervals from the onset of the fever. Bacterial agents considered a frequent cause of BC contamination were excluded.

Results: Of the 407 positive BC, 286 were extracellular bacteria (ECB), most commonly: Neisseria meningitidis (50.7%), Escherichia coli (10.8%), Streptococcus pneumoniae (10.1%) and Staphylococcus aureus (8.4%). Intracellular bacteria (ICB) were identified in 121 BC: Salmonella spp (80%), Brucella spp (19%), Listeria monocytogenes (1%). The time lag between the onset of the fever and the BC positivity in ECB was: <48 hours in 234 (81.8%) BC, <72 hours in 245 (85.7%) BC and >96 hours in 27 (9.4%) BC. For the ICB, the time lag was <72 hours in 19 (15.7%) BC and >120 hours in 92 (76.0%) BC.

Conclusions: The highest percentage of positive BC for ECB was obtained within the first 48 hours of fever. In ICB infection, the time lag was significantly higher than ECB. We emphasize the importance of having a clinical suspicion of ECB or ICB when request a BC as knowing the day of fever.
Background: National data reports that 30% of boys and 19% of girls in the UK sustain a fracture by the age of 18. Both HIV and combination antiretroviral therapy (cART) can affect growth and/or bone metabolism. Literature in adult population recognises the increased risk of osteoporosis and fractures amongst HIV patients. However, this data is scarce in HIV infected children. The aim of this audit was to look at fractures amongst our local paediatric HIV cohort.

Methods: We conducted a retrospective analysis of our electronic notes (e-notes) on patients in our follow up between June 2019 – January 2020. The e-notes were reviewed to determine whether a patient has had previous fracture(s). Further information was requested from GP Practices to avoid missing data in regards to fractures.

Results: 37 children with a median age of 14(IQR11,17) years were included in the audit. All children were on cART, with Triumeq (45%), the commonest fixed dose combination regimen. The remainder received a combination of different cART regimens. Median CD4 count was 889 10^12/L (IQR 643,1110). HIV viral load was undetectable in 25(68%), 3(8%) were <50 copies/ml and 7(19%) children had a detectable viral load between 59-417 copies/ml. 4 patients with a history of fractures were detected. Reported fractures included 2 metatarsal fractures, 1 distal tibia fracture and 1 zygoma fracture.

Conclusions: In our cohort 4 fractures were recorded, however no further conclusions could be drawn due to the small patient population. A larger audit would be needed to compare nationwide fractures in children and young people living with HIV versus the national data of fractures in childhood.
Background and Objective: Hookworm human infections (*Necator Americanus, Ancylostoma Duodenale*) are common in tropical rural areas where people are at high risk of cutaneous and pulmonary manifestations by larval penetration through the skin, or gastrointestinal symptoms due to oral-fecal route. Vertical transmission of larvae can occur through breastfeeding and rarely transplacentally. Although hookworm infections are rare in developed countries, they could always be investigated.

Methods: At present, relatively little is known about vertical transmission of hookworms and the clinical effects of these parasitic infections on infants. In the tropics, hookworms are an important cause of anemia and iron deficiency in children. We report a case of *Ancylostoma Duodenale* infection in a two month-old female infant and a review of the literature about mother to child hookworms transmission.

Learning Points/Discussion: An Italian two month-old female infant was admitted to Emergency Room for vomiting and weight loss. The parents reported a journey to Southeast Asia during the first trimester of pregnancy, where the mother had vomiting. On admission, the laboratory tests showed hypereosinophilia. During hospitalization the microscopic examination of the stools detected eggs of *Ancylostoma Duodenale*, confirmed also by molecular biology techniques. Parents' stools resulted negative, suggesting the vertical transmission of the infection. Immunologic investigations were normal. Although vertical transmission of hookworm is very rare, especially in developed countries, it should always be considered in infants with gastrointestinal symptoms, anemia and protein deficiency. Moreover an unexplained hypereosinophilia may be a major clue to the presence of a parasitic infection and could justify specific investigations on stools. The exposure to hookworm infections during pregnancy could alter the infant's response to unrelated antigens (vaccines, infectious diseases). Infants born from mother with history of parasitic infection should always be investigated immunologically.
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Background: Whooping cough cases and deaths declined dramatically during the 20th century due to public health vaccine initiatives. However, in recent years increases have been observed following the switch from whole cell to acellular pertussis vaccines. The availability of a cost-effective pertussis vaccine that provides improved efficacy and prolonged protection with the potential to reduce or eliminate transmission would present a breakthrough in the prevention of colonizing pertussis infections. BPZE1 is a novel live attenuated pertussis vaccine that elicits both mucosal and systemic responses. The purpose of this study was to assess one and two dose regimens of BPZE1 for safety and immunogenicity (with and without prior Boostrix exposure).

Methods: An observer blinded randomized study of 300 healthy adult volunteers. Volunteers received either BPZE1 (n=200) or Boostrix (n=100) on Day 0 and then each group was further randomized such that half received BPZE1 and half received placebo on day 85. Subjects provided mucosal and serum samples for ELISA IgG and IgA (PT, PRN, FHA, FIM2/3, whole cell extract) prior to and 28 days following each vaccination. Nasal aspirations for B. pertussis colonization were taken prior to and on days 7, 10 and 28 days following the second vaccination. Safety monitoring following each vaccination consisted of safety labs (sentinel), reactogenicity, vitals and all adverse events (AE) through 28 days following each vaccination. A validated electrochemiluminescence based ELISA was performed. Colonization by microbiologic culture, followed by B. pertussis verification by MALDI and colony counting for any positive cultures.

Results: Overall safety, immunogenicity (mucosal and serum) and colonization analyses are ongoing at this time. Primary and secondary outcomes will be presented.

Conclusions: BPZE1 is being developed as a booster indication to reduce transmission of pertussis.

Clinical Trial Registration: clinicaltrials.gov NCT03942406
IMPROVING TREATMENT AND OUTCOMES OF PAEDIATRIC MELIOIDOSIS OVER TEN YEARS IN NORTHERN CAMBODIA

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Background: Melioidosis, infection caused by *Burkholderia pseudomallei*, afflicts approximately 165,000 individuals each year and is responsible for an estimated 89,000 deaths. It remains an under-recognised cause of mortality in many endemic locations, especially in children. This observational study reports epidemiology and treatment of paediatric melioidosis over the last decade at a non-governmental hospital in northern Cambodia.

Methods: Data on culture-confirmed cases of *B. pseudomallei* infection were collected retrospectively (2009-13) and prospectively during an invasive bacterial infection surveillance study (2014-18). Additional patients were identified from the hospital microbiology database. Data were analysed using the statistical package R (v.3.6.1).

Results: Three hundred and fifty-five patients were identified of whom 12.1% (n=43) died. Severe malnutrition (risk ratio (RR=2.69 [95% CI 1.43-5.07]), female sex (RR=1.90 [1.08-3.85]) and age under five years (RR=1.86 [1.05-3.27]) were risk factors for mortality. Admission rate, bacteraemia prevalence and intensive-phase antimicrobial prescribing remained consistent, whilst malnutrition reduced (R=-0.76; p=0.01). Annual case fatality rate declined (R=-0.18; p=0.63), more so in bacteraemic patients (R=-0.43; p=0.20). There was substantial increase in children completing 12-weeks of eradication treatment (R=0.8; p<0.01). Forty-seven patients recovered with only oral treatment, with no culture-confirmed relapses detected.

Conclusions: We demonstrate improvements in treatment and outcomes of paediatric melioidosis at a non-governmental hospital in northern Cambodia, in the context of gains in the nutritional status of the population. The successful outcomes in children treated solely with oral antibiotics lends further support to the idea that some patients with mild infections can be cured with oral agents alone, a question that warrants answering using a randomised-controlled trial.
Title of Case(s): Febrile baby - Is it always sepsis?

Background: Clinical diagnosis of autoinflammatory conditions under six month of age are extremely challenging due to the rarity and atypical presentation of these cases. High level of clinical suspicion is essential to identify these diseases and start treatment in time.

Case Presentation Summary: Two month old baby was transferred to our hospital with one day history of fever, bilateral periorbital oedema and gastroenteritis. Upon presentation the baby was clinically septic so Ceftriaxon was started and a full septic screen was performed. Initial investigations showed raised inflammatory markers, leukocytosis, anaemia, hypoalbuminaemia and thrombocytosis. CSF revealed slight lymphocytosis so Ampicillin was added. During admission fever showed a recurrent pattern but settled after six days, besides, a self-resolving urticarial rash was observed occasionally. Cultures and multiplex PCR were negative so Ampicillin was stopped but Ceftriaxon continued for 2 weeks. US revealed a small amount of free abdominal and pericardial fluid which disappeared with the normalizing albumin. Multiple viral investigations were all negative. Upon discharge white cell count normalized and inflammatory markers were on the downward trend. Five days later the baby represented with the original symptoms plus with urticarial rash and mild periferal oedema. Inflammatory markers were raised again with an extremely high ferritin, low haemoglobin and mild hepatitis. Bone marrow aspiration did not reveal signs of haemophagocytosis. Due to the conflicting clinical picture the suspicion of incomplete Kawasaki syndrome was raised so immunoglobulin and steroid was indicated. During the immunoglobulin administration the baby had a peri-arrest situation and was transferred to ICU. Repeated blood tests showed further elevating liver functions and thrombocytopenia. Abdominal US revealed hepatosplenomegaly. Based on the previous investigations the diagnosis of HLH was made and the baby was transferred to hematology. Genetical tests are currently pending.

Key Learning Points: The diagnostic criteria of HLH might not be all present initially so constant awareness is crucial to avoid delays in the diagnosis.
Title of Case(s): “His illness is a mystery. The medics cannot find it. Doctor, what is wrong with my child?”

Background: Childhood TB is associated with significant morbidity and mortality especially in the developing countries. Abdominal tuberculosis is difficult to diagnose as it presents with unspecific features. Diagnosing abdominal tuberculosis in children presents double the challenge. We present a case of childhood abdominal TB which highlights the hurdles that sometimes widen the time to diagnosis and time to treatment.

Case Presentation Summary: This is KM, a 10-year-old, HIV-negative male who presented with 2 months’ history of high-grade fever, which started in the evenings and was worse at night. This was associated with progressive weight loss and lack of appetite. He had a 2-week history of mild, non-productive cough. He had no known contact with an adult diagnosed with TB. He was fully immunized. He had been treated in 3 private clinics with unspecified oral medication, but with no improvement. On examination, he was febrile T=38.6°C, had mild pallor of mucous membranes but no palpable lymph nodes. Respiratory exam- normal; He was not in distress, RR=32bpm, and had normal breath sounds. Per abdomen: - normal fullness, non-tender, no palpable organomegaly. Chest x-ray- non-specific interstitial pneumonitis; Blood smear- no malaria parasites; Abdominal U/scan- multiple enlarged mesenteric lymph nodes (2.20x1.22cm), no free fluid, liver and spleen normal; sputum Genexpert( after GA)- MTB not detected; CBC- HB 10.1g/dL, lymphocytosis, monocytosis; TST- Not done Diagnosis of EPTB (Abdominal TB) was made and TB treatment started (RHZE). The child improved on treatment.
Key Learning Points: There are limitations in primary care including lack of diagnostics, low suspicion for TB due to inadequate knowledge and stigma. There is lack of awareness on TB symptoms among parents. Abdominal TB can present “atypically” i.e. no abdominal pain, no mass or lump on exam. Sometimes, the diagnosis is only confirmed with good response to anti-TB therapy.
FEBRILE NEUTROPENIA IN A CHILD WITH B-CELL NON-HODGKIN’S LYMPHOMA

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Title of Case(s): Febrile neutropenia in a child with B-cell Non-Hodgkin's lymphoma

Background: Children treated for oncologic diseases suffer from major side effects of chemotherapy. Most chemotherapeutics are highly myelotoxic, leading to an increased susceptibility to infection due to leukopenia. Therefore, one of the major and most dangerous acute side effects of intensive chemotherapy in paediatric cancer is febrile neutropenia, necessitating prompt initiation of empirical broad-spectrum antibiotics.

Case Presentation Summary: This is the case of an 11-year old patient suffering from refractory B-cell Non-Hodgkin's lymphoma who presented with febrile neutropenia at our hospital. The patient had received reinduction chemotherapy two weeks before presentation, leading to a low blood count including leukopenia with severe neutropenia. The patient had developed fever of 38.5 °C at home, but only contacted our hospital on the following day. On clinical examination, she presented with tachycardia, shivering, and a body temperature of 39.5°C. No dermal or mucosal lesions were found, and the central catheter entry point showed no signs of inflammation. According to international guidelines, antibiotic treatment was started with meropenem. Laboratory testing revealed an elevated CRP value of 99 mg/l, and a negative result for virus PCR testing as well as a negative urine culture. Blood cultures were positive for Klebsiella pneumoniae, confirming the diagnosis of sepsis caused by an infection with Klebsiella pneumoniae. Under antibiotic treatment, the patient’s condition quickly improved with stabilisation of vital signs.

Key Learning Points: To conclude, this case demonstrates that febrile neutropenia is an important life-threatening complication in by intensive chemotherapy immunocompromised patients. Febrile neutropenia has to be treated directly with administration of intravenous antibiotics. Often, the etiology and initial localisation of infection remain unclear.
Title of Case(s): Study of biofilm formation of multi drug resistance in strains of Pseudomonas aeruginosa

Background: Pseudomonas aeruginosa is an opportunistic organism that is pathogenic in nature and is in charge of causing both chronic and acute infections in humans. Its capacity to form biofilms on abiotic and biotic surfaces makes it especially resistant to its host’s immune system and defenses and current treatment and therapies with antibiotics as well. The aims of this study are isolation and identification of strains of Pseudomonas aeruginosa from hospitals, the environment and find their degree of biofilm production and its frequency of susceptibility pattern.

Case Presentation Summary: Methodology: The strains of Pseudomonas aeruginosa were collected from various places were collected from medical equipment’s, hospital beds, sinks, bath tubs, basins, sinks and cell phones from homes, and from soil. The strains were identified and isolated using standard microbiology procedures and techniques, which were later subjected to antibiotic susceptibility testing using standardized operative procedures. Biofilm production and detection protocol was done by 3 protocols that are: Tube Method, Congo Red Agar Method and Tissue Culture Plate Method. Results: 16 isolates of Pseudomonas aeruginosa were isolated. 6 samples from hospital giving a probability of nosocomial infection associated strains, 5 from environment that include bath tubs, sinks, cell phones and 5 from soil. 45% of the isolates were strong biofilm producers, while the rest of the 55% remained weak.

Key Learning Points: Conclusion: The ability of Pseudomonas aeruginosa to form biofilm restricts treatments by means of antibiotics and makes them inefficient. As a result of this study infections that are caused by bacterial biofilms are strong and very difficult to treat.
ABDOMINAL PAIN AND RAISED CA-125 IN AN ADOLESCENT GIRL

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Title of Case(s): Abdominal pain and raised CA-125 in an adolescent girl.

Background: A presentation with abdominal pain, ascites, ovarian nodules and an elevated CA 125 is suggestive of ovarian malignancy in 75-95% of cases. A raised CA125 is associated with other malignant conditions (lung, breast, colon, pancreas) and some non-malignant conditions (endometriosis, hepatic cirrhosis, heart failure, pancreatitis). Extra-pulmonary TB disease can similarly present with non-specific symptoms. Both conditions are relatively rare in teenage girls in a London setting. Here we demonstrate that CA 125 can be misleading and potentially cause a delay in diagnosis and start of correct treatment.

Case Presentation Summary: A 16 year-old girl presented to hospital with a short history of abdominal pain, diarrhoea, anorexia, nausea, weight loss and fever. She had no previous medical history, there were no known unwell contacts and no travel history. Abdominal USS showed ascites, ovarian nodules and abdominal lymphadenopathy, confirmed on CT. Apart from a CRP of 140 and CA 125 of 506 Ul/ml, bloods were unremarkable. CXR and CT chest demonstrated normal parenchyma, but mediastinal and perihilar lymphnodes were enlarged on CT chest. Ascitic tap showed signs of acute inflammation, but no malignant cells were seen. Finally, an urgent mediastinal lymph node biopsy (EBUS) was performed 2 weeks after presentation, and PCR confirmed _M.tuberculosis_ Complex (not resistant to Rifampicin). Ascitic fluid cultures confirmed drug sensitive _M. Tuberculosis_ 18 days later. Patient was started on 4-drug TB treatment with good response.

Key Learning Points: Elevated CA 125 is usually correlated to malignant processes, but it is important to consider other possible causes, such as tuberculosis. In fact, CA 125 has been proposed as a potential marker to distinguish pulmonary TB from other infections. In young females presenting with an elevated CA 125 and non-specific abdominal symptoms, it is crucial to consider extrapulmonary TB in the differential diagnosis.
Title of Case(s): Pleural effusion and acute kidney injury - what do they have in common?

Background: This case presents the association of pleural TB with a rare extrathoracic disease manifestation - interstitial glomerulonephritis.

Case Presentation Summary: A 15-year-old female presented to ED with high fever, chills, and abdominal pain. Laboratory testing revealed WBC of 17.700/mm3, CRP of 108.4 mg/dl, and urinalysis with leukocyturia and microscopic hematuria. She was prescribed a course of ciprofloxacin, but symptoms persisted, and she was admitted for further examinations. Her medical history revealed a 4-month-previous admission for pneumonia and left pleural effusion that required draining. Cultures were negative and no TB testing was performed. She responded to empirical therapy with ceftriaxone and vancomycin. No history of exposures or recent travel was documented. On examination she had satisfactory physical condition, no skin lesions, weight of 49 kg, febrile (38.9 C), decreased lung sounds on the lower left side. All else within normal limits. Blood tests showed persistent leukocytosis with neutrophilia, elevated inflammatory markers. Despite an empirical course of IV ceftriaxone, fever persisted and inflammatory markers had an upward trend. Suspicions of infectious or inflammatory systemic disease was raised and additional investigations were performed: aerobic and anaerobic blood cultures, EBV, CMV, HIV serology, ECHO, ANA, ANCA, rheumatoid factor, C3/C4 and an IGRA. Renal function tests revealed a serum creatinine of 3.96 mg/dl with a decrease of GFR, and a fractional excretion of sodium of 1.6% suggestive of an intrinsic AKI (likely interstitial nephritis). Following this discovery, the IGRA test confirmed a TB infection with renal involvement. A renal biopsy being infeasible at the time, she was started on a standard regimen of antituberculous chemotherapy. Follow-up lab work showed decreasing (and eventually normalized) creatinine levels.

Key Learning Points: Tuberculosis should always be considered in a patient with fever and a unilateral pleural effusion. Clinicians should be aware of atypical clinical presentations, perhaps more so in the adolescent population.
A RARE CASE OF SECONDARY HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS

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Title of Case(s): A perfect storm in the little body

Background: Despite its rareness hemophagocytic lymphohistiocytosis (HLH) is a potentially fatal disease of normal but overactive histiocytes and lymphocytes that commonly appears in infancy, although it has been seen in all age groups. Secondary (acquired) HLH occurs after strong immunologic activation, such as that can occur with systemic infection, immunodeficiency, or underlying malignancy.

Case Presentation Summary:
A 5-month-old girl was evaluated in pediatric infectious diseases clinic because of fatigue and fever. The onset was 10 days prior to admission. At the time of presentation patient was conscious with altered mental status and intoxication symptoms. Physical examination revealed paleness of skin and mucosa, difficulty to breathe through nose. During palpation abdomen was non-tender accompanied by enlarged liver and spleen. The rest of organ systems were unremarkable.

Laboratory data: CBC - hemoglobin 80.0g/L (N=120-160g/L), RBC 2.74x10^12/L (N=3.7-5.6x10^12/L), hematocrit 23.27% (N=36.0-48.0%), WBC 2.15x10^9/L (N=4.0-10.0x10^9/L), lymphocytes 1.73x10^9/L (N=1.2-3.0x10^9/L), monocytes 0.17x10^9/L (N=0.09-0.80x10^9/L), neutrophils 0.25x10^9/L (N=2.00-5.80x10^9/L), platelets 0 (N=180-380x10^9/L), ESR 10mm/h (N=2-15mm/h).

Biochemical profile: Glucose 5.9mmol/L (N=4.2-6.4mmol/L), ALT 72.6U/L (N=0-42U/L), AST 194.8U/L (N=0-37U/L), total bilirubin 47.0mmol/L (N=8.55-20.5mmol/L), CRP 10.29mg/L (N<3mg/L), Creatinine 89mmol/L (N=44-80mmol/L), BUN 6.0mmol/L (N=2.1-7.1mmol/L).

Additional investigations showed abnormal ferritin level (12486mg/L, N=12-300mg/L), hypertriglyceridemia (6.78mmol/L, N=1.8mmol/L) as well as elevated level of LDH (491 U/L, N=140-280U/L).

EBV VCA IgM was positive, rK39 rapid test for visceral leishmaniasis was negative. Urine and stool tests were with no significant changes.

Chest X-ray was unremarkable. US scan showed hepatomegaly with poor vascularity and splenomegaly of 9.5cm, moderate ascites and pleural effusion. Bone marrow biopsy revealed hemophagocytic activity. Prophylaxis of infections was started (neutropenia) with ceftriaxone, TMP-SMX, fluconazole. According to clinical, serologic, instrumental and histological findings hemophagocytic lymphohistiocytosis was diagnosed (7th day of hospitalization). IVIG and dexamethasone were administered corresponding to HLH-2004 protocol. Despite of treatment the child died in a week.

Key Learning Points: Epstein-Barr virus is the most common pathogen which triggers infection-associated hemophagocytic lymphohistiocytosis. Such cases are worrying as late diagnosis and absence of treatment can be potentially fatal for patients. Genetic testing, used to differentiate between primary and secondary HLH, is a key for family planning.
THE COUGHING "DOWN" CHILD

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Title of Case(s): The coughing Down child

Background: Down syndrome is the most common genetic disease that often presents with a high frequency of infections especially upper airway infections in their early years, characterized by increased severity and prolonged course of the disease. Individuals with Down syndrome are known to have abnormal function of the B-cell function, which might present with high IgG and low IgM serum levels.

Case Presentation Summary: A one-year-old known Down syndrome child presented with persistent nasal congestion, fever, noisy breathing, and daily cough for 8 months. He had several outpatient consults and treatment with antibiotics but with poor relief of symptoms. Due to persistent symptoms, he was referred to the Ear, Nose, and Throat (ENT) surgeon. His paranasal radiographs revealed sinusitis. He was then referred to a pediatric infectious specialist for further management. Examination revealed a sick-looking, syndromic child who was having marked nasal congestion, global hypotonia, and generalized erythematous rash. He was otherwise well-nourished (BMI 25th centile on Down syndrome growth chart). Serum immunoglobulin test shows marked elevated Ig M with low Ig G and Ig A levels. Rheumatologist and Pulmonologist review was done to rule out possible autoimmune disease and underlying lung pathology. Rheumatologist agreed with the possible diagnosis of primary immunodeficiency. Pulmonologist confirmed no underlying congenital lung pathology from the chest CT scan. The echocardiogram was unremarkable. He received intravenous immunoglobulin (IVIG) as part of the therapy and his symptoms improved markedly. An impression of Hyper Ig M syndrome was made. He received two other courses of IVIG after discharge. Currently, the mother reports a good improvement in symptoms.

Key Learning Points: The association of Down syndrome with primary immunodeficiency is not clearly demonstrated. Warning signs present in children with Down syndrome warrants a detailed immunology investigation to exclude primary immunodeficiency. Diagnosing primary immunodeficiency imposed a great challenge to doctors especially due to the co-existing condition.
3 YEARS OF LONG-TERM FEVER IN A... HEALTHY KID?

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Title of Case(s): Three years of long-term fever in a... Healthy kid?
Background: TB infection in children has a challenging diagnosis due to its unspecific symptomatology. In some cases, it’s a long-term evolution disease with a severe affection.

Case Presentation Summary: We introduce a 6y male referred from his paediatrician due to a 10-days fever episode, as well vomiting, diarrhoea, headache and abdominal pain. He’s a healthy kid, born at our country and well vaccinated. He has short height and suffers intermittent long-term fever episodes for three years. His parents were born in Ecuador, living in Spain for 15 years. He lives with them, two sisters (11-13y) and two uncles (18-23y). He went to Ecuador two years ago. At the time of the admission he had good appearance, with stable vitals. Blood test showed anaemia, high ESR and hyponatremia. Negative urine analysis. Chest-Rx, showed a little infiltrate in upper left lobe. We completed our study with a PPD, which was 11mm at 72h. We collected gastric aspirates and requested for Thoracic-TC.

At 4th admission day, we perceived a subtill neck stickness and photophobia, therefore we asked for a Cranial TC. Image studies confirmed lung and endobronchial TB, as meningo-encephalitis with thalamic and cerebellar TB nodes.

We performed a LP, with hypoglucorrachia, high ADA and a positive PCR in CSF of *M. Tuberculosis*. We started with HRPZ + Dexametasone. All the cultures were positive for multisensible *M. Tuberculosis*. At the contact study, we detected LTBI in his parents and the oldest uncle. Both sisters and the youngest uncle had an active pulmonary TB by multisensible *M. Tuberculosis*.

Currently, he’s on the 4th month of treatment. All the cultures are negative and there’s no side effects.

Key Learning Points: Our patient has a serious illness with a long evolution infection, spreaded in the whole family. Hence, is very important to keep in mind TB infection during the study of unspecific disease, as an early contact study.
Title of Case(s): Unusually Hot

Background: Cerebral malaria remains one of the most common non traumatic encephalopathies. It can be part of a multisystem dysfunction and the combination of these affect prognosis.

Case Presentation Summary: Patient M is a 15 year old girl from Ghana, who was in the UK when she became unwell with a fever up to 40, with no other symptoms. GP review attributed symptoms to a UK heat wave. At the airport two days later, she deteriorated with a generalised tonic clonic seizure. Initial management at a local hospital with benzodiazepines was initially successful. A blood film showed 16% parasitaemia with Plasmodium Falciparum and treatment with IV artesunate commenced. Urgent CT head demonstrated global cerebral oedema, early hydrocephalous and effaced basal cisterns. Treatment escalated due to falling GCS and she was intubated and ventilated for transfer to PICU. Clinical signs of raised ICP (hypertension and bradycardia) were present on admission to PICU. Neuroprotective management included sedation, 3% saline and mannitol and broad spectrum antibiotics given. Repeat CT showed progressive hydrocephalous, crowding of foramen magnum and bilateral tonsillar herniation. An EVD (external ventricular drain) was inserted but intraventricular bleed and blockage required replacement. Severe renal failure was managed by 21 days of haemofiltration. All cultures were negative including CSF. Management challenged included balancing anticoagulation for haemofiltration and intracranial bleeding risks. Despite these, the EVD was removed after 14 days and extubation was successful. Following a 31 day PICU admission and 14 day rehabilitation period on the paediatric ward, she returned home to Ghana neurologically intact.

Key Learning Points: Malaria should always be considered in fever in a returning traveller where malaria is endemic, as early diagnosis and treatment is crucial in preventing rising parasitic load, and reducing complications. The role of neurosurgery in cerebral malaria is not clear, and antimalarial drugs remain the only treatment that unequivocally improves outcome.
SEPSIS AS A TRIGGER OF IMMUNODEFICIENCY

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Title of Case(s): Sepsis as a sign of immunodeficiency

Background: T-cell immunity disorders among primary immunodeficiencies (PID) are 9% in the registry of the European Society of Immunodeficiency (ESID) and 10.5% in the United States. T-cell disorders are characterized by the absence or presence of T-lymphocytes. Because T cells are important for the normal functioning of B cells, most PID with a T-cell disorder lead to combined T- and B-cell disorders. Disturbances of the T-cell link of immunity are clinically manifested in early childhood. The most serious form of PID with violation of the T-cell link of immunity is a severe combined immunodeficiency (SCID).

Case Presentation Summary: Girl N. at the age of 3 months entered the Childrens Infectious Hospital with complaints of cough, high febrile temperature for 5 days, refusal to eat. From the anamnesis of life the girl from the 1st pregnancy, 1 birth, was born full term in 40 weeks gestation, birth weight 4640g. For 3 months of life, a bad increase in body weight was noted and at the time of admission, the weight in 3 months was 5400g. From the anamnesis of the disease on 08.01, the temperature rose to 38.2°C, there was a cough and a mucous discharge from the nose. Then the child refused to eat, the body temperature rose to 39.2°C. According to the immunogram, a sharp decrease in CD3 + 26% was detected, activated T-lymphocytes were 19.9%, T helper / inducers - 26.6% and T suppressors / cytotoxic 0.5%, a high ratio of Tx / Tc was detected 53.2%, cytotoxic non-T cells -1,2, an increase in the number of B-lymphocytes 58.9%, natural killers - 6.6%, natural T-killers - 0.3, leukocyte gates - 99%. Posthumous diagnosis: Primary immunodeficiency (SCID, T0 B + Nk +). Complications: Sepsis. Septic shock. SPON: ARDS, renal failure, DIS, thrombocytopenia, anemia 3. Two-sided lower-lobe pneumonia.

Key Learning Points: infections is trigger of immunodeficiency
A 15 YEAR OLD GIRL WITH WEIGHT LOSS AND ANEMIA

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**Title of Case(s):** A 15 year old girl with weight loss and anemia

**Background:** Tuberculosis remains a major global health problem. Abdominal tuberculosis is an uncommon extrapulmonary form of tuberculosis. Diagnosis is a great challenge even for experienced clinicians as it is a great mimicker presenting with nonspecific and insidious symptoms and therefore treatment is often delayed, especially in the pediatric patient without an obvious history of exposure to the pathogen.

**Case Presentation Summary:** A 15-year-old Indian girl with primary amenorrhea was admitted with one-year history of weight loss and anemia. She reported lack of appetite and weakness. She also suffered from cough, abdominal pain and diarrhea over the last 15 days. Afebrile. On physical examination, she appeared pale and malnourished. Her lungs were clear. Her abdomen was tender. Laboratory results reported anemia, hypoalbuminemia and elevated CRP and ESR. Although the patient had no encounter with any tuberculosis patient and no recent journey to India, we performed tuberculin skin test for differential diagnosis, which was 20mm. The patient had received BCG vaccination in the past. Her chest X-ray revealed mediastinal widening and an infiltration. Her abdominal ultrasonography reported multiple enlarged lymph nodes. Chest CT showed mediastinal lymphadenopathy and multiple nodules. Abdominal CT revealed lymph node enlargement with areas of calcification and circumferential wall thickening in the terminal ileum and right colon. Interferon-gamma-release-assays tests and molecular diagnostic test were positive with no rifampicin resistance. Sputum culture was positive for mycobacterium tuberculosis. Magnetic resonance enterography was also performed. Patient was started four-agent tuberculosis treatment (isoniazid, ethambutol, pyrazinamide, rifampicin) and vitamin-B6. She had good clinical response and gained weight over time. She also visited the endocrinology department. Her family were tested negative for tuberculosis. Differential diagnosis from Crohn's disease is of great importance.
Key Learning Points: It is important to suspect intestinal tuberculosis in patients from endemic countries presenting with nonspecific symptoms of weight loss and abdominal pain, regardless of their BCG vaccination status.
A SERIOUS BELLY-ACHE

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Title of Case(s): A serious belly-ache

Background: An 11 year old girl from Pakistan had treatment for abdominal tuberculosis prior to moving to the London. 3 years later, she was diagnosed with disseminated mycobacterial disease. Multidrug-resistant tuberculosis treatment was commenced, which was modified when she was diagnosed with disseminated BCG disease. This was an unusual presentation in a HIV-negative patient, suggesting underlying immunodeficiency.

Case Presentation Summary: An 11-year old girl from Pakistan presented with three months of abdominal pain, weight loss, headaches, and night sweats. Acid-fast bacilli on gastric washings was confirmed on microscopy, and TB PCR was positive. Rifampicin resistance gene was present on GeneXpert™. Imaging was consistent with disseminated disease, with miliary lesions on CXR, and abdominal imaging demonstrating disease involving the terminal ileum, caecum and ascending colon, lymphadenopathy, liver and spleen lesions. Her MRI-brain had multiple enhancing lesions. She was also treated for HSV stomatitis, and oral candidiasis. HIV serology was negative, and she had normal lymphocyte subsets, normal immunoglobulin levels and normal T-cell functional assays. She was commenced on treatment for suspected multi-drug resistant tuberculosis given her background. Due to burden of gastrointestinal disease, nutritional status, and complications including gastrointestinal bleeding, she was commenced on parenteral nutrition with gut rest. She underwent elective defunctioning ileostomy for management of bowel obstruction. Genetic sequencing and phenotyping confirmed mycobacterium bovis (BCG strain) resistant to rifampicin and pyrazinamide, and her treatment was changed to bedaquiline, moxifloxacin, isoniazid, and cycloserine. Cytokine production studies demonstrated reduced production of interferon-gamma, and reduced production of interleukin-2. Genetic immunodeficiency panel was not diagnostic. She was commenced on subcutaneous interferon-gamma treatment. There was improvement after 11 months of anti-mycobacterial treatment, allowing for successful stoma reversal.

Key Learning Points: BCG strains are intrinsically resistant to pyrazinamide. BCG can cause local and disseminated disease in immunocompromised hosts, including infants with HIV, primary immunodeficiency, and patients with Mendelian susceptibility to mycobacterial diseases.
TB HOUSEHOLD CONTACT WORK UP - THE DIAGNOSTIC DILEMMA OF UNMASKING INCIPIENT TB IN THE VERY YOUNG

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Title of Case(s): TB household contact work up - the diagnostic dilemma of unmasking incipient TB in the very young

Background: Tuberculosis (TB) remains one of the top-ten causes of mortality with approximately 240,000 deaths annually in children. Following exposure, the likelihood of active disease and the form of TB are highly age-dependent. The diagnosis of TB in children remains challenging, even in well-resourced settings such as Germany.

Case Presentation Summary: A 7-month-old boy was referred to the PID department of the Hauner children’s hospital in Munich by the public health department due to a confirmed TB contact (father) in September 2017. The boy born to a Senegalese father and a Belarusian mother was healthy, and no abnormalities, including a negative tuberculin skin test (TST), were found in the initial assessment. On presentation at our PID department, the mother reported a flu-like infection in late August but negated any other relevant abnormalities since birth. The physical examination and laboratory workup were inconspicuous. On the chest X-ray, a questionable opacification in the left upper lobe/hilus was identified. Preventive treatment with Isoniazid/Rifampicin was immediately initiated. A clinical re-evaluation was scheduled after two weeks of treatment, a second TST was applied, which turned out positive, and a follow-up chest X-ray showed a hilar consolidation. Consecutively, a chest CT was initiated, displaying a hilar lymphadenopathy. Anti-tuberculosis treatment was started based on the father’s microbiological findings in early October 2017 (Isoniazid, Rifampicin, Pyrazinamid). The child was followed up for 6 months until the successful completion of treatment, all radiological abnormalities resolved, and treatment was tolerated well.

Key Learning Points: 1) Diagnosing active TB in small children remains challenging. Active TB cannot be ruled out in a clinically well child, or by a negative TST. 2) Progression after contact to active TB can occur at any time, especially in the very young. Even if the initial assessments are inconspicuous, close follow-up needs to be performed.
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Title of Case(s): Unexpected fever in 6 children in long-term follow-up  
Background: In 2019 Bulgaria experienced an outbreak of measles, resulting in more than 1000 cases, 431 of which were treated in our institution. In Jun 2019 within 1 week, we diagnosed several cases of measles in children, treated and followed-up for Tuberculosis. The case report underlines the clinical significance of infection control and compares clinical manifestations and complications in children with Tuberculosis, faced with the Measles virus with children without underlying pathologies prior to the Measles infection.

Case Presentation Summary: The 6 children are regularly followed-up for treatment for Tuberculosis. In early Jun 2019 one of them was presented in our department with early signs of an acute infection. Due to the known measles outbreak, as well as a known family contact of the patient, who had been diagnosed with measles in the preceding 3 weeks, we deduced that the child was infected with measles, which was confirmed via serology test. Immediate response protocol for infection control was implemented, therefore finding all contacts of the child. Five children treated at the same time for tuberculosis were discovered to have been in contact with the patient and were followed-up. All of them developed expected clinical signs of measles within 1-3 weeks. During the hospitalization, the 6 children were treated in isolation from other measles cases. Their hospitalization duration lasted on average 2 days more than measles cases without underlying pathologies. Antibiotic treatment was used prophylactically for all 6 cases. Clinical manifestations beyond the expected, were not noted. Serious complications beyond gastrointestinal and ophthalmic complications were not noted.

Key Learning Points: Infection control measures are essential in ensuring that measles infection does not spread to vulnerable populations with underlying pathologies. Prophylactic usage of antibiotics in children with measles with underlying tuberculosis might reduce risk of complications related to bacterial superinfections.
Title of Case(s): Artesunate treatment in children

Background: Pediatric patients with imported severe *P. falciparum* malaria should receive intravenous artesunate as first-line treatment, however limited data are currently available on its use and potential post-treatment effects in pediatric patients in non-endemic settings.

Case Presentation Summary: A 15-month old child presented with high fever five days after a recent trip of 9 months in Nigeria. Antimalarial prophylaxis was never administered to the child and his mother reported that he was treated for malaria (with unknown drugs) while being in Nigeria. At admission, blood tests were performed showing thrombocythemia (16000/mmc), Hb 9.5 g/dL, increased C-reactive protein (160 mg/L) and increased liver function tests. Peripheral blood smear confirmed a diagnosis of *P. falciparum* malaria with very high parasitaemia (17% red blood cells parasitized). On clinical evaluation, the child was pyretic, well appearing without any neurological sign, physical examination was normal except for a mild spleen and liver enlargement. On DAY 1, due to the very high parasitaemia, intravenous artesunate was administered (3 mg/kg for 5 doses, 0-12-24-48-72 hours), with a rapid decrease of the parasitaemia (1-3% after the first dose and negative after the second dose). A concomitant resolution of fever was observed within the next 48 hours, with transient recovery of platelets and stable haemoglobin level (9.2 mg/dl) (DAY 4). During follow-up visits patient presented: on DAY 7 we observed a haemoglobin decrease, up to 7.7 mg/dl with 12.10% reticulocytes, MCV 71.7 fl, MCH 21.8 pg and haptoglobin <0.08 g/L. On DAY 14 child presented stable level of Hb (7.9 mg/dl) but severe neutropenia (230/mmc). On DAY 21 gradual resolution of anaemia (9.2 mg/dl) and normal neutrophils count (4110/mmc) were observed.

Key Learning Points: Intravenous artesunate seems to be highly effective in children with imported severe *P. falciparum* malaria, however clinicians should be aware that transient moderate/severe anemia and neutropenia may occur even few weeks after treatment.
Title of Case(s): Traveler from Uganda: Tropical infection?

**Background:** This is a first documented case report of tropical infection with rare acquired hematopoietic stem cell disorder in Armenia, describing a 15-years-old boy diagnosed with malaria, who afterwards developed Paroxysmal Nocturnal Hemoglobinuria (PNH).

**Case Presentation Summary:** 15 years old boy was admitted to “Nork” Infectious hospital on the 20th day of the following complaints: general weakness, shivering, chills, fever, abdominal pain, loss of appetite and dark urine. Epidemiological history—traveled to Uganda a month ago, in there four friends got malaria. Laboratory findings CBC—pancytopenia (Hb-84 g/l, RBC-3.1*10^6/μL, WBC-2.5*10^3/μL, Plt-44*10^3/μL), thick blood smear negative (thrice checked), Malaria Ag—negative, RDT malaria falciparum—positive. Ultrasound—hepatosplenomegaly. Based on the above mentioned he received 3 days antimalarial treatment with Lonart forte. Despite of amelioration of symptoms and general condition patient was transferred to pediatric hospital because of the worsening of pancytopenia (Hb-67 g/l, RBC-2.5*10^6/μL, WBC-2.2*10^3/μL, Plt-5*10^3/μL). Considering family history (mother is on colchicine treatment for Familial Mediterranean Fever (FMF)) and medical history (since 2014 the patient had periodic abdominal pains) test for FMF was conducted and showed heterozygote V726A mutation in MEFV gene. Besides persisting pancytopenia further investigations revealed: LDH-1833 U/l, Coombs tests (direct and indirect) – negative, ANA–positive (1:160), coagulation tests—non remarkable, complement parameters—normal (except of haptoglobin-0.01 g/l), hemoglobinuria. CT of chest and abdomen—hepatosplenomegaly, lymphadenopathy. EGDC—duodenal ulcer (followed by eradication therapy). Flow cytometry was performed—PNH clone 91.9% in granulocytes, 88.6% in monocytes, 31.8% in RBC including 2nd type 8.8%, 3rd type 23%. Diagnosis of PNH was confirmed, anticomplement therapy and hematopoietic stem cell transplantation were recommended. However, currently child is under control of hematologists and receives symptomatic therapy when needed.

**Key Learning Points:** In routine diagnostic settings we should keep in mind the rare disorders, even when we have confirmed diagnosis.
STRABISMUS AND DIZZINESS IN THE BOY WITH HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS

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Title of Case(s): Strabismus and dizziness in the boy with hemophagocytic lymphohistiocytosis

Background: Hemophagocytic lymphohistiocytosis (HLH) is a life-threatening clinical syndrome. Recurrent symptoms in a patient with HLH may represent HLH relapse or opportunistic infection due to immunosuppressive treatment and may pose a significant diagnostic challenge.

Case Presentation Summary: Fifteen years old boy with recurrent HLH of unknown etiology treated based on HLH 2004 protocol, was admitted to the hospital for a routine check-up and reported vomiting and dizziness since the previous day. He was treated with tapered corticosteroids at that time, complicated with Cushing syndrome, hypertension, and diabetes. On physical examination, we found the presence of the right-sided facial nerve palsy, convergent strabismus of the right eye, and positive Romberg test. His laboratory results were within normal ranges, and computed tomography of the central nervous system (CNS) revealed no abnormalities. In CNS magnetic resonance imaging (MRI) enhancement of cranial nerves, III-IX, and basal meninges were found, and the abnormalities characteristic for tuberculous meningitis were present in cerebrospinal fluid: cytosis 69/µl, lactate 7.1 mmol/l, protein 1063 mg/dl, glucose 16 mg/dl, chloride 113 mmol/l. We suspected tuberculosis (TB) and started antituberculous treatment with transient improvement in his neurological condition. However, during steroids tapering, he presented with severe headache, nuchal rigidity, deafness, and progressive gait disturbance. No TB confirmatory tests were positive, and there was no improvement in CNS MRI imaging, whereas, in MRI of the spine, full-length leptomeningeal enhancement with massive infiltration at the level of cauda equina was present. CNS reactivation of HLH was suspected, and the boy received dexamethasone, etoposide, and intrathecal methotrexate with hydrocortisone. We observed rapid improvement in both clinical and radiological picture.

Key Learning Points: CNS HLH relapse may mimic CNS TBC in terms of radiological and laboratory findings. CNS HLH relapse may be present in the absence of peripheral blood abnormalities characteristic for the disease.
Title of Case(s): How close is too close? The need to contact trace following exposure to high-mortality infections.

Background: Following exposure to infectious diseases with high mortality rates, it can be challenging to decide who to provide with post-exposure prophylaxis, particularly in resource-poor settings.

Case Presentation Summary: A 9 year old girl, EM, presented to the paediatric ward of a District General Hospital in Uganda with a 2 day history of worsening emotional lability, aggression and confusion. Pronounced dysphagia with painful muscle spasms upon drinking water was observed, progressing to hydrophobia and aerophobia. A healed bite mark was noted on her right hand. Parents reported that she had been bitten by a stray dog 6-weeks previously and had complained of pain and itching at the bite site. EM had not received pre-or post-exposure rabies vaccination. Rapid malaria and HIV tests were negative, and baseline bloods showed a mild leucocytosis only. A presumptive diagnosis of furious rabies was made, based on the clinical features and in the absence of facilities for antemortem rabies diagnosis. Antimicrobial cover for bacterial meningitis and herpes simplex encephalitis was commenced as a precautionary measure. Palliation was provided with codeine, diazepam and haloperidol, along with IV fluids. Progression to coma occurred by the next day, with death occurring 36 hours after presentation. During the course of her illness EM had hypersalivation with episodes of spitting. We were concerned that this represented an exposure risk to her family, health care professionals and, as she travelled to the hospital by mini-bus, members of the public. A literature search reassured us that bystander infection was highly unlikely, and we offered only close family members post-exposure prophylaxis with rabies vaccination.

Key Learning Points: 1. Human-to-human transmission of rabies has never been confirmed, except in very rare cases of infected organ transplantation. 2. Unimmunised carers may be recommended a post-exposure vaccination course, depending on suspected degree of exposure. Rabies immunoglobulin is not deemed necessary.
CUTANEOUS MANIFESTATION OF A WELL-KNOWN DISEASE: AN IMPORTANT CLUE TO REMEMBER

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Title of Case(s): Cutaneous manifestation of a well-known disease: an important clue to remember

Background: The diagnosis of childhood tuberculosis is a known challenge, and a high suspicion approach is mandatory according to the local epidemiology. In high prevalence contexts, atypical presentations and manifestations of tuberculosis require attention to avoid delayed diagnosis.

Case Presentation Summary: A 2 year-old boy presented to our hospital with four months of intermittent fever - five days per week - usually accompanied by sore throat. He went to emergency room consultations during this period, receiving antibiotics for pharyngitis and fever without a source. After two months since symptoms had started, red spots over his legs appeared during one of the fever and sore throat episodes. During a consultation, mother was told they could be insect bites. After many visits to hospitals and different treatments, with no improvement and red spots becoming painful, he was admitted in our hospital for diagnostic elucidation. Infectious disease team investigated aetiologies of fever of unknown origin and tuberculosis; dermatology team suspected of tuberculid and neutrophilic dermatosis, performing a skin biopsy; and rheumatology team made the hypothesis of erythema nodosum. A complete work up was made and the main results were a positive tuberculin test with 20 mm, a pulmonary CT scan showing compatible lesions of pulmonar tuberculosis and mediastinal lymph nodes. There was no mycobacterial isolation in any sample. Treatment for tuberculosis was initiated, leading to a clinical improvement with no adverse effects until now, at his second month of treatment. During the follow up, histopathology came as granulomatous arteritis in subcutaneous adipose tissue, suggestive of a tuberculid.
**Key Learning Points:** Cutaneous lesions are uncommon manifestations of tuberculosis, occurring in approximately 1 to 2% of infected patients. The erythema induratum of Bazin illustrated in this case is one type of this manifestation. Being aware of it enables an adequate workup to make the right diagnosis and start treatment timely.
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BLURRED VISION: EXPECT THE UNEXPECTED

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Title of Case(s): Blurred vision: expect the unexpected

Background: Due to the ongoing conflict in the African continent, Malta has been experiencing a surge in irregular migrants seeking protection, resulting in an increase in the number of cases of tuberculosis being diagnosed, with various presentations, manifestations and complications.

Case Presentation Summary: A 9-year old Eritrean boy underwent routine screening for tuberculosis on his arrival to Malta. He was found to have a Mantoux induration of 15mm with a positive QuantiFERON test. His HIV antibody test was negative and he was not previously vaccinated against tuberculosis. He was asymptomatic, with no signs of active TB. He was diagnosed with latent TB, however just prior to starting treatment, he developed bilateral conjunctivitis, which progressed to keratoconjunctivitis with blurring of vision. Phlyctenules were visible at the corneal limbus, with stromal corneal opacities in both eyes. Polymerase chain reaction assays for Herpes simplex virus and Chlamydia trachomatis were performed on multiple conjunctival swabs and were negative. He was started on repeated courses of topical antibiotics and steroids with minimal improvement. Three months after his initial presentation, a conjunctival biopsy was taken from the left eye, which showed non-necrotising granulomatous inflammation. No acid-fast bacilli were identified on Ziehl Neelsen stain, and Mycobacterium PCR was negative. Cultures for bacteria, fungi and mycobacteria were negative. He was treated with rifampicin, isoniazid, ethambutol, pyrazinamide and moxifloxacin, as well as systemic steroids. Within 6 weeks of starting treatment, his vision improved, his keratoconjunctivitis had subsided and his corneal opacities were fading.

Key Learning Points: Tuberculosis phlyctenular keratoconjunctivitis is a rare complication of TB caused by a delayed hypersensitivity reaction to Mycobacterium antigens. Treatment of tuberculosis disease is indicated, even if there are no clinical signs of active TB. Steroids are essential to reduce inflammation and prevent permanent scarring of the cornea.
THE NEED FOR CHILD-FRIENDLY MEDICINES IN A FAMILIAR DISEASE

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Title of Case(s): The need for child-friendly medicines in a familiar disease

Background: A previously healthy, not BCG-vaccinated, six-year-old girl was diagnosed with tuberculosis (TB) as a result of a household contact tracing study. Her father, with multidrug resistant (MDR) pulmonary TB, was the index case.

Case Presentation Summary: At diagnosis she was asymptomatic, with a normal physical exam, and a positive TST result (13mm). Bilateral mediastinal and hilar enlarged lymph nodes, with bilateral lung nodules, were detected in the thoracic computed tomography (CT). Although her serial gastric aspirates (acid-fast smear, PCR and culture) tested negative, _M. tuberculosis_ culture was positive in her father and brother showing a pattern of resistance to isoniazid, rifampicin, pyrazinamide, ethionamide and streptomycin. An injectable-free treatment regimen was initiated with levofloxacin, linezolid, clofazimine, cycloserine and ethambutol. Three weeks later, she was admitted because of vomiting and refusal to taking the MDR-TB drugs. During admission she presented with behavioural disturbance, right wry neck, and right peripheral facial palsy. A cerebral and cervical CT did not show any abnormal findings. No drug toxicities were found on blood exams. As cycloserine was suspected of being the responsible for these clinical findings, it was discontinued and neuro-psychiatric symptoms progressively disappeared. To appropriately complete the therapeutic scheme, delamanid was then added. Two weeks later, bilateral papilledema was detected after performing a routine ophthalmologic exam. A cerebral magnetic resonance imaging showed a papillary protrusion and posterior flattering of both eyes alongside an increased intracranial pressure (IP) (34cm H2O) confirming the diagnosis of benign intracranial hypertension. Levofloxacin was attributed as the likely cause of this adverse outcome, being discontinued after that. Subsequently, her clinical evolution was good with a progressive decrease of IP. At present, she is on the 4th month of treatment and medications are well tolerated.

Key Learning Points: 1. New oral treatment regimens for childhood MDR-TB 2. Possible MDR-TB drug adverse events
A DIFFICULT ADOLESCENT WITH A CHALLENGING DISEASE.

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Title of Case(s): A difficult adolescent with a challenging diagnosis.
Background: Tuberculous mediastinal adenopathy conventionally requires mediastinoscopy or open biopsy for diagnosis. Endobronchoscopic Ultrasound with Transbronchial Aspiration (EBUS TBNA), promising diagnostic modality, is not widely available in LMICs. We present an adolescent with Rifampicin resistant TB mediastinal adenopathy diagnosed by EBUS TBNA and Xpert MTB/RIF. Issues with drug adherence and toxicities highlighted.

Case Presentation Summary: 17 year old girl from Andaman presented with a 2-month history of cough, low grade fever and weight loss. No known contact with Tuberculosis. Clinically suspected to have pulmonary Tuberculosis in Andaman, started on HRZE. Did not tolerate as persistent nausea and vomiting. All drugs stopped, re-started on Rifampicin which she took for 40 days with improper adherence and follow-up. Presented in February 2019 -cough, central chest pain and weight loss. Chest x-ray -hilar adenopathy. CT chest -necrotic mediastinal nodes with peri-hilar consolidation. Sputum for AFB, Xpert MTB/RIF -negative. 2D-Echo -mild-moderate pericardial effusion with septations, not large enough for pericardiocentesis. HIV ELISA- negative EBUS guided trans-bronchial aspiration (TBNA) of the mediastinal nodes- necrotizing granulomatous inflammation, positive AFB smear, positive Xpert MTB/RIF with Rifampicin resistance detected. Started on Levofoxacin, Amikacin, Pyrazinamide, Ethambutol, Cycloserine, Ethionamide and Linezolid, tapering doses of steroids for 8 weeks. She improved and was discharged after 2 weeks back to Andaman. Amikacin switched to Kanamycin under government regimen. May 2019- reviewed in view of hepatitis. Pyrazinamide, Ethionamide stopped, Clofazimine added. Adherence issues noted, counselled. October 2019- no weight gain, severe paresthesia of both lower limbs. Serum Vitamin B12 -normal. Nerve conduction study- bilateral sural nerve sensory neuropathy. Chest X-ray and Echo showed improvement. Kanamycin stopped, Amitriptyline and Gabapentin added. Paresthesia subsided. She was referred back to government hospital for addition of Bedaquiline or Delamanid.

Key Learning Points: EBUS TBNA is a promising diagnostic modality for mediastinal TB. Challenges in management of Rifampicin resistant TB include drug adherence and toxicities.
Title of Case(s): It’s infection, right? Diagnostic and management challenges in a febrile twelve day old.

Background: Although genetic sequencing has streamlined primary HLH diagnosis, in many cases high-risk treatment is carried out presumptively in the absence of alternative diagnoses. Alternatively treatment may be delayed while awaiting diagnostic confirmation. We present a neonate with fevers, pancytopenia and hepatosplenomegaly who after extensive work-up for congenital/acquired infection was treated with standard and trial therapy followed by a haematopoietic stem cell transplant (HSCT), despite no identified trigger or definitive genetic diagnosis.

Case Presentation Summary: This 12-day old neonate presented febrile and vomiting. She was tachycardic, mottled, and had massive hepatosplenomegaly. Initial blood tests were pancytopenic (Table). She received fluid boluses, cefotaxime, amoxicillin and acyclovir. She was the second child to non-consanguinous white British/North-American parents. Her mother had pyelonephritis, gastroenteritis and cold sores during pregnancy, and travelled to North America (farm visit), Spain and South Africa. In view of hypertriglyceridaemia, hyperferritaemia, hypofibrinogenaemia and abnormal cytotoxic granule release assay the hemophagocytic lymphohistiocytosis (HLH) 94 protocol (etoposide/dexamethasone) was started nine days post-admission, but she suffered a seizure and worsening pancytopenias. Trial-based emapalumab was commenced with partial remission before HSCT (matched sibling donor). Complications included severe mucositis, but resulted in full engraftment and discharge (day 35). Before HSCT, genetic sequencing revealed a heterozygous mutation in the STXBP2 gene (encoding MUNC 18-2 protein), which in a homozygous state has been described causing HLH (FHL-V). Other investigations revealed a maternal Anaplasma antibody positivity. After extensive multidisciplinary discussions including the family, this was considered non-significant and not treated.
Key Learning Points: Learning points Stakes are high in the diagnosis of HLH, and despite recent innovations current diagnostics are not definitive. The broad diagnostic net cast can reveal ‘red herrings’ complicating management decisions and communication with families, especially as here where congenital/acquired infection was also a possibility. False positives can delay HLH treatment and/or lead to unnecessary empiric therapy.
Title of Case(s): Fatal case of extrapulmonary tuberculosis in a child with congenital brain malformation

Background: Extrapulmonary tuberculosis usually presents more of a diagnostic problem than pulmonary tuberculosis. In part this relates to its being less common and, therefore, less familiar to most clinicians, especially in unusual situations with information deficits and combined pathology.

Case Presentation Summary: A child of 3 years old was admitted for observation on the 5th day of the disease with complaints of fever, rejection of food and drink, vomiting, weight loss, general weakness. The child is unvaccinated because of the mother's refusal. General condition is severe, lethargic, positive meningeal symptoms, hyperesthesia, photophobia. Leukocytosis, blood neutrophilosis. CSF was clear, pleocytosis 52 cells/mm³, mostly lymphocytes (82%), normal protein and glucose. Antibiotics (penicillin G, ceftriaxone), infusion therapy, dexamethasone and diuretics were prescribed. On the 5th day of treatment, convulsions of the right extremities, convergent strabismus, and loss of consciousness were observed. CT scan demonstrated cerebrospinal fluid discirculation, involving the cerebellum, an enlargement of the fourth ventricle (Dandy-Walker syndrome) and absence of hyperdense brain abnormalities. CSF was clear, pleocytosis 36 cells/mm³ mostly lymphocytes, normal protein and slightly decreased glucose concentration. The doctor received additional information, after birth, the child lived with a relative suffered from tuberculosis. Tubercular meningitis was laboratory confirmed. The child began to receive specific therapy: kanamycin, rifampicin, pyrazinamide, ethambutol, isoniazid and supportive treatment which proved to be ineffective.

Key Learning Points: So, difficulties of early diagnosis were associated with deviant parental behavior, lack of family complete epidemiological information, unusual changes in CSF in combination with a congenital brain malformation that caused the fatal termination of the disease.
MANAGING A TODDLER WITH LATENT TB: A THERAPEUTIC DILEMMA

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Title of Case(s): Managing a toddler with Latent Tuberculosis Infection (LTBI): a therapeutic dilemma

Background: Treatment of latent TB infection (LTBI) is highly effective in preventing TB reactivation and has a recognised role in the End TB strategy. The available literature is concordant concerning the risk evaluation of children with latent TB who have come into contact with MDR-TB or XDR-TB patients.

Case Presentation Summary: This is a report of a 4.5-year-old girl who was diagnosed with juvenile idiopathic arthritis (extended oligoarthritis) since the age of 2 years old, managed with Methotrexate. Shortly after her JIA diagnosis, her mother was diagnosed with extensively drug resistant TB (XDR-TB) to multiple medications (Rifampicin, Isoniazid, Pyrazinamide, Ethambutol and Streptomycin). Initially mother was treated with IV Capreomycin, Prothionamide, Moxifloxacin, Cycloserine, Linezolid, Pyridoxine for 2 years. Father developed active TB (same organism) much later. The girl was screened with Mantoux test after maternal XDR-TB diagnosis which was strongly positive with inflammation of her forearm. Her repeated Chest X-RAYs every 3 months have been normal. Her clinical examinations have been unremarkable and her weight has been tracking along the 9th centile. As her mother has XDR-TB and this girl is a contact, she’s being followed up very regularly and the parents have been educated to ongoing monitor for early symptoms of active TB disease.

Key Learning Points: When the diagnosis of LTB is established, there are two options for the management of contacts with exposure to MDR-TB or XDR-TB: (a) Education of the patient and/or care giver, with observation over at least two years, with the aim of detecting active TB at the earliest possible stage (b) Preventative drug therapy to decrease the likelihood of progression to active TB. There is insufficient evidence concerning the efficacy of the different post-exposure management and prophylactic strategies. In the context of immunosuppression, the argument for treatment of latent TB might well be stronger.
A PERSISTENT MONOARTHRITIS AND CLINICAL DETERIORATION IN A PATIENT RECEIVING TNF INHIBITOR THERAPY FOR JUVENILE IDIOPATHIC ARTHRITIS

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Title of Case(s): Clinical deterioration and persistent monoarthritis in a patient receiving TNF inhibitor therapy for juvenile idiopathic arthritis

Background: Mycobacterium bovis infections are rare, and there is no consensus regarding the treatment of the infections, especially in immunocompromised patients. We want to emphasize a rare transmission route of Mycobacterium bovis and want to discuss appropriate therapy.

Case Presentation Summary: An 11-year-old girl with left knee involvement is being followed up with the diagnosis of juvenile idiopathic arthritis for almost 12 months. She has been receiving anti-TNF drugs for the last five months. She admitted to the pediatric rheumatology inpatient clinic because of fever, cough, nausea, and vomiting started ten days ago. The left knee was held flexed, and the joint was swollen and tender. Acute phase reactants were elevated. Computed tomography of the chest showed bilaterally diffuse alveolar infiltration in lungs, and there was a granular appearance in liver on abdominal ultrasonography. Tuberculin skin test was measured as 12 mm in diameter. Bronchoscopy and joint fluid sampling were performed. Bronchoalveolar lavage was negative, but joint fluid was positive for acid-fast staining. Mycobacterium bovis BCG ST482/SB0120 was detected in both samples. We learned that the whole family had consumed the meat of a cow with an undiagnosed disease in its lungs and liver before the patient's symptoms began. In this case, our patient was infected with M.bovis most likely via enteral route, and then it was disseminated to liver, lung and damaged joint. Immunosuppressive therapy was discontinued, and antituberculosis treatment was started. Because of severe liver toxicity due to isoniazid, the treatment was switched to ethambutol, moxifloxacin, and rifampicin. She is now in the sixth month of treatment and has only chronic changes in the knee joint.

Key Learning Points: Mycobacterial infections should be kept in mind in opportunistic and possible zoonotic infections in patients receiving immunomodulatory therapy. It should be noted that food may be a source of mycobacterial infections in immunocompromised patients.
Title of Case(s): A 3-Year-Old Girl With a Mediastinal Mass

Background: Recurrent respiratory tract infections can be the presenting symptom of an immunodeficiency. Over the past several years, multiple patients with gain-of-function mutations in PI3Kdelta have been described.

Case Presentation Summary: A 3-year-old girl was referred to a paediatric pulmonologist for dyspnea and recurrent upper respiratory tract infections (RTIs). The year before presentation, she had suffered from pneumonia and > 10 upper RTIs. Apart from the recurrent RTIs, which started in infancy, her medical history was not significant. During the physical examination we saw a dyspnoeic girl with a small stature and appropriate weight. Chest examination revealed mild intercostal retractions and bilateral rhonchi, crackles, and wheezing. The abdomen was nontender with enlargement of spleen and liver. The patient did not have palpable lymph nodes. A chest radiograph showed bilateral pulmonary infiltrations. The chest CT-scan showed compression of the left main bronchus by an undefined subcarinal mediastinal mass as well as diffuse bronchiectasis with atelectasis. Chest MRI additionally showed bilateral hilar lymphadenopathy. Serum levels of immunoglobulins were normal, but the antibody response to pneumococcal polysaccharide vaccination was insufficient. Also, despite previous vaccination, antibodies against poliovirus, pneumococcal conjugate vaccination, and Haemophilus influenzae were not detected. Reduced memory B-cell subsets were found in the peripheral blood together with an inversed CD4/CD8 ratio and increased transitional B cells. Pathological review of the mediastinal mass confirmed lymphatic tissue with dysplastic germinal centers. No malignant cells were found. Other diagnostic tests revealed no signs of viral, bacterial, atypical mycobacterial or yeast infections, or most common immunological diseases. Specific immunological blood tests revealed the Activated PI3Kdelta syndrome.

Key Learning Points: - Patients with APDS commonly suffer from recurrent RTIs (96%) and therefore will usually present first at the pulmonologist. - A mediastinal mass as part of generalized lymphadenopathy may obstruct the airways in APDS, increasing the risk of pulmonary infections and persistent severe damage.
CHRONIC RESPIRATORY SYMPTOMS AND GROWTH FAILURE IN AN EX-PREMATURE WITH PREVIOUS CHRONIC LUNG DISEASE.

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**Title of Case(s):** Chronic respiratory symptoms and growth failure in an ex-premature with previous chronic lung disease.

**Background:** This is an interesting clinical case of the manifestation of a rare autosomal recessive primary immunodeficiency in a 3 year old patient.

**Case Presentation Summary:** This patient was born premature (28 weeks) and was in NICU for 3 months. They developed chronic lung disease for which they required home oxygen for 4 months after discharge. At 3 years of age they were referred for tertiary respiratory review after prolonged admission in a district hospital. Parents reported chronic wet cough, recurrent chest infections and wheezy episodes since 18 months of age with limited effect of repeated courses of antibiotics, inhaled steroids and bronchodilators. During the last admission they required intravenous medication for asthma and antibiotics several times and developed a new oxygen requirement which could not be weaned. Furthermore there had been concerns of growth failure since 8 months of age requiring various feeding regimes. Also there were concerns regarding micro-aspiration and global developmental delay with some dysmorphic facial features. Parents are consanguineous and of Kurdish descent. Investigations on admission showed leukopenia and undetectable immunoglobulins. Broncho-alveolar lavage was positive for Pseudomonas aeruginosa and CMV and high resolution CT chest showed bronchiolitis obliterans. Further immune testing showed HIV serology was negative and lymphocyte subsets were within normal range. Extended lymphocyte subsets showed normal B cells but no IgD+ memory or class switched memory B cells. They were transferred for further specialist evaluation of combined immunodeficiency and consideration for hematopoietic stem cell transplantation (HSCT). Karyotype analysis revealed chromosomal abnormalities consistent with a diagnosis of Immunodeficiency, Centromeric instability and Facial anomalies (ICF) syndrome, a rare autosomal recessive primary immunodeficiency. Treatment with weekly IVIG was commenced and they are awaiting possible HSCT in future.

**Key Learning Points:** It is important to think of primary immunodeficiency in any child presenting with growth faltering and chronic respiratory symptoms also when several other contributing comorbidities present.
THE NEVER-ENDING OSTEOMYELITIS

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Title of Case(s): The never-ending osteomyelitis  
Background: Osteomyelitis is a common infectious disease in children under 5 years-old. S.aureus is the most common cause of acute and chronic hematogenous osteomyelitis. In subacute forms, rare pathogens such as Bartonella, Brucella or M.Tuberculosis, can be isolated.  
Case Presentation Summary: 17-month-old infant, (from Spain, no past-medical-history), brought to the emergency room(ER) because of limping and painful of the right foot without other symptoms. Assessed together with orthopedics, acute bone lesions (by Xray) were ruled out and treatment with anti-inflammatory drugs was prescribed. After one week limping gait persisted so a splint was placed for 2weeks. 4 weeks later he consulted again for persistent limp. At this point he also presented edema on the foot. After an analytical (leukocytosis, elevated CRP and ESR) and radiological study (lesion of talus bone cortex), a T99-scintigraphy was performed, and he was diagnosed with acute osteomyelitis and admitted with cefotaxime and cloxacillin iv. After partial improvement, discharge was decided and he continued oral treatment at home. After 2weeks he still presented swelling and abnormal gait, so an MR was performed. It confirmed the presence of joint effusion, so antibiotic therapy was maintained without definitive improvement. 3weeks later new admission is decided to perform a biopsy of synovial tissue. Also a TST was performed. After 48hours it showed a 15 mm induration, therefore a tuberculosis study was performed (chest x-ray: lymph nodes; IGRA:positive; induced sputum and gastric aspirate: positive PCR for M. tuberculosis) and treatment with 3 drugs was initiated (after knowing sensitivity to rifampicin-isoniazid) to be maintained for 9 months. In the pathological anatomy study of synovial biopsy, necrotizing granulomas were observed, confirming the M. tuberculosis osteomyelitis.  
Key Learning Points: Bone involvement is the second most frequent location in extrapulmonary tuberculosis in childhood, especially under 5 years. The anatomo-pathological study and culture of bone tissue biopsy are the key of the diagnosis.
RELENTLESS FEVERS – A SIGN OF TREATMENT FAILURE OR THE ESSENCE OF THE DISEASE?

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Title of Case(s): Relentless fevers – a sign of treatment failure or the essence of the disease?

Background: Typhoid fever is a severe systemic infection endemic to subtropical and tropical regions. The increasing resistance of Salmonella typhi and the emergence of outbreaks of XDR-strains complicate the choice of antibiotic treatment. Despite of directed antibiotic therapy the resistant strains have been shown to be more difficult to clear and may lead to relapses.

Case Presentation Summary: A 3-year-old girl presented with fever, lethargy and refusal to feed 19 days after returning from Pakistan. She was started on ceftriaxone. Her blood cultures grew S.typhi(azithromycin-and ciprofloxacin-resistant) and stools were positive for Giardia lamblia and Campylobacter spp., so metronidazole was added. She became afebrile on the 6th day of treatment and was subsequently discharged. She received altogether 14 days of parenteral antibiotics. Her family members were screened for S.typhi, they were negative. She developed recurrent fevers and continuous abdominal pain 15 days after being discharged. Due to a suspected UTI and a history of ESBL-producing E.coli, she was started on ciprofloxacin. Her blood cultures revealed a recurrence of S.typhi(azithromycin- and ciprofloxacin-resistant), so she was switched to ceftriaxone. She remained febrile and had persistently high inflammatory markers until the 5th day of treatment. As macrolide-resistance is uncommon in S.typhi, the cultures were sent to the reference-laboratory to be retested which revealed that S.typhi was azithromycin-sensitive. She was discharged on azithromycin and recovered fully. At the time of this presentation her father was symptomatic, although again all the family members’ analyses were negative.

Key Learning Points: When the laboratory reports an unusual resistance pattern, it is worth to discuss the possibility of a problem in the testing process and repeat it. Despite of antibiotics, the fevers may persist for a prolonged time without it being a treatment failure and needing additional broad-spectrum antibiotics. Despite of adequate antibiotic treatment, enteric fever may relapse in 1-3 weeks after the initial presentation, however secondary infection has to be ruled out.
Title of Case(s): Diagnostic Criteria for Tropical Infection

Background: This is a case report of 18-years-old boy with tropical infection. The interest of this case is that the diagnosis was based mostly on the epidemiological and past medical history.

Case Presentation Summary: An 18-years-old boy admitted to “Nork” Infectious Hospital on 5th day of the following complaints: general weakness, shivering, chills, myalgias, fever, dark urine. Epidemiological history: the boy traveled to Africa a week ago. Past medical history: he was treated for malaria (Plasmodium Falciparum) 1.5 years ago. Considering above mentioned information, on the same day the thick and thin blood smears were prepared and ring form trophozoites of Plasmodium Falciparum were detected. Diagnosis of Malaria was confirmed. Other laboratory findings and imaging investigations were unremarkable. The antimalarial treatment was conducted with Lumartem. The patient was discharged on the 2nd day and treatment was continued under outpatient control.

Key Learning Points: Epidemiological, particularly travel history and past medical history are crucial to be considered in diagnostic settings.
Title of Case(s): Acute liver injury in a 13 year old with disseminated Isoniazid resistant Mycobacterium Tuberculosis

Background: This case highlights the clinical dilemma of controlling disseminated TB on a background of anti-tuberculous drug induced liver injury. Interestingly, there was no relapse of liver injury following reintroduction of quadruple therapy. The emerging detail of Isoniazid resistance also raises an important challenge with primary tuberculous treatment in the UK paediatric population.

Case Presentation Summary: A previously fit and well 13 year old girl, presented to her local hospital with a 2 month history of intermittent fevers, night sweats and 7 kg weight loss. There was no known travel or contact history and she was fully immunised, including the BCG. Admission chest Xray and CT Thorax showed extensive miliary shadowing in both lungs, leading to transfer to a Paediatric Infectious Disease unit. Bronchoalveolar lavage (BAL) confirmed Mycobacterium Tuberculosis. Initial MRI head and ultrasound abdomen were both unremarkable. Quadruple therapy of Isoniazid, Rifampicin, Ethambutol and Pyrazinamide was commenced. Nine days after quadruple treatment, she developed vomiting with acute liver injury (ALI). ALT peaked to 636, AST 1012, Bilirubin 39 and APTT 44. Albumin dropped to 21. Hepatitis screen was negative. Quadruple therapy was suspended with Piperacillin/Tazobactam and Amikacin as cover. Routine ophthalmology review revealed evidence of bilateral choroidal tubercles and repeat MRI head showed multiple supratentorial and infratentorial lesions, consistent with disseminated TB. Levofoxacin and Ethambutol were thus restarted with high dose Dexamethasone. The ALI resolved on suspension of anti tuberculous medications with no relapse on gradual reintroduction. Linezolid was used as bridging cover whilst Insoniazid and Rifampicin reached optimum doses, 20 days after suspension. BAL sensitivities, available after discharge, showed that the MTB was highly resistant to Isoniazid. This was then switched to Prothionamide with an extension of intensive phase of therapy.
**Key Learning Points:** Gradual, phased reintroduction of quadruple therapy in order to minimize liver injury. Early consideration of drug resistant tuberculous disease.
A RARE AND FATAL COMPLICATION OF A COMMON VACCINE: BEWARE OF AN UNDERLYING IMMUNODEFICIENCY

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Title of Case(s): A rare and fatal complication of a common vaccine: beware of an underlying immunodeficiency

Background: Disseminated Bacillus Calmette-Guerin (BCG) infection is a very rare complication following BCG vaccination. It mostly occurs in patients with primary immunodeficiency.

Case Presentation Summary: A 5-month-old boy presented with fever and rash for 1 month with cough and respiratory distress for 5 days. On examination, he had pallor, maculopapular rash whole over body, ulcerated BCG vaccination site and hepatosplenomegaly. Investigations revealed anemia, thrombocytopenia and lymphopenia. He had raised C-reactive protein and sterile blood culture. Gastric lavage for acid fast bacilli (AFB) was negative, however, stool examination showed AFB. Ultrasonography abdomen revealed multiple tiny hypoechoic lesions in liver and spleen. Chest X-ray showed bilateral diffuse infiltrates with absent thymus. Skin biopsy revealed collection of foamy cells bordered by histiocytes and macrophages with AFB positivity. Immunological work-up showed low CD 3 (T lymphocytes) and CD 56 (natural killer lymphocytes) with normal CD 19 (B lymphocytes). Immunophenotyping of common gamma chain (CD 132) expression was also low (Table). Possibility of disseminated BCG infection with underlying X-linked severe combined immunodeficiency (SCID) was proffered. Next generation sequencing revealed mutation in IL2RG gene at exon 5 c.598 C>T p. Gln200Ter, confirming the diagnosis of X-linked SCID. Child received intravenous (iv) immunoglobulin, iv vancomycin, meropenem, amphotericin B, isoniazid, rifampicin and ethambutol. However, child gradually deteriorated and expired of decompensated shock.

**Table:** Laboratory investigations

<table>
<thead>
<tr>
<th>Hemoglobin (gm/L)</th>
<th>88</th>
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<tr>
<td>Total leucocyte count (x10⁹/L)</td>
<td>14.9</td>
</tr>
<tr>
<td>Differential leucocyte counts</td>
<td>P₈₅L₁₄M₁E₀</td>
</tr>
<tr>
<td>Platelet count (x10⁹/L)</td>
<td>43</td>
</tr>
<tr>
<td>Aspartate aminotransferase/ Alanine aminotransferase (U/L)</td>
<td>32/22</td>
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<tr>
<th>Lymphocyte subsets</th>
<th>Index child (Normal range) CD3 + (T cells) – 0.61% (51-77%) CD19+ (B cells) – 97.82% (11-41%) CD56+ (NK cells) – 0.22% (3-14%) CD3+CD56+ – 0.04% (NKT cells)</th>
</tr>
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<tbody>
<tr>
<td>CD 132 expression Gated on: Lymphocytes Neutrophils</td>
<td>Index child Control 25.23% 83.53% 17.53% 66.25%</td>
</tr>
</tbody>
</table>
**Key Learning Points:** A high index of suspicion should be kept for an underlying immunodeficiency in patients with disseminated BCG infection.
I THINK YOU’LL FIND IT’S A BIT MORE COMPLICATED THAN THAT...

C. Watterson  
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Title of Case(s): I think you'll find it's a bit more complicated than that…

Background: A rare manifestation in an adolescent of an ubiquitous virus, the Ebstein Barr virus. There is a complex and dynamic interplay between pharmacological immunosupression, virus and host immune components in the development of post-transplant lymphoproliferative disease.

Case Presentation Summary: A sixteen-year-old boy presented six-months post-renal transplant with a one-day history of fever and vomiting. He looked unwell and received intravenous fluids and ceftriaxone to treat suspected sepsis. He had received a living, related donor transplant (CMV-/EBV+ donor) because of underlying nephronophthisis and his immunosuppression regime included tacrolimus, mycophenolate mofetil and prednisolone. Admission bloods showed hyponatraemia, high creatinine, WBC 3.7 (N 2.2, L 0.9, M 0.5), CRP 104 and supra-therapeutic tacrolimus levels. Respiratory viral panel and blood cultures were unrevealing but his urine showed growth of Klebsiella pneumoniae. Despite the addition of gentamicin, the fever persisted. Bone marrow aspirate showed no evidence of haematological malignancy and Xpert MTB/RIF assay was negative. Incidentally, an ultrasound targeting his renal graft revealed multiple solid liver and splenic lesions. MRI scanning showed bony involvement in the vertebrae and pelvis. His EBV viral load had notably doubled in quantity since the previous month. Biopsy of a liver lesion showed heavy infiltration of lymphoid blast cells expressing B-cell antigens CD21 and CD30, there was widespread expression of EBER. This was consistent with a diagnosis of EBV-driven monomorphic post-transplant lymphoproliferative disease (PTLD). He was commenced on rituximab prior to his first round of chemotherapy with prednisolone, cyclophosphamide, vincristine and intrathecal methotrexate. Thirteen days later, he presented with febrile neutropenia. He developed acute kidney injury following first-line intravenous antimicrobial therapy. Despite transitioning to a less nephrotoxic regime (meropenem, ciprofloxacin, teicoplanin and caspofungin), this didn't recover. While he hadn't required dialysis pre-transplant, he was placed on haemodialysis for management of hyperkalaemia and fluid overload.

Key Learning Points: 1. The many ways EBV can affect the adolescent
Title of Case(s): TB or not TB?

Background: This is the unusual and complex case of a teenager who presented with a chronic cough, was initially treated for presumed pulmonary TB, and for whom screening bloods exposed underlying HIV infection. A thorough workup revealed pulmonary *Mycobacterium avium intracellulare* (MAI) infection, HBV with high viral load, EBV and HHV8 viraemia, oral HSV, and cutaneous Kaposi sarcoma. This case illustrates the complexities of managing a patient with chronic HIV and AIDS-defining conditions and highlights the importance of HIV testing as part of baseline workup.

Case Presentation Summary: This 16-year-old girl presented to her GP with a chronic cough, fever, and weight loss. Born in Ghana, she had moved to Italy three years previously and then moved to London three months before presentation. Her father reported she had been seen by doctors in Ghana and Italy, but the reason was unclear. She was suspected to have learning difficulties and had a complex social background with concerns over housing, education, and financial insecurity. Initial investigations showed sputum positive for acid fast bacilli and cavitating lesions on CXR, hence she was started on empiric therapy for suspected pulmonary TB. Screening blood tests revealed HIV infection with CD4 count of 296 and HBV DNA >50 million copies/ml. She was transferred to a tertiary hospital and started on antiretroviral therapy. Serial sputum cultures confirmed MAI infection and her anti-mycobacterial medication was changed accordingly. Biopsy of suspicious lesions on her hand, forehead, and hard palate revealed Kaposi sarcoma in the hand only. HIV sequencing revealed resistance mutations suggestive of exposure to Efavirenz or Nevirapine in Africa. She remained clinically stable on treatment and six months later her HIV viral load is undetectable and CD4 count >300.

Key Learning Points: The importance of HIV testing in suspected TB The need for thorough investigation for infectious/malignant complications in chronic HIV with AIDS-defining conditions
Title of Case(s): Fever with Splenic Abscess

Background: Brucellosis, a zoonotic disease caused by gram negative bacilli of the genus Brucella, occurs due to consumption of unpasteurized milk and contact with infected animals. It is endemic in some Asian countries including Nepal. Salmonella paratyphi, a cause of enteric fever, transmitted by feco-oral route is also common in Nepal. The objective of this case presentation is to describe a fever with spleen involvement and a dual diagnosis.

Case Presentation Summary: A 13 year old boy presented with high grade fever with chills and rigors for 7 days. He also complained of acute onset, dull aching, left upper abdominal pain. He had generalized body aches and malaise. There is no history of diarrhea, vomiting, joint pain or rashes. He was febrile but other vital parameters were normal. His spleen was palpable 1cm below the left costal margin, soft and non tender. Rest of the examination was normal. His investigations showed hemoglobin: 13.1g/dl, WBC: 6.4*10^9/L, Platelets :195*10^9/L, CRP : 18mg/L, Salmonella Paratyphi A isolated in blood culture. Brucella abortus/melitensis antibody was positive. Leptospira IgM, IgG antibody and dengue NS1Ag,lgM and IgG antibody were negative. Chest Xray and urine investigations were normal. USG abdomen showed mesenteric lymph nodes 1.4 cm * 0.8cm and isolated echoic foci adjacent to spleen either splenunculi or splenic abscess. He was initially treated with azithromycin as suspected enteric fever. Due to persistent fever, rifampicin and doxycycline were added after 3 days. He became afebrile after 2 days of doxycycline and was discharged on day 7 with 6 weeks of rifampicin and doxycycline. Child was symptomatically better at 2 weeks follow up. Repeat ultrasound is planned at 6 weeks of antibiotics.

Key Learning Points: Splenic abscess is a rare entity both in brucellosis and enteric fever and should be considered in a child living in endemic areas.
Title of Case(s): Diagnostic challenges from a facial growth from West Africa

Background: An 8 year old Ghanian boy presented with a 7 month history of an evolving, growing nodular lesion over the nasal bridge. He was otherwise systemically well, but the lesion was not responding to topical anti-infective or steroid treatment.

Case Presentation Summary: An 8 year old Ghanaian boy presented to a hospital within the UK with a growing nodular lesion over nasal bridge, which was extending across the mid-facial region. This had been growing for the past 7 months, but he had otherwise systemically well with no fevers. Both steroids and antibiotics had been tried without improvement. He had no significant past medical or family history. His immunisations were up to date and the family had otherwise remained well with no similar lesions noted. On examination, he had a similar nodular lesion over the left deltoid muscle, but otherwise examination was normal. Investigations were performed: The lesion was biopsied and analysis revealed a mycobacterium tuberculosis complex on PCR analysis. This needed further investigation by culture and speciation to distinguish between mycobacterium tuberculosis, bovis or africanum. Mycobacterium bovis was diagnosed, which fitted with the deltoid lesion but raised concerns of an underlying immunodeficiency. Further immunodeficiency investigations, centring on type 1 cytokine analysis showed an interferon-gamma receptor defect, causing an inadequate response to interferon gamma. The lesion was successfully treated with 18 months of rifampicin, isoniazid and ethambutol (as BCG is resistant to pyrazinamide), without requiring interferon gamma treatment. Unfortunately, residual scarring was still present so the child was also followed up with dermatology and plastic surgery specialists.

Key Learning Points: Disseminated and cutaneous tuberculosis can occur and needs careful investigation including speciation of any tuberculosis complex. If Mycobacterium bovis is identified from a previous history of BCG immunisation, an immunodeficiency screen should be performed, including the interferon-gamma pathway.
Title of Case(s): Recurrent fever in a infant

Background: Urinary tract infections are a very common febrile illness in children. The prevalence of UTI in febrile females aged 2 months to 2 years is more than twice as high as that in males and are associated with long-term morbidity.

Case Presentation Summary: We present a 1-month-old female with multiple episodes of urinary tract infections and recurrent pneumonia requiring long-term hospitalizations. She was the 7th child of a low-income family, unvaccinated. In the first year of her life, she was hospitalized 9 times, with a median duration of hospitalization of about 24 days with 6 episodes of bacterial sepsis (positive blood cultures) and 11 episodes of urinary tract infection, most frequently with different gram-negative germs such as Klebsiella, E. coli, Proteus, Pseudomonas aeruginosa or fungi (Candida albicans). Ultrasound - at the age of 2 months, grade I bilateral hydronephrosis can be observed. A subsequent ultrasound performed at the age of 6 months highlights congenital megaureter and vesicoureteral reflux. Bilateral reimplantation of the ureters is performed at the age of 8 months. In spite of surgery, vesicoureteral reflux and third degree hydronephrosis occurs around the age of 1 year. On the other hand, she had 4 episodes of Pneumonia with symptoms of acute respiratory insufficiency and received corticotherapy for more than 14 days per episode. An important mention is that she received long term and aggressive broad-spectrum antibiotic treatment, initial empiric treatment with Ceftriaxon and after escalation of antibiotherapy - association of antibiotics or third line-antibiotherapy (Imipenem, Meropenem, Colistin) with the emergence of multi-resistant germ strains (for example blood culture positive for staphylococcus coagulase negative, with sensitivity only to Teicoplanin).

Key Learning Points: Multiple recurrent urinary tract infections in an infant with congenital renal malformation was associated with progressive renal changes and a negative evolution with long hospitalization and morbidity.
NEONATAL TUBERCULOSIS: AN OUTBREAK?

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Title of Case(s): Neonatal tuberculosis: an outbreak?

Background: Many women display signs of sepsis in the peripartum period and are treated according to local sepsis protocols. In turn their babies are often screened for sepsis. However, most guidelines focus on common and serious causes of peripartum and neonatal sepsis, meaning other diagnoses can be missed. In exceptionally rare circumstances this can result in serious infection control issues.

Case Presentation Summary: A 21-year-old Romanian woman delivered a 37-week-gestation baby girl after an uncomplicated pregnancy. The baby was born in good condition but screened for sepsis due to suspected maternal sepsis. The baby had a raised CRP, and a lumbar puncture, but results were reassuring and she remained clinically well. She received 5 days of antibiotics on the postnatal ward with her mother before being discharged. 16 days postpartum the mother presented to hospital unwell and febrile. A chest x-ray displayed severe cavitation and widespread shadowing, highly suspicious of pulmonary tuberculosis. Sputum cultures revealed acid-fast bacilli and the woman was referred for tuberculosis treatment. The paediatric team were informed and the baby was admitted for investigations and management. Inflammatory markers, blood culture, repeat lumbar puncture, interferon-gamma release assay, and gastric aspirates were all reassuring. The baby received 3 months of rifampicin, isoniazid, and pyridoxine, after which she remained well and had a negative tuberculin skin test. Unknowingly, this mother spent 5 days in an open 5-bedded postnatal bay whilst unwell with smear positive pulmonary tuberculosis. During this time her close contacts included numerous women and their newborns. This resulted in significant difficulties with contact tracing, along with decisions regarding the investigations and management of those contacts.

Key Learning Points: Not all peripartum fever is due to pregnancy-related sepsis but other, rarer causes can be easily overlooked. Contagious pathogens on a postnatal ward pose significant problems, and guidelines regarding screening and treatment in these situations are scarce.
Title of Case(s): A Subtle Presentation of a Serious Illness

Background: Hemophagocytic lymphohistiocytosis (HLH) is a life-threatening but distinct disease in which uncontrolled and ineffective activation of the immune system occurs, leading to multi-organ failure. It can be caused by underlying genetic diseases, or it can be acquired as a result of a wide range of clinical conditions including infections, auto-immune/rheumatologic diseases or malignancies.

Objective: We present a case report of a child with clinical and laboratory characteristics suggestive of HLH.

Case Presentation Summary: Case Report: A previously healthy nine-year-old male, was seen in a pediatric emergency department with a two-month history of low back pain and one week of fever. Physical examination showed a scoliosis and a palpable lumbar mass. A CT-scan revealed a diagnosis of iliopsoas abscess and the patient was admitted. The child’s treatment started with broad spectrum antibiotic (piperacillin tazobactam plus metronidazole) and improved significantly with no additional symptoms. On the sixteenth day after admission, his fever returned suddenly, accompanied by an erythematous rash. Analyses revealed cytopenias, hypertriglyceridemia, hypofibrinogenemia, hyperferritenemia and increased LDH, D-Dimers and AST. These parameters revealed progressive worsening during the following forty-eight hours, despite the child remaining clinically stable. At that point, the diagnosis of HLH was considered, and cortico-therapy with dexamethasone was started. On the twenty-first day, serum level of soluble interleukin-2 receptor showed an elevated value, and on the twenty-second day, a bone marrow biopsy was performed, but no hemophagocytosis was seen. After cortico-therapy, the patient showed improvement and was discharged after twenty-eight days of hospitalization. The cortico-therapy was maintained in progressively lower doses and the child was followed-up as an outpatient.

Key Learning Points: This case highlights the importance of considering this clinical diagnosis, the high index of suspicion that is required and the team-work that can help the early diagnosis and treatment, thereby decreasing the mortality rate.
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Centro Hospitalar São João, Pediatrics, Porto, Portugal

Title of Case(s): Thinl out of the box - the importance of neuroimaging

Background: According to ECDC, Portugal in 2016 had 1836 cases of tuberculosis (17.8 per 100000) being considered a country of low incidence and consequently the BCG vaccination is not universal. In this case, the high index of suspicion by the clinical presentation and the characteristic complementary exams allowed the prompt start of antituberculosis treatment.

Case Presentation Summary: A 20 month old female, previously healthy, was admitted with 4 days fever, cough, nasal congestion and food refusal. She presented in the past 3 months intermittent respiratory infections, weight loss, cervical adenopathies with multiple visits to health care system. On 2\textsuperscript{nd} day, she had a clinical deterioration with drowsiness, gaze eye and positive Romberg’s sign. The cerebrospinal fluid workout revealed 107/ul cells (71% polymorphonucleocytes), low glucose and high protein levels. She progressed to a fluctuating level of consciousness state with a brain MRI showing punctiform focal areas of restricted diffusion in left capsular lenticular region. At this point, she started combined antituberculosis treatment. \textit{Mycobacterium tuberculosis} NAA assays were positive in bronchoalveolar lavage, gastric fluid and cerebrospinal fluid and the father was found to have infectious pulmonary tuberculosis. The repeated brain CT revealed large vessels vasculitis affecting bilateral frontobasal and frontalparasagittal, right temporo-occipital corticosubcortical areas and left lenticulocaudate, also an important meningeal enhancement in the basal cisterns characteristic of tuberculosis (Figure). She is completing treatment. Currently, with 24 months, she has a spastic paraparesis, feeding difficulties and loss of language skills.
Key Learning Points: The authors present a severe case of central nervous system tuberculosis with raised intracranial pressure and vasculitis, all associated with poor outcome. The suspicion was later corroborated by the microbiological positivity and neuroradiologic images of the tuberculosis meningitis triad: hydrocephalus, infarct and basal meningeal increased density and enhancement.
Title of Case(s): A case of a 3-month old girl with fever, cough, hepatosplenomegaly and critical condition

Background: The clinical expression of tuberculosis (TB) in infants and children differs from adults. Children contribute significantly in the global tuberculosis caseload and experience considerable TB-related morbidity and mortality.

Case Presentation Summary: A 3-month old girl presented with fever, cough and gasping. On examination she was febrile (39.5°C), pale, with enlarged liver and spleen but no abnormal rales on lung auscultation. The infant was born with caesarian section at 32 weeks’ gestational age and was hospitalized in NICU for 20 days due to prematurity and low birth weight. Her parents were immigrants of Romanian ancestry. Laboratory tests showed blood leukocytosis, anemia and CSF findings revealed 28 cells/μl, glucose: 52 mg/dl, protein: 43 mg/dl. Intravenous fluids and ceftriaxone were initiated. One day after admission the infant became critically ill with fever, respiratory distress and coagulation disorders and was transferred to PICU. Vancomycin and metronidazole were added to treatment. Progressively, the girl developed anasarca oedema and renal insufficiency and left exophthalmus. Chest x-ray revealed right upper lobe consolidation. MRI findings were suggestive of either TB or fungal infection. The second lumbar puncture revealed pleiocytosis, low glucose and high protein levels and CSF PCR was positive for M.tuberculosis. Anti TB treatment for central nervous system (CNS) infection (isoniazid, rifampin, pyrazinamide, streptomycin, steroids) was administered and a CNS shunt was placed. The infant survived but with severe neurological sequelae. Investigation of family members revealed genital TB of the mother with positive PCR for M. tuberculosis from the vaginal discharge and an aunt in the same household with cavitary lung TB.

Key Learning Points: This is an interesting case of an infant that presented with lung consolidation, multi-organ failure, severe neurological complications and CSF and MRI findings attributed to TB infection that was transmitted either prenatally or postnatally.
13-YEAR-OLD FEMALE WITH ABDOMINAL PAIN, FEVER AND WEIGHT LOSS

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Title of Case(s): 13-year-old female with abdominal pain, fever and weight loss

Background: My case presentation refers to a major public health issue that occurs mostly in Sub Saharan countries and raises special interest due to the difficulty in diagnosis and treatment.

Case Presentation Summary: A 13-year-old female, immigrant from Congo, with medical history of sickle cell-thalassemia, was referred to the “Aghia Sophia” Children’s Hospital (Athens), because of abdominal pain and fever for the last two days and weight loss during the last months. Laboratory examinations were normal apart from hyperproteinemia. Abdominal ultrasound revealed hepatosplenomegaly with multiple splenic infarctions. Although she was diagnosed and treated as sickle cell crisis, she continued to present fever and malaise. Imaging with CXR and chest CT scan was performed and revealed pulmonary disease. Mantoux test was also positive and pulmonary Tuberculosis was confirmed by the Xpert MTB/Rif molecular test in sputum. Before the initiation of TB treatment, the patient was tested for HIV antibodies and she was found HIV-positive. According to WHO guidelines all HIV-positive individuals with active TB disease should begin ART within the first 2 months of TB treatment. So she was started immediately on a 4-drug regimen empiric treatment for TB. One month after the initiation of TB therapy the patient’s condition was improved and the implementation of ART was decided according to WHO guidelines for drug interactions. During the initiation of ART she presented fever, cough, respiratory distress and deterioration of chest radiological findings. Sputum cultures showed no MDR TB strains. Steroid treatment was implemented with suspicion of TB-IRIS. In the following days patient’s condition was improved while carrying on both ART and TB treatment.

Key Learning Points: The HIV/TB “cursed duet” is a major public health issue because of delayed diagnosis especially in African countries. Treatment of HIV/TB coinfection is a challenge for the PID specialists. TB-IRIS is usually associated with HIV/TB patients who have recently started ART.
PYLORODUODENAL STENOSIS SYNDROME REVEALING ABDOMINAL TUBERCULOSIS.

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Title of Case(s): Pyloroduodenal stenosis syndrome revealing abdominal tuberculosis.

Background: Tuberculosis is still endemic in Africa. The pulmonary forms predominate widely, followed by lymph node and osteo-articular localizations. Abdominal tuberculosis is the fourth location and most often concerns the peritoneum. Pancreatic involvement is extremely rare even in endemic areas. We report the case of a 9-year-old immunocompetent patient with pancreatic tuberculosis revealed by pyloroduodenal stenosis and emphasize the diagnostic difficulties.

Case Presentation Summary: This is a 9-year-old female child received for postprandial vomiting associated with intense abdominal pain, all evolving for 3 months. The physical examination found a good general condition. The abdomen was painless, with no palpable mass. The abdominal ultrasound showed lymphadenopathies achieving a mass effect on the duodeno-pancreas with significant gastric stasis upstream. The eso-gastro-duodenal transit showed gastric distension in connection with pyloro-duodenal stenosis. Exploratory laparotomy found confluent mesenteric lymphadenopathies and an irregular firm pancreatic tumor compressing the pylorus. The accidental break-in of this mass left a caseiform liquid. A gastro-entero-anastomosis, biopsies on the mass and a fluid sample were performed. Postoperatively, the tuberculin test was positive at 16 mm. The amylasemia was raised to twice normal. Examination of the sample fluid isolated Mycobacterium tuberculosis. An anatomopathological examination of the biopsies revealed an epithelio-giganto-cellular granuloma in favor of tuberculosis. The child received anti-tuberculosis treatment for 6 months. After 15 months of follow-up, the child was symptom-free and the abdominal ultrasound was normal.

Learning Points/Discussion: In endemic areas, one must think of tuberculosis in front of a chronic abdominal pain and a compressive abdominal mass evolving in an unspecific clinical and para-clinical picture. From this point on, tuberculin test can be helpful in showing strong positivity. This test would have allowed the surgeons to avoid the child an unnecessary laparotomy. Anti-tuberculosis medical treatment gives good results.
Title of Case(s): An unexpected finding in a child with febrile neutropenia, anemia, and thrombocytopenia developed during intensive chemotherapy in a patient affected by ALL

Background: ALL is the most common cancer amongst children. Prolonged use of intensive chemotherapy and subsequent immunodepression are associated with an increased risk of infections. There are few data available on the risk of MDR-IPD in children undergoing intensive chemotherapy. Meningitis sustained by *Streptococcus pneumoniae* has been already described in this particular setting, while, although rare, cardiac involvement has not to be neglected in immunocompromised children.

Case Presentation Summary: A 2 y/o child in febrile chemo-induced neutropenia was admitted and empirical treatment with ceftazidime was started. At admission, blood samples collected by the central and peripheral lines showed positivity for MDR *S. pneumoniae* susceptible only to levofloxacin and vancomycin. A treatment with vancomycin and vancomycin associated to levofloxacin was initiated as lock and systemic therapy, respectively. For worsening symptoms with persistent fever, treatment was switched to meropenem and linezolid. Pneumonia was radiologically excluded and lumbar puncture was performed showing highly suggestive features for bacterial infection and positivity for *S. pneumoniae* antigen. Brain-MRI showed a necrotic-cystic involvement of pachimeninges and numerous intraparenchymal microabscesses. Echocardiography revealed massive vegetation on the tricuspid valve extended to the right ventricle suggestive for endocarditis. The association of meropenem and linezolid was continued and fever remitted on day 13 of treatment.

Learning Points/Discussion: IPD in immunocompromised hosts requires long-term treatment. The child described received 3 weeks of meropenem and 7 weeks of linezolid. Complete resolution of meningitis was achieved at 6-months-FUP. 1 year after the discharge, cardiac vegetation was decreased in size but still present. A herd immunity around immunocompromised hosts could be helpful with the aim of reducing complications of IPD, being this fragile population at risk for losing vaccine-derived immunity.
OLIGOSACCHARIDES: A DEFENSE FACTOR AGAINST PATHOGENS IN BREAST MILK

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Background and Objective: Human milk is considered the best nutrition for newborn infants because it contains optimal ingredients for healthy growth and development. Human milk oligosaccharides (HMOs) are a group of complex and diverse sugars found in breast milk. Most recently, extensive research has been conducted to understand the beneficial role of human milk oligosaccharides (HMOs) in infant health. The aim of this review was to investigate the role of oligosaccharides against pathogens in infants.

Methods: For this Review, we used the standard search strategy of the Cochrane Neonatal Review group to search the Cochrane Central Register of Controlled Trials; MEDLINE via PubMed (2012 to 25 January 2020); Embase (2010 to January 2020); and CINAHL (2013 to January 2020). We also searched clinical trials' databases, conference proceedings, and the reference lists of retrieved articles for randomized controlled trials and quasi-randomized trials.

Learning Points/Discussion: HMOs act as prebiotics to promote the growth of beneficial bacteria in the infant gut and have been proposed to act as anti-adhesive antimicrobial agents. Recent studies have shown that HMOs isolated from donor human milk samples demonstrated anti-microbial and antibiofilm activity against different strains of Group B Streptococcus (GBS), a leading cause of neonatal infection. Some HMOs also produced structural alterations in GBS biofilms, resulting in more densely packed biofilms with less prominent nutrient channels. Growth and biofilm assays in other bacterial species showed that HMOs possessed antibiofilm activity against methicillin-resistant Staphylococcus aureus (up to 60% inhibition) and antimicrobial activity against Acinetobacter baumannii (up to 11% inhibition). HMOs have also been shown to potentiate antibiotic activity. However, HMOs did not potentiate the function of antibiotics that inhibit cell wall synthesis (β-lactams and glycopeptides), suggesting that HMOs may help to permeabilize the cell membrane.
FEATURES OF CARDIOVASCULAR CHANGES IN CHILDREN WITH NOROVIRUS INFECTION

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Background: Acute intestinal infections (AII) of viral etiology may be accompanied by certain disorders of the function of various organs. The cardiovascular system reacts to the infectious process one of the first.

Purpose of research. To study the frequency, nature and severity of changes in the cardiovascular system in children with norovirus infection.

Methods: We observed 125 children aged 6 months and older up to 10 years with norovirus infection. The majority of patients (92%) had a medium-severe form. All children underwent a clinical examination, standard General clinical blood and urine tests, verification of the etiology of AII by polymerase chain reaction, and biochemical blood analysis with quantitative determination of MB-creatine kinase, lactate dehydrogenase, aspartate transaminase, and alanine transaminase. Electrocardiography (ECG) data were recorded and analyzed in patients. Clinical examinations were performed daily. Laboratory and instrumental examinations were performed a month later.

Results: The main manifestations were repeated vomiting, intoxication and increase temperature in 100%. The most frequently detected violation of repolarization - in 52%, decrease in voltage – in 17%, extrasystole - in 6%. We recorded an increase in the levels of MB-creatine kinase in isolation or simultaneously with an increase in the values of lactate dehydrogenase, aspartic transaminase, ratio of aspartic and alanine transaminases in 33%. Early initiation of therapy with gelatin tannate, a rehydration solution and probiotics reduced the disorders on ECG to 21%. Repolarization disorders remained after a month in 7% of children.

Conclusions: More than half of children have ECG repolarization disorders, and 33% have increased enzyme levels, which correlates with long-term asthenia.
CHALLENGES IN TREATING TUBERCULOSIS IN A CHILD WITH INFLAMMATORY BOWEL DISEASE.

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Title of Case(s): Challenges in treating tuberculosis in a child with inflammatory bowel disease

Background: 15-year-old child with a background of Crohn’s disease was on infliximab and azathioprine which were started after an initial negative QuantiFERON screen. He started having fever spikes with weight loss, repeat tests during this admission showed a positive QuantiFERON with chest xray showing signs of pulmonary tuberculosis. This involved a multidisciplinary team in view of the complexity of the case.

Case Presentation Summary: Infliximab was stopped and standard antitubercular therapy was started. To add to the challenges, child developed drug induced liver injury (DILI) after starting on ATT. DILI being major concern impairing efficacy of treatment it is essential for early recognition and management. Medications were stopped and phased introduction was done according to BTS (British Thoracic Society) guidelines. We found that DILI was secondary to Isoniazid and Pyrazinamide. Child was started on amikacin, moxifloxacin and clofazimine. During the phased re-introduction the child developed further weight loss with worsening xray suggestive of military TB. USS abdomen showed involvement of the bowel and MRI brain was normal. Child needed nasogastric feeds in view of poor appetite and weight loss which challenged the tolerance of ATT as well. Eventually was discharged once drug regime, weight gain was well established.

Learning Points/Discussion: 1. QuantiFERON screen sensitivity is about 80% hence important to be aware of the risk of missing latent TB. 2. Children with IBD on immunosuppression, be aware of risk of miliary TB which needs to be managed appropriately. 3. IBD does add to the challenges as associated nausea, vomiting episodes threaten the compliance to therapy with already narrowed bioavailability due to altered pharmacodynamics secondary to bowel inflammation. 4. Diagnostic dilemma whether symptoms are secondary to flare up of tuberculosis or due to drug induced DILI as newer mechanisms come to light (especially immune mediated).
Background: Tularemia, a rare zoonosis, is caused by *Francisella tularensis (F.t.)*, a gram-negative intracellular bacterium transmitted by insects, contaminated environment and contact with infected animals. From 2010 to 2017 an increase (0.3 to 1.4 per 100’000 per year) of reported cases (24% in < 24 years) has been observed. We performed a first audit at our institution to review management and outcome and compare clinical data from children and adults.

Methods: Retrospective review of ambulatory and hospitalised cases (confirmed with positive *F.t.* serology or PCR) from 2010 to 2019. 22 confirmed cases (8 children) were found. All children and 12 adults had ulcero-glandular and 3 adults had pulmonary tularemia. Mean age in children and adults was 9.25 years (range 4-14) and 49.6 years (range 18- 84 years) respectively. 6 children (mean 3d) and 10 adults (mean 8d) had to be hospitalised.

Results: In adults it took longer (range: 11d – 2 months) to establish the diagnosis than in children (range: 3d – 1month). 7 children and 9 adults were treated with beta-lactam antibiotics for 1-3 weeks prior diagnosis. All adult patients were exposed to X-rays during medical work-up. In children US was the primary imaging modality. All children received Ciprofloxacin as final treatment with neither adverse events nor recurrence whereas 3 adults had recurrent disease.

Conclusions: The disease was longer and more complicated in adults compared to children. For adult cases more diagnostics were used and it took longer to establish the diagnosis. Inadequate antimicrobial use was seen in both age groups. Tularemia should be part of differential diagnosis in children and adults with lymphadenopathy to avoid inadequate antibiotic treatment, minimize imaging and to reduce hospitalization duration and costs.
MALNUTRITION AND MALARIAL INFECTION IN RURAL MALAWI

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Background: Multiple studies have been conducted regarding the link between malaria and malnutrition with varying results. Malawi is a predominantly rural population with high malaria infection rates. Mid-upper arm circumference has been regarded as a simple and effective tool for screening for malnutrition within the rural community in low-income countries. Therefore I undertook an observational study reviewing the link between malaria infection and malnutrition within the Malawian rural paediatric community.

Methods: This was an observational study within Nkhotakota, Malawi. Those included were 126 children aged 3-60 months attending paediatric outreach clinics with clinical suspicion of malaria. These children underwent rapid malarial diagnostic testing and mid-upper arm circumference (MUAC) measurement. Raw data was analysed via the use of a Mann-Whitney U test. Age was then accounted for by recalculation with age-adjusted variations from the WHO mean MUACs for age.

Results: 76 children were malaria +ve and 50 were malaria -ve. The average age for positive children was 28.9 months (+/- 14.3) and for negative children was 19.1 months (+/- 16.1), p=<0.01. The average MUAC for positive children was 15.0cm (+/- 1.34 SD) and for negative children was 14.7cm (+/- 1.44 SD), p=0.242. Accounting for age, the average number of standard deviations away from age-adjusted WHO means for positive children was -0.19 SD (+/- 1.08) and for negative children was 0.08 SD (+/- 1.20), p=0.332.

Conclusions: In conclusion, there was no significant difference in the rates of malnutrition between children with and without malaria in this region of rural Malawi. This suggests that nutritional status may prove a poor determining factor in excluding potential for malarial infection in similar demographical settings. This may be confounded by heightened community outreach teams resulting in a more nourished population.
Background: Premature neonates are particularly at risk of many organs and systems complications resulting from the immaturity, associated with prematurity and intensive treatment.

Methods: We present a case of Pneumocystis jiroveci infection, which occurred in a newborn with extreme immaturity. The child has gone through severe circulatory and respiratory failure after birth, a few episodes of infection including the central nervous system, and has gone through a lot of invasive procedures like intubation, long-term central catheters and parenteral nutrition.

Results: There were severe complications like gastrointestinal obstructions with the necessity of stoma, haemodynamically significant patent ductus arteriosus requiring surgical ligation and severe retinopathy of prematurity treated with ocular inhibitor supply of human vascular endothelial growth factor A (VEGF-A). Pneumonitis with very severe course occurred after another surgical intervention. Multidirectional diagnosis allowed identifying the infection of Pneumocystis jiroveci etiology. Inclusion of trimethoprim and sulfamethoxazole targeted therapy resulted in clinical improvement and gradual resolution of inflammatory changes.

Conclusions: We indicate that Pneumocystis jiroveci is still a dangerous pathogen for a selected group of patients. The risk of disease is important in patients with a significant immaturity, a history of previous infections, intensive antibiotic therapy and the use of many invasive diagnostic and therapeutic procedures.
CLINICAL FEATURES OF ACUTE EBV INFECTION IN CHILDREN AT ADMISSION IN THE HOSPITAL.

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Background: Epstein-Barr virus-related infectious mononucleosis (IM) is well studied and it is clinically characterized by a triad of symptoms: sore throat, cervical lymph nodes enlargement, fever mostly in young adults. Our study was to evaluate the recent trend in clinical manifestations of EBV-associated IM in children at the moment of hospital admission.

Methods: Data of 101 children were collected before they got hospitalized. Patients presented symptoms resembling those of EBV-associated infectious mononucleosis. Two groups were formed: group I comprised children aged 1-7 (mean=3.7) group II: 7-17(mean=12.4)years. In all cases, was not confirmed. Data gathering and analysis were performed with MS Excel 2019.

Results: On average, patients in the group I sought medical attention on the 6th day of illness, while those in the 2nd group did seek medical help on the 8th day. The predominant complaints in group I were high fever and fatigue (94%), enlargement of cervical lymph nodes (78%), blocked nose (80%) sore throat (2%). The main symptoms in the 2nd group were: high fever (96%), enlargement of cervical lymph nodes (86%), sore throat (63%), blocked nose (59%). IM was clinically suspected in 90% of patients of group I, and 100% in patients of group II.

Conclusions: The study showed that EBV-associated IM is still characterized by its classical symptoms. Also, The symptoms are well expressed, therefore IM is easily recognizable at the hospital admission level in elderly children. In younger children, IM can occur under the mask of a respiratory viral infection.

Clinical Trial Registration: not applicable
UMBILICAL CORD BLOOD UNITS: DETECTION OF HHV-6 AND PARVOVIRUS B19 WITH MOLECULAR TECHNIQUES

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Background: Viral infections are major causes of morbidity and mortality in patients undergoing stem cell transplantation (HSCT). Umbilical cord blood (UCB) is an alternative source of HSCT. Human herpesvirus 6 (HHV6) and Parvovirus B19 may be transmitted through UCB to immunosuppressed patients causing mainly myelosuppression, encephalitis, acute graft versus host disease, delayed engraftment or even graft failure [1]. HHV-6 intrauterine transmission is recorded in 1% of births. Congenital infection is mainly due to the presence of chromosomally integrated HHV-6 (ciHHV6) in mothers which represents 1% of the population. CiHHV-6 can lead to virus reactivation, especially in immunosuppressed patients, with a variety of known complications. The purpose of this study is to examine the presence of HHV-6 and Parvovirus_B19 in cord blood units (CBUs) by Real-Time PCR.

Methods: Plasma samples (n=82) from cryopreserved cord blood units were thawed and tested. CBUs were collected during the period 2011-2018 and were processed using the automated system Sepax (Biosafe). DNA was isolated from plasma (DNA-Sorb-B kit, Sacace). Molecular detection of HHV-6 and Parvovirus B19 was performed by Real-Time PCR using the HHV6_Real_TM_Quant and Parvovirus_B19_Real_TM_Quan(Sacace) kits respectively, on Rotor-GeneQ cycler(Qiagen).

Results: There was 1 positive sample (1.22%) in 82 plasma samples analysed for HHV-6, while all samples were negative for Parvovirus B19. 52.44% of the samples were CMV IgG positive and 6.09% CMV IgM positive. The HHV-6(+) sample was also CMV IgG(+)IgM(+) without reaching statistical significant correlation. All samples were negative for HTLV_I-II, HCV, HBsAg and HIV_I-II.

Conclusions: Our data shows that the parvo_B19 virus is not required to be examined in CBU excluding the epidemic periods. The percentage of HHV6 was 1.22%. Our experimental results indirectly indicate the need for molecular control of this virus in the transplanted CBUs mainly for the detection of ciHHV-6.

Clinical Trial Registration: No clinical trial - Basic medical research
THE EFFECT OF AN ANTIMICROBIAL GUIDELINE ON THE MANAGEMENT OF LATE ONSET SEPSIS IN THE NEONATAL INTENSIVE CARE UNIT.

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**Background:** The use of broad spectrum antibiotics as empiric therapy in cases of suspected late onset sepsis (LOS), a leading cause of morbidity and mortality among very low birth weight (VLBW) infants, has contributed to the emergence of multidrug resistant organisms (MDRO). The WHO and national health institutes recommend that hospitals institute guidelines to restrict the use of broad spectrum antibiotics as part of antimicrobial stewardship. Objective: To evaluate the efficacy and safety of implementing an antimicrobial guideline to restrict the use of vancomycin in the NICU.

**Methods:** An antibiotic guideline for the management of LOS was introduced in a tertiary level NICU and antibiotic usage compared between the pre- and post-implementation periods using interrupted time series analysis. The primary outcome was measured as days of therapy (DOT) per 1000 patient days (PD) for antibiotics received after 72 hours of life. Information relating to birth weight, gestational age, blood culture positivity, duration of bacteraemia and central line associated bloodstream infection (CLABSI) was collected before and after guideline implementation.

**Results:** Use of glycopeptides was reduced from 46.07 DOT/1000 PD to 19.94/1000 PD (P = ). The incidence of confirmed and suspected cases of LOS and duration of bacteraemia decreased post-guideline implementation; 10.2% (5/49) vs 6.8% (4/59); 43% (21/49) vs 37% (22/59), respectively. No death or complication related to LOS occurred during either study period. Guideline compliance was 69.5%. A positive blood culture was the most frequent reason (38.9%) given for non-adherence to guideline recommendations.

**Conclusions:** Use of an antibiotic prescribing guideline for the management of LOS in the NICU is a safe and effective means of reducing vancomycin usage. Guideline compliance may be optimised through education, training and multidisciplinary input.
A CONFUSING URINARY TRACT INFECTION IN CHILDREN

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Background: Acute pyelonephritis (AP) is one of the most serious infection throughout childhood. The diagnosis of AP is initially made on the basis of urinalysis results and the presence of clinical systemic signs of inflammation.

Methods: A 8-year-old boy was referred to our Pediatric Emergency Department (PED) because of a prolonged high-grade fever. The first episod of hyperpyrexia was dated back 3 weeks. During the first medical visit, the Primary Care Paediatrician (PCP) observed signs of localized pneumonia, therefore prescribed a co-amoxiclav therapy. Without fever for three days, hyperpyrexia started again. On the day 13th, the patient went to PED. A positive chest X-Ray was performed, azithromycin prescribed and fever disappeared after two days. On day 5, the child was feverish again with headache and vomit. The physical examination still showed a slight reduction of murmur. The PCP prescribed blood tests documenting WB 20.000/mmc (N 90%), CRP 46.8 mg/dl, PCT 70.6 ng/ml, creatinine 0.86 mg/dl. The physical examination still showed a reduction of murmur. On that time, during the Covid19 outbreak, he didn’t have the epidemiologic criteria to test the Corona Virus.

Results: At the admission to our ward, blood cultures and urine dipstick resulted negative. With suspicion of brain abscess, he performed an encephalon (negative) and abdomen MRI finding out the presence of a globose right kidney with several abscess foci. The urine culture documented a multi-sensitive Pseudomonas Aeuruginosa. Piperacillin/tazobactam with amikacin were started. After 5 days of therapy he stopped amikacin because of an improvement of acute phase reactants, at the day 7 the saw-tooth pattern of high temperature 'spikes'(maximum 40°C) disappeared.

Conclusions: Fever may be the only symptom of AP. A negative dipstick in a persistent feverish child has to be repeated.

Clinical Trial Registration: ClinicalTrials.gov 0123456789
CLINICAL MANIFESTATIONS OF VARIOUS ETIOLOGICAL FORMS OF ACUTE RESPIRATORY INFECTION IN CHILDREN

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Background: In recent decades new pathogens of ARI have been discovered: metapneumovirus, bocavirus, and coronavirus. They persist in combination with RSV, rhinovirus, adenovirus and parainfluenza. They affect children of preschool age, causing damage of the upper and lower respiratory tract. Objective: to evaluate the clinical manifestations of the disease, depending on the type of pathogen in children.

Methods: This study included 41 children from birth to 13 years old with the symptoms of acute respiratory infections. Most of children were aged 1-5 years (n=20; 48,8%), less - children of the first year of life (31,7%; n=13) and 8 children (19,5%) were older than 5 years. All patients underwent swab smear by polymerase chain reaction to isolate viral pathogens of respiratory infections.

Results: The most common pathogens were rhinovirus infection (n=9; 21,9%) and RSV (n=8; 19,5%). Metapneumovirus and adenovirus were rarely found. Mixed infection was detected in patients of the first 5 years of life (7,3%). Children over 5 years old more often suffered from upper respiratory tract disease (15%), while in patients 1-5 years old of life suffered from lower respiratory tract lesion (50%). In children of the first months of life the main disease was acute rhinopharyngitis of unknown etiology. Complicated forms of respiratory infection occurred in infants in the form of otitis, sinusitis and pneumonia. Acute bronchitis was caused by RSV, metapneumovirus and rhinovirus. The main pathogens of obstructive bronchitis and rhinopharyngitis were of unclear etiology.

Conclusions: Children of the first five years of life had signs of lower respiratory tract damage in the form of tracheobronchitis, obstructive bronchitis and acute bronchitis, while older children had upper respiratory tract infection. The pathogen was not associated with clinical manifestation of the disease.

Clinical Trial Registration: Clinical trial registration N/A
IDENTIFICATION, CHARACTERIZATION AND ANTIBIOTIC RESISTANCE OF STREPTOCOCCUS AGALACTIAE CLINICAL SAMPLES ISOLATED IN GEORGIA

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Background: Streptococcus agalactiae colonizes the gastrointestinal and genitourinary tracts of up to 50% of healthy adults and newborns; it is associated with pathogenicity in immunocompromised, elderly and pregnant adults as well as infants and neonates. Mostly responsible for two different clinical presentations: early-onset neonatal sepsis and late neonatal sepsis. Intrapartum antibiotic strategies have limited impact on disease but according to the CDC 2012 report GBS is the leading cause of culture-confirmed neonatal sepsis. In GBS case the treatment mainly performed with penicillin but Erythromycin, Vancomycin and Clindamycin are recommended for penicillin-allergic women.

Methods: Between March 2019 and September 2019 an anovaginal swabs were collected from 80 women at 35-37 weeks of gestation and 39 were identified as str. agalactiae. 24 str. agalactiae strains were isolated from urine, vagina and rectum at clinic „Curatio“. Culturing and identification GBS were carried out according to standard microbiological methods and sero-grouping was done by multiplex PCR. Antimicrobial susceptibility profiles were determined by disk diffusion method for penicillin, vancomycin, erythromycin, clindamycin, levoflaxacin, cefotaxim, Pefloxacin.

Results: Our results revealed that in total from 104 samples 29% were Str. agalactiae. All GBS strains were all sensitive to Penicillin, 16% were resistant to Erythromycin and Clindamycin. 6% showed intermediate sensitivity to Erythromycin and 4% to Pefloxacin. We detected antibiotic resistance genes and determine resistance mechanism for each Erythromycin resistant isolates by PCR.

Conclusions: As we detected resistant strains to Erythromycin it is important to study prevalence, serotype distribution of Str. agalactiae and antibiotic resistance mechanism. The given data cannot be projected on the population in our country because we had small sample size for report but this could be used as a base for further epidemiological studies and also for managing targeted new approaches of treatment and prevention strategy.
DISSEMINATED STAPHYLOCOCCAL DISEASE: THREE YEAR EXPERIENCE FROM PEDIATRIC INTENSIVE CARE UNIT IN NORTH INDIA

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Background: *Staphylococcus aureus* is one of the most virulent organisms causing infection in humans ranging from skin infections to fatal disseminated disease (DSD). Literature is scanty regarding the critical care needs in children with DSD. However, with the dearth of pediatric critical care beds in developing economies, we review the clinical presentation, management and outcome of children with DSD. Here we present clinical and microbial data of 22 patients with DSD admitted in our Pediatric Intensive Care Unit (PICU) over a 3-year period.

Methods: Retrospective medical records of patients with DSD managed in PICU over 3 years (2017–2019) were reviewed. DSD was defined as pyogenic infection of two anatomically non-contiguous organs, and either culture of *S. aureus* or demonstration of clustered Gram-positive cocci from at least one normally sterile body fluid. The data was retrieved on clinical and demographic characteristics, various laboratory studies, critical care problems and their management details.

Results: Twenty two patients with a mean age of 59 ± 50 months were admitted, out of which 13 were female. Presenting complaints included fever, soft tissue swelling and breathing difficulty. Respiratory distress (19) followed by shock (6) were the main indication for PICU admission. Pyothorax (9) and pyomyositis (8) were commonest foci. Fifteen grew staph. aureus, eleven were Methicillin resistant (MRSA) and four were methicillin sensitive. Seven patients needed ventilation for median 48 (30,96) hours. The median duration of PICU stay was 12.5 (7,19) days. Seventeen (77%) children were discharged.

Conclusions: Pleuro-pulmonary involvement was the commonest presentation. Identifying metastatic foci is crucial for instituting source control measures, which forms an integral part of management of these patients. Emergence of MRSA is a matter of concern and needs revision of antibiotic policy.
COVID-19 VIRAL INFECTION ROMANIAN PHYSICIANS RISK PERCEPTION

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Background: December 2019, Wuhan- China, SARS-CoV2 induces a severe epidemic outbreak. 11 March 2020, as a result of the global rapidly spread of the infection, WHO declares pandemia. Circumstances: 118,000 cases of Covid-19 infections, 4921 deaths worldwide. 16. March 2020 Romania declares emergency status. Purpose Analysis of the Covid-19 infection risk perception among the Romanian health care professionals (HCP)

Methods: We applied a research instrument (questionnaire) with 28 items addressed online to HCP from Romania. Respondents - 311 doctors, family medicine specialists 70%, 25% of respondents from other specialties, age: 31-45 years (31%) and 46-64 years (51%),80% are from urban area, 20% - rural areas.

Results: 80% of the respondents need more medical informations. 60% felt risk exposure to Covid-19 infection. 54% perceive that infection can evolve severely in Romania compared to other countries. 70% feel a sense of insecurity because they do not have access to the official new treatment protocols. 60 % of the respondents feel concerned about severity of Covid-19 pandemia. 33% feel a sense of fear in front of the unknown infection evolution. Major concern - lack of medical protection equipment: only 38% have gloves, 60% protection mask, 1% overalls and glasses.

Conclusions: Primary HCP remains the gate-keeper of the healthcare system in Romania. The perceived risk at personal and professional level is in invers correlation with the level of medical knowledge about the major risk situation we are going through. For maximum capacity, medical personnel require: - medical information, - working protocols adapted to the reality from the field, - protection equipment, - social protection.
HYPERBILIRUBINEMIA IN NEWBORNS WITH CONGENITAL CYTOMEGALOVIRUS INFECTION

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Background: Congenital cytomegalovirus infection (cCMVI) causes liver damage in the form of hyperbilirubinemia in newborn. The goal is to determine the clinical and laboratory signs of jaundice in newborn with cCMVI.

Methods: The clinical and laboratory signs of jaundice in 70 newborns were studied. The study group included (n = 50) children with cCMVI. The control group (n=20) included newborns with hyperbilirubinemia and negative results of blood and urine tests on DNA CMV. In the study were determined: bilirubin, liver enzymes (alanine aminotransferase (AlАT), aspartate aminotransferase (AsAT)). The results were processed using “Statistica 10.0”.

Results: In the main group, the total bilirubin level was 162.5 (98–214) µmol / L, in the control group 204.9 (164.9–237) µmol/L (p<0.05). In children with cCMVI, direct bilirubin was higher (p <0.05) and amounted to 66.8 (41.6–85) µmol / L than in control group 21.4 (17.5–23.8) µmol/L. In the study, an increase in liver enzymes was noted in 16 children (53.3%) of the main group and in 2 children (10%) in the control group, which significantly differed (p <0.05). The median AlАT level in the main group was 65.4 (72–155) U / L, which was significantly higher (p <0.05) than in the comparison group 24.5 (18–36) U / L. The median AsAT level in the main group was 85.7 (60.4 - 90.6) U / L, and higher (p <0.05) than in the control group 43.0 (34.8 - 52, 6) U / L.

Conclusions: Hyperbilirubinemia in newborn with cCMVI is characterized by increasing liver enzymes. Clinical Trial Registration: identifying number: N/A
PROGNOSIS OF PERTUSSIS IN INFANTS IN TUNISIA: ABOUT 79 CASES

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Background: Pertussis is increasingly affecting infants under the age of 6 months who have not been vaccinated or have been inadequately vaccinated. In Tunisia, there is no mandatory national vaccine booster in adolescence or adulthood. The infant is then particularly exposed. Our aim was to study the severity of pertussis in infants under the age of 3 months.

Methods: Our study was retrospective extending over a period of 5 years (2015-2019). It included all cases of pertussis confirmed by PCR in infants less than 3 months old. Data were collected from medical records.

Results: We collected 79 infants with a median age of 50 days [11-90]. Thirteen patients had already received one dose of cell vaccine. Patients were admitted mainly because of cyanogenic paroxysmal cough (n=50) associated with dyspnea (n=11). Fever was present in 18 cases. Lymphocytes ratio over 10,000 / mm³ was present in 29 cases [2560-47330]. A macrolide was administered in 58 patients. Twenty patients were transferred to intensive care unit. Thirteen among them needed mechanical ventilation and seven transfusion exchange. The median duration of the hospital stay was 9 days. Four patients died.

Conclusions: Pertussis was severe in a quarter of our patients. The prevention of the disease among infants through a booster vaccination in adolescents and adults is urgent.
COMPLICATIONS OF VARICELLA IN TUNISIAN CHILDREN: ABOUT 23 CASES

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Background: Varicella is often mild in immunocompetent children. However, in recent years severe cases have become more and more frequent. Our aim was to study the complications of varicella in children.

Methods: Our study is retrospective extending over a period of 10 years (2010-2019). It concerned 23 children with complicated varicella. The diagnosis of varicella was based on a characteristic feverish rash. For each patient, we analyzed the clinical and biological data and the outcome of the disease based on medical records.

Results: Our 23 patients were aged 2.5 years on average. A non-steroidal anti-inflammatory drug has previously been administered in 6 cases. Feverish rash was developed 4 days before hospitalization on average. The complications were a bacterial cutaneous infection (n=8) with a scalded-skin syndrome in one case and face cellulitis in another case, pneumonia (n=8) complicated by pleural empyema in one case and acute respiratory distress syndrome in another case, cerebellitis (n=4), hepatitis (n=4), pancytopenia (n=3), and seizure (n=2). Twenty patients were treated with intravenous Aciclovir and antibiotics. The outcome was positive.

Conclusions: Varicella is likely to cause severe complications which can compromise the vital prognosis of children with immunodeficiency but also of immunocompetent children. A national registry of complicated varicella cases is needed to better assess the importance of the varicella vaccine in our country.
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**Background:** Nigeria has one of the highest under 5 mortality rates worldwide, and meningitis accounts for 3% of such mortality. The diagnosis of meningitis is challenging in LMICs because there is often poor laboratory support for carrying out timely cerebrospinal fluid analysis. Viral meningitis accounts for 50% of meningitis in children in developed countries, the incidence is not known in this setting. This study set out to determine the incidence of cytomegalovirus and herpes simplex virus 1 & 2 among patients presenting with suspected meningitis at the children’s emergency room.

**Methods:** It was a prospective study of consecutive paediatric emergencies presenting with fever and neurological signs. Cerebrospinal fluid samples were obtained at admission and sent to the Laboratory in a cold box for deoxyribonucleic acid extraction and testing for HSV 1&2 and CMV by polymerase

**Results:** Forty patients were recruited, 29 (72.5%) males and 11 (27.5%) females, with a mean age of 27.1±18.3 months. The common presenting clinical features were seizures 37 (92.5%), fever 35 (87.5%), lethargy 29 (72.5%), poor feeding 23 (57.5%) and coma 11 (27.5%). Twenty (50%) patients had CSF positive for HSV 1, 13 (32.5%) of whom were also positive for CMV and 12 (30%) for HSV 2. Eleven (27.5%) were positive for all three viruses.

**Conclusions:** The high incidence of viral meningitis among children with suspected meningitis is consistent with findings from high income countries. Antiviral agents should therefore be considered in the management of meningitis in this setting in order to improve outcomes of patients and promote judicious use of antibiotics. Further research in the viral aetiology of meningitis in this setting is required.
NEONATAL MENINGITIS IN TUNISIA: CLINICAL, MICROBIOLOGICAL AND OUTCOME FEATURES

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Background: Neonatal meningitis (NNM) is a rare but serious infection. It involves both the vital and neurological prognoses given the severity of neurosensory and psychomotor sequelae that it may cause. The aim of our study was to describe the clinical, biological, microbiological, radiological and the aspects of NNM as well as its treatment and outcome.

Methods: A retrospective study of cases of NNM conducted at the department of Pediatric Medicine B in the Bechir Hamza Children’s Hospital over a 15-year period (2004-2018).

Results: Forty-seven newborns with meningitis were included, aged 13.2 days on average. The NNM was bacterial in 26 cases and viral in 21 cases. PCR detected the enterovirus genome in two cases. Antibiotics were prescribed in 34 cases. Bacterial NNM were complicated by hydrocephalus (n=3) and ventriculitis (n=4). Six patients, among those treated for bacterial NNM, had neurological sequelae. In the bacterial NNM group, the mean age was significantly lower (p=0.02), prematurity, axial hypotonia and squeaking were significantly more frequent (p<0.05). A C-reactive protein value greater than 50 mg/l was statistically associated with bacterial NNM (p<0.001).

Conclusions: Viral NNM are benign and rarely require a specific treatment, but they are underestimated in the absence of systematic Polymerase Chain Reaction. Bacterial NNM, which are more severe and may cause neurological sequelae are rarely documented.
Background: Pediatric community acquired pneumonia is frequent and represent one of the major childhood death causes, especially in developing countries. We proposed to analyse clinical, microbiological and radiographic features of community acquired pneumonia in hospitalized children.

Methods: We conducted a retrospective descriptive study in the pediatric department B of Children Hospital Béchir Hamza of Tunis. We analyzed medical reports of children hospitalized for community acquired pneumonia, during the period from January 2015 to December 2016.

Results: We enrolled 120 patients with a median age of 18 months. Oral antibiotic was previously received in 49 cases. Physical examination revealed fever (89.2%), tachypnea (65%), retractions (40.8%), hypoxemia (13.3%), and crackles (30.8%). Chest radiograph revealed a unique alveolar condensation in 79.2% of the cases, with pleural effusion in 22.5% of the cases. Bacteria was identified in 10 cases by blood, pleural or sputum culture: Haemophilus influenzae, Pneumococcus, Staphylococcus aureus, Brahamella catarralis and Stenotrophomonas maltophilia. Ampicilline was prescribed in 54.9% of the cases. Seven patients required chest drainage and eight patients were transferred to intensive care unit.

Conclusions: Bacteriological diagnosis in community acquired pneumonia is insufficient, due to the high level of ambulatory antibiotic consumption and the low profitability of bacterial diagnostic methods. Therefore antibiotic therapy is based on clinical, radiographic and laboratory presumption characteristics of causative germ.
MENINGOCOCCAL CARRIAGE IN YOUNG ADULTS IN THE MALTESE ISLANDS

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Background: Invasive meningococcal disease (IMD) has an annual incidence of 0.4-3/100,000 in Malta. Meningococcal carriage studies shed light on the epidemiology, transmission, and pathogenesis of IMD. We present the first study to investigate the prevalence and genomic characteristics of meningococcal carriage in young adults aged 18-24 years attending the only university in Malta.

Methods: Two posterior pharyngeal swabs were taken from 404 university students, and tested for Neisseria meningitidis (Nm) by culture and polymerase chain reaction. Isolates were assigned a serogroup and genogroup, and sequenced by whole genome sequencing. Post-sequence analysis assigned sequence type (ST), clonal complex (CC) and Bexsero antigen sequence type (BAST) for each isolate. Diversity amongst isolates was assessed using Simpson’s Index of Diversity (D).

Results: Twenty-five students (6.2%; 95% CI 4.9%) were carriers for Nm. While most of the cultured isolates were non-serogroupable (n=14; 66.7%; 95% CI 43-85.4%), the predominant genogroup was B (n=9; 36%; 95% CI 18–57.5%), followed by Y (n=6; 24%; 95% CI 9.4 – 45.1%). Fourteen different ST distributed among 9 CC, and demonstrating 17 different BAST, were identified amongst the carried meningococcal isolates. The ratio of unique BAST to isolates was 1:1.12, and there was a high degree of BAST diversity (D=0.98). No single CC predominated in carriage, though CC53, CC23 and the hyperinvasive CC41/44 accounted for 4 (19%; 95% CI 5.4-41.9%), 4 (19%; 95% CI 5.4-41.9%) and 3 (14.3%; 95% CI 3.0-36.3%) isolates respectively.

Conclusions: Our findings demonstrate a wide biodiversity in meningococcal carriage, with CC23, CC41/44 and CC53 being important. The high degree of BAST diversity amongst carriage isolates is likely to undermine any potential for MenB vaccination to impact meningococcal carriage. These results may influence a future meningococcal vaccination strategy in Malta.

Clinical Trial Registration: This is a basic science study, and not a clinical trial. Therefore, there is no registration number.
RISK FACTORS FOR INVASIVE INTERVENTION IN HOSPITALIZED CHILDREN WITH SUPPURATIVE CERVICAL LYMPHADENITIS

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Background: While some cases of Suppurative Cervical Lymphadenitis resolves with oral antibiotic treatment, many children are hospitalized for IV antibiotic treatment and some of them require invasive procedure such as needle aspiration or open surgical drainage. The optimal setting and timing for this procedure as well as clinical and laboratory parameters indicating its necessity are not well described in literature. Aims of study: to examine clinical and laboratory predictors for invasive intervention in hospitalized children that may lead to early intervention, hasten recovery and shorten length of hospitalization.

Methods: Retrospective study included pediatric patients with lymphadenitis according to clinical impression at the ER department, who were hospitalized 2010-2017. From this list, only children with the diagnosis of Suppurative cervical lymphadenitis were included in the study and their electronic data base including clinical, laboratory and total length of antibiotic treatment pre-hospitalization was examined. They were categorized according to the presence of needle aspiration intervention, open surgical drainage and conservative adequate antibiotic treatment.

Results: 383 pediatric patients with the diagnosis of Suppurative cervical lymphadenitis were hospitalized during 2010-2017. Average length of hospitalization and length of antibiotic treatment pre- hospitalization was longer in children who went through intervention, as well as the presence of local erythema and fluctuation described in physical examination. There were no association to laboratory parameters.

Conclusions: In hospitalized pediatric patients with the diagnosis of Suppurative cervical lymphadenitis there were no laboratory risk factors found to be in association with the need for intervention. The main predictor is clinical assessment and physical examination of the pediatrician. In addition during oral antibiotic treatment without clinical improvement, consider hospitalization and invasive intervention.
THE ROLE OF INFECTIONS IN THE STRUCTURE OF CAUSES OF LONG-TERM SUBFEBRILITY IN CHILDREN

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Background: Increased body temperature in children is a frequent symptom of many diseases. Finding the cause of fever is very important in the practice of a pediatrician. However, long-term subfebrility remains one of the most problematic symptoms in terms of the volume of examination of the patient to find out the causes of its causes and the choice of tactics for further management.

Methods: A retrospective analysis of 90 medical records of patients hospitalized in the US GDIKB of Minsk in the period from 2012 to 2019 with the diagnosis of "long-term subfebrility" was conducted.

Results: In the age aspect, all patients were distributed as follows: children older than 11 years were 58.9%, 7-10 years – 24.4%, 1-6 years – 8.9%, children under 1 year - 7.8%. The average age was 10.6±4.6 years. Among the children studied, the number of girls was higher than boys – 54 (60%) and 36 (40%), respectively. There was a wave dynamics of morbidity: a third of all cases (38.8%) occurred in the spring, less often there were admissions in winter (25.6%) and autumn (28.9%); during the summer months, only six children were hospitalized (6.7%). The average duration of hospitalization was 7.6±4 bed days.

The causes of long-term subfebrility were both infectious (in 40% of cases) and non-infectious (in 60%), and the role of non-infectious pathology increases with age. Among the infectious causes were the following: transmitted EB-infection (25%), streptococcal infection (13.8%), acute sinusitis (11.1%), urinary tract infection (11.1%), enterovirus infection (8.3%), acute intestinal infections (8.3%), infectious mononucleosis (5.6%), giardiasis (5.6%), acute otitis (5.6%), toxocarosis (2.8%), congenital toxoplasmosis with damage to the nervous system (2.8%).

Conclusions: The exclusion of major infectious pathogens as possible causes of long-term subfebrility should be mandatory in such patients.

Clinical Trial Registration: no unique identifying number
ARTHROCENTESIS, ARTHROSCOPY OR ARTHROTOMY FOR SEPTIC KNEE AND ANKLE ARTHRITIS IN CHILDREN: A SYSTEMATIC REVIEW

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Background: Septic knee and ankle arthritis in children can be treated by arthrocentesis (articular needle aspiration) with or without irrigation, arthroscopy or arthrotomy followed by antibiotics. The objective of this systematic review is to identify the most effective drainage technique for septic arthritis of the knee and ankle in children.

Methods: The electronic MEDLINE, EMBASE and Cochrane databases were systematically searched for original articles that reported outcomes of arthrocentesis, arthroscopy or arthrotomy for septic arthritis of the knee or ankle joint. The quality of all included studies was assessed with the Methodological Index for Non-randomized Studies (MINORS) criteria.

Results: Out of 2428 articles, 11 studies with a total of 297 knees and ankles were included in the systematic review. The quality of evidence was low (MINORS median 4 (range 2-7)). A meta-analysis could not be performed because of the diversity and low quality of the studies. In septic knee arthritis, additional drainage procedures were needed in 54 of 156 (35%) knees after arthrocentesis, in 4 of 96 (4%) after arthroscopy and in 2 of 12 (17%) after arthrotomy. In patients with septic ankle arthritis treated with arthrocentesis, additional drainage procedures were needed in 4 of 18 (22%) ankles.

Conclusions: Included studies on treatment strategies for septic arthritis of the knee and ankle in children are diverse and the scientific quality is generally low. Knee arthroscopy may have a lower risk of additional drainage procedures as compared to arthrocentesis and arthrotomy, with acceptable clinical outcomes and no radiological sequelae.

Systematic Review Registration: International Prospective Register of Systematic Reviews (PROSPERO) under registration number CRD42018117795.
POST-HOSPITAL SYNDROME: DOES HOSPITAL STAY CAUSE VULNERABILITY AFTER DISCHARGE IN INFANTS IN LOW-INCOME COUNTRIES?

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Background: After discharge from the hospital, patients face a transient period of generalized susceptibility to disease, deaths and hospital readmissions that is called post hospital syndrome. This syndrome has been described recently and only in adults and in high-income countries, while no studies investigated the risk in children in low-income countries. Thus, the aims of this work are to estimate the burden of the post-hospital syndrome in terms of mortality and morbidity and identifying risk factors and the period of vulnerability after discharge among hospitalized infants in low-income countries.

Methods: We used data from the BIRDY cohort, a community-based multi-centric paediatric study implemented in Madagascar, Cambodia and Senegal that followed 3,651 infants from birth to up to 24 months. Mortality, infectious events (diarrhea, respiratory infection, sepsis) were considered. In order to estimate the burden of post-hospital syndrome, hospitalized infants were compared with those not hospitalized with survival analysis after stratification matching using propensity score.

Results: Globally, 598 infants (16%) were hospitalized at least once, with the great majority during the two first weeks of life in Madagascar and Senegal. The three quarters of deaths (54/72) occurred during the neonatal period of which half occurred at home within one month after discharge. Compared to matched infants with health adverse events without a hospitalization, we showed that hospitalized infants were more at risk of death and very severe infection, diarrhea and bronchiolitis within the six months after discharge.

Conclusions: Our results showed that hospitalization during the first weeks of life is clearly at high risk of death and infections after discharge. These children represent an accessible high-risk population in which targeted interventions to prevent morbidity and mortality are clearly needed.
Background: Respiratory syncytial virus (RSV) is a major cause of pediatric morbidity, with increasing recognition of its burden within older populations. Mathematical models are valuable tools for characterizing annual epidemics, investigating underlying transmission dynamics and assessing the impact of emerging vaccination strategies. Compared to other common respiratory pathogens, relatively few RSV transmission models have been developed to date and none are specific to Canadian populations.

Methods: We constructed a seasonally forced, age-structured, deterministic compartmental mathematical model for the Canadian province of Ontario, fit to local seasonal epidemic curves of RSV-related hospitalizations among Ontario infants aged <2 years for the period April 2002 through December 2014. Ranges for six model parameters were explored and plausible values were identified using Latin Hypercube Sampling; the top 1% best-fitting parameter sets were identified on the basis of maximum likelihood.

Results: Our model accurately reproduced the observed patterns in seasonal RSV peaks in hospitalizations, with model projections estimating a peak of 500-600 monthly admissions among children <2 years of age occurring annually around February. We estimate an average annual admission rate of 39.7 (95% CrI: 34.5–45.0) and incidence of 57,408 (41,223–75,058) per 100,000 population; however, these varied substantially by age group. This calibrated model suggests that the burden of RSV is greatest at both ends of the age spectrum, including a large, likely under-diagnosed burden of RSV among adults aged 65+. 
Conclusions: Our age-structured compartmental model accurately captured the observed seasonal RSV epidemic curves in children. This calibrated base model can be further adapted to investigate the potential impacts of emerging RSV vaccination strategies on RSV incidence and admissions across the age continuum.

**Figure 1.** Observed and model-based (top 1% best-fitting parameter sets) estimates of the monthly RSV admission rate among Ontario infants <2 years of age; April 2002 through December 2014
INFECTION OR INFARCTION - ABDOMINAL MANIFESTATIONS OF SICKLE CELL DISEASE

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**Background:** Sickle cell disease can affect any part of the body. Nearly 10% of patients with SCD are hospitalized due to acute abdominal pain. It usually occurs during vaso-occlusion or distal tissue ischemia. Sickle cell hemoglobinopathy is a common genetic disorder which is prevalent in certain areas of the Kingdom of Saudi Arabia. Affected individuals present with a wide variety of gastrointestinal disorders mimicking vasoocclusive episodes causing diagnostic confusion and delays that may catch the unwary clinician.

**Methods:** A retrospective case record based study was performed in Radiology department at our hospital including pediatric patients (under 14 years) with known sickle cell disease who presented with abdominal or lower back pain and underwent imaging for diagnostic workup between June 2018 - June 2020. Post operative cases were excluded. Abdominal manifestations were categorized as solid abdominal visceral (SAV) including liver, spleen and kidneys, hollow visceral (HV) including gastrium, gallbladder and bowel, vascular (Vas) including sma/smv thrombosis, and bony (Bon) including lower ribs and spine. US and CT/ MRI reviewed to document imaging findings.

**Results:** In total 55 paediatric patients, SAV manifestations, followed by HV and Vas were seen with estimated frequencies of about 45%, 38%, 12% respectively. Bon/ spine manifestations (5%) usually required further evaluation by bone scintigraphy. Clinical and laboratory parameters helped in more than half of cases in suspected event of infection or infarction.

**Conclusions:** Recognition of common abdominal manifestations of sickle cell disease help clinicians to adopt methodical imaging approach.
HIV-RELATED ENCEPHALOPATHY IN CHILDREN

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Title of Case(s): HIV-RELATED ENCEPHALOPATHY IN CHILDREN

Background: Children with HIV can develop HIV-related encephalopathy in 20-50% of cases (1). Hereby we represent clinical cases of children with neurological and developmental problems who late received antiretroviral therapy (ART).

Case Presentation Summary: 1-year-5-months male with complaint on fever, rapid loss of developmental milestones. On the examination: can not sit and stand up without support, can not hold the neck, however he had a normal neural development at the first year of life. Blood test: Hb – 67 g/l, ESR-44 ml/H, HIV test – positive. CD4: 9%-298 cells/ml, blood viral load (VL): 3,499,452 RNA copies/ml, VL of liquor: 347 RNA copies/ml. His mother was HIV tested - results was positive. 6-year-old female was admitted with fever and pneumonia, weight loss. Weight and height was less than 5 percentile. During the treatment in the department child developed aggressive behavior, loss of developmental milestones. She was tested on HIV – result positive. CD4: 0.7% -3 cells, VL: 10,590 RNA copies/ml. Child had a blood transfusion after birth. 1-year-5-months male was admitted in the hospital with complaint on the fever and dyspnoea. Also he had developed loss of motor function during the last 3 months. His HIV-positive mother had been on ART almost 9 years before this pregnancy. Child was tested on HIV PCR DNA twice and results were negative. At the admission he had positive antibody to HIV and HIV PCR RNA, VL: 62053 RNA copies/ml, CD4-15% - 420 cells/ml.

Learning Points/Discussion: Loss of developmental milestones in any age should be an indication for HIV testing, especially when children had a blood transfusion or who's mothers are HIV-positive. ART should be prescribed to children irrespective of age and CD4 cells.
IMPACT OF EARLY VERSUS DEFERRED ANTIRETROVIRAL THERAPY ON GROWTH AND IMMUNOLOGICAL STATUS IN PERINATALLY HIV INFECTED CHILDREN

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Background: Current research demonstrates that early initiation of antiretroviral therapy (ART) reduces dramatically the risk of disease progression and improves significantly the survival of vertically HIV infected children. However, there are limited data on the effect of early versus deferred ART initiation on growth and immunological status among seropositive children entering puberty.

Methods: A cohort study including 21 vertically infected HIV children followed at our Division of Infectious Diseases was performed. Patients were grouped according to the time of ART initiation. Patients' medical records were reviewed from diagnosis until 15 years of age and a number of parameters were collected retrospectively.

Results: In six patients (group A) ART was initiated between 5 to 10 years of age following the initial treatment with AZT+ IVIG given in the first years of life. Fifteen patients (group B) received ART since birth. Group B had significantly higher median BMI and CD4+ levels at 10 years of age (21.6 vs 15.1 kg/m2; P=0.003, 729.5 vs 151 cells/mm3; P=0.017, respectively). Median height was significantly higher at 10 and 15 years of age (136 vs 118 cm; P=0.011, 165 vs 147 cm; P=0.03). Moreover, hospitalizations were lower taking into consideration the follow-up period as a confounding factor (1 vs 3; P=0.012).

Conclusions: Early ART has improved significantly BMI, height and immunological status in perinatally HIV infected children in Greece entering adolescence. In addition, the significant decrease in hospitalizations may reflect the impact of ART on patients’ quality of life. Further follow-up studies are necessary to evaluate the role of early versus deferred treatment on long-term growth and viral suppression from adolescence to adulthood.
WHOLE GENOME SEQUENCING OF MALTESE INVASIVE MENINGOCOCCAL ISOLATES FROM 1998–2015

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Background: Invasive meningococcal disease (IMD) has an incidence of 0.4-3/100,000 in Malta, while vaccines targeting MenB have only recently been introduced on the national immunisation schedule locally. We present a genomic analysis of all Maltese invasive meningococcal isolates from 1998-2015, with an estimation of the vaccine coverage against invasive genogroup B meningococci with the four component MenB (Bexsero, MenB-4C) and Bivalent rLP2086 (Trumenba, MenB-fHbp) vaccines.

Methods: Invasive meningococcal isolates (n=95) obtained from patients at Mater Dei Hospital in Malta from 1998-2015 were recovered from storage. DNA extracts from the isolates underwent whole genome sequencing to identify genogroup, sequence type (ST), and clonal complex (CC). Vaccine coverage was estimated based on genomic data using Bexsero® antigen sequence typing (BAST).

Results: Genogroup B predominated (n=68; 71.6%; 95% CI 61.4 – 80.4%) amongst the invasive meningococcal isolates. Most isolates belonged to the ST-32 CC (n=45; 47.4%; 95% CI 37.0-57.9%), followed by the ST-11 (n=13; 13.7%; 95% CI 6.8-20.6%) and ST-41/44 (n=8; 8.4%; 95% CI 3.7-15.9%) hyperinvasive CCs. Thirty-six different BAST were recorded, predominated by BAST-10 (n=35; 38.9%; 95% C.I. 28.8 – 49.7%). Amongst genogroup B isolates, BAST-1 antigens present in the MenB-4C vaccine were present as follows: fHbp 1: 70.6%, NadA 8: 0%, NHBA 2: 5.9%, and PorA VR2 4: 10.3%. MenB-4C and MenB-fHbp vaccine coverage amongst invasive genogroup B meningococci were estimated to be 89.7% (95% CI 79.9-95.8%) and 91.2% (95% CI 91.8-96.7%) respectively, though the difference was not statistically significant (p=0.77).

Conclusions: MenB accounted for most IMD in Malta, with CC32 found to be important. The estimated vaccine coverage of IMD-MenB with MenB-4C and MenB-fHbp were equivalent, and the introduction of protein-based MenB vaccines on the national immunisation schedule could reduce endemic IMD in Malta.

Clinical Trial Registration: Not applicable to this study.
NEONATAL OUTCOMES FROM ARBOVIRUSES IN THE PERINATAL PERIOD

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Background and Objective: Since the 2016 Zika outbreak and the understanding of the teratogenic effect of this infection, there has been a newfound interest in arbovirus infections and their effects on pregnancy, resulting in a significant number of publications in the last five years. However, limited literature focusses on arbovirus infection in different stages of pregnancy and their effect on the neonate. There is currently no consensus management of perinatal transmission of arboviruses, and current evidence is largely anecdotal observational reports.

Methods: A review was conducted of scientific publications on arboviruses in pregnancy and neonatal outcomes, focussing on those infections in the perinatal period.

Learning Points/Discussion: As teratogens may have different effects on the developing foetus depending on the time of infection, the time of infection during pregnancy should be analysed by trimester. A better understanding of arbovirus infection in the perinatal period is required to assist obstetric, neonatal, and paediatric clinicians in making decisions about the management of mother and neonate. There are eight types of arbovirus for which perinatal transmission has been reported, with the most concerning dengue and chikungunya virus infections. These both demonstrated a risk of neonatal infection if the mother contracted the illness during the perinatal period, and also a risk of premature delivery with a perinatal dengue infection. The other arboviruses investigated were Crimean-Congo haemorrhagic fever virus, Rift Valley fever virus, Western equine encephalitis virus, West Nile virus, Yellow fever virus and Zika virus. The evidence reviewed supports the adoption of preventative strategies to avoid ticks and mosquitoes close to the date of delivery. For the other arbovirus infections not reported, further community-based cohort studies during outbreaks are required to evaluate whether these infections have a similar teratogenic impact.
Background: In endemic areas, human echinococcosis (HE) annual incidence varies from 1-200/100,000 inhabitants, with mortality of 4%. In Chile, there’s an average of 302 cases annually (240-384). 32% of national cases occur in patients between 0-15 years. In the BioBio province, Chile, the incidence is 3.54/100,000, compared to the country’s 1.4-1.8/100,000 inhabitants. The objective is to describe clinically and epidemiologically HE in pediatric population between 2003-2017 in the province of BioBio.

Methods: Descriptive, observational and retrospective study, using secondary data. Case notifications from Ministry of Health, Los Angeles hospital discharge records. All tabulated in Minitab Express. Chi square test, Fisher’s exact test, post-hoc bonferroni correction were used.

Results: 56 patients with HE. Average age 9.3 years (SD ± 4.4 years). 58.9% presented under 10 years, 62.5% were female (p <0.05), 23% native population (p <0.05), 62.5% from rural areas (p<0.05), 83.9% no morbid history (p <0.05). Diagnosis performed either hospital or primary care (p=ns). 34 cases, diagnosis of HE was incidental (p <0.05). HE location was distributed as following: hepatic-pulmonary (35.7%), pulmonary (26.8%) ,hepatic (23.2%), retroperitoneal (3.5%), cardiac, renal and intrauterine 1.7% each. All patients with hepatic-pulmonary involvement presented with respiratory symptoms. Multiple cystic lesions found in 33 patients

Conclusions: This is the first national study that analyzes the epidemiological characteristics of HE in pediatric population. The greater presence of disease in children under 10 years, especially under 5 (28.6%) stands out compared to international studies. The native populations are exposed to a higher risk of infection with multiple cysts, complications and morbidity. Preventive health policies should focus on the populations at risk, mainly those with little access to basic healthcare.
CONSENSUS-BASED ANTIMICROBIAL RESISTANCE AND STEWARDSHIP COMPETENCIES FOR UK UNDERGRADUATE MEDICAL STUDENTS

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Background: Antimicrobial resistance is a global threat due in part to overuse and misuse of antimicrobials by healthcare workers. Evidence shows that final year medical students in the United Kingdom (UK) have insufficient antimicrobial stewardship teaching and feel underprepared to judiciously prescribe antimicrobials. To standardise a high level of understanding education must be improved for all prescribers, including doctors. Our aim is to provide a UK national consensus on competencies for antimicrobial resistance and stewardship for undergraduate medical education.

Methods: The modified Delphi method was used, identifying an expert panel of leads for UK undergraduate medical school infection teaching, who reviewed competency descriptors for antimicrobial resistance and stewardship over two online survey rounds. Experts ranked descriptors on a 6-point Likert scale (1=strongly disagree; 6=strongly agree) to the extent to which they felt it was important to be included in the undergraduate curriculum. Medians and interquartile ranges (IQRs) were calculated for each descriptor.

Results: There was a 100% response rate with 28 experts representing the UK medical schools responding to the first-round survey. Of the initial 55 descriptors, 43 reached consensus (i.e. median 5 and IQR 1.5) by the expert panel. The remaining 12 descriptors which had disagreement, four amended descriptors and 12 new descriptors formed the second round of the survey. Following the second-round survey, a consensus was reached on a set of descriptors.

Conclusions: It is essential that antimicrobial resistance and stewardship competencies are included into the curricula of all healthcare professionals, including medical students, and the consensus-based competency descriptors defined here can be used to inform standards and direct UK undergraduate medical education.
ATTITUDE TOWARDS IMMUNIZATION AMONG SCHOOL CHILDREN IN MALAYSIA

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Background: Attitude towards immunization has been extensively studied among parents/carers. However, there is little evidence in the reduction of vaccine hesitancy among adults. Interestingly, at present less is known regarding immunization attitude among children. Addressing vaccination attitude among the younger generation may provide an avenue to reduce vaccine hesitancy in the future, by identifying their concerns at an earlier age. Here, we aim to identify the attitude towards vaccination as well as illness concerns among children.

Methods: Children attending secondary schools were identified and consent obtained from their respective schools between January-November 2020. Data was collected using a self-administered questionnaire. The questionnaire assessed three main areas: 1) demographics, 2) vaccine attitude (score between 1-5; a higher score a more positive attitude towards vaccination) and 3) concern towards illness (score between 1-10; a higher score showed more concern towards illness).

Results: Overall, a total of 400 respondents have been identified. Respondents were between the ages of 11-17 years old (mean 13.9±2.2). The majority perceived that they had good (n=242, 60.5%) health, compared to 68 (17.0%) that had excellent, 82 (20.5%) fair and 8 (2%) poor health. A total of 390 (97.5%) admitted to having felt ill within the previous year. The average score on vaccination attitude was 3.48 (0.27), whilst illness concern was 6.06 (SD 0.98). There was a positive correlation between vaccination attitude and illness perception (r=0.11, p=0.031).

Conclusions: The current data demonstrated that respondents with a more concerned perception towards illness had a more positive attitude towards vaccination. Further work is being performed to collect more data among school children in Malaysia.
INFECTION AS A TRIGGER OF ACUTE URTICARIA IN CHILDREN

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**Background:** Exanthema is one of the most striking and significant diagnostic and differential diagnostic symptom. In the clinical practice of an allergist, it is often necessary to make a differential diagnosis of an allergic and infectious rash. Of particular difficulty are patients without clinical signs of viral and/or bacterial infection. The aim of our study: to identify the infectious etiology of exanthema in children with a diagnosis of acute urticaria.

**Methods:** The study included 40 children hospitalized in the allergology department of the 4th city children's clinical hospital in Minsk with a diagnosis of acute urticaria in 2019. To identify the infectious agent that manifested exanthema syndrome, the PCR method was used with the isolation of parvovirus B19 DNA, enterovirus RNA, human herpes virus type 6 (HHV-6) DNA and Mycoplasma pneumoniae. All patients were admitted to the allergy department without symptoms of an infectious disease.

**Results:** According to laboratory studies, 30% (12 patients) of children with a diagnosis of acute urticaria were diagnosed with infectious diseases accompanied by exanthema syndrome. Parvovirus B19 DNA was detected in blood serum in 8 (20%), enterovirus RNA in 2 (5%), and HHV-6 DNA in 2 (5%) patients. Parvovirus B19 DNA in 4 (10%), enterovirus RNA in 4 (10%), HHV-6 DNA type in 10 (25%) patients were detected in a mucus smear from the nasopharynx.

**Conclusions:** Infectious diseases accompanied by exanthema can be regarded as an acute allergic reaction, causing children to be hospitalized in the allergy department. In 12 (30%) patients diagnosed with acute urticaria, infectious exanthema was detected. These children did not need standard methods of treatment for allergopathology, which dictates the need to examine patients with acute urticaria for infectious agents.
PERIANAL STREPTOCOCCAL DERMATITIS IN ARMENIAN CLINIC

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Background: Perianal infectious dermatitis is a superficial inflammation of the perianal skin caused by bacteria (mainly group A beta-hemolytic streptococci [Strep A]). Classical presentation of PID is itchy, red, sharply demarcated, edematous perianal erythema, affecting children between the ages of 6 months and 10 years old. We report cases of Strep A induced PID diagnosed in the pediatric outpatient visits at Wigmore clinic (University teaching hospital, Yerevan, Armenia) from October 1, 2018 to May 1, 2020.

Methods: Strep A PID was diagnosed based on complaints, clinical findings and positive results of Streptococcal rapid antigen test. Data were extracted from patient’s medical records retrospectively. The study included 21 patients (males 13[61.9%], females 8[38.1%]), mean age 4.2±2.1 years. Median duration of complaints was 88.7 ±142.3 days.

Results: Observed complaints and clinical findings were: perianal itching and pain(7/21[33.33%]), constipation and bloody discharge(5/21[23.8%]), perianal hyperemia (3/21[14.3%]), perianal pruritus(2/21[9.52%]), abdominal pain(2/21[9.52%]), painful defecation, purulent discharge (1/21[4.76%]), abdominal and perianal pain(1/21[4.76%]). Strep A detecting rapid antigen test was positive in all the included children. All the patients received oral Amoxicillin 50 mg/kg/day: 3(14.3%) for 21 and 18(85.7%) for 14 days respectively. 10 children(47.6 %) were advised to use topical antiseptic in addition to oral antibiotics. None of the included children developed recurrence of PID or acute rheumatic fever during follow up.

Conclusions: Streptococcal PID should be considered in differential diagnosis of children presenting with perianal pruritus/pain, abdominal pain and constipation. The recognition of the disease and timely initiation of systemic antibiotics are important, especially for developing countries, where rheumatic fever remains common.
INTESTINAL PARASITIC INFECTIONS AMONG OUTPATIENT VISITS IN PEDIATRIC CLINIC IN ARMENIA

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Background: Parasites are one of the frequent causes of morbidity in developing countries. We aimed to demonstrate frequency and assess the spectrum of helmintosis-related diagnoses in outpatient settings.

Methods: We performed a survey of parasitic infections frequency among pediatric outpatient visits at Wigmore clinic (University teaching hospital, Yerevan, Armenia) and main clinical features in infected children, between September 2018 and June 2020. All outpatient medical reports were evaluated retrospectively. The data of patients with intestinal helmintosis were extracted and analyzed. In total 12305 patients’ medical reports were evaluated. 76 of 12305(0.61%) were diagnosed with intestinal parasitic infection. Mean age of patients was 68±34 months old, 40(52.6%) males, 36(47.4%) females.

Results: The following infection-rates were found: Ascaris lumbricoides 23(30.3%), Entamoeba histolytica 5(6.6%), Enterobius vermicularis 22(28.9%), Giardia intestinalis 16(21.1%), Cryptosporidium parvum 8(10.5%), Toxocara canis 1(1.3%) and 1(1.3%) coinfection with ascaridosis and giardiasis. The main complaints were abdominal pain 31/76(40.8%), diarrhea 21/76(27.6 %), anal itching 18/76(23.7%), vomiting 10/76(13%). 13 of 76(17.1%) reported systemic symptoms such as failure to thrive (FTT)[3], cough[3], nausea[3], stomatitis[2], fever[2], rash[1]. 13/76(17%) patients manifested with nutritional deficiencies: zinc, vitamin d, vitamin b12, folic acid, iron. 12/76(15.8%) required hospitalization of which 1 patient with criptosporiasis had severe hemocolitis and developed HUS.

Conclusions: Parasites are one of the leading causes of outpatient visits, especially in non-industrialized nations, though their role is often underestimated within the cases with FTT and nutritional deficiencies. Early identification of parasitic infections is important and can prevent complications such as malnutrition and growth failure.
THE USING OF CLINICAL SCENARIOS IN SIMULATION TRAINING OF DIAGNOSTICS AND TREATMENT GENERALIZED FORM OF MENINGOCOCCAL INFECTION

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Background: For modern and proper training in treatment methods, it is necessary to use simulators that allow you to acquire manual skills and make them automated in a safe environment for the patient. Safe mastery of the manual skills used in the providing of medical care for patients with generalized meningococcal infection (GFMI) is possible in simulated conditions. Interactive training in algorithms and skills to assist patients with GFMI allows you to objectify the assessment at all stages of medical care.

Methods: The “GFMI” scenario was developed using the CBL (Case-Based Learning) method. There are 47 clinical scenarios were conducted among students of clinical residents in 2018 – 2019 and there were trained 379 people. The assessment of skills formation was carried out according to the developed checklists. The patient was imitated by a Sim Junior mannequin with feedback and remote control technologies.

Results: The lessons consisted of two parts: conducting a scenario with an assessment of the initial skills and knowledge level and debriefing. Students were assigned the roles of health workers, parents, and observers. The tasks of medical workers were: collecting anamnesis, full examination, taking biological material, beginning intensive therapy, treatment of complications, working with a simulated patient. Observers were filling out checklists. After passing the first round a debriefing was conducted with the identification and analysis of mistakes which are made, followed by the reference implementation of the case.

Conclusions: Case-Based Learning method during the training allows you to evaluate teamwork and individual skills of each student. The development of analytical thinking in the use of CBL methodologies facilitates effective learning and application of theoretical knowledge in solving practical problems contributes to the consolidation of existing skills.
ETIOLOGICAL STRUCTURE OF ACUTE DIARRHEA AMONG CHILDREN IN OUTPATIENT CLINIC IN ARMENIA

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Background: Diarrhea is the second leading cause of death in children below 5 years. While rotavirus is identified as the most frequent cause of gastroenteritis in children all over the world, the distribution of bacterial pathogens is more dependent on the economic status of the country. The aim of the study is to demonstrate the etiological structure of acute diarrhea among children in the outpatient clinic (Wigmore clinic, University teaching hospital, Yerevan, Armenia).

Methods: We performed a retrospective laboratory based study. We included patients below 18 years, presenting with acute diarrhea, whose stool examination was ordered by a caring pediatrician, from April 2019 to April 2020. Pathogens were identified by Multiplex polymerase chain reaction (RT-PCR) including 4 bacteria (Enterohemorrhagic E. Coli [EHEC], Salmonella, Shigella, Campylobacter) and 3 viruses (Norovirus, Rotavirus, Adenovirus) and/or stool culture. We analyzed the results of 543 stool samples: RT-PCR 529/543(97.4%) and culture 14/543(2.58%).

Results: In RT-PCR group, no pathogen was identified in 185/529(34.97%), 339/529(64.08%) were positive for virus, bacteria, and both in 200/339(58.9%), 162/339(47.7%), 19/339(5.6%) respectively. Rotavirus was the leading pathogen among all specimens 101/339(50.5%), followed by Norovirus 69/200(34.5%), Adenovirus 32/200(16%). The following bacteria were found: EHEC 80/162(49.3%), Campylobacter spp. 64/162(39.5%), Shigella spp.17/162(10.4%), Salmonella spp. 5/162(3.08%). 7/339(2.06%) PCR positive samples underwent further culture, 6/7(85.7%) confirmed bacterial growth (3 Salmonella enteritidis, 2 Shigella flexneri, 1 EHEC). No growth was documented in 10/14(71.4%) cultures, in 4/14(28.6%) Salmonella enteritidis was detected.

Conclusions: Our study showed that the distribution of pathogens in the diarrheal disease is similar to developing countries. Although Rotavirus vaccine has been implemented in Armenia since 2012 and has rather high coverage (99%), Rotavirus remains the most frequent cause of acute diarrhea among children.
TRAINING OF PERCUTANEOUS ENDOSCOPIC GASTROSTOMY USING SIMULATION TECHNOLOGIES

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Background: Percutaneous endoscopic gastrostomy (PEG) is a minimally invasive way of providing nutrition to patients who cannot eat by themselves. For the training of the PEG it is necessary to use simulators that allow you to acquire manual skills and do them to automatism in a safe conditions for the patient with subsequent implementation in practical health care. The lack of mannequins and simulation methodologies techniques for training doctors determines the relevance of this work.

Methods: A literature review was carried, a simulator was developed allowing you to perform all stages of the operation. Practical exercises have been worked out in the conditions of the endoscopic office of the clinic using the branded kit Freka PEG, FR 20 with control of the pressure of the pressure plate during fixation of the gastrostomy tube. Simulation trainings were held for students with an assessment of the assimilation of the material.

Results: The developed mannequin imitates the upper half of the body and internal organs, it has a removable stomach and anterior abdominal wall. The simulation was carried out in an endoscopic operating mannequin with phased execution of all stages of the operation. External part of the gastrostomy is fixed with a pressure plate with a tension 200 mg. At the end of this procedure there was a control the standing of the tube in the stomach. The operation is performed as many times as necessary to bring the skill to automaticity.

Conclusions: The methodology for training percutaneous endoscopic gastrostomy on a mannequin allows you to repeatedly perform manipulation in simulated conditions. The practicing of manual skills before meeting with a real patient reduces the risk of the iatrogenic complications.
LEARN TECHNOLOGIES AS AN EFFECTIVE METHOD OF OPTIMIZATION OF THE VACCINATION CABINET

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Background: Optimization of the first medical aid in the system of Health Ministry has objective region peculiarities. Lean-manufacturing instruments are the effective mechanisms which engage to increase the productivity while minimizing the usage of material and non-material resources in medicine.

Methods: While implementing the Health Ministry programme “Medical organization model providing first medical aid” in 2019 the project “Optimization of the vaccination cabinet activity” is implemented. There are 367 members of the medical staff have been trained. The specialists demonstrated the modeling of the fabrics of the processes “Vaccination cabinet” which indicated medical loses, the route of medical staff and patients inside and out of the vaccination cabinet. The practical period consisted of three sessions in vaccination cabinet with the defining of the possibilities in optimization during the inter-round debriefing.

Results: While primary testing the low level of professional knowledge of lean-manufacturing instruments (36%) was registered while in the end of studying the result gained up to 84%. Simulation of similar medical processes helped find optimization paths after each round. A decrease in the waiting time for vaccination was noted and opportunities were found to improve the quality of admission for each patient. Typical mistakes of mapping were registered while using such methods as “5S”, “Spaghetti” and visualization of losses. Special attention was paid to the issues of organization of medical processes.

Conclusions: Implementing of educational fabrics of processes promote to raise knowledge of the standartization process used while medical help. Modeling of vaccination cabinet in simulation centre promotes indicating the losses and optimization of the work by means lean-manufacturing instruments.
SUCCESSFUL PREVENTION OF SARS-COV-2 INFECTION IN CHILDREN AND ADOLESCENTS WITH UNDERLYING HAEMOTO-ONCOLOGICAL DISEASES IN A PAEDIATRIC HOSPITAL IN MAINZ/GERMANY

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Background: Paediatric patients seem to be less affected by Coronavirus disease (COVID-19) than adults and in majority develop only mild or asymptomatic disease. However, paediatric patients with haemato-oncological diseases might carry an increased risk for a complicated course of COVID-19. Therefore, we established a diagnostic and hygiene strategy to prevent viral exposure and spread among this particularly vulnerable patient group.

Methods: Nasopharyngeal swabs were routinely obtained from children with underlying haemato-oncological diseases presenting at the Centre for Paediatric and Adolescent Medicine, University Medical Centre Mainz during March to June 2020. Swabs were collected at every hospital admission and from outpatients with potential symptoms of SARS-CoV-2 infection. Respiratory samples were analysed for SARS-CoV-2 using real-time PCR. Corresponding clinical data was obtained using a standardised questionnaire.

Results: In total, 209 and 9 respiratory samples were obtained from 85 oncological and 6 haematological patients, respectively. Most of them (83.9%; n=183/218) were routinely taken upon hospital admission, whereas 16.1% (n=35/218) of samples were obtained from outpatients with clinical signs of infection. Most of the hospital admissions were scheduled admissions (90.7%; n=166/183), whereas 9.3% of hospitalizations occurred for signs of infection or bad general condition. Overall, 41.3% (n=90/218) of all patients reported symptoms or showed clinical signs of infection upon physical examination. All respiratory samples were tested SARS-CoV-2 negative.

Conclusions: No SARS-CoV-2 infection was detected in paediatric patients with haemato-oncological diseases in Mainz/Germany. The adoption of infection prevention measures plays a major role in the daily routine of immunocompromised patients and might therefore be especially effective during the SARS-CoV-2 pandemic. However, paediatric patients with haemato-oncological diseases undergoing intensive chemotherapy or other immunosuppressive treatments represent an extremely vulnerable population and should therefore be considered a high-risk group for SARS-CoV-2 infections.
RISK OF STREPTOCOCCUS PNEUMONIAE-ASSOCIATED HAEMOLYTIC URAEMIC SYNDROME IN EUROPE, CANADA, AUSTRALIA, NEW ZEALAND, AND UNITED STATES: A SYSTEMATIC REVIEW OF THE LITERATURE.

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Background: Haemolytic uraemic syndrome (HUS) is a triad of haemolytic anaemia, thrombocytopenia, and acute renal failure. It is a leading cause of acute renal damage in children, and therefore could have a poor prognosis. *Streptococcus pneumoniae*–associated HUS (SpHUS) is a rare complication from pneumococcal disease. Thus, the diagnosis of SpHUS has often been overlooked until recently following reports of poor long-term outcomes and mortality associated with this disease. This article systematically reviewed SpHUS following the introduction of pneumococcal conjugate vaccines.

Methods: A comprehensive literature search was conducted in MEDLINE, EMBASE, and the Cochrane library from 01 January 2000 to 27th May 2020.

Results: Nine studies were eligible for inclusion in the final analysis. This involved a total of 6,708 children with HUS, of which 306 cases were associated with Streptococcus pneumoniae. Six studies (81.0%, 248 cases of SpHUS) were during the PCV era, whereas 3 studies (19.0%, 58 cases of SpHUS) were before the PCV was incorporated into the national vaccination programme in the specified countries. Thus, the rate of SpHUS from all HUS cases was 4.6%. The average age was below 27 months. The commonest clinical presentation was pneumonia (80.0%, n=72/90), followed by septicaemia (51.9%, n=28/54) and meningitis (27.8%, n=25/90). Most cases presenting with pneumonia were complicated by empyema (54.7%, n=47/86) and pleural effusion (51.9%, n=28/54). The most prevalent serotype was 19A (47.6%, n=20/42), which was followed by serotype 3 (14.3%, n=6/42) and 7F (9.5%, n=3/42). Furthermore, the mortality rate was 7.6% (n=8/105).

Conclusions: SpHUS is uncommon, but commonly presents in children younger than 2 years old. There remains a high risk of long-term complications and relatively high mortality even in the era of conjugate vaccines.

Systematic Review Registration:
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Background: The COVID-19 pandemic has so far shown an increased number of cases and a higher risk of severe disease with increasing age. Worldwide, the number of infections with the novel coronavirus in children remains low, and deaths in this group are exceptional. The role of children in the epidemiology of SARS-CoV-2 needs to be well clarified. We set out to present our experience in caring for children hospitalized with COVID-19 in the first months of the pandemic.

Methods: We performed a descriptive analysis of the clinical and epidemiological characteristics of the first 49 pediatric cases of COVID-19, hospitalized in the National Institute of Infectious Diseases "Prof. Dr. Matei Bals", Bucharest, Romania in March and April 2020.

Results: The male-to-female ratio was 2:1. The average age at hospitalization was 7.3 years (range 17 days-15 years). A percentage of 40% of those hospitalized were asymptomatic, 39% had mild forms of the disease and 21% had moderate forms. Of the symptomatic cases: 58.3% had fever, 54.2% cough, 41.7% rhinorrhea, and 20.9% diarrhea. The average length of hospital stay was 16 days, and discharge occurred in all cases after clinical remission and two consecutive negative RT-PCR results. In all cases, the transmission of SARS-CoV-2 infection was within the family. No deaths were reported.

Conclusions: We identified an increased rate of mild and asymptomatic forms of SARS-CoV-2 infection among children who were managed in our clinic. To a certain extent, this might be a reflection of the epidemiological surveillance applied in the country during the studied time span, which initially included RT-PCR testing of all contacts of confirmed cases. Close follow-up and a better understanding of the clinical and epidemiological characteristics of pediatric cases of COVID-19 are still needed.
YOUNG PEOPLE EXPERIENCING HOMELESSNESS: COMPARING PSYCHOSOCIAL AND PHYSICAL HEALTH RISK FACTORS IN LGBT AND NON-LGBT UNSHELTERED POPULATIONS

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Background: Young people experiencing homelessness is a public health issue associated with increased risk of substance use, HIV positivity, sexual abuse, and other issues. Despite the overrepresentation of LGBT individuals among homeless young individuals, few studies explore the differences in health risk factors between homeless youth who identify as LGBT and as non-LGBT, particularly those who are unsheltered. This study compares LGBT and non-LGBT identifying persons on multiple risk factors including substance use, HIV status, physical and sexual abuse, and chronic homelessness in a population of young people experiencing homelessness.

Methods: This study utilized survey data from Los Angeles County, California, 2015-2016 collected from 2,519 unsheltered young people, ages 13 – 30. LGBT individuals (n = 374) were compared to their non-LGBT counterparts (n = 2145). The sample was predominately African American (35.1%) and Hispanic (33.2%), and male (66.3%). This study examined differences on several mental, physical, and behavioral variables utilizing multiple regression analysis.

Results: In adjusted analyses, individuals who identified as LGBT were more likely to have used substances in their lifetime (AOR: 1.59, CI: 1.26-2.00), to report severe depression (AOR: 1.99, CI: 1.50-2.63), and to experience chronic homelessness (AOR: 1.98, CI: 1.55-2.53). LGBT individuals were also particularly at risk for physical or sexual abuse (AOR: 2.47, CI: 1.95-3.13). Findings suggest that LGBT individuals have an increased odds of being HIV positive, though the direction of this effect could not be confidently determined (AOR: 1.88, CI: 0.94 – 3.74).

Conclusions: Unsheltered young people experiencing homelessness who identify as LGBT are at an increased risk for serious psychosocial and physical health issues. This study provides evidence for the need for enhanced and targeted outreach, mental health support, and substance abuse treatment efforts for this population.

Clinical Trial Registration: Not applicable.
THE TRIAGE SYSTEM IMPLEMENTATION AS THE EFFECTIVE METHOD OF THE EMERGENCY MEDICAL HELP TO CHILDREN IN INFECTIOUS DISEASES HOSPITAL

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Background: The increase in the number of patients in children's infectious diseases hospitals has identified the need for redistribution of patient flows. The sequence of emergency and emergency care does not depend on the route and time of patient arrival at the medical facility. The diagnosis of such conditions is based on a unified system of medical sorting measures - triage.

Methods: The scale chart developed on the basis of the Pediatric Observation Priority Score Chart has been introduced. The analysis of the correspondence of the triage data and the objective data obtained during the initial examination, as well as the doctor's waiting time, depending on the results, were carried out. Upon admission of each child the performed triage must take 7 parameters into account. The parameters are the following: general parameters (consciousness, body temperature, saturation data, pain response according to the modified Wong-Baker scale) and determined parameters depending on age.

Results: Each question has 3 possible answers (corresponding to the degree of compensation), the choice of which determines the order of assistance (i.e. "corridor"). In a retrospective study, 128 patient records were analyzed. Upon admission of patients by the fake nurse, the "green" corridor was determined to be 47%, the "yellow" - 43.75%, the "red" - 9.25%. The reference point in determining the "corridor" in 68.75% of the cases was saturation, in 23.44% - temperature, 7.03% - heart rate, 0.78% - consciousness. Patients of the "red" corridor received help immediately.

Conclusions: 1. The introduction of triage allows to determine the sequence of medical care depending upon the severity of the patient state. 2. The implementation of pre-hospital care assistance algorithms allows to standardize care approach to patients.
HEALTHCARE PROFESSIONALS’ AND PARENTS’ PERSPECTIVES AND EXPECTATIONS AROUND HEXAVALENT VACCINATION AND DIFFERENCES BY COUNTRY: A SURVEY IN INDIA AND FRANCE

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Background: Hexavalent diphtheria-tetanus-pertussis vaccines are the cornerstone of infant vaccination and often among the first to be administered to an infant. In India, a whole-cell pertussis vaccine is part of the National Immunization Program and hexavalent combination vaccines containing acellular pertussis components are only available for use in private practice. In France, the acellular pertussis hexavalent vaccination is mandatory and fully reimbursed, since January 2018.

Methods: To gather insights on the perspectives/expectations of parents and healthcare professionals (HCPs) on hexavalent vaccination experience, a survey was conducted in India and France, during February–March 2020. It targeted parents/guardians of infants aged 0–3 years (online in France; face-to-face in India) and HCPs (online in both countries) and was focused on attitudes towards vaccination and motivation in vaccine decisions.

Results: In our survey, HCPs care how parents perceive them and agreed on the importance of discussing parents’ concerns around hexavalent vaccination. In France, short-term experience after vaccination was significantly more important to parents than to HCPs, for whom long-term protection was more important. In India, both these aspects were equally important to parents and HCPs, and vaccination cost was also a key decision factor. Whilst high overall, parents in France were more likely to express being not very/not at all accepting of hexavalent vaccination vs parents in India (Table).

<table>
<thead>
<tr>
<th>Survey item</th>
<th>Item rating</th>
<th>India</th>
<th>France</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agreement/disagreement with each statement</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I care how parents perceive me as a professional</td>
<td>Strongly/tend to agree</td>
<td>87%</td>
<td>80%</td>
</tr>
<tr>
<td>It is important for HCPs to acknowledge and discuss concerns with parents</td>
<td>Strongly/tend to agree</td>
<td>84%</td>
<td>82%</td>
</tr>
<tr>
<td>Importance of different stages of the vaccination journey</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short-term experiences (3 days post-vaccination)</td>
<td>Essential/very important</td>
<td>80%</td>
<td>55%</td>
</tr>
<tr>
<td>Long-term protection offered by the vaccine</td>
<td>Essential/very important</td>
<td>86%</td>
<td>90%**</td>
</tr>
<tr>
<td>Parent acceptance/HCP perceptions of parent acceptance hexavalent vaccination</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parents’ acceptance towards hexavalent vaccination</td>
<td>Not very accepting/not at all accepting</td>
<td>4%</td>
<td>0%</td>
</tr>
</tbody>
</table>

*Statistically higher vs HCPs at 95% confidence intervals; **Statistically higher vs parents at 95% confidence intervals; ***Statistically higher vs HCPs in France and vs parents in India at 95% confidence intervals; N, number of participants in each category; NA, not applicable.
Conclusions: Parents’ perceptions/concerns were equally important to HCPs from both countries, however acceptance of hexavalent vaccination tended to be lower in France. The differences in the importance attributed in France and India to short-term events vs long-term protection could be due to the different vaccines historically available on the market. This survey highlighted country-specific differences between parents’ and HCPs’ perspectives/expectations around hexavalent vaccination. Funding: GlaxoSmithKline Biologicals SA
A CASE OF PARVIMONAS MICRA INFECTION AMONG A SERIES OF PEDIATRIC BRAIN ABSCESES IN A SINGAPORE TERTIARY CHILDREN'S HOSPITAL

T.A. Pham Nguyen¹, K. Kam², K. Nadua², C.Y. Chong², K.C. Thoon², J. Li², C.F. Yung², M.G. Maiwald³, W.T. Seow⁴, L. Qiu⁴, N.W.H. Tan²
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Background: Bacterial brain abscess is a rare life-threatening infection in children and in developed countries. While anaerobic bacteria are known to play an important role, they are rarely identified by conventional culturing methods. Here we report the first case of an anaerobe Parvimonas micra identified in KK Hospital, Singapore, among a series of 12 pediatric brain abscesses during a 13-year period (Jan 2007 - Jun 2020).

Methods: We conducted a retrospective study of our pediatric infectious disease registry from 2007, which included 12 cases of brain abscess. The mean age was 2.7 ± 3.9 years with a male predominance (1.4:1). A majority (67%) of patients had at least one predisposing condition, including cardiac defects (33%), prematurity (16%), otorhinological or odontogenic infections (16%). Fourteen pathogens were found by bacterial cultures, with Streptococcus intermedius being the most common (Table). 16S RNA sequencing was applied to two patients, both also showing S. intermedius. Parvimonas micra was the first anaerobe isolated.

Results:

<table>
<thead>
<tr>
<th>Microorganisms</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptococcus intermedius</td>
<td>3</td>
</tr>
<tr>
<td>Coagulase-negative Staphylococcus</td>
<td>2</td>
</tr>
<tr>
<td>Streptococcus constellatus</td>
<td></td>
</tr>
<tr>
<td>Streptococcus agalactiae</td>
<td></td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td></td>
</tr>
<tr>
<td>Enterococcus faecium</td>
<td></td>
</tr>
<tr>
<td>Bacillus sp.</td>
<td></td>
</tr>
<tr>
<td>Enterobacter cloacae</td>
<td></td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td></td>
</tr>
<tr>
<td>Acinetobacter baumannii</td>
<td></td>
</tr>
<tr>
<td>Parvimonas micra</td>
<td>1 each</td>
</tr>
<tr>
<td>Mycobacterium bovis</td>
<td></td>
</tr>
<tr>
<td>Candida albicans</td>
<td></td>
</tr>
</tbody>
</table>
Case summary: A 3-year-old boy with trisomy 21, history of otitis media and gingivitis presented with prolonged fever and lethargy. After initial response to ceftriaxone, he re-presented with an inability to walk. MRI brain showed a large fronto-temporo-parietal brain abscess. Surgical drainage anaerobic culture revealed *Parvimonas micra*, while 16S RNA sequencing from the abscess material revealed a sequence matching *Streptococcus intermedius*. He was treated with ceftriaxone and metronidazole, with clinical and radiological improvement.

Conclusions: Pediatric brain abscesses are rare in our institution and comprised mainly of Gram-positive pathogens. However, we should maintain a high index of suspicion for anaerobic pathogens and always consider anaerobic coverage.
ETIOLOGICAL DIAGNOSIS OF CHILDHOOD PNEUMONIA - A COMPARATIVE EVALUATION OF DIAGNOSTIC METHODS

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Background: The etiological diagnosis of community acquired pneumonia (CAP) among children, an important cause of mortality and morbidity in developing countries, is challenging due to absence of a gold standard diagnostic test. The present study was undertaken to compare the different diagnostic methods for aetiology and to determine the etiological agents of CAP in children in a developing country setting.

Methods: This cross-sectional study was conducted from January 2019 - March 2020, on 50 children (2-59 months) with CAP. Oropharyngeal swabs and blood were taken from each patient and processed as per standard operating procedures by microscopy and culture for bacterial and fungal pathogens in the laboratory. Further, real-time multiplex PCR of oropharyngeal swabs was done for detection of various bacterial and viral agents by FTD™ Respiratory Pathogen 33 kit.

Results: Majority of cases were within one-year of age. Bacterial pathogens were grown in 46% of the patients, on culture of oropharyngeal-swab and blood. In contrast, there was 100% detection by real-time multiplex PCR in all samples. The commonest agent detected was HRSV(A/B) (50%) followed by S. pneumoniae (42%), M. catarrhalis (32%) & HRV (30%). The oropharyngeal-swab culture had a moderately high sensitivity (66.7%-85.7%) & high specificity (90.9%-93%) when compared to real-time multiplex PCR. Blood culture performed poorly with a very low sensitivity (14.2%-16.7%) though the specificity was very high (100%).

Conclusions: The study concludes that though culture is a good method for detecting aetiology of CAP in children, real-time multiplex PCR has a better yield for detection, especially for viruses. There is need to standardize the various detection methods for aetiology of CAP in children as it would be helpful in reducing the morbidity of the disease.
THE IMPLEMENTATION OF THE EMERGENCY ASSISTANCE ALGORITHM FOR CHILDREN WITH FEBRILE SEIZURES WITH ACUTE INFECTIOUS DISEASES

Saint-Petersburg State pediatric medical university, General Medical Practice, Saint Petersburg, Russian Federation

Background: Febrile seizures (FS - R.56.0) are the complication of acute infectious disease in 3-7% of all the cases. The optimization of medical care for children with the development of febrile seizures reduces the risk of neurological complications. The implementation of the diagnostic and treatment algorithm helps to define therapy in a timely and adequate manner.

Methods: An assessment of the primary medical documentation of children seeking medical care with the diagnosis “convulsions due to fever” from 2018 to 2020 was carried out. The analysis of 784 medical records of children was also carried out. The implemented algorithm includes determining the time, place of examination of the child by doctors, indications for resuscitation, neurosonography, clinical, laboratory monitoring. In a state of ongoing convulsions, 132 children asked for medical help during three years.

Results: At the prehospital stage, the primary resuscitation measures were required for 7 patients (2.4%) in 2018, 8 (2.34%) in 2019, and 2 (1.27%) in 2020. The relief of convulsive syndrome required the introduction of antipyretics (Ibuprofen, Acetaminophen) was registered in the treating of 120 patients. The other children suffered from the FS attack which lasted more than 15 minutes. In those cases Relanium was administered. In 54.0% of all monitored children, iron-deficiency anemia was detected. To reduce neurological complications, the introduction of Pyridoxine hydrochloride is included to the algorithm.

Conclusions: The introduction of an assistance algorithm has accelerated the provision of medical care to children with a complicated course of acute infectious diseases. The drugs of the first line of seizures relief are Ibuprofen and Acetaminophen (rectally or orally). The identified risk factor, in addition to the burdened anamnesis, was the presence of iron deficiency anemia.
Background: The interpatient pharmacokinetic parameters of intravenous immunoglobulin (IVIG) varies widely causing difficulty in optimizing individual dosage regimen. This prospective clinical study was conducted to estimate the population pharmacokinetic parameters of IVIG in patients with primary immunodeficiency.

Methods: Blood samples were withdrawn from recruited patients for pharmacokinetic and genetic studies, whereas clinical data were obtained from patients' medical records. Gender, ethnicity, weight, age, genetic polymorphism of the FcRn gene and presence of bronchiectasis were the covariates investigated. Nonlinear mixed-effects modeling in Monolix® version 2019R1 was used to estimate population pharmacokinetic parameters. Difference in objective function value, goodness-of-fit plots, visual predictive check and bootstrap analysis were utilized to evaluate the model.

Results: Ten patients with median age of 9.5 years (range: 3 - 64 years) were recruited. The IgG concentration data from 30 serum samples were best described by a one-compartment model with linear elimination. Weight was an important covariate for both Vd and CL. For an adult weighing 70kg, the estimated population Vd and CL were 5.2L and 0.006L h⁻¹, respectively. Elimination rate and terminal half-life were 0.00115h⁻¹ and 25 days, respectively. The pharmacokinetics of IVIG were not affected by the FcRn gene genetic polymorphism and presence of bronchiectasis.

Conclusions: The pharmacokinetic parameters of IVIG in patients with primary immunodeficiency were significantly affected by body weight but not the genetic and clinical factors investigated.
E-POSTER VIEWING
E-POSTER VIEWING - ALL OTHER TOPICS
10-28-2020 8:00 AM - 7:00 PM

CHILD REHABILITATION AFTER ENCEPHALITIS ASSOCIATED WITH NEUROBORRELIOSIS

S. Nykytyuk1,2, O. Yavorska3, T. Vorontsova1, N. Haliyash2
11. Horbachevsky Ternopil National Medical University, Department Of Children's Diseases And Pediatric Surgery, Ternopil, Ukraine, 21. Horbachevsky Ternopil National Medical University, Department Of Children's Diseases And Pediatric Surgery, TERNOPIL, Ukraine, 31. Horbachevsky Ternopil National Medical University, Department Ofof Physical Rehabilitation, Human Health And Physical Healthy, TERNOPIL, Ukraine

Background: The causative agent of Lyme disease, Borrelia burgdorferi, causes damage to the meninges. Within a few weeks (rarely 10-12 days) or months from the disease onset, 15% of patients experience obvious signs of nervous system damage. The consequences of neuroinfection in these patients are encephalitis associated with borreliosis with a predominant damage of the cortical-subcortical-stem structures of the brain.

Methods: 10 children aged 3-12 years were under supervision at the neurological department. General clinical studies, EEG, cerebrospinal fluid testing, MRI of the head, ELISA, Western Blot were performed.

Results: 10 children were diagnosed with Lyme disease of a disseminated form, neuroborreliosis. In these children, the disorders like cephalgia, myatonia were still evidenced; relapsed paresis of the facial nerve took part in 1 patient in 2 years. Therefore, the rehabilitation therapy for children with neuroborreliosis is being developed and implemented in the rehabilitation department. Physiotherapeutic procedures involve plasmaphoresis, lymphophoresis, laser therapy, intra-articular irradiation, intravenous irradiation, UFO method. Therapeutic baths are used to relieve pain, improve peripheral hemodynamics, relieve muscle spasms, and have a calming effect. Sea, lake salts or complex, standardized products with plant extracts (Tonus + C) are used. In magnetic therapy a low-frequency alternating magnetic field (Polus-1 device) is applied on the joints and reflexogenic zones. It has an analgesic, resorbing and vasodilating effect, also affects tissue trophism. The magnetic field has an effect on the peripheral nerves and enhances inhibition in the cerebral cortex. Massage is performed twice a day, 15-20 minutes.

Conclusions: The consequences of the neuroinfection in the patients are mainly damage of the cortical-subcortical-stem structures of the brain. Rehabilitation therapy is a necessary for normal quality of life of the patients, who suffered from Lyme disease.

Clinical Trial Registration: has not list of registry
GROUP B STREPTOCOCCAL COLONIZATION DURING PREGNANCY IN GREECE: COMMON PITFALLS IN CULTURE COLLECTION

M. Berikopoulou¹, A. Pana², A. Soldatou³, V. Papaevangelou⁴
¹National and Kapodistrian University of Athens, School Of Medicine, ATHENS, Greece, ²General Hospital of Sparta, Department Of Pediatrics, Sparta, Greece, ³General Children Hospital "Pan. & Aglaia Kyriakou", Second Department Of Pediatrics Of National And Kapodistrian University, Athens, Greece, ⁴National and Kapodistrian University of Athens, School of Medicine, Third Department Of Pediatrics, University General Hospital “attikon”, Chaidari, Greece

Background: Group B Streptococcus (GBS) is a leading cause of serious neonatal infections. Maternal GBS colonization is associated with early and late onset neonatal disease, even though the majority of the neonates from colonized mothers remain asymptomatic. In Greece, a screening-based strategy is suggested, in which vaginal-rectal cultures are obtained between 36 0/7 and 37 6/7 weeks’ gestation. If maternal GBS colonization is identified, administration of intrapartum antibiotic prophylaxis (IAP) is required. Yet, are the guidelines being followed or do we tend to under-estimate their importance?

Methods: We questioned 604 postpartum women from three maternity clinics (University General Hospital Attikon, University General Hospital Aretaieio and IASO General Maternity and Gynecological Clinic), both private and public ones, in Athens about their GBS status. Among the questions, additional data about the cultures’ sampling techniques were obtained from patients’ records.

Results: Almost 1/3 of the questioned population did not have a culture taken at all or they had taken one only during the first trimester of their pregnancy. From the remaining 2/3, a main issue was the wrong timing of culture collection as many were obtained more than 5 weeks before childbirth. In addition, 231 pregnant women reported collection of a vaginal sample only, instead of the proper vaginal-rectal one.

Conclusions: Inappropriate timing and site of sample collection for cultures are not infrequent and may lead to false negative results. Therefore, pediatricians, should be alert in recognizing GBS screening pitfalls, provide close neonatal observation and recognize false negative results to ensure prompt intervention.
TWO CASES OF MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN AND ADOLESCENTS TEMPORALLY RELATED TO COVID-19 (PIMS-TS) WITH CLINICAL DISTINCT PRESENTATIONS

A. Panciu¹, C. Neaga¹, M. Popov¹, A. Ivan¹, F. Popa¹, A. Bilasco¹, C. Dogaru¹, C. Kouris¹, C. Negulescu¹, A.C. Draganescu¹, R. Matei¹, G. Jugulete¹,², M.L. Luminos¹,²
¹INBI Prof Dr Matei Bals, Pediatric Infectious Disease, Bucharest, Romania, ²University of Medicine and Pharmacy Carol Davila, Infectious Diseases, Bucharest, Romania

Background: Recently, several countries affected by the COVID-19 pandemic have reported clusters of children and adolescents requiring admission to intensive care units, with a multisystem inflammatory condition with some features similar to those of Kawasaki disease and toxic shock syndrome. A possible temporal association with SARS-COV-2 has been hypothesized. The World Health Organization (WHO) has published in May, preliminary case definitions.

Methods: In this retrospective study, we report two cases with different clinical presentations that meet the WHO preliminary case definitions for PIMS-TS.

Results: Case 1, 14-year-old male patient admitted to our hospital with a severe form of COVID-19, 9th day of disease evolution, with acute respiratory and heart failure symptoms. Chest scan showed bilateral multilobular ground-glass opacities, consolidations and sub-segmental arterial branch thromboembolism. The echocardiography showed a dilated left ventricle with severely impaired left ventricular function (LVEF=30%). Blood test showed extremely elevated NT-pro-BNP (22,558 ng/L), inflammatory markers and D-dimers. Case 2, 7-year-old male patient with prolonged fever, rash, bilateral non-purulent conjunctivitis, features of myocardial dysfunction and elevated D-dimers. No coronary abnormalities. Both patients had elevated markers of inflammation, evidence of COVID-19 infection and negative bacterial screening. Both cases had favorable outcomes.

Conclusions: We report two different clinical cases that meet the preliminary criteria for multisystem inflammatory syndrome in children and adolescents temporally related to COVID-19. PIMS-TS is considered a rare condition and its potential link with COVID-19 is neither established nor well understood. The is a need to characterize this syndrome and its risk factors, to understand causality and describe treatment interventions. Clinicians should be aware of this severe presentation of COVID-19 in children.
ASSOCIATION BETWEEN BREASTFEEDING AND HUMAN CALICIVIRUS GASTROENTERITIS IN A NICARAGUAN BIRTH COHORT


1University of North Carolina at Chapel Hill, Department Of Epidemiology, Chapel Hill, United States of America, 2University of North Carolina at Chapel Hill, School Of Medicine, Chapel Hill, United States of America, 3National Autonomous University of Nicaragua, Department Of Microbiology And Parasitology, León, Nicaragua, 4Centers for Disease Control and Prevention, Division Of Viral Diseases, Atlanta, United States of America, 5University of North Carolina at Chapel Hill, Department Of Family Medicine, Chapel Hill, United States of America

Background: Caliciviruses, including norovirus and sapovirus, are important causes of childhood acute gastroenteritis (AGE). Breastfeeding protects against all-cause AGE; however, there is limited information about the benefits of breastfeeding against human calicivirus AGE.

Methods: We investigated the association between breastfeeding and human calicivirus AGE in a Nicaragua birth cohort. Weekly information on breastfeeding and AGE episodes were captured during the first 18 months of life. Stools were collected from children with AGE and tested by RT-qPCR for norovirus GII and sapovirus. Time-dependent Cox models were used to evaluate the association between breastfeeding and the first human calicivirus AGE episode. From June 2017 to July 2018, 444 newborns were enrolled in the study.

Results: Through January 2020, 72 and 87 norovirus and sapovirus first AGE episodes were reported, respectively. The exclusive and any breastfeeding median duration was 2 and 42 weeks, respectively. The norovirus and sapovirus AGE hazard ratios among children who received any breastfeeding compared to none were 2.10 (95% CI: 1.19-3.71) and 1.38 (95% CI: 0.87-2.18), respectively, adjusting for child’s sex, delivery mode, household crowding, and maternal age, education, and occupation. C-section delivery was associated with a 57% reduced sapovirus AGE hazard compared to vaginal birth (HR = 0.43; 95% CI: 0.26-0.71).

Conclusions: Exclusive breastfeeding in this population was rare and brief. Mixed breastfeeding did not provide protection against sapovirus AGE, and was associated with an increased hazard of norovirus AGE. Additional analyses are ongoing to identify confounders of the breastfeeding-norovirus association. Similar analyses should be repeated in populations with high exclusive breastfeeding prevalence to understand its benefits in preventing symptomatic calicivirus infections. Mechanisms for sapovirus risk via delivery mode are being explored.
DISTRIBUTION AND EPIDEMIOLOGICAL CHARACTERISTICS OF PEDIATRIC INFECTIOUS DISEASES IN CENTRAL MOROCCO

S. Jbari, W. Lahmini, S. Boussaa, M. Bourrous
university cadi ayyad, Science And Environnement/Marrakech, Morocco

Background: Infectious diseases represent the world’s leading cause of premature death as shown in the WHO report. In Morocco, infectious diseases are more widespread among the poor and vulnerable populations, including children, and are still a major public health problem.

Methods: With the aim to analyze the distribution and epidemiological characteristics of pediatric infectious diseases in central Morocco, a retrospective study was carried out in pediatric emergency services of the Mother-Child hospital in University Hospital of Marrakech. Data of 1658 patients, hospitalized in the pediatric emergency service between March 2015 and December 2018, were collected. It concerns mainly the socio-demographic and clinical profile, evolution status, mode of admission and medical history.

Results: The characterization of the study population by sex and age showed a predominance of the boys with a sex ratio of 1.36, infants (1 month to 2 years) with 625 patients. Regarding the region, Marrakech-Safi was the most represented with 88.8%. Concerning the final diagnosis, the most frequent pathologies are infection of the respiratory system (28%) with recurrence of pertussis (21 cases), followed by other infectious and parasitic diseases (10.7%), mainly Meningitis (70 cases), then urogenital infections (9.8%). A percentage of 7.40% of deaths was recorded in the emergency room.

Conclusions: According to our results, infectious diseases still the main cause of medical consultation and hospitalization in the study area. Raising awareness around vaccination campaigns seem to be fairly effective way of reducing the incidence of pediatric infectious diseases and consequently infant mortality. Surveillance of emerging diseases is therefore essential in order to detect any changes or evolutions.
Autism Genes Overlap with Cancer Genes, and Genes Targeted by Viruses

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Background and Objective: As many autistic individuals have now had whole exome testing, genetic pathways associated with autism demonstrate substantial overlap with those commonly associated with cancer. [1-3] Like cancer, viruses often alter genes to prolong cell life. The aim is to see if viruses associated with autism might also target a few of these highly overlapping genetic pathways, in particular, the Ras-MAPK and the PI3K-AKT-mTOR with regulation by PTEN, or sometimes termed singly as the RAS signaling pathway. [4]

Methods: Some viruses scrutinized for an association with autism include: Rubella [5,6], CMV, EBV, HSV1, HHV6, and polyomaviruses [7]. A limited literature search of the above viruses was performed to see if they could alter genes along the Ras-MAPK and the PI3K-AKT-mTOR with regulation by PTEN pathways.

Learning Points/Discussion: -The search demonstrates that viruses associated with autism alter genes along the Ras-MAPK and the PI3K-AKT-mTOR with regulation by PTEN pathways as shown in Table 1. -In regards to whether viruses target genes with an overlap in autism and cancer, this shows that viruses can, but not necessarily to any given extent. -More research regarding the overlap of genes involved in autism that also serve as viral targets is warranted. Table 1: Viruses target Ras-MAPK and PI3K-AKT-mTOR/PTEN

<table>
<thead>
<tr>
<th>Virus Type</th>
<th>Ras-MAPK</th>
<th>PI3K-AKT-mTOR/PTEN</th>
</tr>
</thead>
<tbody>
<tr>
<td>CMV</td>
<td>Johnson 2001 Hutton 2017</td>
<td>Shen 2006</td>
</tr>
<tr>
<td>EBV</td>
<td>Morris 2018</td>
<td>Turnell 2012 Zhou 2016 Morris 2018</td>
</tr>
<tr>
<td>HSV1, HSV2</td>
<td>Colao 2017 Filippakis 2010</td>
<td>Vink 2017 Filippakis 2010</td>
</tr>
<tr>
<td>HHV6</td>
<td>Engdahl 2018</td>
<td>Filippakis 2010</td>
</tr>
<tr>
<td>Polyomavirus (JC virus, BKV, SV40)</td>
<td>DuShane 2018</td>
<td>Link 2009 Turnell 2012</td>
</tr>
</tbody>
</table>
STUDY OF INVASIVE FUNGAL DISEASE IN CHILDREN WITH FEBRILE NEUTROPENIA

M. Nathani¹, R. Kaur², J. Chandra³
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Background: Profound and prolonged neutropenia following chemotherapy is a major risk factor for systemic fungal infection. The early diagnosis of invasive fungal infection (IFI) is quite difficult leading to high morbidity and mortality. There is an urgent need for reliable screening methods facilitating timely diagnosis and treatment. The aim of the study was to diagnose IFI in children of febrile neutropenia and compare the different laboratory procedures for diagnosis of IFI.

Methods: The study was performed from November 2018 to April 2020 in the department of Pediatrics KSCH and department of Microbiology LHMC, New Delhi. Fifty five children diagnosed with lympho-reticular malignancies or aplastic anemia and presenting with fever and neutropenia were evaluated and their samples were sent to the laboratory for testing. Samples were subjected to microscopy, culture, antigen detection and fungal Polymerase chain reaction (PCR).

Results: We had 23 proven invasive fungal infective cases, probable in 3 and possible in 21 cases. 10 of proven cases were Panfungal and Candida multiplex PCR positive which included 5 fungal growth positive cases (growing Candida spp.) On comparison of blood culture and PCR results, blood culture showed sensitivity, specificity, positive and negative predictive values of 50.00%, 93.30%, 62.50% and 89.40% respectively. Microscopy showed a sensitivity of 70% specificity of 31.11%, positive and negative predictive values of 18.42% and 82.35% respectively.

Conclusions: The Panfungal real-time PCR assay can detect common fungal genera and it may be used as an adjunct to conventional methods for screening of IFI specially in cases where deep seated samples are difficult to access for diagnosis. Combining microscopy, culture and PCR may improve the diagnostic outcome to a greater extent.
Background: AIDS-related deaths in children and adolescents were estimated at 120,000 in 2018, accounting for 15% of all AIDS related deaths globally. Each day in 2018, approximately 980 children were infected with HIV and 320 children lost their lives from AIDS-related causes. In Kenya, there are 139,000 children aged less than 15 years living with HIV. With the scale up of universal Anti-Retroviral Therapy, HIV associated morbidity and mortality has been declining. We sought to study the patterns of HIV associated morbidity and mortality through this survey.

Methods: This study is a retrospective survey of hospital records of children and adolescents living with HIV who had been admitted in Kenyatta National Referral hospital between 2013 and 2019. Records were abstracted from the electronic medical record (EMR) system then were placed onto excel sheets which were then used for analysis using SPSS. Mortality rates were calculated yearly throughout the time period from 2013 to 2019. Univariate and Multivariate analysis were then used to describe the factors associated with mortality.

Results: 566 children and adolescents admitted in Kenyatta National Referral hospital between 2013 and 2019. All were included in analysis. Seventy percent were known HIV infected. Males were 55%, and 60% presented in WHO Stage 3. Most (22%) presented with Pneumonia. The median hospital stay was 15 days. The overall mortality was 29%, with Pneumonia and TB being major causes of mortality. Factors noted to be associated with mortality include age 15-19 years (p=0.002), WHO Stage 4 (p=<0.001), diagnosis of cryptococcal meningitis(p=0.024), extrapulmonary TB (p=<0.001)

Conclusions: Pneumonia and TB are significant contributors of HIV associated morbidity and mortality. Adolescents suffer highest mortality, and interventions targeting adherence and retention to HIV care would assist in reducing this.
N.M. Wijesundara1,2, S. Lee3,4,5,6, Z. Cheng4, H.P.V. Rupasinghe1,2,5
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Background: *Streptococcus pyogenes* causes streptococcal pharyngitis, which is a significant pediatric infectious disease worldwide. The identification of natural antibacterial phytochemicals has renewed interest due to the current paucity of antimicrobial development. This study aimed to study the antibacterial activity and mechanisms of carvacrol, a monoterpenoid phenol found in herbs such as oregano and thyme, against *S. pyogenes*.

Methods: Carvacrol was evaluated for the bactericidal effect, killing time, and cytoplasmic leakage against four strains of *S. pyogenes*. Flow cytometry (FCM) was employed to determine the permeability and membrane potential changes. Morphological changes of carvacrol treated intact bacterial cells, protoplasts, and isolated membranes were visualized using transmission electron microscopy (TEM), scan electron microscopy (SEM), and fluorescence microscopy (FM). The cytotoxicity of carvacrol on human tonsil epithelium cells (TonEpiCs) was assessed.

Results: All four tested strains were susceptible to carvacrol with a minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) of 125 and 250 µg/mL, respectively. Time to kill was 5 min for carvacrol at MBC, when compared to 24 hours for benzylpenicillin at MBC. The effect on lactate dehydrogenase release from cytoplasm was observed in a dose-dependent manner. Loss of cell integrity was observed through TEM. Ultra-structural and functional membrane damages induced by a shorter period of carvacrol exposure were demonstrated by using protoplasts of *S. pyogenes* model and isolated bacterial membranes *in-vitro*. Carvacrol exhibited selective cytotoxicity towards bacterial cells in comparison to TonEpiCs.

Conclusions: Overall, carvacrol alters bacterial membrane fluidity and integrity, leading to increase membrane permeability, cell lysis, and ultimately death of the bacteria. Therefore, carvacrol could be used for developing as an efficient antimicrobial agent for the management of pediatric streptococcal pharyngitis.

Clinical Trial Registration: non-applicable
Nosocomial candidaemia in paediatrics - a retrospective analysis of patient demographics, epidemiology, species distribution and antifungal susceptibility

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Background: Bloodstream infections (BSI) caused by Candida species are responsible for significant morbidity and mortality in hospitalised children. This study aimed to compare epidemiological and demographic trends in paediatric invasive candidiasis.

Methods: In this comparative analysis, paediatric patients with BSI caused by candida species were identified from hospitalised paediatric patients. There were 29 cases of candidaemia in 22 patients over the time period January 1st 2016 - December 31st 2019. Recurrence was identified using a 14 day repeat infection time frame (RTT) - 3 incidences totalled. Six different species isolated. This was then compared with previous data from Jan 1st 2004 to December 31st 2015.

Results: Candidaemia continues to be more common in younger children than in the older age group (mean age 4.7). The majority of patients had central venous catheters. There was a high prevalence of neutropenia or immunodeficiency amongst patients (9/22, 41%). Candida albicans was the most prevalent species isolated on this occasion 12/26, 42.5%. Previously Candida parapsilosis was the most prevalent. In terms of antifungal resistance, all isolated Candida species demonstrated susceptibility to Amphotericin B. Caspofungin had previously demonstrated 100% susceptibility from 2004-2015. However, analysis from 2016 onwards showed susceptibility of 87.5%.

Conclusions: Although all isolates remain sensitive to Amphotericin B, there is evidence of reduced susceptibility to certain antifungal agents. This is demonstrated by the recent decrease in susceptibility to Caspofungin, therefore continued vigilance is required to detect any changing trends in susceptibility and epidemiology.
LEVELS OF HEPATITIS B ANTIBODY TITERS ARE AFFECTED BY AGE AND SEX IN CHILDREN FROM A HIGH ENDEMIC AREA OF THE WESTERN AMAZON

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**Background:** Despite completion of the vaccine schedule for hepatitis B virus (HBV), children may display levels of HBV surface antibodies (anti-HBs) that are considered inadequate for sufficient protection (<10 IU/L). Our aim was to investigate if age and gap time between HBV vaccine doses may negatively affect the levels of anti-HBs in children, and if these relationships are modified by sex.

**Methods:** In a high-endemic HBV region of the western Brazilian Amazon we enrolled children who had completed the HBV vaccine schedule. All children underwent analysis of anti-HBs and a clinical examination.

**Results:** We included 522 children (mean age 4.3 ± 0.8 years; 50% male). Median anti-HBs was 28.4 [interquartile range (IQR) 5.4 to 128.6] IU/L and 32% had anti-HBs <10 IU/L. The median gap time from last to preceding dose was 2.4 [IQR 2.1 to 3.3] months. Levels of anti-HBs decreased with higher age (-25% per year increase [95%CI -37% to -11%], p=0.001; Figure 1A) but not with longer gap time (-1% per month increase [95%CI -5% to +4%], p=0.80). After adjusting for relevant confounders, age remained a significant predictor of anti-HBs (p=0.002). Sex modified the relationship (p interaction<0.001; Figure 1B), such that age was a significant predictor of anti-HBs in boys (p<0.001) but not in girls (p=0.36). The sex did not modify the relationship with gap time (p interaction=0.12).

**Figure 1.** (A) Association between Hepatitis B antibodies and age; (B) the interaction stratified by sex.
**Conclusions:** One third of assessed children displayed anti-HBs <10 UI/L. Levels of anti-HBs decreased with higher age, but not with longer gap time. Sex influenced the level of antibodies, such that anti-HBs decreased with higher age in boys but not in girls.

**Clinical Trial Registration:** This clinical study was not registered in Clinicaltrials.gov.
Background: Streptococcus pneumoniae is the first cause of bacterial pneumonia in children. Since the implementation of routine immunization in 2004, the incidence of severe pneumococcal infections has decreased in Luxembourg. Thirteen-valent conjugated vaccine (PVC13), used routinely since 2010, is the only licensed PCV with serotype 3 (ser3) polysaccharide in its formulation. The incidence rate of pediatric empyema in Luxembourg was 6/100000 person-years (children aged 0 to 6 years old) between 2015 and 2019, representing an average of 2.6 admissions per year in our children's hospital.

Methods: Demographical, clinical and microbiological data from a cluster of cases of complicated pneumonia (empyema, necrosis and abscess) in children hospitalised in our National Paediatric Reference Center were retrospectively collected and analysed.

Results: We identified a cluster of 6 cases of pediatric complicated pneumonia between December 2019 and February 2020 (9 weeks period). The median age was 4 years. All patients had been vaccinated with PCV13 according to the national vaccination schedule (2 + 1). All were treated with intravenous antibiotics (median length 12 days). Four were admitted to the intensive care unit. Two underwent video-assisted thoracoscopic surgery. All patients recovered. Pneumococcus infection was confirmed in 5 patients (positive PCR on pleural fluid) with serotyping performed in 4 of them and identifying ser3.

Conclusions: We present a cluster of cases of complicated pneumococcal pneumonia caused by ser3 in children vaccinated with PCV13. Several other European countries have reported cases of complicated ser3 pneumococcal pneumonia in previously vaccinated children, indicating the need for close monitoring and larger studies to evaluate the protection afforded by PCV13 against ser3 complicated pneumonia.
LYME CARDITIS IN PEDIATRIC PRACTICE: A RARE PRESENTATION OF SINUS BRADYCARDIA WITHOUT ANY CONDUCTION DEFECTS

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¹Ternopil National University, Department Of Pediatrics With General Surgery, Ternopil, Ukraine,
²Ternopil National University, Department Of Emergency And Emergency Care, Ternopil, Ukraine

Background: Lyme disease is the most commonly reported vector-borne disease in Europe and is endemic in Ukraine. In Europe, only 0.3–4% of all Lyme borreliosis cases manifest with myocarditis. Erythema migrans rash (80% of the patients) usually appears on the early localized stage of Lyme disease. Most cases of LB appear to be clinically asymptomatic.

Methods: Case history. Laboratory examinations: CBC, Rheumatic tests: Serologic testing: Elisa, Western blot. ECG. echo-cardiography of heart

Results: A 14-year-old girl was with complaints of pain in the ankle and metatarsal joint. Tick bite 2 months ago, CBC: leukocytosis (12.12 * 10⁹/L). C-reactive protein – 40.7 mg/l, Antistreptolysin-O (ASL-O) – 201 IU/ml Elisa anti-B. burgdorferi– IgM antibodies – 17.77 U/ml, antibodies IgG – 77.6 U/ml. Western blot analysis was positive for specific anti-Borrelia burgdorferi IgM and IgG antibodies too. ECG- sinus bradycardia without conduction disorders. Echo-cardiography of heart: the chambers of the heart were not dilated, and a small amount of fluid up to 4.2 ml was visualized on pericardium cavity.

Conclusions: This report describes case of Lyme carditis and sinus bradycardia as its only presenting symptom.
SCHISTOSOMIASIS IN CHILDREN, A RETROSPECTIVE 6 YEARS STUDY IN SPAIN

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¹Hospital Universitario Infantil La Paz, Department Of Infectious Diseases And Tropical Pediatrics, Madrid, Spain, ²Hospital General de Valdepeñas, Pediatrics, Ciudad Real, Spain, ³Hospital de Torrejón, Paediatrics, Madrid, Spain, ⁴Hospital Universitario Quirón Madrid, Paediatrics, Madrid, Spain, ⁵La Paz University Hospital, Microbiology, Madrid, Spain

Background: Schistosoma is a trematode prevalent in tropical and subtropical areas. Schistosomiasis, considered a neglected, affects 240 million people. We aim to describe clinical and epidemiological characteristics of pediatric patients.

Methods: A retrospective descriptive study (2014-2019) of patients ≤18 years old diagnosed with schistosomiasis was performed in a Spanish referral Pediatric Tropical Unit. Of 1504 patients attended, 69 suffered schistosomiasis (4.6%), median age 15.3 (IQR 12.5). 47/69 (68.1%) were males, 23/69 (33.3%) adoptees, 20/69 (21%) immigrants, 4/69 (5.8%) VFRs, 1/69 (1.4%) Spanish traveler. Median time since arriving Spain was 60 days (IQR 113). Reasons for consultation: 23/69 (33.3%) adoptees health control, 18/69 (26.1%) tuberculosis-screening, 16/69 (23.2%) to discard tropical pathology and 12/69 (17.4%) eosinophilia; 28/69 (40.6%) had symptoms (12/28 cutaneous, 12/28 gastrointestinal, 4/28 hematuria).

Results: On physical examination 12/69 (17.4%) presented low weight-for-age and 18/66 (27.3%) low height-for-age. Regarding blood test, 16/69 (23.2%) presented anemia and 36/69 (52.2%) eosinophilia (22/36 <1000/mm³), IgE was increased in 16/24 (66.6%) (1789 IQR 2394 KU/L). All patients presented positive serology and in 1 case S. haematobium eggs were found in urine sample. Serology for Toxocara or Strongyloides was positive in 15/57 (26.3%); 29/69 (42%) had co-parasitosis: 7/29 by helmith, 5/29 by Giardia 5/29 by protozoa and helminth; 18/29 by non-pathogenic protozoa. All patients from Europe and South America presented co-parasitosis (p = 0.025).
Conclusions: All patients were treated with praziquantel at 20mg/kg/day every 8 hours 1 day, repeating in 2 weeks. No significant side effect were observed (only 1 hypertransaminasemia). 54/69(78.2%) patient were followed-up, median time until serology was negative was 9 months (IQR 18). At the last visit 19/54(35.2%) persisted positive, 9/54(16.6%) lost during follow-up. Children coming from countries where schistosomiasis is endemic must be screened. Usually are asymptomatic although chronic infection can lead to malignancy, portal-hypertension or compression of spinal cord.
ANALYSIS OF THE POLIOVIRUS VACCINE COVERAGE RATE IN CHILDREN AND THEIR RELATIONSHIP WITH SOCIOECONOMIC INDICATORS IN A STATE IN BRAZIL

F.R. Gonçalves, Y. Pamplona, C. Barbieri, L. Martins
Universidade Católica de Santos, Programa De Saúde Coletiva, Santos, Brazil

Background: Vaccination is responsible for the control and elimination of several vaccine-preventable diseases. The National Immunization Program (PNI) in Brazil, created in 1973, pointed to a drop since 2017 in routine vaccine uptake rates. It is committed to the return of measles and puts the return of some diseases like polio at risk. This study aims to analyze the vaccination coverage rates of the poliovirus vaccine and its relationship with socioeconomic and health characteristics in the State of Paraiba, Brazil, in 2016.

Methods: This is an ecological study that used secondary data. Polio vaccine coverage rates were calculated using doses applied to children under 1 year old and live births in 2016, stratified by 223 municipalities. Descriptive analyzes, chi-square test and linear regression analysis were performed. SPSS 24.0 software was used, adopting a significance level of 5%.

Results: In Paraíba, vaccination coverage is not homogeneous, 51.1% of the municipalities had low and very low coverage vaccination coverage and 43% of the municipalities showed a high dropout rate. In the multivariate analysis, the illiteracy rate is inversely proportional to low coverage (OR 0.23; CI 0.087-0.604), so the municipalities with the highest prenatal (OR 0.150, CI 0.056-0.399). Municipalities with a higher proportion of population with a higher density per bedroom (OR 2.912; CI 1.062-7.983) and with more inadequate water treatment and sanitation (OR 3.656; CI 1.389-9.622) has a greater chance of low polio vaccination coverage.

Conclusions: Vaccination coverage against polio is below the target in most municipalities, not achieving collective immunity and putting the return of the disease at risk. The findings indicate that trained professionals are needed, awareness of the population, adequate immunization to achieve the established goal.
INTESTINAL PARASITES AMONG CHILDREN COMING FROM 4 CONTINENTS.

J. Bustamante Amador¹, T. Sainz Costa², S. Perez Muñoz³, M.F. Ara Montojo⁴, P. Rodríguez-Molino⁵, M. García López-Hortelano⁶, M.J. Mellado-Peña⁶
¹Hospital General de Valdepeñas, Pediatrics, Ciudad Real, Spain, ²Hospital Universitario La Paz, Pediatric Infectious Diseases, Madrid, Spain, ³Hospital de Torrejón, Paediatrics, Madrid, Spain, ⁴Hospital La Paz, Pediatrics, Madrid, Spain, ⁵La Paz University Hospital, Pediatrics, Madrid, Spain, ⁶Hospital Universitario La Paz, Paediatrics, Madrid, Spain

Background: Parasitic infection caused by intestinal helminth and protozoa are among the most prevalent infections in developing countries. We aim to describe clinical and epidemiological characteristics of these patients.

Methods: A retrospective descriptive study (2014-May 2018) including children ≤18 years old with parasitosis was performed in a referral Spanish Center for Pediatric Tropical diseases. Diagnosis was by serology or microscopic stool-sample evaluation. Epidemiological and clinical data were recorded.

Results: Totally 272/938 (29%) children suffered parasitosis and 406 parasites and 12 bacteria were found. Median age was 6.70 (IQR 8.43), 113/272 (41.5%) females. Symptomatic 145/272 (53.3%) more common diarrhea 68/145 (46.9%), 13/145 (8.9%) abdominal pain, pruritus 32/145 (22.1%). At the physical examination: 14/38 (36.8%) abdominal swelling, 13/38 (34.21%) eczema, 4/38 (10.53%) visceromegaly, 1/38 (2.6%) abdominal-pain, 6/38 (15.8%) several. 99/272 (36.4%) anemia, 120/272 (44.1%) eosinophilia and 40/272 (14.7%) leukocytosis, increased IgE in 19/80 (23.7%) (median 1363 IQR 1226kU/L). Among all, 220/272 (80.9%) children presented ≥1 pathogenic parasite, 113/272 (41.5%) children were infected exclusively by helminthic, 106/272 (38.9%) protozoa, 6/272 (2.2%) by bacteria and 47/272 (17.3%) mixed. More than 2 parasites were found in 94/272 (34.5%).

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**Conclusions:** Parasites could be asymptomatic so screening in children coming from abroad or with eosinophilia, could avoid complications such as malignancy, chronic disease, intestinal malabsorption or hypereosinophilic syndrome. At the logistic-regression, coming from sub-Saharan Africa (OR 2.8 IC95%: 1.7-4.7), and presenting eosinophilia (OR 12.9 IC95%: 8.1-19.9) were risk factors for parasitization. For co-parasitization, coming from sub-Saharan Africa (OR 2 IC95%: 1.1-3.8), being refugee (OR 6.9 IC95%: 1.1-42.3) and presenting eosinophilia (3OR 3.4 IC95%: 2.0-5.8).
Background: Parasitic infection caused by intestinal helminth and protozoa are among the most prevalent infections in developing countries. We aim to describe clinical and epidemiological characteristics of these patients.

Methods: A retrospective descriptive study (2014-May 2018) including adopted children with parasites was performed in a referral Spanish Center for Pediatric Tropical diseases. Diagnosis was by serology or microscopic stool-sample evaluation. Epidemiological and clinical data were recorded.

Results: Totally 140/394(35.5%) presented parasites: 24/100(24%) European, 15/38(39.5%) Latin-American, 48/90(53.3%) African, 53/166(31.9%) Asiatic. Symptomatic 77/140(31.4%) most common: 58/77(75.3%) gastrointestinal, 15/77(19.5%) cutaneous. At physical examination 15/28(53.6%) abdominal-swelling, 5/28(17.8%) eczema, 2/28(7.1%) visceromegaly, 1/38(3.6%) abdominal pain. 76/140(54.3%) presented anemia, 51/140(36.4%) eosinophilia and 25/140(17.8%) leukocytosis and 10/59(16.9%) increased IgE. Among all, 113/140(80.7%) children presented ≥1 pathogenic parasite. 35/140(25%) exclusively by helminthic, 69/140(49.3%) protozoa, 2/140(1.4%) bacteria and 34/140(24.3%) mixed. ≥2 parasites were found in 60/140(42.8%). Statistically significant difference was found when comparing the presence of symptoms, age and eosinophilia with the regions (p 0.001, 0.001, 0.002).
Conclusions: At the logistic regression age 6-10 years old (OR3.7 IC95%:1.1-12.3), Africans (OR 4.4, IC95%: 2.4-8.2) and eosinophilia (OR 10.8 IC95%: 5.6-21.0) were risk factors for being infected by a parasite. For ≥1 parasite age 6-10 years old (OR4.3 IC95%: 1.0-18), Africans (OR 2.8 IC95% 1.4-5.9), and eosinophilia (OR 4.2 IC95% 2.1-8.3) were risk factors too. Screening for parasites in adoptees should be done as up to 35% are infected. It could improve nutrients absorption and avoid severe complications.
EXPLORING THE PAEDIATRIC RESPIRATORY INFECTIOUS DISEASE LANDSCAPE: THE EVOLUTION OF IMMUNISATION SCHEDULES IN THE UK AND IRELAND AND THEIR IMPACT ON EPIDEMIOLOGY AND DISEASE BURDEN

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¹Sanofi, Sanofi Pasteur, Reading, United Kingdom, ²Sanofi, Sanofi Pasteur, Dublin, Ireland

Background and Objective: Globally, respiratory tract infections (RTIs) are amongst the most frequent childhood diseases and have a considerable impact on public health, morbidity and mortality. This review evaluated the evolution of the paediatric immunisation schedule in the UK and Ireland protecting against pathogens that can cause RTIs and assessed the impact of vaccination on disease epidemiology and burden in children 0–5 years.

Methods: We undertook a review of publicly available national health surveillance data for the UK and Ireland (1930/1940 to 2020) for children aged 0–5 years. Epidemiological data was cross referenced to changes in the vaccination schedules.

Learning Points/Discussion: The paediatric vaccination schedules in the UK and Ireland have led to significant reductions in the incidence of RTIs caused by vaccine-preventable pathogens such as influenza, pneumococcus, pertussis, and Hib. Reductions in the incidence of these diseases have led to corresponding reductions in the healthcare burden. Continuous disease monitoring and surveillance have enabled the vaccination schedule to be modified and evolve in response to changing epidemiology, in order to protect those most at risk. There continue to be a number of pathogens that cause RTIs in the under 5’s for which there are currently no vaccines and these include coronaviruses, adenoviruses and respiratory syncytial virus. These can represent a considerable health, caregiver and economic burden. Efforts are currently underway to develop immunisations for some of these pathogens.
PERIPHERAL EOSINOPHILIA ASSESSMENT IN CHILDREN. A 4.5 YEARS’ EXPERIENCE IN A PEDIATRIC TROPICAL REFERRAL UNIT.

J. Bustamante Amador¹, T. Sainz Costa², M.F. Ara Montojo³, S. Perez Muñoz⁴, P. Rodríguez-Molino⁵, M. García López-Hortelano², M.J. Mellado-Peña²
¹Hospital General de Valdepeñas, Pediatrics, Ciudad Real, Spain, ²Hospital Universitario La Paz, Pediatric Infectious Diseases, Madrid, Spain, ³Hospital Universitario Quirón Madrid, Paediatrics, Madrid, Spain, ⁴Hospital Universitario Infantil La Paz, Department Of Infectious Diseases And Tropical Pediatrics, Madrid, Spain, ⁵Hospital Universitario La Paz, Pediatrics, Madrid, Spain

Background: Peripheral eosinophilia can be the manifestation of a wide spectrum underlying conditions including allergies, parasites, autoimmune disorders, malignancy and immunodeficiencies.

Methods: A retrospective descriptive study (2014-May 2018) including children ≤18 years old with peripheral eosinophilia (≥500 eosinophils/mm³ or >5% of leukocytes) was performed, in a referral Spanish Center for Pediatric Tropical diseases. Epidemiological and clinical data were recorded.

Results: Totally 163/938(17.4%) presented peripheral eosinophilia. Symptoms 56/163(34.4%) gastrointestinal (27/56(48.2%), cutaneous 22/56(39.3%), 7/56(12.5%) both. 49/163(30%) presented anemia, 29/163(17.8%) leukocytosis. 113/163(69.3%)suffered parasitosis (helminth 58/113(51.3%), protozoa 25/113(22.1%), both 28/113(24.8%)); 41/113(36.3%) ≥2 parasites. 123/163(75.5%) mild eosinophilia (500-1000/mm³), 20/163(12.2%) moderate (1000-1500/mm³) and 20/163(12.2%) hyper-eosinophilia (>1500/mm³), 62.6, 85 and 95% with any parasite respectively. Most common parasites: Schistosoma (27/113(23.9%), Toxocara (23/113(20.4%), Giardia 22/113(19.5%), Strongyloides (20/113(17.7%). The aetiology wasn’t clarified in 50/163(44.2%); 5/50(10%) presented indeterminate serology for helminths. In 46/50(92%) eosinophilia was mild, 3/50(6%) moderate, 1/50(2%) hypereosinophilia. 6/50(12%) patients improved with albendazole (1 hypereosinophilia and 5 symptomatic).
Conclusions: At the logistic regression, suffering parasitization was the main risk factor for eosinophilia (OR 11.9 IC-95%: 7.4-19.1), and helminths for eosinophilia >1000/mm³ (OR 6.7 IC-95%: 2.1-21.4). Determining the cause of eosinophilia is challenging. Parasites represent an important etiology so should be screened.
**TOXOCARIASIS IN CHILDREN, A RETROSPECTIVE 6 YEARS STUDY IN SPAIN**

J. Bustamante Amador¹, S. Perez Muñoz², T. Sainz Costa³, M.F. Ara Montojo⁴, P. Rodríguez-Molino⁵, L. Montes Martín⁶, S. González Martínez⁶, M. García López-Hortelano⁷, M.J. Mellado-Peña⁷

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**Background:** *Toxocara* spp. is a nematode spread worldwide although more common in tropical regions. Toxocariasis occurs when ingesting embryonated eggs, causing lung, liver and eye damage.

**Methods:** A retrospective, descriptive study (2014-2019) including children ≤18 years old diagnosed with toxocariasis (serology) was performed, in a referral Spanish Center for Pediatric Tropical diseases. Epidemiological and clinical data were recorded.

**Results:** Totally 51/1504 (3.4%) diagnosed with toxocariasis. Of them, 27/51 (52.9%) were males, 21/51 (41.1%) immigrants, 20/51 (39.2%) adoptees, 5/51 (9.8%) refugees, 3/51 (5.9%) Spanish, 2/51 (3.9%) VFRs. Risk factors: 17/22 (77.3%), puppies contact, 5/17 (22.7%) walked barefoot. Symptoms in 19/51 (37.2%): 10/19 (52.6%) gastrointestinal, 5/19 (26.3%) cutaneous symptoms, 1/19 (5.3%) cough, 3/19 (15.8%) gastrointestinal+cutaneous. Physical examination 4/51 (7.8%) lymphadenopathy, 5/51 (9.8%) eczema, 1/51 (2%) both. Normal chest-radiography in 18/19 (94.7%) (1 bilateral-peribronchial-infiltrates), abdominal ultrasound in 16/18 (88.8%) (1 liver-granuloma and 1 mesenteric-lymphadenitis) and funduscopy in 24/24 (100%); 15/51 (29.4%) presented anemia, 29/51 (56.8%) eosinophilia, increased IgE 4/15 (26.6%). 15/51 (29.4%) presented co-parasitization. All were treated with albendazole 10-20 mg/kg/day, 42/51 (82.3%) 21 days and 14/51 (27.4%) 14 days.

**Conclusions:** Although more common asymptomatic, toxocariasis can lead to severe complications such as blindness, hepatitis or pneumonitis. Usually is underdiagnosed as pediatricians are not familiar with it.

**Table 1. Main characteristics of patients with toxocariasis.**

<table>
<thead>
<tr>
<th>Region</th>
<th>Europe n: 12 (%)</th>
<th>South America n: 10 (%)</th>
<th>Central America n: 7 (%)</th>
<th>Subsaharan Africa n: 10 (%)</th>
<th>Asia n: 12 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>5.28 (8.18)</td>
<td>12.49 (4.03)</td>
<td>13.79 (3.57)</td>
<td>11.84 (11.22)</td>
<td>10.11 (9.71)</td>
</tr>
<tr>
<td>Gender (Male)</td>
<td>3 (25)</td>
<td>6 (60)</td>
<td>2 (28.6)</td>
<td>6 (60)</td>
<td>10 (83.3)</td>
</tr>
<tr>
<td>Symptoms</td>
<td>3 (25)</td>
<td>6 (60)</td>
<td>4 (57.1)</td>
<td>1 (10)</td>
<td>5 (41.6)</td>
</tr>
<tr>
<td>GI</td>
<td>2 (16.6)</td>
<td>3 (30)</td>
<td>3 (42.9)</td>
<td>0 (0)</td>
<td>4 (33.3)</td>
</tr>
<tr>
<td>Cutaneous</td>
<td>0 (0)</td>
<td>3 (30)</td>
<td>1 (14.3)</td>
<td>1 (10)</td>
<td>1 (8.3)</td>
</tr>
<tr>
<td>Anemia</td>
<td>4 (33.3)</td>
<td>3 (30)</td>
<td>1 (14.3)</td>
<td>1 (10)</td>
<td>5 (41.6)</td>
</tr>
<tr>
<td>Eosinophilia</td>
<td>6 (50)</td>
<td>6 (60)</td>
<td>5 (71.42)</td>
<td>7 (70)</td>
<td>5 (41.6)</td>
</tr>
<tr>
<td>≥2 parasites</td>
<td>2 (16.6)</td>
<td>4 (40)</td>
<td>1 (14.3)</td>
<td>4 (40)</td>
<td>4 (33.3)</td>
</tr>
</tbody>
</table>
Background: Community-acquired pneumonia in children remains the most common cause of hospitalization for children and the leading cause of morbidity and mortality worldwide. The incidence of these complications is significantly increased. However, the causes of this increase are not clearly identified. The aim of this work is to describe the demographic, clinical and microbiological characteristics of immunocompetent patients hospitalized for community-acquired pneumonia with suppurative complications.

Methods: Retrospective analytical study over a period of 10 years from January 2010 to December 2019 collecting all cases of complicated community-acquired pneumonia occurring in immunocompetent patients.

Results: We collected 63 patients. 20% of patients took nonsteroidal anti-inflammatory drugs before hospitalization. Pre-hospital antibiotic use was noted in 25% of cases. Purulent pleurisy was diagnosed in 30 patients, pulmonary abscess in 26 patients, pyopneumothorax in 5 patients and necrotizing pneumonia in 2 patients. The germs responsible were staphylococcus aureus, pneumococcus in 20% of cases. The outcome was unfavorable in two cases with death secondary to macrophagic activation syndrome and refractory septic shock. Two patients had sequelae of localized bronchiectasis and three patients had a pneumatocele cavity.

Conclusions: Community-acquired pneumonia still represent an important threat to children. Early identification of the diagnostic and therapeutic procedures can help to improve the outcomes of these patients.
LYME DISEASE DISSEMINATION IN UKRAINE

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Background: The natural focus of Lyme disease (LD) in Ukraine are caused by Borrelia burgdorferi sensu lato Spirochaeta Complex and are spread all over the territory of Western and Eastern Ukraine. An important component of epidemiological surveillance is the prediction of the epidemic situation, including the assessment of the epidemic potential of natural cells of tick-borne infections.

Methods: Used materials of Region Laboratory Centre of Ministry of Health Care of Ukraine (State statistical reporting (ф. №1) from 2000 to 2019

Results: During 2000–2018, the incidence increased 93.4 times (Ukraine), 75.5 times (Sumy region). The incidence of Lyme disease in Ukraine for 2018 was 5419 cases, which was 12.8 cases per 100 thousand people, for 2019 year-4482 cases (10.6 cases per 100 thousand population), which may be due to insufficient attention of doctors to this disease. In the Sumy region, when comparing the quantitative characteristics of diseases among rural and urban children's population there was a more intense growth of Lyme disease in the city and central regions -39.45-40.01 100 000.

Conclusions: LD incidence in Sumy and Ternopol region, and Ukraine is on the rise. It concerns the lack of a clear organization of disease accounting in separate districts, which adversely affects the authenticity of statistical indicators. This can prompt to conduct inadequate medical tactics among children
Background: Urinary tract infection is a common pathology in children and adolescents, with a prevalence between 1 and 8%, depending of age. Antibiotics have been indiscriminately administered in the last years, generating mechanisms of bacterial resistance. In Mexico, there is a lack of information about resistance and prevalence of infections due to ESBL bacteria. The objective of the present study was to report the prevalence of urinary tract infections due to ESBL bacteria in Mexican children and adolescents during 2015 to 2016 in a third-level hospital.

Methods: A retrospective cross-sectional study was conducted using a database of various culture samples, between January 2015 and December 2016 at the Pediatric Hospital of the National Medical Center of Occident, Guadalajara, Mexico. Criteria inclusion was urine cultures of female / male patients from 0 to < 18 years. The most common bacterial pathogens were determined in the following age groups: < 1 year; 1-4 years; 5-9 years; 10-14 years, and 15-17 years.

Results: Of 3,474 records only 700 cases were urine samples which 353 (50.4%) from female, and 347(49.5%) from male. UTIs were highest (270) in the age group of < 1 year, followed by 5-9 years group (109). The most frequent microorganism was E. coli (47.5%), followed by Klebsiella pneumoniae (16.7%) and Pseudomonas spp (11.2%). The prevalence of ESBL-producing bacteria was 46.7 % and was most common in males. E.coli and Klebsiella were the only ESBL pathogens. Male patients presented more resistance than females (72.7% vs 27.7%;p = <0.001) respectively. Ampicillin reported the highest resistance.

Conclusions: UTIs are most common in males < 1 year. However, the frequency is higher in females in the subsequent age groups. E. coli was the most common uropathogen. Almost half of the isolates were from ESBL pathogens and males were the most affected. Only E.coli and Klebsiella were ESBL-producing bacteria. Ampicillin showed the highest resistance.
Background: Protein C reactive (CPR) is an acute – phase reactant, widely used in neonatal units to support and monitor the diagnosis of sepsis combined with clinical signs and other laboratory tests. Recent evidence question its diagnostic accuracy, based on the influence of noninfectious factors in CPR levels. We conducted this study to evaluate the correlation of CPR levels in cases of neonates with bacteremia or bacterial meningitis.

Methods: A retrospective study in a NICU of a tertiary center was conducted between January 2016 and December 2019. Neonates with bacteremia or bacterial meningitis were included. Data of blood cultures, cerebrospinal fluid (CSF) cultures and protein C reactive levels within the first 72 hours of each episode were collected.

Results: During the study period 4864 neonates were admitted. There were 108 patients with sepsis diagnosis, isolating microorganisms in 109 blood cultures and 8 cerebrospinal fluid culture. The organisms more frequently involved in sepsis diagnosis were Staphylococcus epidermidis (22%), Escherichia coli (15.3%) Streptoccus agalactiae (11.9%) and Klebsiella spp (11.1%). Levels of CPR > 1 mg/dL were associated with 76 (69%) positive blood cultures and 6 (75%, all cases > 3 mg/dL) positive CSF cultures; and CPR levels > 2 mg/dL associated with 65 (59%) of positive blood cultures.

Conclusions: There is a correlation in neonates with bacteremia or bacterial meningitis and increased levels of CPR in this serie, considering the most commonly used cutoff of 1 mg/dL.
PEDIATRIC ECHINOCOCCOSIS AT HIGH ALTITUDE: BIGGEST PEDIATRIC CASE SERIES STUDY IN THE PERUVIAN ANDES

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Background: Echinoccosis or cystic hydatidosis is a zoonotic parasitic disease due to the larval stage of taenia Echinococcus granulosus. In children that are the endangered group that gets the infection initially, it is believed to have special features such as higher rate of lung infection rather than in liver. The objective was to evaluate the features of this disease in a high incidence setting in Cusco in the Peruvian Andes at 3400 meters above sea level.

Methods: Through observational study and protocolised review of medical records during the last five years. We sought to characterize epidemiologically, clinically and therapeutically a series of 132 patients younger than 20 years diagnosed with echinococcosis through a descriptive analysis.

Results: More than 274 cysts and 132 medical records were found and evaluated. In this region hydatidosis affects mainly male (63.6%). The organ most affected was the lungs with 75 cases, in second place the liver 30 cases, and there were 26 cases with both liver and lungs affected. 81.1% of cases mentioned exposure to dogs, 11.4% had relatives with cystic echinococcosis and 65.2% had family who raised sheep. In pulmonary echinococcosis the most common symptom was cough (88%). The predominant therapeutic approach was surgery plus albendazole (93.3%).

Conclusions: Results differ from the series at sea level, this is the biggest case series in high altitude in our understanding. In this study the most common postoperative complication in pulmonary Echinococcosis was atelectasis and the most common approach in pulmonary hydatid disease was posterolateral right (93.1%). The complex social, cultural and physiological role of this disease in high Andean areas reveals why echinococcosis is frequent in the pediatric population.
SPATIAL ANALYSIS OF DIPHTHERIA-TETANUS-PERTUSSIS VACCINE IN BRAZIL

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Background: Childhood vaccination is a preventive health measure of great impact in reducing child morbidity and mortality. Diphtheria-Tetanus-Pertussis Vaccine (DTP) is provided free of charge by the National Immunization Program (PNI) in Brazil, included in the pentavalent vaccine. Despite the successes of the PNI, the country has been presenting cases of pertussis in the last two decades. This study aims to perform spatial analysis of DTP vaccine coverage in Brazil in 2016.

Methods: Ecological study mixed with secondary data from the PNI information system. Vaccination coverage of DTP in children under 1 year of age, in 2016, was calculated stratified by municipalities. Descriptive analysis and spatial analysis were performed using R and Qgis 3.4 software. The significance level was 5%.

Results: DTP vaccination coverage is heterogeneous across the country. There is a predominance of coverage below the 95% target by the WHO, in the states of the north and northeast regions, where some municipalities negatively influence their neighbors (p <0.05); except the state of Ceará. Adequate coverage is observed in the states of the south and southeast regions, where some municipalities positively influence their neighbors (p <0.05). In the central-west region, there is adequate vaccination coverage in the state of Mato Grosso do Sul that positively influence their neighbors (p <0.05).
**Conclusions:** In addition to its innovative character, the spatial analysis makes it possible to identify municipalities or regions of the greatest vulnerability, providing a different look at the logic of health equity, in understanding the low vaccination coverage in children and, thus, it allows guiding public policies.
INTESTINAL PARASITES IN CHILDREN WITH DIARRHEA FROM SANTIAGO, CAPE VERDE

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Background: Intestinal parasitic infections are significant cause of morbidity and mortality in children in developing countries. In Cape Verde, although there is a high incidence of diarrhea in children, in most cases an adequate clinical diagnosis is not made. Therefore, the aim of this study was to assess the intestinal parasitic infections in children with diarrhoea at the central hospital in Cape Verde.

Methods: A total of 105 stool samples were collected from children with diarrhea aged 0 to 12 years during 2018-2019 at the Dr. Agostinho Neto Hospital and all samples was submitted to morphological and molecular analyzes. It has been used in the Biofire® Filmarray® gastrointestinal panel with an integrated Biofire® Filmarray® system for detection of Giardia lamblia, Cryptosporidium sp., Entamoeba histolytica and Cyclospora cayetanensis, other parasites were detected by microscopy. Demographic information was obtained by questionnaire.

Results: Nine fecal intestinal parasite species were detected in 60% of the analyzed samples. The overall prevalence of protozoa and helminths was 29.5% (31/105) and 41.9% (44/105), respectively. The analyzes showed the presence of G. lamblia (34/105; 32.4%), A. lumbricoides (20/105; 19%), Cryptosporidium sp (10/105; 9.5%) Strongyloides sp. (7/105; 6.7%), Enterobius sp. (6/105; 5.7%), Taenia sp. (5/105; 4.8%), H. nana (4/105; 3.8%), Entamoeba coli (4/105; 3.8%) and Blastocystis sp. (1/105; 0.9%). Cyclospora cayetanensis and E. histolytica were not found. 20.9% of the samples had polyparasitism.

Conclusions: This study shows a high incidence and diversity of intestinal parasites in children with diarrhea in Cape Verde. The identified parasites are transmitted mainly by contaminated drinking water. In Cape Verde there is a need to implement water quality control measures. The results could help to establish adequate diagnosis and effective treatments for diarrheal disease.

Clinical Trial Registration: The project was approved by the National Ethical Commission for Health Research of the Ministry of Health and Social Security of Cape Verde with the reference nº 28/2018.
ATTITUDES AND KNOWLEDGE REGARDING TUBERCULOSIS IN HIGH SCHOOL STUDENTS, A CROSS SECTIONAL SURVEY IN NORTHWEST PERU

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Background: Teenagers is a vulnerable group that should be protected against tuberculosis (TB). TB incidence and resistant forms remain high despite government efforts in Peru. The objective of this study was to determine the level of knowledge and attitudes about tuberculosis that high school students have in a district of Peru Northwest coast (Chiclayo).

Methods: A cross-sectional-descriptive survey (self-administered) was performed. A knowledge score in the survey above or equal to 11 was considered adequate. A survey was created based on recommendations from the World Health Organization and validated by infectologists and pulmonologists in Peru. The sample included 319 students selected by simple random sampling. Representative schools from Chiclayo, an endemic region of northern Peru, were selected. Univariate and bivariate analyzes were performed with chi-square.

Results: The average knowledge score was 8.39 out of 20 possible points as maximum. 18.8% of the students had adequate level of knowledge about TB. 51.41% showed positive attitudes towards patients with TB. Only 43.26% showed adequate knowledge in prevention. Lower values were obtained in treatment (19.12%). There was association between adequate knowledge and having more schooling years, urban origin, and positive attitudes towards tuberculosis (p<0.05). Women displayed more positive attitudes as well as students from urban areas.

Conclusions: The level of knowledge about tuberculosis in the high school children is not adequate some factors. Endemic diseases such as tuberculosis should be taught in endemic regions of Peru. This is a way to carry out health promotion in community and country low-income.
PAEDIATRIC USE OF ANTIBIOTICS IN CHILDREN WITH COMMUNITY ACQUIRED PNEUMONIA

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Background: Antibiotic is the main weapon to reduce death caused by bacterial pneumonia. However, inappropriate antibiotic use can lead to antimicrobial resistance and adverse pneumonia outcome. Factors that may encourage unnecessary antibiotic use by doctors working in an urban paediatric hospital setting have not been explored in Vietnam. We did a survey to characterise paediatricians’ antibiotic prescribing behaviour managing pneumonia in Vietnam.

Methods: We conducted a questionnaire survey of paediatricians practising at a regional provincial hospital in central Vietnam over a 2-week period (from December 12 to December 29, 2017). We explored doctors’ perception of antibiotic use (or misuse), knowledge of pneumonia guidelines, factors that influenced hospital admission, discharge and antibiotic prescription decisions, as well as their attitudes towards antibiotic regulation and stewardship.

Results: Of 79 paediatricians 87.3% completed the questionnaire, of whom 94.2% thought that antibiotics were overused in Vietnam. Half of doctors indicated that they routinely hospitalised children with pneumonia to provide intravenous antibiotics. Older doctors generally continued intravenous antibiotics for more than 7 days. The two important factors driving discharge decisions were clinical assessment and completion of the full course of intravenous antibiotics. Antibiotic prescription was influenced by local guidelines, drugs used before admission. Most doctors believed antibiotic stewardship was necessary and over the counter use of antibiotics should be restricted.
Conclusions: Paediatricians in Da Nang, Vietnam, routinely hospitalise children diagnosed with pneumonia for a full course of intravenous antibiotics; identifying a potential opportunity to reduce unnecessary hospitalization. A need for better drug (antibiotic) regulation in Vietnam was universally acknowledged. Most doctors recognised an urgent need for better microbiology services and antibiotic stewardship programs to reduce empiric use of broad spectrum antibiotics.
Background: *Haemophilus influenzae* is one of the main and most interesting pathogens causing community-acquired respiratory infections in children. Previous studies have shown that *H. influenzae* is the second most common pathogen causing pneumonia and accounts for 30–50% of bacterial meningitis among Pakistani children. *H. influenzae* carriage in children and its resistance to commonly used antimicrobials varies widely both geographically and over time.

Methods: Surveys of *H. influenzae* carriage in children younger than 5 years of age with acute respiratory tract infection (ARI) were conducted in Karachi Hospital. *H. influenzae* carriage in children & its resistance to commonly used antimicrobials varies geographically. Surveys of nasopharyngeal carriage of *H. influenzae* in children younger than 5 years acute respiratory tract infection (ARI) were conducted in Karachi Hospital, Pakistan in 2010, 2013, 2015 & 2018.

Results: The *H. influenzae* among children with ARI were 35.5%, 20.6%, 14.4%, and 18.7%, and *H. influenzae* isolates producing β-lactamase were 4%, 13%, 27.1%, and 31%. Ampicillin susceptibility decreased from 96% (2010) to 87% (2013) to 63% (2015) to 61% (2018), ampicillin-resistant isolates were found to be beta-lactamase producers. Tetracycline susceptibility increased from 54% (2010) to 60% (2013) to 91.5% (2015) to 94.5% (2018). No statistically significant differences observed in cefaclor, cefuroxime, sulfamethoxazole, and chloramphenicol susceptibility. Amoxicillin/clavulanic acid and ceftriaxone were the effective antimicrobials for *H. influenzae* across 10-year period.

Conclusions: This report on the *H. influenzae* carriage rates in children and the susceptibility of these bacteria to commonly used antibiotics showed that *H. influenzae* carriage decreased from 2010 to 2018. Additionally, the percentage of β-lactamase-producing isolates increased while their susceptibility to ampicillin progressively decreased during this time. These results indicate that the appropriate empirical antimicrobial therapy should be changed for pediatric patients in Pakistan.
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Background: Blood culture (BC) sampling can be a challenging process in paediatrics. Cultures are often taken without correct indications and using a sub-standard technique. This is complicated by a lack of ‘child-friendly’ blood culture sampling equipment, with a perceived high rate of contaminant growth. Our aim was to assess compliance with correct indications for blood culture sampling, results of cultures taken and subsequent management of same.

Methods: We obtained records of all blood culture results sampled over a four week period in September and October 2019. Approval was prospectively obtained from our local audit committee. We included all patients attending our paediatric Emergency Department (ED) who were reviewed by a paediatric medical doctor. We cross-referenced BC records and results with patient attendance notes, to determine what proportion of the cultures were taken under correct indications.

Results: A total of 110 blood cultures were tested during the study period. 21 patients (19%) had a fever of 38 degrees Celsius or higher at time of assessment. 59% of our patients sampled were tachycardic at time of assessment. 27% had clinically significant indications for blood cultures documented in notes (n=30). This included suspected sepsis (n=5), urinary tract infection (n=8), and suspected meningitis (n=4). The remaining 80 patients had no documented reason for BC sampling. 10 BC samples grew bacteria consistent with contamination from skin or mouth flora.
Conclusions: Blood culture sampling technique is poor, and this is evident from our high rate of contaminant growth in paediatric blood culture bottles (10/110, 9.1%). Blood culture samples are being taken where no indication is found. This results in important patient-care and cost implications. We require further guidelines on indications for blood culture sampling, and education on correct sampling technique in our paediatric ED.
THE PROPHYLACTIC ANTIMICROBIAL THERAPY CRITERIA FOR VERY-LOW-BIRTH-WEIGHT INFANTS PROMOTE APPROPRIATE ANTIMICROBIAL THERAPY

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Background: Appropriate antimicrobial therapy is essential for the prevention of antimicrobial resistance and adverse neonatal outcomes. However, most very-low-birth-weight infants (VLBWI) (<1500 g) receive antimicrobial agents soon after birth because of the high risk of early-onset sepsis (EOS). Many of deaths from EOS occur among VLBWI. It is important to consider approaches to the appropriate use of antimicrobial agents for VLBWI.

Methods: We included VLBWI who received antibiotics in the first week of life and were admitted to the NICU of one of the three hospitals (A, B, or C) associated with Juntendo University between 2014 and 2018. We retrospectively investigated blood culture results, and EOS morbidity, defined by the isolation of a pathogenic species from the blood culture by 7 days of age. The dicision to use antibiotics was based on the criteria of the facility at Hospital A, or the attending physician’s discretion at Hospital B and C, respectively.

Results: 48, 127, and 77 infants were included at Hospital A, B and C respectively. 12% and 27%, 39% and 43%, and 70% and 71% of included infants recibed antibiotics on 0 and 7 days of age at Hospital A, B and C, respectively. At Hospital A, B, and C, the average duration of prophylactic antimicrobial therapy and the morbidity of EOS was 4.3, 6.6, and 7.1 days and 0, 0, 6.5%, respectively.

Conclusions: The use of the prophylactic antimicrobial therapy criteria for VLBWI is likely associated with appropriate antimicrobial therapy administration and reduced exposure to antimicrobial agents among infants without culture-proven sepsis. The prevalence of EOS may affect antibiotic use rates and days of use. We may need to work with obstetrics and gynecology to review treatment strategies for pregnant women and infants.
IN VITRO ACTIVITY OF CEFTAZIDIME-AVIBACTAM AGAINST CARBAPENEMASE-PRODUCING ENTEROBACTERIACEAE CAUSING BLOODSTREAM INFECTIONS IN PEDIATRIC PATIENTS

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Background: Enterobacteriaceae producing carbapenemase (EPC) are a major health threat in the world. Specific data for the pediatric population are still scarce, although the number of cases is increasing and associated with high morbidity and mortality. New therapeutic options need to be evaluated for pediatric population. This study aimed to evaluate the susceptibility profile to ceftazidime-avibactam of EPC isolated from pediatric patients.

Methods: Strains from December 2012 to December 2018, of the pediatric population at Santa Casa de Misericordia de São Paulo, were included. For each strain microbiological and molecular biology test were performed. Strains were tested for: polymyxin, amikacin, meropenem and tigecycline. All of them were tested by the epsilometer test, except polymyxin which was tested by the micro-dilution test. Then the strains were tested to ceftazidime-avibactam by disc-diffusion testing method. Regarding the molecular tests used, the RT-PCR was performed aiming to detect resistance genes. Clinical data were collected from medical records.

Results: There were 41 patients and 44 episodes of bacteremia due to EPC during the studied period. We observed high rates of antimicrobial resistance to the drugs used in the patients treatments. All strains, except one, were susceptible to ceftazidime-avibactam, with MIC50 = 0.75µg/mL and MIC90 = 2µg/mL. RT-PCR revealed that 100% of the strains were positive for gene blaKPC.

Conclusions: The study concluded that these infections have great impact among the pediatric population, however they are still presented as a challenge due to the fact that there are few effective therapeutic options, and few studies in pediatric population. Ceftazidime avibactam has a good susceptibility profile to the strains tested and may be an option for treating EPC infections in pediatrics.
CLOSTRIDIUM DIFFICILE IN THE COUNTRY GEORGIA – WHY CHILDREN ARE AFFECTED?

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Background: Worldwide Clostridium difficile infection development in pediatric patients hospitalized due to different medical conditions, mainly is associated with the exposure to antibiotics. Our study aim was to determine the association between antibiotic exposure in hospital settings and risk of Clostridium difficile associated infection in pediatric population of Georgia. Wide objective of our research was to determine main characteristic factors responsible for Clostridium difficile associated infection development in children.

Methods: 310 pediatric patients meeting our study criteria were enrolled. Study design was Cross-Sectional. Samples from 2 hospitals in Tbilisi, were tested by EIA kits for presence of toxin A and B. EIA test positive samples were evaluated by real-time PCR for confirmation of the infection and for simultaneous detection of additional gastrointestinal infectious agents. Patient’s data were collected from their medical health records.

Results: Presence of Clostridium difficile was documented in 34 patients (11%). Out of 34 Clostridium difficile positive children, in 6 patients study detected co-infection with Giardia lamblia (17.6% co-infection rate) and 4 patients study detected co-infection with Adenoviruses (11.7% co-infection rate). Several factors were associated with the development of Clostridium difficile infection (Table). The study showed that independent risk-factor for Clostridium difficile infection development was age more than 4 years old, while ethnicity and gender was not associated with the infection.

Table. Association of different factors with the development of Clostridium difficile infection

<table>
<thead>
<tr>
<th>Factor</th>
<th>Total number</th>
<th>Clostridium difficile positive</th>
<th>Odds Ratio (OR)</th>
<th>95% Confidence Interval (CI)</th>
<th>Statistical significance p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;4 years</td>
<td>198</td>
<td>14 (7.07%)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;=4 years</td>
<td>112</td>
<td>20 (17.86%)</td>
<td>2.86</td>
<td>1.38-5.91</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>157</td>
<td>19 (12.10%)</td>
<td>1.27</td>
<td>0.61-2.59</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>Female</td>
<td>153</td>
<td>15 (9.80%)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Georgian</td>
<td>280</td>
<td>29 (10.36%)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>30</td>
<td>5 (16.67%)</td>
<td>1.73</td>
<td>0.62-4.87</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>Antibiotic use</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>185</td>
<td>30 (16.22%)</td>
<td>5.86</td>
<td>2.01-17.07</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>No</td>
<td>125</td>
<td>4 (3.20%)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Conclusions: In Georgia, Clostridium difficile is significant cause of healthcare-associated diarrhea in pediatric population. Antibiotic administration within 2 months before the onset of diarrhea was related to increased risk of Clostridium difficile infections. The highest risk was related to cephalosporins, followed by penicillins, carbapenems and macrolides. Application of combination of first-line (EIA) and confirmatory (PCR) diagnostic methods yield simultaneous and accurate identification of the pathogens responsible for gastrointestinal infection.
PEDIATRIC PATIENTS COLONIZED BY CARBAPENEMIC RESISTANT ENTEROBACTERIACEAE: WHEN TO SUSPEND CONTACT PRECAUTIONS?

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Background: The establishment of contact precautions and collection of surveillance cultures are proposed strategies for control of dissemination and outbreaks of carbapenem resistant Enterobacteriaceae (CRE). However, the implementation and maintenance of these measures presuppose a great commitment and dedication of the infection control teams, besides implying costs with collection, exam processing and infrastructure for precautions. The aim of the study was to evaluate the duration of CRE colonization in readmissions of previously colonized or infected pediatric patients.

Methods: The readmission of pediatric patients from Santa Casa de São Paulo Hospital, with previous history of infection or colonization by CRE, was carried out from January 2012 to December 2018. We included patients who, on readmission, underwent surveillance cultures within 72 hours of admission. Patients with positive cultures with resistance profile or intermediate resistance to imipenem and/or meropenem were considered antecedents of CRE infection or colonization.

Results: During the study period, 169 patients colonized or infected with CRE were detected. These patients had 48 episodes of readmission and in 21 episodes surveillance cultures were collected within 72 hours of admission. Surveillance cultures were positive in 42.8% (n = 9) of readmission cases within six months. In cases of readmission after six months the positivity decreased to 14.3% (n = 3). There was no positivity in readmissions after 12 months.

Conclusions: We conclude that prevention and control measures remain essential. In our study we demonstrated that patients previously infected or colonized by CRE can maintain colonization for a long time, justifying the maintenance of surveillance strategies for at least 12 months. The aim of this strategy is to reduce the spread of resistant agents in the hospital environment, and reduce future infections.
PERIPHERAL INTRAVENOUS CATHETER RELATED BLOOD STREAM INFECTION AND ITS COMPLICATIONS: A STUDY AT PEDIATRIC ONCOLOGY UNIT IN TERTIARY CARE HOSPITAL KARACHI.

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the indus hospital, Infection Control Department, karachi, Pakistan

**Background:** Peripheral Intravenous devices are commonly practice in health care system and are used in utmost hospitalized patients. Studies has proven that microorganisms that most often caused infection related to devices are coagulase negative staphylococci and staphylococcus auerus, gram negative bacilli and fungus. The purpose of this study was to find out the type of organisms and its effects on immunocompromised children and determine the complications or death.

**Methods:** Data was collected retrospectively from January 2018 to December 2019 at pediatric oncology unit and laboratory result were collected from hospital information system at tertiary care hospital Karachi, Pakistan. Total 24546 patient’s data was studied. Emphasis on health care associated blood stream infections in peads oncology and their laboratory results, type of organisms and complications on positive in BSI of hospitalized patients.

**Results:** The causative pathogens were Gram-positive microorganisms in 19.0% out of 132 cases, Gram-negative microorganisms in blood were 75% of cases, and Candida spp were 5.3%. Patients who were died because of Peripheral Venous Catheter related Blood Stream Infection’s had a higher proportion of gram negative carbapenem resistant enterobacteriaceae infection that is 37.8%. enterobactericeae are included E.Coli, Klebsiella and candida spp along with Acinetobecter and pseudomonas aeruginosa.

**Conclusions:** Immunocompromised patients always on high risk in acquiring blood stream infection and can major cause of health care-associated infection and death. Provision of quality care practices in immunocompromised children is essential. We observed that patients with severe PVC-BSI may require intensive and long-term care along with antibiotic treatment. Application of PVC care bundle can also help to reduce microbiological related morbidity and mortality in immunocompromised populations.
ASSESSMENT OF EFFICACY AND SUSTAINABILITY OF AN ANTIMICROBIAL STEWARDSHIP PROGRAM FOR PERIOPERATIVE PROPHYLAXIS IN PEDIATRIC SURGERY

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Background: Appropriate antibiotic prophylaxis (PAP) is essential to prevent surgical site infections (SSIs) and to avoid the misuse of antibiotics. The aim of this study is to determine the effectiveness of an Antimicrobial Stewardship Program (ASP) based on Clinical Pathways (CP) and education to improve adherence to the guidelines for PAP in the tertiary care pediatric surgical referral center of Padua.

Methods: This quasi-experimental study was performed 6 months before (PRE) and the 24 months after (POST, divided into 4 periods) the CP implementation. All patients who underwent a surgical procedure were enrolled in the surveillance, according to the inclusion criteria. The ASP was addressed to all surgeons and attending physicians of the department. The main outcome measures were appropriateness of PAP (agent, timing of the first dose and the duration) and antimicrobial consumption. The SSI rate was calculated during both pre and post interventional period.

Results: 1771 patients were included in the study and 676 received PAP. The overall correctness of the PAP, in terms of agent, timing and duration, increased significantly after the CP implementation. In particular, what changed most was the PAP discontinuation within 24-hours (p <0.001) Cefazolin was the mostly used antibiotic, with a significant increase in the POST period (p<0.001) with a concomitant reduction in use of other broad-spectrum antibiotics. No variations in the incidence of SSIs were reported in the five periods (p =0.958).
Conclusions: The implementation of CP has proved to be a valid means of ASP. The increase of the correct indication, the antibiotic discontinuation within the twenty-four hours, the use of first-line antibiotics with the reduction of broad spectrum ones configures it as an effective and sustainable tool for improving the correct use of PAP.
KNOWLEDGE AND PERCEPTION OF MALARIA RDT AMONG HEALTHCARE WORKERS IN SOKOTO METROPOLIS, NORTH-WESTERN NIGERIA.

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Background: In order to adequately implement the World Health Organisations’ 3T( test, treat and track) policy. Healthcare workers need to be knowledgeable on the point of care test such as malaria rapid diagnostic test (mRDT) which are feasible to conduct at the lower level of the healthcare system. Our study aimed at determining the healthcare workers (HCWs) knowledge and perception of mRDT in Sokoto metropolis, north-western Nigeria.

Methods: We conducted a cross-sectional study amongst 262 healthcare workers in Primary and Secondary health centres’ in Sokoto metropolis. A multi-stage sampling technique was used to select 262 respondents from different cadres of health care workers. An interviewer-administered questionnaire was used to collect data on respondents’ demographic characteristics, knowledge and perception of mRDT. Knowledge and perception scores were categorised into poor, fair and good.

Results: The mean age was 33.3±7.9 years, 155 (59.2) were females, 112 (42.8%) were community health workers, 260 (99.2%) knew the meaning of mRDT, 261 (99.6) knew what RDT assesses and 258 (98.5) use mRDT for diagnosis. Only 47 (17.9%) do not know the time it takes to read the test, Overall knowledge was good in 92% of the respondents. Regarding perception, 218 (83.2) perceive the test to be a screening test while 127 (48.5%) perceive the time slated for the test is long. Overall perception of RDT was fair (55.7%)

Conclusions: Although health care workers have good knowledge of mRDT, their perception of the test is sub-optimal which may affect the implementation of the 3T policy. We recommended context-specific interventions such as health education, training and increase awareness among healthcare workers on misperceived concepts on RDT. Such an approach may upscale the use of the policy and reduce the overuse of antimalarial drugs.
Background: Antibiotic resistance is rising to dangerously high levels in all parts of the world. Considerable portion of antibiotic use lacks clear warrant; in some Neonatal Intensive Care Units (NICUs), antibiotics are overused. Our aim to show the most frequent antibiotics administered in NICU of Muratsan University Hospital Complex (Yerevan, Republic of Armenia) and subsequently to avoid the huge burden of antibiotic resistance.

Methods: We retrospectively reviewed the case records of randomly selected patients admitted to Neonatal Intensive Care Unit of Muratsan hospital during the period of January 1 – June 1, 2017. Only the patients with recovery were included (lethal outcome was exclusion criteria). Information obtained included patient diagnoses; antibacterial drugs used for treatment. The collected data were analyzed by our team and depicted on table.

Results: Of 133 patients, 131 received antibiotic treatment, of which 39(29.8%) were treated with only 1antibiotic, 45(34.4%) with 2antibiotics and 43(32.8%)–3antibiotics. Totally, 13 different antibiotics were used in 266 courses of treatment. The most common antibiotics used in this period were gentamycin–69(25.9%), penicillin–55(20.7%), moxifloxacin–35(13.2%).

Table1. Complete list of drugs.
Penicillin+gentamycin combination was given to 37(28.2%) neonates. In most cases(120) antibiotics were administered for treatment of respiratory tract disorders(congenital and community-acquired pneumonias, RDS, bronchitis etc.) and sepsis. Alas, there were no data about etiology of infectious diseases such as pneumonia or sepsis.

**Conclusions:** It is a necessity to use our arsenal of antibiotics carefully. Greater than half of patients received treatment with 2 and more antibiotics in NICU without identifying infectious agent and its susceptibility to antimicrobial drugs. Identifying of infectious agent and implementation of guidelines can prevent deleterious effects of antibacterial resistance. Educating the guidelines is another option of reducing inappropriate antibiotic use.
ANTIBIOTIC USE ON A TERTIARY NEONATAL INTENSIVE CARE UNIT IN THE UK

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¹St George’s University Hospitals NHS Foundation Trust, Department Of Paediatrics, London, United Kingdom, ²St George’s Hospital, Neonatal Intensive Care Unit, Tooting, United Kingdom

Background: Neonatal units use many antibiotics, yet there are few published data on neonatal antibiotic prescribing practices. Antimicrobial stewardship practices have been undertaken on our Neonatal Intensive Care Unit (NICU) since the early 2000s. We aimed to evaluate the antibiotic prescribing trends on the NICU between 2014-2018, including subgroups of patients with necrotising enterocolitis (NEC) and central-line associated bloodstream infections (CLABSI).

Methods: A retrospective analysis of all antibiotic prescriptions between 2014-2018 was performed using data from the NICU database, BadgerNet. Prescriptions for antifungals and antivirals were excluded. Antibiotics were categorised according to the WHO Access, Watch and Reserve recommendations. We investigated overall antibiotic use on the NICU and investigated antibiotic use in infants with necrotising enterocolitis (NEC) born at 30 weeks and under and those with central-line associated bloodstream infections (CLABSI).

Results: The mean duration of antibiotics received per infant decreased significantly from 13.9 (SD 6.2) to 10.3 (SD 6.2) days between 2014-2018 (p=0.009). Approximately 80% of prescriptions were from the Access category, with minimal variations between years. Infants who developed NEC received significantly more antibiotics over their NICU stay compared with infants who did not; 35 (SD23.2) versus 14 (SD17.5) days (p=0.003). Of 127 infants with a positive blood culture with a central line in situ, 70.3% were staphylococci (93.1% coagulase-negative staphylococci, 6.9% staphylococcus aureus) and 19.3% were Gram-negative bacteria.

Conclusions: We have shown an overall reduction in the use of antibiotics on our NICU over the last five years, demonstrating the benefit of ongoing antimicrobial stewardship practices. We have also highlighted that infants who develop NEC will, on average, be on antibiotics for over twice as long compared to infants who don’t develop NEC, making it a target for antimicrobial stewardship.
RETROSPECTIVE REVIEW OF PAEDIATRIC BLOOD CULTURE CONTAMINATION RATES IN A LARGE TEACHING HOSPITAL IN EAST MIDLANDS, UK.

S. Koo, N. Elhefnawy
University Hospitals of Leicester NHS Trust, Microbiology, Leicester, United Kingdom

**Background:** Blood cultures remain the mainstay of laboratory diagnosis of bloodstream infections. Positive blood cultures enable the identification of the pathogen and allow for antimicrobial susceptibility testing. Blood culture contamination may result in unnecessary use of antimicrobials and increased resource implications for both the laboratory and healthcare facility. There are currently no standards for allowable blood culture contamination rates in children. The agreed international standard in adults is 2–3%. We have taken this as our standard.

**Methods:** All blood cultures from patients aged ≤ 16 years received by the microbiology department at University Hospitals of Leicester NHS Trust over 1 year period was obtained using the hospital’s laboratory electronic reporting system. A retrospective review of the organisms isolated was then performed against information obtained from documented clinical discussions and electronic patient records. The presence of skin-type or environmental organisms in the absence of intravascular devices or prosthesis were deemed as contaminated blood cultures.

**Results:** In total, there are 1544 sets of blood cultures received by the laboratory. 115 (7.4%) samples were culture positive with ≥1 organisms. 63 (4%) of these were considered as true pathogens and 52 (3.36%) were regarded as false positives or contaminated. The most common organism regarded as a contaminant was *Coagulase-negative Staphylococci* (CoNS). Among other contaminants isolated were *Streptococcus viridans*, *Propionibacterium species*, *Corynebacterium species*, *Bacillus simplex* and *Kocuria Rhizophila*.

**Conclusions:** The overall paediatric blood culture contamination rate in our trust is at 3.36%. Although this is short of the international standards for adults, we believe that it is an acceptable contamination rate in children considering the challenges and difficulty in obtaining sterile blood cultures, especially from the very young population where the majority of the blood cultures were taken from.
Background: Sepsis represents a common cause of morbidity in the Neonatal Intensive Care Unit (NICU). Although empirical antibiotic treatment pending blood culture results is the rule when sepsis is suspected, many infants present non-specific symptoms that may delay the initiation of treatment. Our objective was to assess the value of clinical and laboratory parameters in predicting septicemia (positive blood culture) in NICU infants.

Methods: Initially (derivation study), we retrospectively reviewed clinical files of 120 neonates with suspected sepsis symptoms (63 with positive blood culture) and we identified clinical and laboratory parameters associated with proven sepsis: 48 hours prior, 24 hours prior and on blood culture day. These parameters were combined into a sepsis prediction score (SPS). Subsequently (validation study), we prospectively validated the performance of SPS in a cohort of 145 neonates.

Results: Identified parameters were: temperature >38°C, PLTs <150.000/mm3, feeding volume decrease >20%, blood glucose changes >50%, CRP >1mg/dL, peripheral circulation disturbances, increased oxygen requirements, respiratory symptoms. The derivation cohort AUC combined parameters was 0.918 on the blood culture day, 0.747 at 24 hours prior and 0.752 at 48 hours prior. The validation cohort AUC was 0.912 on the blood culture day, 0.729 at 24 hours and 0.579 at 48 hours prior. On the blood culture day, SPS >3 could predict sepsis with 89.4% sensitivity, 84.3% specificity, and 5.7 positive LR.

Conclusions: Prediction of neonatal sepsis remains a challenge as many non infectious conditions may resemble septicemia. A combination of selected clinical and laboratory parameters may predict septicemia in Neonatal Intensive Care Unit infants and contribute in early confrontation. The sepsis prediction score may be very helpful for the clinicians in order to prescribe antibiotics on time, given the severity of neonatal sepsis.
Background: Factors linked to the antibiotic-resistance in preterms were not much studied. Integrons are genetic elements widely involved in antibiotic-resistance dissemination in Gram-negative bacteria (GNB). They acquire, exchange and express antibiotic-resistance genes embedded within gene cassettes. The aim of our study was to determine the dynamic acquisition of integron in stools of preterms during their hospitalization in neonatology units.

Methods: The study was prospective and realized in 5 different neonatology unit on preterms of 28 to 34 weeks of gestational age. Meconium and stools at 7 days and all the 15 days after until the neonatology unit out of newborns and a stool of the mother were sampled. Integrons were detected by a real time PCR method, directly on samples and different acquisition factors of integrons were also studied.

Results: 201 duos (newborns/mother) were included with an average gestational age of 31 weeks +1 day. 838 samples of newborns and 165 stools of mother were analyzed, for all newborns at least 3 samples were realized. 7 newborns had a positive meconium and 61 in total at their exit of the neonatology unit, whereas 66 stools of mother were found positive. The twinship absence, the presence of integon in the mother stool, a gestational age > 32 weeks and a breastfeeding were found as risk factors of integron acquisition.

Conclusions: The integron acquisition could occur before the birth and progress in the first weeks of the preterms. We described 4 risk factors of integron acquisition.
**E-POSTER VIEWING**
**E-POSTER VIEWING - ALL OTHER TOPICS**
10-28-2020 8:00 AM - 7:00 PM

**RISK FACTORS AND ANTIBIOTIC SUSCEPTIBILITIES OF ACINETOBACTER INFECTIONS IN CHILDREN**

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**Background:** *Acinetobacter* spp are gram-negative coccobacilli which have the ability to survive in hospital environment leading to health-care associated infections. Treatment is difficult due to development of resistance to the major antibiotic classes. We aimed to evaluate antibiotic resistance profiles of *Acinetobacter* spp. identified from blood, urine, cerebrospinal fluid, respiratory or wound culture of children hospitalized in a tertiary care hospital in Istanbul during a six-year period.

**Methods:** Data of children with *Acinetobacter* spp growth between January 2012 and September 2018 were retrospectively analyzed. Age, sex, underlying illness, reason of hospitalization, culture sample type, clinical illness, antibiotic susceptibility, and outcome of patients were evaluated. The organism was considered insignificant (either colonization or contamination) if clinical disease was absent and as true infections if the patients received appropriate treatment.

**Results:** 58 patients with *Acinetobacter* spp growth were identified. Mean age of patients was 66 months. 28 growths were true infections (12 bloodstream infections, 11 pneumonia, 3 urinary tract infections, and 2 wound infections). Most common underlying disorders were neuromuscular disorders (28.6%) and hematologic malignancies (32.2%). Previous use of antibiotics (87.3%) and presence of central venous catheters (67.9%) were the most common risk factors. Mortality rate was 25%. Resistances to ampicillin-sulbactam (SAM), piperacillin-tazobactam, ciprofloxacin, meropenem, amikacin, and trimethoprim-sulfamethoxazole were 73.1%, 56%, 55.6%, 50%, 44.4%, and 30.8%, respectively.

**Conclusions:** Multidrug-resistant *Acinetobacter baumannii* has emerged as an increasingly important pathogen that causes nosocomial infections. In this study the most frequent clinical manifestations of *Acinetobacter* infections were bloodstream infections and ventilator-associated pneumonia. 20 percent of *Acinetobacter* growths were polymicrobial. Resistance rates to SAM and carbapenems were significant. None of the isolates were resistant to colistin. Colistin was given in combination with meropenem in carbapenem resistant cases.
**SAFE INTRODUCTION OF DRY CORD CARE OF UMBILICAL CORD REQUIRES GOOD CONTROL OF HYGIENE FACTORS**

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**Background:** Omphalitis may cause serious complications and contribute to neonatal morbidity and mortality. Staphylococcus aureus is the most common cause. Umbilical cord care is important to prevent omphalitis. In Gynecology-Obstetrics department of General Hospital of Rhethymnon (Greece) 70% Alcohol is used as anticeptic umbilical care since 5 years the incidence of omphalitis was 0.5-1% per year. We introduced Dry Cord Care according to WHO recommendations.

**Methods:** For 3 months (from July to September of 2019) we just introduced dry Cord Care withdrawing the use of Alcohol to healthy full term neonates. An increase of omphalitis cases was mentioned and, the next three months (from October to December of 2019), measures of proper hand hygiene and better drying of the cord was decided to be applied.

**Results:** During the first 3 months, 9/130 (7%) neonates developed omphalitis. Six of them were treated topically by Mupirocin. Three were hospitalized and Staph. aureus, Mupirocin resistant but MSSA was cultured from the cord sample. During the 2nd trimester the rate was 2/135 (1.4%), both neonates were hospitalized and Staph. aureus, one of them MRSA, was cultured. The incidence of omphalitis increased about 7 times during the first trimester and decreased 5 times after introducing hygiene measures (2nd trimester), but incidence was still >1%.  

**Conclusions:** Hand hygiene of the personnel and care givers should be ensured, before changing the umbilical care to simple Dry Cord Care, as this is the most common way of bacteria contamination. The use of Alcohol could have substituted the hand hygiene in the past. Mother’s training and surveillance of hand hygiene was further planned. Increase in cases of omphalitis treated by antibiotics could lead to resistance of the causing bacteria.
INTEREST OF INTEGRONS IN CHILDREN’S URINARY INFECTION AT THE PEDIATRIC EMERGENCY

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¹CHU Limoges, Pédiatrie, Limoges, France, ²Faculté de médecine, Limoges, Inserm U1092, Université De Limoges, Chu Limoges, Limoges, France

Background: Integrons are genetic elements widely involved in antibiotic-resistance dissemination in Gram-negative bacteria (GNB). Integron can acquire, exchange and express antibiotic-resistance genes. A previous study on sepsis has shown that integrons had a Negative Predictive Values (NPV) > 95% for predicting antibiotic resistance particularly for third-generation cephalosporins (3GC). Urinary tract infections (UTIs) are a common reason for presentations at paediatric emergency departments (PED). The aim of our study was to determine the NPV of integrons detection for predicting antibiotic resistance in a PED for UTIs.

Methods: This study was conducted in the PED of a tertiary hospital from 1st February 2018 to 31st March 2019. Children, with a positive urine culture for GNB, were included after consent was signed. Children included were eligible for analysis provided that they had retrospective validation of the diagnosis of UTI. Integrons were detected by a real time PCR method, directly on urinalysis and on isolates.

Results: 72 children were enrolled, 54 with a pyelonephritis and 18 a cystitis. In 70.8% of UTI, 3GC were used as probabilistic treatment. An integron was detected in 15 urine samples (20.8%). NPVs for cotrimoxazol (SXT) and cefotaxim were 100%.

Conclusions: To our knowledge, this study is the first to examine the clinical value of integrons as a genetic marker of antibiotic resistance, in UTIs managed at PED. The NPV of integrons detection could be high enough to affect empiric antimicrobial strategy and help to select a first-line treatment better tailored to each individual patient, using SXT whenever possible.
PERIOPERATIVE ANTIMICROBIAL PROPHYLAXIS IN A TERTIARY CHILDREN’S HOSPITAL

A. Vlachou¹, I. Kopsidas¹, A. Tzortzopoulou², F.-E. Dasoula¹, I. Kaliviotis³, A. Passalidis², N. Spyridis¹, M. Tsolia¹

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Background: Antibiotic overuse has led to the development of multidrug resistant microorganisms with an impact on patients' length of stay and hospital costs. Perioperative Antimicrobial Prophylaxis (PAP) is the administration of antibiotics before an operation to prevent surgical site infections. We sought to describe practices in the surgical departments of a tertiary Children's hospital in Greece in order to identify targets for improvement of judicious antibiotic use.

Methods: All operations performed in the Surgery Departments of a tertiary Children's hospital were recorded prospectively for 2 months. Data recorded included patient demographics, type of operation and wound class, antibiotic agents administered along with time, dose and duration of regimen. Study data were collected using REDCap electronic data capture tools.

Results: 81 surgeries were recorded at the First Surgery Department. PAP was administrated at 33.3% of the clean and 100% of the clean contaminated surgeries. 61% of the patients received the first dose of antibiotics after the surgery. In all cases the antibiotic administration continued after the surgery. The mean duration of the regimen was 6 days for clean and 10.8 days for clean contaminated surgeries. 101 surgeries were recorded at the Second Surgery Department. PAP was administrated at 50% of the clean and 100% of the clean contaminated surgeries.

Conclusions: [Results] 79% of the patients received the first dose of antibiotics less than 60 minutes before surgery. In 66/71 (93%) cases the antibiotic administration continued after the surgery. The mean duration of the regimen was 2 days for clean and 4.2 days for clean contaminated surgeries. [Conclusions] We identified injudicious antibiotic use regarding PAP both in the indication (type of operation) as well as in the time of initiation and the duration of the regimen prescribed. These targets are used to educate the design of an intervention with the aim of decreasing unnecessary antibiotic use.
CONCORDANCE OF BLOOD CULTURE AND COLONIZATION IN NEONATES WITH LATE ONSET SEPSIS ON THE NEONATAL INTENSIVE CARE UNIT

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**Background:** Late-onset neonatal infection (LOS) is still an important cause of morbidity and mortality in neonates admitted to the Neonatal Intensive Care Unit (NICU). Weekly surveillance cultures of rectum and throat identify potential pathogen microorganisms colonizing the individual neonate. In case of suspicion of LOS, empiric antibiotics are started. Individual surveillance culture results are taken into account, the standard empirical antibiotic policy is adjusted as necessary. We studied the degree of similarity between the causative microorganism of LOS in the blood culture and the microorganisms found in the individual surveillance cultures.

**Methods:** A retrospective, descriptive study, including all late-onset sepsis episodes with a positive blood culture from January 2009 to January 2019 at the NICU Isala, Zwolle. After data selection, 98 positive blood cultures were analysed and compared with the results of the surveillance cultures taken 1 week before the sepsis period.

**Results:** The causative agent in the blood culture correspond in 61/98 (62%) to the results of the previously taken surveillance cultures, with the highest agreement for the gram-negative causative agents (79%) and for Staphylococcus aureus (88%). If only positive surveillance cultures were analysed, the correspondence was higher: 82% for the total, 86% for gram-negative causative agents and 97% for Staphylococcus aureus. In case of lower gestational age or birth weight an increase in similarity between positive blood culture and surveillance cultures was seen.

**Conclusions:** A great similarity was found between the causative agent in the blood culture and a positive surveillance culture in case of LOS, in particular with gram-negative pathogens and Staphylococcus aureus. Therefore, performing surveillance cultures seems useful for the individual patient and adjusting the empirical antibiotic policy on the base of known colonisations justified.
Laboratory Reporting of Positive Blood Culture in Paediatric Patients at Prince Sultan Military Medical City - KSA

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Background: Laboratory reporting of positive blood cultures (PBCs) at any medical care institution is crucial and essential for infection control purposes, antibiotic stewardship programs, and guidance for proper antimicrobial coverage. The aims of this study were to describe epidemiological and microbiological data of pediatric patients with PBCs, and to determine resistance patterns of blood isolates.

Methods: A retrospective, descriptive study conducted at Prince Sultan Military Medical City, Riyadh KSA, from February to July 2019. All PBCs from pediatrics were daily identified from microbiology reports and analyzed for demographical and microbiological data.

Results: 132 PBCs were isolated from 108 patients. 97 cases (73.5%) were true PBCs, 52 cases were categorized as hospital-acquired infection (HAI), 21 cases occurred in ICU. The most frequent bacteria were Klebsiella spp (12 cases), Serratia spp (10 cases), Staphylococcus aureus (9 cases) and Enterococcus spp (9 cases). Interestingly, 44% of all Klebsiella spp were resistant to cephalosporin 3rd generation and 100% were sensitive to Carbapenems. In addition, 22% of Staphylococcus aureus were methicillin resistant, and 14% of Enterococcus spp were vancomycin resistant.

Conclusions: Our study showed a high rate of contaminated blood culture. CONS were the most frequent bacteria isolated in hospital and community true PBCs and Klebsiella spp had high resistance rate to cephalosporin 3rd generation.
A COMPARISON OF TRADITIONAL AND MOLECULAR TECHNIQUES OF IDENTIFYING PATHOGENS IN SUSPECTED PAEDIATRIC MENINGITIS IN A PERIPHERAL CENTRE.

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Background: BioFire FilmArray meningitis/encephalitis (BioFire-ME) panel is a diagnostic tool which uses multiplex PCR to identify 14 of the most common viral, bacterial and yeast pathogens on CSF samples in as quickly as one hour. Biofire-ME is more sensitive and timely than CSF cultures and remains highly sensitive if antibiotics have been given prior to lumbar puncture. We aimed to evaluate if an earlier diagnosis improves patient outcomes regarding mortality, transfer to tertiary centres, LOS or duration of antibiotic therapy.

Methods: A retrospective analysis of the CSF samples of all children under the age of 16 years for the indication of suspected meningitis over a 2 year period was performed. The BioFire-ME was performed on samples with a pleocytosis or in young infants with a high index of suspicion for meningitis/encephalitis but without pleocytosis. Organisms identified were compared with CSF protein, glucose, cell counts and culture, and blood culture and other microbiology samples.

Results: Overall enterovirus was the most common pathogen detected on BioFire-ME. The primary endpoints of CSF-Culture positive results were compared with case matched controls from before the introduction of the panel. BioFire-ME significantly reduced time to diagnosis in most instances. BioFire-ME did not reduce LOS, transfer to tertiary care or duration of treatment in culture positive cases. Cases with negative BioFire-ME and traditional microbiology studies had a significantly shorter LOS than children with a positive result on BioFire but negative CSF and blood cultures.

Conclusions: Suspected meningitis/encephalitis is a common presentation to peripheral hospitals, particularly in young infants and neonates. These patients contribute a significant proportion of our admissions although confirmed cases remain relatively rare. BioFire-ME led to both quicker positive and negative results however this did not improve our primary endpoints.
SCRIPT FOR PAEDIATRICS- CREATING A SMARTPHONE APPLICATION (APP) THAT IMPROVED ANTIMICROBIAL PRESCRIBING FOR CHILDREN

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Background: Paediatrics is an often overlooked group for antimicrobial stewardship interventions. However, 97\% of New Zealand five year olds have received antibiotics (median 8 courses/child). Prescribing is complex due to age- and weight-based adjustments, unpalatable preparations and inappropriate allergy labelling. Starship Hospital’s >250 guidelines, 15\% including antimicrobials, are frequently poorly utilised. Using these, community guidelines, national formulary and subspecialist consultation, 31 algorithms were developed. Each algorithm used information including diagnosis, age, antibiotic allergy history and resistant organism colonisation to give antimicrobial prescribing advice. These formed the basis for the Script for Paediatrics smartphone app.

Methods: Paediatric inpatient and emergency department prescriptions were reviewed before launch of the app and six months afterwards. These included all patients with diagnoses included in Script for Paediatrics and excluded targeted prescribing and medications commenced prior to admission. Two independent graders, blinded to whether data was pre or post-app then graded each prescription as appropriate, inappropriate or high risk.

Results: >4500 patients records were reviewed to identify 711 antimicrobial prescriptions that matched inclusion criteria. During the initial audit period, 239/346 (69\%) of the presciptions were considered appropriate, following launch of Script for Paediatrics this rose to 304/365 (83\%). This demonstrated a significant improvement ($x^2$, p<0.001). High risk errors also decreased from 7/346 (0.02\%) to 3/365 (0.008\%).
Conclusions: While antimicrobial prescribing smartphone apps in adults have shown mixed results, our study has demonstrated significant improvements in paediatric prescribing. This may reflect the greater complexity and need to consult guidance felt by paediatric prescribers. The improvements seen mean both improved clinical care for individual patients and optimised antimicrobial prescribing in the era of antibiotic resistance. We intend to repeat the audit in one year to assess whether the improvement seen is sustained.
THE AVAILABILITY AND USE OF RAPID POINT-OF-CARE TESTS FOR THE MANAGEMENT OF ACUTE CHILDHOOD INFECTIONS IN EUROPE: A CROSS SECTIONAL SURVEY OF PAEDIATRICIANS

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Background: Correctly identifying which of the children presenting with an acute febrile illness have a potentially severe bacterial infection is difficult and results in unnecessary admissions, invasive investigations and overuse of antibiotics. Rapid point of care tests (POCTs) are recommended to reduce the use of antibiotics and medical resources but the extent of their availability and use by paediatricians in Europe is unclear. The aim of this survey was to describe the availability and use of POCTs by paediatricians for the management of acute childhood infections across Europe.

Methods: A cross-sectional survey of paediatricians was conducted between September and November 2019 using an online-questionnaire translated into 11 languages. Paediatricians working in primary care and hospitals across Europe were recruited through several research and clinical networks.

Results: 2,581 paediatricians (48% primary care paediatricians; 52% hospital paediatricians) from 24 countries completed the survey. The availability of POCTs varied across countries, e.g.: from 12% (Poland) to 91% (Austria) for C-reactive protein tests, from 4.6% (UK) to 99% (Slovenia) for group A streptococcal tests, and from 35.6% (Poland) to 99% (Spain) for urine dipsticks. The use of any diagnostic in a clinical scenario of an infant with undifferentiated fever varied from 42% (France) to 93% (Poland) among primary care paediatricians, and from 40% (France) to 91% (UK) among hospital paediatricians.

Conclusions: The availability and use of rapid POCTs for the management of acute childhood infections vary widely in primary care and hospital services across Europe. Additional research is needed to identify the reasons for this variability, including clinicians’ perceptions of POCTs and health systems factors. This study was conducted as part of the PERFORM project which is funded by the European Union’s Horizon 2020 research programme (grant No. 668303).
EVALUATION OF THE CAMPYLOBACTER QUIK CHECK TO DETECT CAMPYLOBACTER IN STOOL SAMPLES

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Background: Campylobacters are the main cause of bacterial diarrhea in the world. Antibiotic therapy is of interest in the first 3 days in order to shorten carriage and duration of the disease. Stool culture, the reference test to detect campylobacter, is obtained in a minimum of 48h. Now, several other different rapid tests are available. One of them is a rapid membrane enzyme-linked immunosorbent assay, the CAMPYLOBACTER QUIK CHECK™, commercialized by Abbott and providing a result in less than 30 minutes. The aim of this study was to evaluate its performance.

Methods: This retrospective study was conducted in the Bacteriological Laboratory of Bordeaux University Hospital, France. One hundred and eight samples were analyzed. Culture was systematically performed, then specimens were frozen at -80°C until use. After thawing, specimens were tested by the rapid CAMPYLOBACTER QUIK CHECK™ following the manufacturers’ instructions, and by a molecular method. The reference test was a composite reference standard: a positive case corresponded to a positive culture and, in case of a negative culture result, by the association of a positive molecular test and the ELISA.

Results: Following the composite reference test, 53 stools were positive and 55 were negative. The Abbott test detected 1 additional positive sample and missed 2 cases, corresponding to e-swab stools, whereas culture did not detect 5 positive samples. Sensitivity of the CAMPYLOBACTER QUIK CHECK™ was 97% and specificity was 98%. In contrast, culture sensitivity was 90% and its specificity was 100%.

Conclusions: The CAMPYLOBACTER QUIK CHECK™ showed an excellent performance. It is a very easy test to use. Its main advantage is the rapidity in obtaining a result, enabling an adapted medical care if needed. The place of this test in daily clinical practice needs to be evaluated.
OUTBREAK OF A YERSINIABACTIN-PRODUCING STRAIN OF KLEBSIELLA AEROGENES IN AN AUSTRIAN NEONATAL INTENSIVE CARE UNIT


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Background: Yersiniabactin (Ytb) is a siderophore with a high affinity to iron, facilitating enhanced iron uptake in bacteria. Thus, it has been described as a potential pathogenic factor in some gram-negative rods. Klebsiella aerogenes is a gram-negative rod known to cause late-onset sepsis in newborn and premature infants, but an unusual pathogen to cause outbreaks in neonatal intensive care units. We describe an outbreak of a non-resistant, yersiniabactin-producing K. aerogenes strain, colonizing 16 infants at a single Level III NICU in Vienna, Austria.

Methods: K. aerogenes isolates were tested for resistance according to current EUCAST recommendations. All isolates obtained from colonized patients and 7 comparative samples were genotyped using whole genome sequencing (WGS) combined with core genome multilocus sequencing type analysis. Ytb production was evaluated by luciferase assay.

Results: 16 cases were colonized with K. aerogenes over a three-month period. 13 patients showed no signs of infection with K. aerogenes, whereas three patients developed blood culture-proven necrotizing enterocolitis, two complicated by sepsis, one of whom died. No sample showed acquired resistance. In total, 25 K. aerogenes samples were further analyzed. Genetic sequencing revealed no significant genetic difference between 17 of 18 isolates from colonized patients. All 18 strains mentioned expressed the high pathogenicity island, necessary for the production of Ybt. Six exemplary cases were proven to produce Ybt in vitro.

Conclusions: This is the first report of an outbreak of a yersiniabactin-producing K. aerogenes strain causing infection in preterm infants. We hypothesize that, due to improved iron-uptake, this strain depicted higher virulence than non-yersiniabactin producing ones. Additional to containment measures, early initiation of WGS and extended search for pathogen virulence factors could be pivotal in the management of ICU outbreaks in the future.
DIFFERENT FORMS OF THE TROPICAL INFECTION IN ONE PATIENT

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Title of Case(s): Different Forms of the Tropical Infection in One Patient

\textbf{Background:} This is a unique case report from Armenia describing cutaneous and visceral forms of Leishmaniasis infantum in one patient: 2.5 years old girl presented with symptoms of Localized Cutaneous Leishmaniasis (LCL) one year after recovery from Visceral Leishmaniasis (VL).

\textbf{Case Presentation Summary:} The first admission was in 05.2017 with the following complaints: fever, general weakness, abdominal mass, loss of appetite and pallor. The patient has not traveled abroad. Laboratory analysis and instrumental investigations showed pancytopenia and hepatosplenomegaly. Taking into consideration the complaints and endemic region for leishmaniasis (Syunik region), bone marrow puncture was performed and Leishmania infantum was detected. Additionally, serological tests of VL were positive. After the confirmation of diagnosis of VL treatment was initiated with Meglumine Antimonate, but after 6 injections patient developed prolongation of QT interval and the treatment was interrupted. It was continued with Amphotericin B deoxycholate which was also unsuccessful. Hence, the patient had intolerance against 2 main antileishmanial medications. The management was completed with intravenous injections of Liposomal Amphotericin B. The patient was discharged after full recovery with 1-year follow-up. In 08.2018 she was admitted second time with a single lesion on the right cheek. Physical examination revealed an erythematosus nodule with a central hyperkeratotic crust. The results of Laboratory investigations were unremarkable. Based on the presence of VL in the past medical history and resemblance of the lesion to LCL (caused by L. infantum) cutaneous leishmaniasis was suspected. For the confirmation of the diagnosis biopsy of the lesion followed by microscopy/PCR are warranted. However, the lesion was spontaneously resolved without treatment as in most of the cases of LCL.

\textbf{Key Learning Points:} Although, spontaneous resolution of the lesions is expected in most of the cases with LCL, further investigations (biopsy of the lesions with microscopy and/or PCR) are warranted for the confirmation of diagnosis.
Title of Case(s): Fever in a returning traveller

Background: This is a case of an unwell child, who may well have died were it not for a broad range of differential diagnoses and empirical management choices.

Case Presentation Summary: A 7-year-old boy became unwell after returning to the UK from a holiday in Queensland, Australia and Kuala Lumpur, Malaysia. Shortly before travelling he had minor surgery to remove a verruca on his foot, and he noticed erythema tracking from the wound site after playing in the sand in Queensland. This improved after oral flucloxacillin for presumed cellulitis. 8 days after returning home he began vomiting and had a fever of >40C. After 48-hours he developed rigors, abdominal pain and muscle aches, prompting attendance to the emergency department. His C-reactive protein was 394mg/L, and he was lymphopaenic (0.6x10^9/L). He was treated for suspected bacterial sepsis with ceftriaxone and gentamycin. Blood cultures grew Streptococcus epidermis, a presumed contaminant, but his condition did not improve after 3 days. He was transferred to a tertiary paediatric infectious disease unit. On examination he was noted to have tender hepatosplenomegaly and generalised lymphadenopathy. He was not meningitic, had no rashes, and cardiovascular/respiratory examinations were unremarkable. An ultrasound scan demonstrated 13cm hepatomegaly, 10cm splenomegaly, and gallstones without cholecystitis. CRP was 360mg/L, malaria films were negative. Doxycyline was empirically added to the antimicrobial regimen to cover Rickettsial disease, after which he quickly improved clinically. Subsequent serology confirmed a diagnosis of scrub typhus (Orientia tsutsugamushi).

Key Learning Points: This case highlights the need to consider a broad range of differential diagnoses when managing fever in a returning traveller, especially when initial antimicrobial choices do not result in clinical improvement. It also highlights the need for empirical treatment based on a good history and clinical examination, because confirmatory diagnostic tests will often take too long to complete.
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Title of Case(s): Do not forget about additional risks of treatment with tumor necrosis factor - alpha( anti-TNFα) therapy

Background: Treatment with Tumor necrosis factor -alpha( anti- TNF-α) agents has been associated with reactivation TB and progression from latent TB infection (LTBI) to TB disease in adults [1]. In pediatric cohort this data are limited.

Case Presentation Summary: 10-year old girl was hospitalized in the tertiary hospital in December 2016 for the planned anti- TNF-α (Adalimumab) injection as a treatment of ulcerative colitis. She had complains on weigh lost, worsening of intestinal syndrome which had started 3 weeks before admission and fever and cough - 1 weeks before hospitalization. Anamnesis vitae: She was diagnosed with ulcerative colitis in 8 years old and received treatment mesalozine and prednisolone since May 2014. Mantoux test have been performed irregularly: in 2007 (10 mm) and in 2009 (8 mm). Chest X-ray was done before initiation of anti-inflammatory treatment and was normal. In May 2014 she had a prolonged pneumonia which resolved on the cefoperazone, amikacin, rifaximinum, levofloxacin. At that time she was on immunosuppressive therapy (prednisolone). Anti-TNF-α therapy started at August 2015. Results of examination at the current admission: Blood test: WBC- 14.2 *10^9/L, Hb- 81 g/L, ERS -46 mm/h. CRP - 69.5 mg/L. CT scans : mediastinal lymph nodes enlargement, pleural and pericardial effusion, disseminated changes in lungs were found. Gastric aspirate on MBT was collected: microscopy for AFB and culture for M.tuberculosis were positive. Sensitivity test was performed: isoniazid, rifampicin, ethambutol, pyrazinamide - sensitive, streptomycin - resistant. She received antituberculosis treatment for 10 months, including rifampicin, ethambutol, pyrazinamide orally and isoniazid, levofloxacin -intravenous administered for 4 months of intensive phase.

Key Learning Points: - TB screening before TNF- treatment must carried out mandatory, using tuberculin skin test (TST) or /and interferon-gamma release assay (IGRA). - Aminoglycosides using in routine practice ( for example, for treatment pneumonia) in country with high MDRTB burden should be avoid.
Title of Case(s): The key is in the origin.

Background: Chagas disease is endemic in Latin American countries, especially in Bolivia. Spain is the European country with the most Bolivian migrants.

Case Presentation Summary: A 10-year-old boy was referred by his primary care doctor for suspected Chagas disease. He had negative serology when he was born, but after that he lived in Bolivia for 7 years. Chagas serology was done when he came back because his mother had a positive serology picked up by routine screening during current pregnancy. He denied palpitations and chest pain. No constipation, reflux symptom, neither paresthesia. We diagnosed Chagas disease by positive T. cruzi antibody by ELISA and positive T. cruzi antibody by immunochromatographic test. Quantitative IgG by ELISA was 7.85. Although, T. cruzi PCR was negative. General analysis, chest x-ray, EKG and echocardiography were normal. Neither esophagogram nor barium enema were performed because of the absence of symptoms. He started benznidazole treatment at 5mg/kg/day. 5 days after starting, he presented with an itchy rash in periumbilical region. 10 days later it extended to his trunk, face, ears, extremities and genital area. No mucosal involvement. Benznidazole was stopped and the rash improved. After a month we restarted benznidazole together with prednisone at 1mg/kg/day. He completed 2 months of treatment. After that, T. cruzi PCR persisted negative but IgG titers remained positive at 7.94. He continues asymptomatic during follow up after 2 years.

Key Learning Points: Chagas disease should be suspected in individuals who have lived in endemic areas, even if they were not born there. Attention should be paid to possible adverse effects of the treatment. Treatment in patients in indeterminate or chronic phase is controversial. However, it is generally recommended to treat under 18 years old.
Title of Case(s): Six months old previously healthy boy - prolonged severe respiratory virus infection

Background: The patient is a six months old full term healthy boy born in Finland, he was abroad on vacation with the family, got rhinovirus infection, was referred to local university hospital intensive care unit for two weeks, and finally transferred to Finland by ambulance flight. In Finland untypical pneumonia, later absence of T and NK cells in blood and ultimately high copy number of pneumocystis jirovecii in BAL aspirate was diagnosed. Finally, cord blood stem cell transplantation was performed. Newborn screening for SCID is under heavy discussion and debate in Finland and in other European countries.

Case Presentation Summary: The patient is a 6-months-old full-term healthy boy. He travelled for vacation with family. Due to infection symptoms, he was referred to hospital, tested positive for rhinovirus, admitted to PICU for two weeks, and finally transferred home. At home country he was treated in PICU at university hospital. Untypical pneumonia was diagnosed. Lymphocyte count was decreased (1.46 e9/l). Flowcytometry revealed absence of T cells and NK cells. B-cell count was normal, IgG and IgA levels were under detection limit, IgM 0.4 g/l. Bronchoscopy was performed, and high copy number of pneumocystis jirovecii and rhinovirus were detected. CMV was tested negative. Intravenous sulfa-methoxazole, fluconatsol and gammaglobulin were initiated. HLA genotyping of the patient and the first-degree family member were performed. Later, HSCT with umbilical cord blood stem cells was successfully performed, however, T-cell engraftment, especially CD8 T-cell engraftment, has been slow. Neonatal screening for SCID is under discussion and debate. In clinical point of view, early detection of SCID, before emergence of infections, is crucial for the survival of SCID patients. Unfortunately, in absence of SCID screening, most of the SCID patients are diagnosed after the emergence of first infection(s).

Key Learning Points: Early detection of SCID, before emergence of infections, is crucial for survival of SCID patients.
HOW TRAVEL HISTORY HELPED DIAGNOSING A CHILD WITH FOCAL SEIZURES

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Title of Case(s): How travel history helped diagnosing a child with focal seizures

Background: Neurocysticercosis is a clinical syndrome caused by the larval stage of Taenia solium. Approximately 29% of seizures in endemic areas are caused by neurocysticercosis. We present a case of neurocysticercosis successfully treated in a child who presented focal seizures.

Case Presentation Summary: A two-year-old girl of Indian origin was taken to the emergency department in Italy for a nonfebrile focal seizure. On arrival, physical examination was normal. Patient history was negative for previous seizures and the child was otherwise healthy. To assess the possible origin of the seizure, a CT scan was performed, which showed in the right occipital lobe and in the left parietal lobe, two hypodense round lesions (max diameter 5 mm and 7 mm) with a small hyperdensity within, associated with perilesional edema. The MRI scan confirmed the lesions (fig A-B) and suggested a cystic infectious process. Laboratory findings, including cultural exams on blood, liquor and stool, were negative for infection. In particular serology for cysticercosis on blood and liquor were negative. Chest X-ray and abdominal ultrasound did not demonstrate other localizations of infection. A more focused travel history revealed that the patient had travelled to a rural area in India one week before. The neuroimages were reviewed and, despite negative serology, neurocysticercosis was diagnosed. Treatment with Albendazole (7.5 mg/kg every 12 hours for 15 days) and Prednisone (10 mg for 7 days, then decalage) was therefore stared. In addition, seizure prophylaxis with Carbamazepine was administered. One year later, MRI images (fig. C-D) showed a substantial decrease in size of the lesions. The patient did not experience other seizures, Carbamazepine was therefore discontinued.
**Key Learning Points:** In conclusion, when confronted with infectious diseases an accurate travel history is of the utmost importance, especially in patients originally from tropical regions. Neurocysticercosis must be considered in the presence of suggestive neuroimaging, even with negative serology.
Title of Case(s): 9 year old girl with purple lesions in the back of her legs

Background: Cutaneous tuberculosis is very rarely seen nowadays. It represents 1-2% of newly diagnosis cases of tuberculosis. However it should be suspected in children with slow healing lesions.

Case Presentation Summary: A 9 year old girl presented to the Emergency Department (ED) with purple lesions in the back of her legs which had started four weeks before after a common cold. She was of Spanish descent, had never travelled abroad and was previously healthy. A chest X-ray was performed, which was normal and a raised CPR of 2.79 mg/dl was found in blood tests. She was diagnosed of erythema nodosum, ibuprofen was prescribed and she was sent home. Several days later she returned to the ER because the lesions had worsened, she was referred to Dermatology. A skin biopsy was performed and the PCR for \textit{M. tuberculosis} was positive. The mother of our patient remembered that she had had pulmonary tuberculosis while she was pregnant with her. An IGRA was performed when she was 2 months old and it was positive. She was treated as a latent tuberculosis with 6 months of isoniazid. The patient was diagnosed of cutaneous tuberculosis and treatment with isoniazid, rifampicin, pyranzinamide and ethambutol was started. It was deescalated to isoniazid and rifampicin after two months. It had to be extended to 9 months because of the slow improvement.
Key Learning Points: There are several lesson to learn from this case. The first one is that tuberculosis may have an atypical presentation and we must consider it in the differential diagnosis of cutaneous lesions. The second one is that children exposed to tuberculosis during pregnancy have a high risk of extrapulmonary tuberculosis, and latent tuberculosis infection in this group should be treated for 9 months per Spanish guidelines. Finally, there is not an established duration of treatment for extrapulmonary tuberculosis so we must consider each case individually.
A SLAM DUNK DIAGNOSIS

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Title of Case(s): A slam dunk diagnosis

Background: This case report will focus on the epidemiology, risk factors, investigations and management of this rare manifestation of Histoplasma. It will highlight the diagnostic uncertainty which frequently occurs. Ultimately this case was discussed with the United States of America’s leading expert in Histoplasma who reassured us that on reviewing the full history and investigations it was a “slam dunk diagnosis” of CNS histoplasmosis.

Case Presentation Summary: A seven year old boy born in South Africa with an extensive travel history developed a metastatic medulloblastoma while he was resident in Singapore. He was successfully treated in the United States of America with debulking surgery, radiotherapy and chemotherapy. He returned to Singapore in remission and developed a slowly progressing encephalopathy and encephalitis complicated by a hemispheric stroke. He was extensively investigated and ultimately diagnosed with a probable histoplasmosis infection of the central nervous system (CNS). Following his diagnosis he was transferred to the United Kingdom for rehabilitation and a second opinion. In Singapore he started treatment with voriconazole but as per international guidelines for CNS histoplasmosis infection he was switched to itraconazole. During his stay he underwent repeat investigations including a brain biopsy. His imaging and cerebral fluid investigations suggested progressive disease with a CNS vasculopathy and the targeted therapy for the histoplasmosis CNS infection was intensified including steroids for the anti-inflammatory effect.

Key Learning Points: Diagnosing central nervous system histoplasmosis is challenging and treating it might be even more challenging. Ultimately discussion with multiple specialists, including national and international fungal experts, was needed to reach a consensus regarding the diagnosis and optimal treatment for this patient.
AN INFANT WITH MULTIPLE EPISODES OF PNEUMONIA, RECURRENT WHEEZING, SKIN ABSCESSES AND SEVERE MILK ALLERGY

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Title of Case(s): An Infant with Multiple Episodes of Pneumonia, Recurrent Wheezing, Skin Abscesses and Severe Milk Allergy

Background: Recently, a novel Hyper immunoglobulin E syndrome (HIES) has been attributed to mutations in the gene encoding ARPC1B, a key molecule of the cytoskeleton. Omozygous ARPC1B mutation cause an autosomal recessive syndrome of Combined immune deficiency and hypersensitivity. Less than 20 individuals have been diagnosed with ARPC1b deficiency syndrome worldwide.

Case Presentation Summary: In November 2018, a 6-month old infant was urgently transferred to our tertiary hospital due to severe Lower Respiratory Tract Infection (LRTI). Previous Hx: Six previous admissions due to wheezing, DIB and significant leukocytosis (WBC 20,000-48,000). Family Hx: This is a family of consanguineous parents with 5 living children. The second child of the family has died aged 3 due to CNS infection. The eldest son suffers from recurrent infections and hypothyroidism and the 10-year old daughter from severe failure to thrive. Treatment and Outcome: Upon admission, the infant was treated with IV Teicoplanin and Piperacillin-Tazobactam, nebulizers and supplemental oxygen. Imaging revealed a large opacity occupying nearly all the left lung and blood tests showed WBC 41,720 (Neu 78%) & CRP 136 mg/L. He gradually improved over the next 3 weeks until he developed a Pseudomonas perianal abscess and became systemically unwell. While under treatment with IV Ceftazidime & Clindamycin, he developed a second severe LRTI on Day 30. On Day 35 he developed anaphylactic shock after having formula milk. He then gradually developed severe eczema. Immunological work up revealed elevated IgA & IgE, normal IgG & IgM, normal C3, C4 & CH50. Lymphocyte phenotyping showed normal counts of T, B and NK-cells, but reversed ratio of naïve and memory T-cells. Th17 count was normal and DHR and IRAK-4 tests were normal. Specific IgE tests (RAST) were high for multiple food allergens. Whole exome sequencing was performed and revealed an omozygous ARPC1b mutation. The diagnosis of autosomal recessive HIES was made and the patient was referred to BMT. He received BMT in August 2019 and he has recently been discharged home.

Key Learning Points: Recurrent and/or severe infections and allergy should rise the suspicion of primary immunodeficiency. Early diagnosis can lead to favourable outcomes.
Title of Case(s): A presentation of ear pain

Background: The overall incidence of tuberculosis in England is low, approximately 8.3 per 100,000. The majority of cases occur in London, with very few cases identified in Caucasian children on the Southern coast of England. While tuberculosis remains an uncommon presentation, difficulties arise as variable clinical manifestation can delay diagnosis.

Case Presentation Summary: A 2-year-old boy presented to a tertiary paediatrics hospital in the South of England with a 6-week history of ear pain, malaise and irritability. He had been seen in the community over the previous 6 weeks and had been prescribed 4 courses of antibiotics. On presentation he was febrile and lethargic. Examination found a left mastoid mass, with a dull, tense tympanic membrane. There were no neurological signs. CT head demonstrated subperiosteal parietal abscess and an extradural abscess, felt to be bacterial in origin, for which he underwent urgent surgical incision and drainage. Cultures were sent intra-operatively. He improved and was ambulated on IV ceftriaxone and oral metronidazole. Despite ongoing medical management, he represented 3 weeks later with worsening headache and ear discomfort. MRI demonstrated a persistent collection and he underwent repeat drainage of the collection. Cultures subsequently were identified as being positive for mycobacterium. This was considered most likely to be an atypical mycobacterium and he was commenced on clarithromycin and ritabutin. Two weeks later, the sample was identified as having grown mycobacterium tuberculosis, fully sensitive to first line therapy. The patient was commenced on two months of quadruple therapy (isoniazid, rifampicin, ethambutol, pyrazinamide), after which he was switched to dual therapy (isoniazid, rifampicin) with pyridoxine for a further ten months.

Key Learning Points: This case highlights the clinical variability of tuberculosis presentation, and the need to consider tuberculosis in the differential diagnosis, even in populations of low tuberculosis incidence. Delays in diagnosis and commencement of appropriate treatment are associated with further complications.
DIAGNOSTIC CHALLENGE AND TREATMENT OF NEWBORNS WITH INTRAUTERINE CONGENITAL MALFORMATION

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Title of Case(s): Diagnostic challenge and treatment of newborns with intrauterine congenital malformation

Background: Cytomegalovirus (CMV) is the main cause of congenital infection and can cause severe intrauterine malformations and especially damage in the central nervous system. To date, CMV treatment is performed only in postnatal period, only preventing the evolution of existing damage. The choice of prenatal treatment is of relevance as it may contribute to the reduction of sequelae left by the virus.

Case Presentation Summary: A 23-year-old woman at 9 weeks of pregnancy had fever, diarrhea, vomiting and skin rash, with spontaneous improvement. At 30 weeks, obstetric ultrasonography showed fetal brain malformation, being referred for high-risk antenatal care. At 30 weeks, CMV serology proved IgM: positive and IgG: positive, with high avidity, and Dengue IgM: positive. Valaciclovir 8g daily was prescribed at the 34th week, totaling 34 days of treatment. She underwent cesarean section at 39 weeks and gave birth to a 3975g boy with head circumference of 36cm. Peripheral blood CMV serology was IgG: positive, IgM: negative and urine CMV PCR: undetectable. At the age of 13 days, was performed a Panherpes PCR in urine: negative. No cerebrospinal fluid collection was possible due to technical difficulties. Transfontanelle ultrasound and brain magnetic resonance presented with multiple periventricular calcifications, ventriculomegaly and cerebral atrophy. Electroencephalogram showed diffuse depression of brain electrical activity. Fundoscopy and transient evoked otoacoustic emissions showed no alterations. The neonate was diagnosed with intrauterine treated congenital CMV infection.

Learning Points/Discussion: Intrauterine treatment with valaciclovir may have influenced negative PCR results at birth. However, severe brain damage was already present, what may have prevented a successful neurological outcome. Prenatal CMV screening may allow early treatment with valaciclovir. Further studies are needed to assess whether the use of valaciclovir really treats the concept or just makes postnatal diagnosis difficult, preventing virus isolation.
OBTURATOR EXTERNUS PYOMYOSITIS IN AN IMMUNOCOMPETENT ADOLESCENT

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Title of Case(s): Obturator externus pyomyositis in an immunocompetent adolescent

Background: Obturator pyomyositis is a rare condition in children. Diagnosis is often delayed because of its rarity, and the varied forms of its presentation cause it to be easily be missed. Pediatricians should therefore familiarize themselves with this condition and consider it as a possible differential diagnosis in patients presenting with an acute hip pain so that early surgical intervention is done if required.

Case Presentation Summary: A fourteen year old adolescent boy presented with complaints of fever, pain lower abdomen and groin and painful left leg movements. On examination child was febrile with a temperature of 39 degree celsius, pulse rate of 156 beats/minute, wide pulse pressure, respiratory rate of 40/minute and a blood pressure of 100/50 mmHg. Local examination revealed tenderness and swelling over upper part of left thigh and painful hip joint movements. Keeping a diagnosis of sepsis intravenous cefuroxime was started. Ultrasound left thigh and hip was suggestive of loculated collection over anteromedial aspect of upper thigh. MRI of left hip and thigh revealed myofascitis and collection in left obturator externus muscle, no involvement of hip joint. In view of persistant fever spikes antibiotics were upgraded to ceftriaxone and vancomycin. However over next 5 days fever and pain persisted. So incision and drainage was done and pus send for culture. Both pus and blood culture grew streptococcus pyogenes. Child was discharged after 2 weeks hospital stay on oral antibiotics.

Learning Points/Discussion: 1. Primary pyomyositis involving obturator externus muscle is rarely seen in children. 2. Usually there is a history of prior trauma or child is immunocompromised but in our case there was no history of any injury and child was immunocompetent. 3. Diagnosis can be difficult because pelvic pyomyositis is often mistaken for more common pathologies such as septic arthritis, osteomyelitis etc. So an early MRI scan is very important in management.
INSIDIOUS ARTHRITIS AND ITS DIFFERENTIAL DIAGNOSES

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Title of Case(s): Insidious Arthritis and its Differential Diagnoses

Background: Tuberculosis is one of the top 10 causes of death among children worldwide, and may affect many systems, including the osteoarticular which is responsible for 10 to 20% of cases of extrapulmonary tuberculosis. It's of potential relevance in the infant universe and usually appear in higher load joints, such as hip and knee. Its evolution is insidious, so the time elapsed for treatment can be very long.

Case Presentation Summary: Patient with left knee injury and edema four months ago. He went to a health service, with a knee radiograph without changes and discharged with splint for one week, without improvement. In another service, was evaluated by an orthopedist, with ultrasound presenting a heterogeneous collection in suprapatellar recess. Local puncture had no fluid outlet, being referred for rheumatology, which requested some exams, showing alterations in ANA (anti-hep 2 1/160) and PPD: 11 mm. Referred to pediatric infectology, presented suprapatellar and infrapatellar edema, without phlogistic signs. A knee radiograph, knee ultrasound and chest X-ray was requested. The ultrasound showed a thick fluid and a local puncture was performed, with purulent discharge. On return in pediatric infectology ambulatory, he presented phlogistic signs and limitation of movement in the left knee. A synovial biopsy was performed, presenting BAAR: positive and genexpert: rifampicin-sensitive Mycobacterium tuberculosis. Tuberculosis treatment started, with significant improvement in arthritis.

Learning Points/Discussion: - The diagnosis of osteoarticular tuberculosis is very hard, especially when there is no concomitant pulmonary condition. - Tests such as genexpert, BAAR and tuberculin skin test can be used to guide the investigation, but the definitive diagnosis is only performed with biopsy. - When faced with an insidious arthritis condition, tuberculosis should be part of the differential diagnosis in order not to delay treatment.
Title of Case(s): Surge in Invasive Group B Streptococcus (GBS) Disease

Background: Our institution sees around 15 infants with invasive GBS disease a year. From 14/10/19 to 15/11/19, the Infectious Disease team observed 8 infants who were diagnosed with invasive GBS early onset disease (EOD) or late onset disease (LOD). This prompted our team to notify the Ministry of Health and an investigation was conducted to ascertain if a clonal outbreak in the community was likely.

Case Presentation Summary: 2 EOD and 6 LOD infants were identified via positive culture in the cerebrospinal fluid and/or blood cultures. The 2 EOD neonates had symptoms of sepsis at birth. Both mothers had pyrexia and 1 had prolonged rupture of membrane. Maternal GBS colonization were unknown at delivery and only 1 mother received adequate intrapartum antibiotics. The 6 LOD infants were born in other hospitals and had no significant intrapartum risk factors. Fifty percent of LOD infants had bacteremia and meningitis. Whole genome sequencing of the EOD isolates showed type II ST1 and type VI ST1. The LOD isolates belonged to serotype III; five were ST17 and one was ST17-like. They were diverse by core genome analysis. The type III ST17 isolates carried hygA, a gene that encodes for GBS adhesin that is associated with hypervirulence. HvgA was not detected in the EOD isolates.

Learning Points/Discussion: Whole genome sequencing showed that the likelihood of a clonal outbreak was remote given that the EOD isolates had different capsular types and LOD isolates were diverse by core genome analysis. We are uncertain of the reason behind this surge of invasive GBS disease in our centre for the month. Previous analysis in our institution also showed that ST17 had been the dominant ST in GBS LOD since 2016.
TYPHOID FEVER IN AN ADOLESCENT GIRL WITH LUPUS VULGARIS AND ABDOMINAL TUBERCULOSIS

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Title of Case(s): Multifocal Tuberculosis In An Immunocompetent Adolescent Girl

Background: Tuberculosis in Adolescent children is a common occurrence in developing countries including India. Multifocal tuberculosis can occur in immunocompromised children but it occurs rarely in the immunocompetent children like our case. In addition, our case suffered from one more infectious disease that is typhoid fever. Also, our child was not immunised against tuberculosis which is provided under the national immunisation schedule free of cost.

Case Presentation Summary: A 14 year old female child admitted with complaints of pain abdomen and fever (low grade) for last 2 years, decreased appetite for last 6 months, weight loss for last 6 months. On examination vitals were PR—108, RR—20, BP—100/60 and temperature—100 F. Per abdomen examination showed a distended abdomen with doughy consistency, shifting dullness positive. There was a healing ulcer with undermined edges on nape of neck. It was diagnosed as lupus vulgaris and skin biopsy was taken. There was a history of contact with an open case of pulmonary kochs in maternal uncle. USG Abdomen—moderate septate ascites, mesenteric thickening with clumping of gut loops in central abdomen. Diagnostic ascitic tap was done showed a cell count of 600 cells/100ml, MNC—90 %, Neutrophils—10 %, CBNAAT done on fluid showed mycobacterium tuberculosis. Mantoux Test—16 mm, Blood culture grew salmonella typhi. Patient was initially started on IV ceftrioxone as per sensitivity. In view of chronic illness suggestive of tuberculosis child was started on ATT. Child was unvaccinated.

Learning Points/Discussion: 1. Child was not immunised against any disease till date. As per parents it was against their religion to get children vaccinated as they should develop immunity on their own without any artificial means like vaccination. 2. Child belongs to a lower socioeconomic strata and live in a joint family with one of her paternal uncles suffering from pulmonary tuberculosis. 3. Tuberculosis of two extrapulmonary sites (abdominal and skin) with no pulmonary involvement is uncommon in immunocompetent children.
FACIAL NERVE PALSY - SHOULD WE PERFORM A LUMBAR PUNCTURE?

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Title of Case(s): Facial nerve palsy – should we perform a lumbar puncture?

Background: Lyme disease (LD) is the most common cause of facial nerve palsy among children in endemic areas, including Poland, with a prevalence of 55 per 100 000 population per year. The treatment recommended for peripheral and central neuroborreliosis and idiopathic facial nerve palsy differs considerably. However, the question of whether children with facial nerve palsy need a lumbar puncture remains unanswered.

Case Presentation Summary: A 6-year-old girl was admitted to our ward with facial nerve palsy and lethargy. She had been hospitalized in another hospital for two weeks and received glucocorticoids, with no improvement. A day before admission, she became weak and apathetic. Apart from facial nerve palsy and weakness, there were no abnormal findings on clinical examination. Lumbar puncture revealed cytosis of 224/μL and protein concentration of 85 mg/dl. Serum and cerebrospinal fluid (CSF) serology were positive for LD. Ceftriaxone was administered, and the girl improved significantly within the first days of treatment. A 10-year-old boy was admitted to the hospital because of facial nerve palsy and a history of a tick bite. He had been febrile for two weeks before admission. He became irritable and tearful, and developed facial nerve palsy three days before admission. CSF showed cytosis of 175/μl and protein level of 150 mg/dl. Serum and CSF serology confirmed neuroborreliosis. He recovered fully after six days of ceftriaxone treatment.

Learning Points/Discussion: Facial nerve palsy may be the principal symptom of LD. Proper diagnosis of central neuroborreliosis is crucial because it warrants intravenous antibiotic therapy, which is not routine in patients with facial nerve palsy. Therefore, a lumbar puncture should be performed as a routine diagnostic procedure in children with facial nerve palsy, especially with positive serology for LD or history of tick exposure.
"PERSISTENT FEVER, ATYPICAL AND RESISTANT PATHOGEN- CASE REPORT OF COMMUNITY ACQUIRED PNEUMONIA IN A 7 YEAR OLD GIRL"

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**Title of Case(s):** Persistent fever in a child with Community Acquired Pneumonia

**Background:** Community Acquired Pneumonia (CAP) in children is the most common diagnosis requiring medical attention and accounts for majority of antibiotic prescriptions despite most of the etiologies being viral which usually resolves with symptomatic & supportive treatment. With adequate vaccine coverage the incidence of bacterial etiologies (Pneumococcus, Haemophilus) has decreased. Atypical organisms (Mycoplasma, Chlamydia) causing CAP neither have preventive vaccines nor definitive diagnostic tools and antibiotics are essential for clinical recovery.

**Case Presentation Summary:** A 7 year old girl presented with a sub-acute onset of CAP with respiratory distress starting in the 2nd week. There was no clinical improvement despite appropriate use of antibiotics (oral) recommended for treatment of CAP. Her clinical examination and radiological features were suggestive of bacterial pneumonia with effusion. She was empirically started with Ceftriaxone and Azithromycin.

| Lecuopenia, thrombocytopenia, CRP-32, Scrub IgM, Mycoplasma IgM-Negative, Blood culture-Sterile; |
| NPA- Mycoplasma pneumoniae (Film-Array); Pleural fluid-Exudate; PCR-Mycoplasma pneumoniae (Film-Array) |
| CXR- Right lower zone consolidation with effusion CT- Lower lobe consolidation with effusion with paratracheal and hilar lymphadenopathy. |

Over the next 48 hours, there was clinical worsening (shifted to PICU), antibiotics were escalated, Doxycycline was added and an ICD was placed. She had **persistent fever spikes** for a week despite clinical recovery which resolved with NSAID’s.

**Learning Points/Discussion:** Persistent fever in CAP (with clinical recovery) could be a non-infective complication (HLH, SIRS) and is not an indication for escalation of antibiotics. Worsening clinical and laboratory features should suggest a complication of CAP rather than a resistant pathogen which will avoid inappropriate antibiotic escalation. Mycoplasma pneumoniae can present like a classical bacterial pneumonia with a sub-acute onset and progression. We suggest use of PCR and empirical Doxycycline (as opposed to Azithromycin) for management of CAP (due to Mycoplasma)
Title of Case(s): Oral Human Serum Immunoglobulin Treatment in a Child with Human immunodeficiency Virus infection and Rotavirus Diarrhea

Background: Rotavirus is one of the most common cause of infectious gastroenteritis in children worldwide. It may cause severe diarrhea in both immunocompetent and immunocompromised patients. Literature suggests that oral immunoglobulin therapy may be of value in severe gastrointestinal infections. Here we report a case with human immunodeficiency virus (HIV) infection and rotavirus diarrhea who had treated with intravenous immunoglobulin given by oral route.

Case Presentation Summary: Case presentation
An 8–year-old boy diagnosed with HIV infection was admitted to emergency room with complaint of fever, vomiting, abdominal pain and watery diarrhea. He was severely dehydrated but had normal blood pressure (100/70 mmHg). On admission, physical examination revealed dry oral mucous membrane and poor skin turgor. Laboratory tests was as following: white blood cell count: 6800/µl., absolute lymphocyte count :400/µl. and C-reactive protein: 3 mg/dl. Rotavirus antigen was detected in the stool sample by ELISA method. Intravenous fluid therapy was commenced. Intravenous immunoglobulin (300 mg/kg) was given by oral route. After this intervention, his diarrhea which is continuing for 3 days was revealed at same day. His clinical condition improved rapidly and he was discharged without any sequelae.

Learning Points/Discussion: Severe diarrheacaused by rotavirus in patients with immunodeficiency diseases increases morbidity and is challenge to physicians in terms of establishing treatment regimens useful in managing the diarrhea. Previous studies indicate that orally administered serum immunoglobulin can survive passage in the gastrointestinal tract in an immunologically active form. Intravenous immunoglobulin given by oral route may improve the clinical condition in immunocompromised patients with rotavirus diarrhea.
SUCCESSFUL TREATMENT OF ALLERGIC BRONCHOPULMONARY ASPERGILLOSIS WITH POSACONAZOLE IN A CHILD WITH CYSTIC FIBROSIS

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**Title of Case(s):** Successful Treatment of Allergic Bronchopulmonary Aspergillosis with Posaconazole in a Child with Cystic Fibrosis

**Background:** Aspergillus fumigatus is the main fungus isolated from the airways of patients with cystic fibrosis. Allergic bronchopulmonary aspergillosis (ABPA) is recognized as a rare, progressive, allergic disorder in patients with cystic fibrosis and asthma. Treatment of ABPA mainly includes systemic corticosteroids and antifungal agents. Here, we report posaconazole treatment in a 9-year-old boy with ABPA and also review the literature on antifungal management of ABPA.

**Case Presentation Summary:** A 9-year-old boy with the diagnosis of cystic fibrosis (CF) presented with complaints of fever, productive cough and acute dyspnea. CF was diagnosed at two months following presentation of persistent cough. On admission he was hypoxic, tachypneic and dyspneic. His oxygen saturation was 92% while breathing room air and his respiratory rate was 30 breaths per minute. His body temperature was 38.5. Auscultation of the lungs revealed obvious bilateral fine crackles and bilateral rhonchus. Intravenous meropenem and amikacin therapy was started for the acute exacerbation. The patient was diagnosed with ABPA because of his failure to respond to antibiotherapy, elevated serum immunoglobulin IgE, specific IgE to *Aspergillus fumigatus* levels and sputum growth of *A. fumigatus*. Because of his failure to respond to itraconazole, the drug was discontinued, he was then started on voriconazole. Voriconazole was discontinued after 1 month of the treatment because of severe photosensitivity. He was successfully treated with posaconazole with marked clinical and laboratory improvement and no adverse effects.

**Learning Points/Discussion:** Allergic bronchopulmonary aspergillosis is usually a progressive disease. If left untreated, it can cause recurrent pulmonary consolidation, bronchiectasis, pulmonary fibrosis and lung destruction. Defining optimal treatment practices for ABPA is controversial. Corticosteroids and antifungal agents are the mainstay of therapy in patients with ABPA based on observational studies in children. Posaconazole is a useful treatment option for patients with ABPA.
COULD THIS SOMEHOW BE LINKED TO THE GUT? A MYSTERIOUS CASE OF POLYMICROBIAL MENINGITIS

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Title of Case(s): Could this somehow be linked to the gut? A mysterious case of polymicrobial meningitis

Background: Polymicrobial meningitis is associated with cerebrospinal fluid (CSF) contamination caused by gastrointestinal/genitourinary tract malformation, or post-neurosurgical intervention. We describe a child with meningitis caused by multiple commensal gut bacteria in association with an occult anterior meningocele.

Case Presentation Summary: A previously well 4-year-old girl presented with fever and dysuria. Urine culture revealed *Escherichia coli* and she received oral nitrofurantoin. In the following days, she developed acute encephalopathy and opisthotonus. Lumbar puncture yielded frank pus: polymorphs 2960 cells/mm³; lymphocytes 230 cells/mm³; glucose <0.3 mmol/L; protein 2.1 g/L. CSF culture yielded *Bacteroides fragilis* and *Bacteroides ovatus*, with *Prevotella denticola* also identified on 16S ribosomal polymerase chain reaction. She received intravenous ceftriaxone and metronidazole, but developed seizures secondary to acute hydrocephalus necessitating external ventricular drain (EVD) insertion. Abdominal discomfort was also noted, and imaging revealed a 6x5x10cm pelvic abscess extending into the right buttock and sacral spinal canal. The collection was surgically drained and culture yielded *E. coli* and mixed anaerobes. She recovered well, her EVD was removed, and after three months of intravenous antibiotics, her treatment was changed to oral co-amoxiclav. Magnetic resonance imaging during convalescence demonstrated an anterior sacral bony defect with anterior meningocele (Figure 1). Enterothecal fistula between the anterior meningocele and colon was deemed to be the underlying cause of meningitis. She remains on oral co-amoxiclav and is awaiting definitive surgical repair. (Figure 1)
Learning Points/Discussion: 1. Polymicrobial meningitis caused by gut flora should prompt consideration of enterothecal fistula. 2. Anterior sacral meningocele usually manifests with constipation or urinary retention but can present with polymicrobial meningitis caused by enterothecal fistula in the previously well child. 3. Long-term antibiotic treatment may be required until the anatomical defect can be surgically corrected.
Title of Case(s): A PREVENTABLE DISEASE, AN UNPREVENTABLE FATALITY

Background: Recently, measles outbreaks have been reported globally, both due to migration processes and the increasing number of unvaccinated children. Early complications of measles are usually unproblematic to recognize while rare long-term sequelae, particularly, subacute sclerosing panencephalitis (SSPE) having the highest case-fatality rate among all rubeola complications, may outstand the acute infection for years and thus might be confusing for differential diagnosis.

Case Presentation Summary: We observed a case of a progressive degenerative CNS disease in an eight year old male who was fully immunized including two doses of MMR vaccine. Prior to MMR vaccination he had measles at the age of eight months. Behavioral changes and school performance deterioration started five months prior to admission. However, parents had not sought for medical advice until the episode of tonic-clonic afebrile seizures and syncope developed regarded as an epilepsy onset. Two weeks later he was admitted to the pediatric ICU with lethargy, seizures, hallucinations and tetraparesis. Acute encephalitis was suspected but CSF PCR screening for common pathogens including human herpes viruses was negative. Cerebral MRI showed bilateral temporal and occipital changes. Further differential diagnosis included Schilder’s disease versus SSPE. The latter was confirmed with CSF testing for rubeola IgG (12000 mIU/ml). CSF and serum oligoclonal IgG test was positive confirming intrathecal synthesis of antibodies. The child received symptomatic treatment; fatality occurred two months later.

Learning Points/Discussion: The ongoing measles outbreak in Ukraine has already involved over 70000 children since 2017. Incidence of SSPE may reach 18-27 cases per 100000 cases of measles, thus, it is immensely important to raise awareness about SSPE and its prophylaxis. Measles vaccination is the only effective way to prevent SSPE and may be given as early as six months of age during outbreaks.
Title of Case(s): An ancient disease that remains a modern day problem: How can we definitely fight this global public health issue?

Background: Tuberculosis (TB) continues to be a public health problem. Even though in these days it can be preventable and curable, most cases are misdiagnosed. Infants and young children are at higher risk of developing severe disseminated disease and have higher rates of mortality. The various options for intervention while facing this diagnosis are prophylatic treatment, vaccination, preventive chemotherapy and adequate treatment.

Case Presentation Summary: A previously healthy 3-month-old male infant was admitted due to disseminated tuberculosis. His father and cousin were diagnosed with pulmonary tuberculosis 2 months earlier and initiated isoniazid, rifampicin, pyrazinamide and ethambutol (HRZE) and HRZ, respectively. The drug susceptibility test for Mycobacterium tuberculosis (DST-MT) was ongoing by the time they were discharged and the other household contacts were not screened. On the following month his siblings became symptomatic and were also diagnosed with TB. Our patient initiated chemoprophylaxis with isoniazid but no imaging exams were performed. After 3 weeks disseminated TB (pulmonary, ganglionic and meningeal) was diagnosed. We contacted the father’s hospital in order to know his DST-MT and it was resistant to H. By this time his father was at home, still bacilliferous, his cousin got worse and was re-admitted at the hospital. All the antibacillary drug schemes were changed and the infant initiated RZE and levofloxacin.

Learning Points/Discussion: TB is still a challenge. Besides the prematurely stop of the treatment by the patients, incorrect prescriptions by health care providers also increase the number of drug resistant MT cases. In this case, the diagnosis of a severe form of TB after BCG immunization, rises awareness for the real effectiveness of the vaccine. Appropriate screening and adequate articulation between the different health care services are the key to combat this public health problem.
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ACUTE LARYNGO-TRACHEOBRONCHITIS IN NEPHROTIC SYNDROME: CHALLENGES IN AIRWAY MANAGEMENT

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Title of Case(s): Difficult Airway in an Immunocompromised Child

Background: We highlight a rare presentation of nephrotic syndrome presenting with relapse and stridor along with severe neck and glottic oedema. The child was admitted to pediatric emergency in acute respiratory distress with neck edema extending till the upper chest. Airway management being a priority and anticipating difficulty, child was electively intubated by videolaryngoscopy by a multidisciplinary team comprising paediatricians, intensivists and otorhinolaryngologist.

Case Presentation Summary: A10 year old boy presented with generalized anasarca and neck swelling for a week. He was conscious, had respiratory distress with stridor and neck swelling extending until the sternal angle. Neck girth was 40 cm, 1.5 times of normal for age and sex (normal: 26.4-27.2cm). Possibility of local-site infection of neck or fluid collection due to nephrotic syndrome with relapse with bilateral pleural effusion and ascites was considered. Aspiration of neck swelling revealed clear fluid with no pus cells. X-Ray neck frontal view revealed a positive steeple sign consistent with acute laryngo-tracheobronchitis. Ultrasound of neck showed subcutaneous oedema with extension into muscular plane. On direct laryngoscopy, there was severe glottic edema with inadequate glottic opening. Child was graded as Mallampati class 3. After failed conventional intubation, he was successfully intubated using C-MAC videolaryngoscope with acute-angle D-blade.

Learning Points/Discussion: Acute onset of respiratory distress with positive steeple sign on xray neck and glottic stenosis on direct laryngoscopy was consistent with acute laryngo-tracheobronchitis in this diagnosed case of nephrotic syndrome with relapse and severe neck edema. Close differentials included Ludwigs angina and submandibular abscess. Elective intubation with video-laryngoscopy was lifesaving in the index child and is an attractive option to be considered in failed conventional intubation while encountering difficult airway.
ANGIOSTRONGYLUS CANTONENSIS: AN EMERGING CAUSE OF EOSINOPHILIC MENINGOENCEPHALITIS

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Title of Case(s): Angiostrongylus cantonensis: an emerging cause of eosinophilic meningoencephalitis

Background: Angiostrongylus cantonensis is a natural parasite found in lung arteries of rats, considered the most important cause of eosinophilic meningitis in humans. Human infections are most commonly diagnosed in Southeast Asia, and it was recently described in Brazil. We report two cases of infants with different presentations of eosinophilic meningitis caused by A. cantonensis in the non-endemic city of Sao Paulo, Brazil.

Case Presentation Summary:

Case 1: healthy 11-month-old girl presented with sudden onset of unilateral convergent strabismus. Ophthalmological evaluation of the affected eye revealed exodeviation. Funduscopy and brain MRI were normal. Cerebrospinal fluid (CSF) analysis revealed 1.792 leukocytes/µL (56% eosinophils), glucose=40mg/dl, proteins=85mg/dl. Extensive etiologic evaluation in CSF was negative, positive ELISA and Western Blot for Angiostrongylus led to the treatment with albendazole and prednisolone. She recovered completely.

Case 2: healthy 11-month-old boy presented with a 2-day history of fever, weakness and prostration, which developed a decreased level of consciousness. Brain CT showed hyper signal in caudate and putamen nuclei. CSF analysis revealed 435 leukocytes/µL (48% eosinophils), glucose=37mg/dl, proteins=68mg/dl. Extensive etiologic evaluation in CSF was negative, ELISA and PCR for A. cantonensis were positive. The patient developed flaccid paralysis, areflexia, irreversible unilateral amaurosis. Both were born and raised in São Paulo, without recent travels and didn't consum slugs, snails, uncooked vegetables. They lived on a slum. Snails and rats were reported near their houses.

Learning Points/Discussion: The epidemiological and clinical data, the CSF alterations, the seroconversion and the positive PCR confirmes A. cantonensis eosinophilic meningitis and demonstrate the presence of A. cantonensis roundworms in São Paulo. A timing suspicion and prompt initiation of treatment can reduce adverse neurologic outcomes. This present aims to aware health care professionals about A. cantonensis as a cause of eosinophilic meningitis.
A CASE OF DISSEMINATE CYSTIC ECHINOCOCOSIS RESISTANT TO ALBENDAZOLE TREATMENT

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Title of Case(s): A case of disseminate cystic echinococcosis resistant to albendazole treatment

Background: Cystic echinococcosis is a zoonotic infectious disease caused by the larval stage of Echinococcus granulosus. The liver and lungs are the most frequently affected organs. Benzimidazoles have therapeutic potential in patients with multiorgan and multicystic echinococcosis. Here, we present a patient controlled by praziquantel and nitazoxanide combination therapy, who had drug resistant echinococcosis located to lungs and liver and who had evaluated as inoperable.

Case Presentation Summary: A 13-years-old boy diagnosed with cystic echinococcosis had been operated twice because of cystic echinococcosis of the lung. His lesions located to lungs and liver were continued to spread under the albendazole treatment. The patient was evaluated for cellular and humoral immune deficiencies. No any immunodeficiency was detected. This medical treatment was changed to albendazole plus praziquantel. The patient was followed for 3 years. There was an increase in cyst size in lung and liver. Nitazoxamide added to treatment. Patient received albendazole, praziquantel and nitazoxanide combination therapy regularly for 1 year. Within this period, cyst size was decreased and calcification was observed in cysts. His disseminated echinococcosis is under control with 3 drugs is given. This is the first child in the literature in which the combination therapy.

Learning Points/Discussion: The management of cystic echinococcosis is still controversial and treatment recommendations are based on the opinions of experts. There is no “best” treatment option for cystic echinococcosis and no clinical trial has compared all the different treatment modalities, including “Watch and Wait”. Combination of nitazoxamide, praziquantel and albendazole may be useful in some rare cases which there is no opportunity of surgical excision under albendazole treatment.
A PARTICULAR CASE OF CYTOMEGALOVIRUS INFECTION IN INFANCY

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Title of Case(s): A particular case of cytomegalovirus infection in infancy

Background: The clinical spectrum of perinatal infection varies from asymptomatic infection or mild disease to severe systemic involvement. CMV hepatitis is relatively common in early ages, especially early infancy, and, during this period, is associated with cholestasis. CMV infection in infancy is important; it might result in cirrhosis and even death. Severe neonatal symptoms of congenital CMV occur more often in infants born to mothers with primary infection in pregnancy. The aim of this paper is to present a severe intrauterine infection, which led to difficulties in diagnosis and unfavorable evolution.

Case Presentation Summary: M.E., 6-weeks-old, born small for gestational age, was admitted in our Hospital for gastrointestinal signs: diarrhea, abdominal distension, observed three days earlier. Clinical and biological exams revealed hepatic disease related with hepatic cytolysis and cholestasis. Abdominal ultrasound showed large amounts of ascitic fluid, cirrhotic liver, enlarged portal vessel with hepatopetal flow, normal gallbladder and biliary tract. Computed tomography angiography revealed a wide hepatic artery and absence of splenic vein. Markers were sero-negative for infection with hepatitis viruses A, B or C and positive for CMV (both IgM and IgG). Postmortem macroscopy revealed important liver enlargement, micronodularity, green discoloration due to marked cholestasis, all elements of primary biliary cirrhosis, end stage; cell free CMV antigens were found among alveoli with atelectasis.

Learning Points/Discussion: The onset of hepatic disease was acute or chronic? Anamnesis offered reliable diagnostic criteria for intrauterine infection (flu during first trimester of pregnancy, intrauterine growth restriction, prolonged jaundice). The mother had been tested for all TORCH infections other than CMV. The strict liver cell tropism raised questions regarding virulence, host immunology. The late diagnosis of this case led to the impossibility of etiological treatment.
EXTRALOBAR PULMONARY SQUESTRATION MASQUERADING AS PNEUMOCOCCAL PLEURAL EMPYEMA IN AN INFANT

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Title of Case(s): An Infant With Recurrent Pleural Empyema

Background: Pulmonary sequestration (PS) is a rare congenital broncho-pulmonary malformation. Pulmonary sequestration is classified into intralobar sequestration and extralobar sequestration according to the absence or presence of independent visceral pleura encase in abnormal lung tissues. One of the complications associated with extralobar sequestration is pleural empyema. We report a young infant who presented with empyema thoracis due to streptococcus pneumoniae masking an underlying left basal sequestration.

Case Presentation Summary: 11 month infant presented with complaints of fever since 12 days, cough 6 days and increased rates of breathing since 3 days. On chest examination air entry was reduced on left side. Xray chest showed left lower zone opacity with CP angle obliteration with mediastinal shift to right side. There was a past history of chest tube insertion and drainage about 6 months back also. Intercostal chest tube was inserted and pleural fluid sent for analysis. Antibiotics were changed to vancomycin and clindamycin as per pus culture sensitivity which grew streptococcus pneumoniae. CT Chest showed heterogeneously enhancing soft tissue in the region of left lobe draining its blood supply from aorta suggestive of Extralobar sequestration with multiple cystic areas within the sequestered segment. Pediatric Surgery consultation was taken and Operative intervention was advised after the resolution of acute event. Another review US Chest was suggestive of resolution of empyema and intercostal chest tubes were taken out. Patient was discharged on oral antibiotics.

Learning Points/Discussion: Intralobar pulmonary sequestration is characterized by aberrant formation of nonfunctional lung tissue that has no communication with the bronchial tree and receives systemic arterial blood supply. Failure of earlier diagnosis can lead to recurrent pneumonia, failure to thrive, multiple hospital admissions, and more morbidity. In our case also there was past history of pleural empyema. So an early CT scan chest can be helpful.
VACCINE-ASSOCIATED MEASLES IN AN IMMUNOCOMPETENT INFANT DURING A LARGE OUTBREAK

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Title of Case(s): Rush and fever in an immunocompetent child

Background: During 2019 Brazil has experienced a measles outbreak that reached 50,000 suspected cases with 14,000 confirmed mainly in Sao Paulo. Children younger than 1 year old were predominantly affected. A massive Measles vaccination campaign started, including children from 6 to 12 months and young adults until 30 years old. We present a case of vaccine-associated measles infection in an immunocompetent infant.

Case Presentation Summary: Case Presentation Summary: A previously healthy, 13-month-old immunocompetent male presented to the emergency with a nine-day history of a runny nose, followed by a two-day history of diffuse maculopapular rash and fever. The runny nose developed 2 days after receiving his first dose of the measles, mumps, and rubella (MMR) vaccine and the rash and fever after 9 days. He had no previous adverse reactions to immunizations. The child resided in an orphanage, with almost 20 inhabitants, including 8 children. He had no known sick contacts or any known contacts with a rash. On examination, the patient had a full-body blanchable maculopapular rash. The patient's rash resolved after 5 days. All routine laboratory values were normal. Serologies were negative for HIV, cytomegalovirus, Epstein-Barr, and parvovirus B19. Reverse transcriptase-polymerase chain reaction (RT-PCR) testing for measles RNA from saliva and urine was positive, as well as measles-specific IgM and IgG. Viral sequencing confirmed a vaccinal virus.

Learning Points/Discussion: Adverse reactions after Measles Mumps Rubella (MMR) vaccine administration are generally absent or mild. Rash and/or mild clinical illness following MMR vaccine are not uncommon, but clinically significant vaccine-associated illness is rare. In the period of a large outbreak and vaccine campaign, these cases can increase. When it occurs, can be clinically indistinguishable from wild-type measles disease, except by genotyping.
PNEUMOCOCCAL MENINGITIS WITH FETAL OUTCOME: CASE REPORT

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Title of Case(s): Pneumococcal menengitis with fetal outcome: case report

Background: Streptococcus pneumoniae is an important pathogen causing invasive infections such as pneumonia, meningitis, and bacteremia. These infections result in hospitalization, complications with long term sequelae, multisystem organ failure, or death. Bacterial meningitis caused by S. pneumoniae is an emergency condition requiring rapid diagnosis and treatment. We report a patient with fatal pneumococcal meningitis which is considered as secondary to middle ear cholesteatoma.

Case Presentation Summary: A 12-years-old boy with a history of ear pain and hearing loss has admitted to another hospital because of otitis and a ventilation tube is inserted. The patient was admitted to our hospital because of headache and decreased level of consciousness, 20 days after the ventilation tube insertion. CSF cell count was 320 leukocytes/mm³. There were gram-positive cocci on gram-staining. Ceftriaxone and vancomycin treatment was started. Blood and CSF cultures yielded Streptococcus pneumoniae. Anaphylactic reaction was developed after ceftriaxone administration. Meropenem and vancomycin combination was given. CranialMRI showed multiple infarcts in cerebellar hemispheres and fluid collection in mastoid bone. Cortical mastoidectomy was performed. Cholesteatoma was detected during operation and removed. CSF culture was sterile. On the 7th day of admission, diffuse edema and tonsillar herniation were detected. Decompression surgery was performed. His antibiotic therapy was revised as vancomycin plus ciprofloxacin. The patient was hemodynamically instable and arrhythmia was developed. The patient died on the 12th day of admission.

Learning Points/Discussion: Invasive pneumococcal infections such as meningitis are major cause of morbidity and mortality worldwide despite pneumococcal vaccines. Pneumococcal meningitis has higher mortality and morbidity then other bacterial causes of meningitis. Middle ear ventilation tube insertion may induce bacterial invasion especially in patients with cholesteatoma. High mortality of these infections may reflect need to increase vaccination coverage in children with predisposing factors to pneumococcal infections.
YELLOW FEVER VACCINE-ASSOCIATED NEUROLOGIC DISEASE: A PEDIATRIC CASE SERIES.

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Title of Case(s): Yellow fever vaccine-associated neurologic disease: A pediatric case series.

Background: Yellow fever (YF) is endemic in many regions of Brazil. During the 2017/2018 YF outbreak, more than 13.3 million people were vaccinated in a mass vaccination campaign in São Paulo. YF vaccine-associated neurotropic disease (YEL-AND) is a potentially severe adverse event of the live-attenuated vaccine (YFV), presenting as several neurologic syndromes. We describe the clinical and laboratory characteristics of 12 cases of meningoencephalitis occurring in children after the first dose of YFV.

Case Presentation Summary: All children with suspected YEL-AND were healthy, and the median age was 6.5 years. Neurological symptoms started within 30 days after the YFV (average 21.5 days). All were hospitalized for investigation, with an average hospital stay of 9.3 days. The main signs and symptoms reported were fever, headache, vomiting, mental confusion, ataxia, seizure, meningeal signs or loss of muscle strength. All CSF samples were collected within 48 hours of admission and revealed elevated protein, increased white cell count, and negative cultures for bacteria. Five patients had positive YF IgM, one IgM was inconclusive, four with negative results, and serology was not performed in two samples. Among the confirmed cases and the other seven suspected cases, all presented clinical and laboratory characteristics compatible with YEL-AND. Additionally, all had a temporal relationship with the vaccine administration and the onset of symptoms. No sequelae were described.

Learning Points/Discussion: YFV adverse events are mostly mild. However, an increase of the vaccinees (such as during massive vaccination campaigns during outbreaks) will lead to more adverse events to be seen in a reduced period. YEL-AND cases described in the literature are rare and usually have a favorable prognosis. Therefore, the decision to vaccinate must be individualized according to the epidemiological situation and individual risk factors.
BACTEREMIA DUE TO ACTINOMYCES VISCOSUS IN A CHILD WITH FEBRILE NEUTROPENIA

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Title of Case(s): Bacteremia due to Actinomyces viscosus in a child with febrile neutropenia

Background: Actinomycosis is an uncommon infectious disease caused predominantly by Actinomyces israelii. Other species and A.viscosus are less common and rarely affects children and adolescents. These organisms are found in the normal flora of the oropharynx, gastrointestinal and female genital tract. Hematogenous dissemination can rarely occur and blood cultures generally remains negative. Here we report a case of bacteremia due to A.viscosus in a 2-year-old boy with acute myeloblastic leukemia (AML).

Case Presentation Summary: A 2-year-old boy underwent a biopsy due to a mass in his right cheek, and a granulocytic sarcoma was detected. Bone marrow aspiration was performed due to the detection of granulocytic sarcoma and the patient was diagnosed with AML. Four days after the induction phase, the patient was hospitalized with febrile neutropenia. Laboratory investigations revealed a white blood cell count of 100/mm³, neutrophil count of 0/mm³. Peripheral blood culture was taken and cefepime was started empirically. Galactomannan and CMV-PCR were found negative. Gram stained smear revealed the presence of gram-positive bacilli. Actinomyces viscosus and Rhizobium radiobacter were isolated from a blood culture. The antibiogram showed clindamycin and penicillin susceptibility. Clindamycin was continued during hospitalization and oral penicillin V was given for 1 year after discharge.

Learning Points/Discussion: Actinomycosis caused by Actinomyces species is an indolent, slowly progressive, uncommon bacterial infection. Three important sites of involvement are cervicofacial, abdominopelvic and thoracic. Actinomycosis characterized by formation of abscesses, fistulae, fibrosis and sinus tracts discharging sulphur granules. A.viscosus may rarely cause localized and disseminated infections. Patients who have underlying disease and immunocompromised status are at particularly high risk for infection. We would like to emphasized that rare anaerobic microorganisms including A. viscosus may cause bloodstream infection in immunocompromised children.
NEUROLOGICAL COMPLICATIONS CAUSED BY EPSTEIN-BARR VIRUS IN CHILDREN

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Title of Case(s): Neurological Complications Caused by Epstein-Barr Virus in Children

Background: Epstein-Barr virus (EBV) usually causes benign, self-limited infections in children. Although rarely, EBV can lead to central nervous system complications such as encephalitis, meningitis, myelitis, cranial nerve palsies, polyradiculomyelitis and Alice-in-Wonderland syndrome.

In a period May 2008-December 2019 there were 3 children hospitalised in the University Hospital for Infectious Diseases "Dr. Fran Mihaljević" with EBV detected in cerebrospinal fluid (CSF).

Case Presentation Summary: The first case was a 3-year-old girl, previously healthy, who presented with mononucleosis disease and seizures. Magnetic resonance imaging (MRI) revealed oedema and elevated signal of the entire cerebral cortex, nucleus caudatus and putamen, bilaterally. The girl was treated with acyclovir for 14 days. The second CSF EBV positive case was a 5-year-old boy with a transplanted liver who presented with peripheral facial palsy. Brain MRI showed imbibition of both trigeminal and facial nerves. He was treated with acyclovir for 19 months. During that period immunosuppressive therapy was reduced. The third case was a 5-year-old girl with ventriculoperitoneal drainage system who presented with fever and somnolence. Computerized tomography was uninformative. She was treated with meropenem for 14 days and acyclovir for initial 3 days. Afterwards, EBV was detected in CSF, but since the patient’s condition improved as she showed no signs of CNS involvement, further acyclovir therapy wasn’t administered. All 3 patients recovered fully.

Learning Points/Discussion: EBV must be considered as a causative agent in children with neurological symptoms, especially in immunocompromised patients or if no other causative agent has been identified. Neurologic symptoms can occur alone or in the course of mononucleosis disease. Most children recover fully. The impact of antiviral therapy on clinical course of disease and the optimal duration of treatment have not been precisely defined.
Title of Case(s): Tachycardia as a sign of life-threatening condition in a nearly 3-month-old infant

Background: Group B streptococcal (GBS) infection is the most common cause of early-onset sepsis, but it should be taken into consideration also in all young infants with signs of invasive infection. The clinical picture of the life-threatening infection in the first months of life may be insidious. We present a case of 3-months-old child with sinus tachycardia as a principal symptom of GBS sepsis.

Case Presentation Summary: An 82-day-old previously healthy male baby presented with a history of four hours of poor feeding and irritability. The mother of the child received ampicillin for intrapartum antibiotic prophylaxis (IAP) because of maternal GBS colonization. On initial assessment, the child had a fever (38°C) and tachycardia of 250 per minute. Electrocardiography showed a narrow QRS complex, typical for supraventricular tachycardia. Routine lab tests (complete blood count, C-reactive protein, serum electrolytes), except for elevated procalcitonin, did not reveal any significant abnormalities. Due to the patient’s poor general condition, we treat him empirically with ceftriaxone plus vancomycin. On the fourth day of hospitalization, the blood culture identified Streptococcus agalactiae, so the antibiotic therapy had been replaced with penicillin G, the drug of choice. Ten days after admission, we discharged the boy in good general condition.

Learning Points/Discussion: Sinus tachycardia in an infant should rise suspicion of noncardiac life-threatening conditions, such as sepsis. IAP does not protect infants from late-onset GBS-associated sepsis, and 25% of children born to GBS-positive mothers who received it, becomes colonized with GBS at the age of 1 month. One should consider GBS as an etiologic agent of bacteriemia in all infants up to 3 months of age.
SEVERE COMPLICATIONS OF VARICELLA IN A 20-MOTH-OLD BOY

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Title of Case(s): Severe complications of varicella in a 20-moth-old boy

Background: Skin and soft tissue bacterial infection is the most common complication of varicella. Untreated skin infection may lead to septicemia. In Poland varicella-zoster virus (VZV) infection remains one of the most common predisposing factors to severe group A streptococcus (GAS) infections in children. We present a case of a boy who developed GAS complicated bacteriemia in the course of chicken-pox.

Case Presentation Summary: We admitted a 20-month-old boy due to fever, bilateral otitis media, and limping in the course of chickenpox. The child had been feverish 12 days before admission and had been receiving ibuprofen for five days until chickenpox was diagnosed. After transient improvement, on the 7th day of varicella, fever reached 40°C, and the boy became lethargic. On admission, the child was in a stable condition, and there were numerous superinfected lesions on his skin, he had scarlatina-like erythema, whitlow on two fingers, purulent conjunctivitis, and bilateral otitis media. Laboratory tests revealed moderately elevated inflammatory markers and S.pyogenes growth from both the blood culture and skin lesions. We treated the patient initially with ceftriaxone and clindamycin and then with penicillin G with a significant improvement in the boy's general condition after the first day. The boy is on the sixth day of treatment now, and due to persistent limping, we plan to perform imaging in search of osteomyelitis.

Learning Points/Discussion: Prolonged or recurrent fever in the course of varicella warrants prompt diagnostics for bacterial complications. Skin and soft tissue infection in the course of varicella may lead to life-threatening GAS bacteriemia. Limping in a child with GAS bacteriemia may be a red flag symptom of osteomyelitis. Nonsteroidal anti-inflammatory drugs (NSAIDs) seem to enhance the risk of skin and soft tissue complications of VZV infection.
Title of Case(s): Slow-baked fever

Background: Extrapulmonary tuberculosis diagnose remains a challenge. An 8-year-old boy arrived at Emergency Department with daily fever that started 15 days ago. The only symptoms were mild cough and one vomit. A chest x-ray on the 8th day showed a small infiltrate in median lobe so amoxicillin and azithromycin was administered without disappearance of fever. He had lost 2 kg in two weeks.

Case Presentation Summary: Physical examination was normal. In Emergency Department, chest x-ray was repeated and was normal; blood exam showed elevated CRP 23 mg/dl, and thrombocytosis (734000/ml). No liver nor kidney parameters were altered. He was admitted with cephotaxime for study. He was a healthy child born in Spain. His parents were Bolivian. Last travel to Bolivia was 2 years ago where they stayed for 3 months. No other exposures were reported. During admission, daily fever persisted and he had mild abdominal pain. HIV test was negative. TST was 0 mm, and IGRA test was also negative. An abdominal echography evidenced moderate ascites and thickening of greater omentum. Paracentesis was done, and peritoneal fluid had 46 mg/dl of glucose, 5.9 gr/dl of proteins, 65% mononuclear leukocytes and increased ADA (110 UI/l) and LDH (595 UI/l). PCR test for Mycobacterium tuberculosis and Auramine stain in peritoneal fluid and 3 gastric aspirates were negative.

Learning Points/Discussion: An echography-guided percutaneous biopsy of greater omentum was performed, in which PCR for M. tuberculosis complex was positive. It was confirmed by culture. Culture isolation in one previous gastric lavage was positive afterwards. The patient was diagnosed of peritoneal tuberculosis. According to sensitivity status treatment were started and prednisone was added. TST and IGRA test are not necessary to diagnose tuberculosis. Clinical suspicion is essential when sensitivity of microbiological tests is low.
Title of Case(s): Investigation of the index case contacts of an airborne disease in a school

Background: WHO classifies Brazil as one of the TB priority countries. One of the ways to fight tuberculosis is through those with latent infection. Latent TB is in a common problem, it has an easy diagnosis, and free treatment is available, the biggest challenge remains been attendance to investigation and treatment adherence. It would be interesting to discuss how people handle this issue.

Case Presentation Summary: a. A teacher was diagnosed with bacillary tuberculosis. All classroom children (8 to 9 years) were considered as contacts. We describe the difficulties faced during the investigation in the school environment. b. The planning process started with meetings between the municipality secretary of health, education and surveillance departments. Only after that the children caregivers were summoned for evaluation of their child. At inicial moments school resisted in collaborating and compreending the need to evaluate all children. d. 20 children contacts were identified, only 8 (40%) completed all steps. Of these 20 children, 13 (65%) came for evaluation at the tuberculosis reference service, 4 (30.8%) had a diagnosis of latent TB (LTB); one (7.7%) did not attend the TT (tuberculin test) reading, 4 (30.8%) were discharged as non-infected; and 5 (38.4%) did not complete the investigation. e. From those diagnosed with LTB, 75% completed treatment. For those that lost follow-up the social service was triggered. These children live in constant social vulnerability.

Learning Points/Discussion: The main obstacles were intersectoral communication. It was evident the lack of knowledge about the pathology among the school teachers and the failure to understand the severity of the risk of illness among the parents. Tuberculosis is a public health problem in Brazil, with failures in understanding and communication between the actors involved in the support network of these children.
Title of Case(s): Fever, rash, conjunctivitis – (not) an easy diagnosis? A case of a 4-year-old girl.

Background: Measles is a highly contagious disease usually manifested by fever, dry cough, bilateral conjunctivitis, and rash. Despite typical clinical presentation, measles can be mistaken for other exanthematous illnesses. Until recently, measles was an uncommon disease that young doctors knew only from the literature or older colleagues. In the last decade, the epidemiologic situation of measles in Europe has worsened significantly.

Case Presentation Summary: We admitted a 4-year-old girl due to high fever with cough, red throat, bilateral conjunctivitis, enlarged cervical lymph nodes, and maculopapular rash on the face and thorax, which appeared two hours after she received amoxicillin. She was immunized up to date but without the measles-mumps-rubella (MMR) vaccine. Three weeks earlier, the patient's mother (who received one dose of MMR in the past) had a fever with mild rash lasting two days. Laboratory testing revealed elevated CRP, normal WBC with lymphopenia, and negative EBV antibodies. Measles antibodies results’ waiting time was two weeks. The girl also met Kawasaki disease criteria (fever lasting at least 5 days, bilateral nonexudative conjunctivitis, cervical lymphadenopathy, redness of lips and throat and morbilliform maculopapular rash), therefore on the 8th day of fever, she received immunoglobulins. The patient was afebrile since then and her condition was much improved. IgM antibodies against measles virus in both mother's and daughter's blood samples were found.

Learning Points/Discussion: Making a diagnosis of measles can provide a challenge, especially when the disease is rare, and serology results are unavailable. In the presence of increasing measles morbidity, it must be taken into consideration while making a differential diagnosis in patients with fever and rash. Although a single dose of MMR vaccine is highly effective in preventing measles, it does not exclude the possibility of disease.
IS IT JUST A MILD DISEASE OF CHILDHOOD? A CASE OF A 15-YEAR-OLD BOY WITH A RASH.

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Title of Case(s): Is it just a mild disease of childhood? A case of a 15-year-old boy with a rash.

Background: Measles is usually a mild infection in children. However, complications may occur, including relatively benign like diarrhea and vomiting, otitis media, laryngitis, and severe such as pneumonia, acute encephalitis, and sporadically, subacute sclerosing panencephalitis. Pneumonia is the most common cause of measles-related death in children. According to the Centers for Disease Control and Prevention, five out of every 100 children with measles will develop pneumonia.

Case Presentation Summary: We admitted to the hospital a 15-year-old male without significant past medical history due to high fever, fatigue, and photophobia. Maculopapular rash on the skin and Koplik's spots appeared on the 4th day of fever. The patient developed dyspnea and significant lethargy. IgM antibodies against measles virus were positive. His immunization status was unclear. On physical examination, we found paleness, maculopapular rash on the trunk, tachypnoea 30 per minute, dull sound on percussion, and bronchial respiratory sound over the left lung. The chest x-ray showed parenchymal consolidation with atelectasis in the left lower lobe. The patient received ceftriaxone. Laboratory testing revealed hemoglobin level 7.6 g/dl with mean corpuscular volume (MCV) of 56 fL. Due to severe fatigue, dyspnea, and anemia, the boy received red blood cell transfusion, and his general condition improved significantly.

Learning Points/Discussion: Despite the typically mild course of measles, severe complications can arise, especially in patients with an underlying chronic condition. Etiologic factors of measles-related pneumonia include S. pneumoniae, H. influenzae, but also S. aureus and S. pyogenes. In most severe cases, necessitating ventilatory support, ribavirin treatment should be taken into consideration. Measles may also reveal previously not known medical problems, such as microcytic anemia in the presented patient.
SEVERE COAGULOPATHY IN A CHILD UNDER TUBERCULOSIS TREATMENT


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Title of Case(s): SEVERE COAGULOPATHY IN A CHILD UNDER TUBERCULOSIS TREATMENT

Background: Tuberculosis and tuberculosis drugs may produce several adverse hematological effects. An 8-month-old infant presented with multiple ecchymotic, non-pruritic lesions in lower limbs in the previous 24 hours. There was no fever, trauma, nor any other symptoms. He had been diagnosed with pulmonary tuberculosis (TB) sensitive to first-line drugs when he was 5 months old and he was receiving rifampicin 15 mg/kg/day and isoniazid 10 mg/kg/day at the moment.

Case Presentation Summary: He was breastfed and received complementary feeding. His mother had been diagnosed with latent TB infection and was receiving isoniazid 300mg/day. Blood tests showed a severe coagulopathy (Prothrombin activity 4%, Prothrombin time 175 seconds, INR 15.64, partial thromboplastin test 160 seconds and fibrinogen 131 mg/dl). Platelet count, liver and kidney function were normal. He was admitted to Pediatric Intensive Care Unit. Symptoms, blood test and coagulation factors study (II 3%, VII 2%, IX 3% and X 1% while the others were normal) were compatible with vitamin K deficiency. Intravenous vitamin K and fresh frozen plasma were administered achieving normalization of values 6 hours later. A transfontanelar ultrasound ruled out intracranial bleeding. TB treatment was restarted 3 days later and he was discharged with oral vitamin K. He remained asymptomatic and coagulation values continued stable and normal. TB and TB drugs may produce several adverse hematological effects. However, rifampicin-induced vitamin K deficiency is a rare condition reported only once before, possibly related to an inhibition of vitamin K cycle. It may not resolve unless vitamin K is administered despite interruption the drug.

Learning Points/Discussion: Vitamin K deficiency is a rare issue that could be related to rifampicin treatment. The mechanism may be interaction with vitamin K cycle. Clinicians may be aware of this condition.
GUIDELINES FOR ACUTE OTITIS MEDIA IN CHILDREN WORLDWIDE: USEFUL OR USELESS?

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Background and Objective: Our aim is to identify, analyze and compare the international guidelines or national consensus reports on the diagnosis and management of acute otitis media (AOM) in children.

Methods: We performed a systematic search on PubMed database. From all the items found in the guidelines we refer here only to diagnosis and pharmacologic treatment.

Learning Points/Discussion: There are only 11 countries in the world having a specific AOM guidelines published in Pubmed (English or French): USA, Spain, France, Germany, South Africa, Australia, Korea, Canada, Italy, UK and Japan. Prompt antibiotic treatment is recommended for: children with temperature over 39 gr C or with otorrhea (Germany, Italy), children with intracranial complications and/or a history of recurrence (Italy, South African), children under the age of 2 years (Italy, South Africa, France), children over 2 years old with severe bilateral AOM (Italy), or with failure to respond to symptomatic treatment after 48 to 72 hours (Australia), children with signs of severe infection (temperature > 38, otorrhea, otolagia >48 hours) (South Africa, France), recurrent AOM (South Africa, Italy), children with risk factors (malnourished, immunodepression, ear malformation) (France and South Africa), day-care attendance or siblings of children attending day care centers (South Africa). Some of the guidelines mention the importance of preventive strategies (Italy, Germany, Australia, USA, Spain, Japan, Korea and South Africa), including pneumococcal and influenza vaccination. Amoxicillin is universally accepted as the first-line antibiotic therapy in all included guidelines. The alternative for children allergic to penicillins is the use of macrolides. The Australian guideline is the only one which recommend Cotrimoxazole for the penicillin sensitive patients. All the guidelines excepting the International Consensus, Spain and USA, recommend Amoxicillin-Clavulanic acid or third-generation cephalosporins as second-line therapy.
RECURRENT GROUP B STREPTOCOCCAL INFECTION IN INFANCY: IDENTIFYING THE FOCUS

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Title of Case(s): RECURRENT GROUP B STREPTOCOCCAL INFECTION IN INFANCY: IDENTIFYING THE FOCUS

Background: Group B streptococcus (GBS) is the leading cause of neonatal sepsis worldwide. Recurrent bacteraemia is a rare complication and has been associated with the presence of GBS in maternal breastmilk, and deep-seated infections such as osteomyelitis.

Case Presentation Summary: A preterm infant born at 27 weeks’ gestation deteriorated clinically on day 34 of life. He had a previously uncomplicated neonatal course and was establishing breast milk feeds with minimal respiratory support. GBS was identified from blood cultures, but not urine nor cerebrospinal fluid (CSF). He received 14 days’ intravenous benzylpenicillin with good clinical response. Following discontinuation of antibiotics, he deteriorated clinically within 4 days with a further GBS bacteraemia (urine/CSF cultures negative). Culture of maternal breast milk did not yield GBS. An echocardiogram revealed a small patent ductus arteriosus but no evidence of endocarditis. He was treated with 21 days of intravenous benzylpenicillin, during which surveillance blood cultures were negative. However, within 48-hours of discontinuing antibiotics, he again deteriorated clinically with GBS bacteraemia. Clinical examination, cranial and abdominal ultrasound, and whole-body magnetic resonance imaging did not identify a nidus of infection. However, repeat echocardiogram demonstrated a 9x9mm vegetation at the bifurcation of the main pulmonary artery (Figure 1). The lesion was not amenable to surgical intervention and he received 6 weeks’ intravenous antibiotic treatment, initially with benzylpenicillin, and then ceftriaxone to facilitate outpatient administration. The treatment was successful and he has subsequently remained well.

Learning Points/Discussion: Recurrent GBS bacteraemia should prompt further investigation for a deep-seated nidus of infection. Although GBS is a recognised cause of endocarditis in older adults, it can also occur in infants. Prolonged antibiotic treatment may be a successful strategy for lesions not amenable to surgery.
DIAGNOSTIC AND THERAPEUTIC CONSIDERATIONS IN A CHILD BORN TO A MOTHER WITH OPEN PULMONARY TB

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Title of Case(s): Diagnostic and therapeutic considerations in a child born to a mother with open pulmonary TB

Background: Childhood tuberculosis (TB) is acquired from adult index patients, most often from household contacts. Perinatal exposure to TB carries a high risk for infection and fast progression to active and disseminated TB. Guidelines for management are clear but based on limited evidence.

Case Presentation Summary: A 2 year old child presented with three weeks of fever and progressive neurological symptoms. After a delayed diagnosis of TB meningitis in the two year old, the asymptomatic mother and older brother were tested for TB. The mother, who was pregnant at 38 weeks gestational age, was diagnosed with open pulmonary TB. Fetal ultrasound showed a small for gestational age fetus and unspecific lesions in the placenta. PCR detected no resistance mutations in the mother's TB strain. The neonate was born by uncomplicated vaginal delivery at term, i.e. after 12 days of TB treatment, and was started on preventive TB therapy with isoniazid and rifampicin on the third day of life due to inability to tolerate medication on the first two days. Breastfeeding was initiated after preventive therapy was successfully established. Placenta histology and PCR were negative for TB, culture is currently still negative at 3 weeks. After delivery, the mother developed a fever and cervical lymphadenopathy under therapy. This was assessed as immune activation after the end of pregnancy. Gastric aspirates in the child were microscopy and PCR negative with culture still in progress.

Learning Points/Discussion: - diagnostic steps and therapy in TB close to delivery - breastfeeding and preventive therapy in neonates exposed to TB from the mother - increasing symptoms as a consequence of immune activation after delivery
Background: The MenB-FHbp vaccine (Trumenba®; bivalent rLP2086; Pfizer Inc, Philadelphia, PA) is licensed to prevent meningococcal serogroup B (MenB) disease in individuals aged ≥10 years in Europe and 10–25 years in the United States. This phase 3 postapproval study further assessed the immunogenicity and safety of a 2-dose MenB-FHbp schedule.

Methods: Participants aged 10–25 years received MenB-FHbp (months 0,6) and MenACWY-CRM (month 0). Primary immunogenicity endpoints included percentages of participants achieving ≥4-fold increase from baseline in serum bactericidal assay using human complement (hSBA) titers for 4 diverse, vaccine-heterologous primary MenB test strains and titers ≥lower limit of quantitation (LLOQ; 1:8 or 1:16) for all 4 primary strains combined (composite response) after dose 2; a titer ≥1:4 is the accepted correlate of protection. Percentages of participants with hSBA titers ≥LLOQ for 10 additional, vaccine-heterologous MenB test strains were also assessed; positive predictive values (PPVs) of primary strain responses for secondary strain responses were determined. Safety was assessed.

Results: Percentage of participants (n=814–850) achieving ≥4-fold increases in hSBA titers against each primary strain after dose 2 ranged from 67.4%–95%; composite response was 74.3% (Figure 1A). Primary strain responses were highly predictive of secondary strain responses for FHbp subfamily A (≥84%) and B (≥72.8%) (Figure 1B). Most reactogenicity events were mild-to-moderate in severity. Adverse events (AEs), serious AEs, medically attended AEs, and newly diagnosed chronic medical conditions during the vaccination phase were reported by 40.7%, 0.8%, 26.7%, and 0.8% of participants, respectively.
Conclusions: MenB-FHbp administered at 0,6 months was well-tolerated and induced protective bactericidal antibody responses against diverse MenB strains. Findings provide further support for the continued use of MenB-FHbp on a 2-dose schedule in this population. Funded by Pfizer.

Clinical Trial Registration: ClinicalTrials.gov: NCT03135834.
LINCOLN’S HIGHWAY ABSCESS PRESENTING AS SUPERIOR MEDIASTINAL SYNDROME

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Title of Case(s): A rare cause of Superior Mediastinal Syndrome

**Background:** One of the rare sites of neck abscess is the carotid space, commonly known as The Lincoln’s Highway. The Lincoln’s Highway is the longest highway from California to New York in United States. Involvement of this space has a significant potential for spread to the mediastinum. We report a case of carotid space abscess with descending mediastinitis in a 17 month immunocompetent child presenting as Superior Mediastinal Syndrome.

**Case Presentation Summary:** A 17-months girl was admitted with fever for 5 days and progressively increasing, non-discharging, soft, cystic, fluctuant swelling in right cervical region, approx. 5*5 cm, with bilaterally engorged neck veins and prominent chest veins. A possibility of superior mediastinal syndrome was kept secondary to pyogenic collection - mediastinal mass. USG neck revealed infected fluid collection in right carotid space, encasing the carotid vessels extending to contralateral side. CECT neck showed multiple peripherally enhancing irregular intercommunicating collections, involving right para-tracheal, para-pharyngeal, prevertebral, peri-cervical space on right side and right carotid space with extension into superior and posterior mediastinum up to T5. Child was started on broad spectrum antibiotics and taken up for open thoracotomy after 24 hours. She showed remarkable clinical recovery and was well on last followup visit.

**Learning Points/Discussion:** Superior Vena Cava Syndrome (SVCS) refers to clinical signs caused by obstruction of the superior vena cava. Superior mediastinal syndrome is when SVCS coexists with obstruction of trachea as occurred in our case. Management includes antibiotic therapy and timely incision and drainage of the abscess. Complications include upper airway obstruction due to laryngeal oedema or extrinsic compression, pneumothorax, pneumomediastinum, vocal cord paralysis and descending mediastinitis. Differentials are lymphoma and leukaemia, none of which was the cause in our case.
A 15-YEAR-OLD BOY WITH SKIN LESIONS 10 DAYS AFTER HEART TRANSPLANT

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Title of Case(s): A 15-year-old boy with skin lesions 10 days after heart transplant

Background: The differential diagnosis of cutaneous lesions in children using immunosuppressive therapy after heart transplantation can be challenging.

Case Presentation Summary: A 15-year-old boy, born and raised on a farm in the Netherlands, was admitted to the intensive care unit after a heart transplant because of a dilated cardiomyopathy of unknown origin. Previous to the cardiomyopathy he had been healthy. On day 10 after heart transplant two sharply demarcated erythematous nummular plaques with multiple yellowish grouped vesicles and crustae on his right hand and his left elbow appeared (Figure 1). The most likely cause based on appearance of the skin lesions was herpes simplex infection with Staphylococcus aureus superinfection. However, the culture remained negative for S. aureus and other bacterial pathogens and viral PCR was negative. Skin biopsy showed a granulomatous necrotic inflammation with hyphae and spores. Fungi were seen in PasD and Grocott staining. Fungal culture showed Aspergillus fumigatus and voriconazole treatment was initiated.
Learning Points/Discussion: Fungal infection should be included in the differential diagnosis of children after transplant presenting with a clinical picture that mimics herpes infection. Cutaneous aspergillosis can either be caused by a primary cutaneous infection or can be secondary due to hematogenous dissemination of aspergillus infection. In our patient primary cutaneous aspergillosis was suspected because two days before, bandages had been removed from the exact same locations. Since primary cutaneous aspergillosis can disseminate, as was the case in our patient, timely recognition and prompt treatment is of utmost importance.
PHAGE THERAPY FACILITATING A LIVER TRANSPLANTATION IN A TODDLER INFECTED BY AN EXTENSIVELY-DRUG RESISTANT PSEUDOMONAS AERUGINOSA

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Title of Case(s): Challenging bacterial infection to treat in a child transplanted for biliary atresia

Background: Multi-drug resistant bacterial infections are difficult to treat especially in the context of scarcity of new antibiotics. Management is even more challenging in case of severe immunosuppression. Phage therapy (PT) represents a real opportunity, in synergy with last-resort antibiotics, to treat such infections.

Case Presentation Summary: A 14-month-old infant was transplanted for biliary atresia, using an ABO-incompatible living donor. At day 53 post-transplantation he developed an XDR Pseudomonas sepsis (colimycin R, aztreonam I and gentamycin S) treated with IV colimycin, aztreonam and gentamycin. Blood cultures remained positive and intrahepatic collections appeared on the abdominal ultrasound. Decision was taken to drain one of the collections and to start with IV and in situ PT after ethical committee approval. Twenty milliliters (2 mL/kg) of purified bacteriophage cocktail BFC1 (phage load of 107 pfu/mL) were administered as a 6-h intravenous infusion for 72 days once a day till two weeks after he received a new ABO compatible liver transplant. Intralesional injections with BFC1 were performed with 1 mL during 7 days and stopped due to abdominal swelling and discomfort. During liver transplantation 250 mL of BFC1 was used to rinse the abdominal cavity; the procedure was well tolerated. Phage productions of the Queen Astrid Military Hospital, Brussels, are in agreement with an adapted Belgian framework, set up in concertation with the Federal Agency Medicinal and Health Products.

Learning Points/Discussion: To our knowledge, this is the first case of life-saving IV PT in a transplanted infant. The long IV PT treatment of 86 days was safe. One year after retransplantation the 30-month-old child remains well on immunosuppressive medication. This case highlights the challenge of treating complicated infections due to multi-drug resistant bacteria in immunocompromised children.
Title of Case(s): NOT JUST A LUNG PROBLEM

Background: Starting from a pulmonary location (primary infection), *Mycobacterium tuberculosis* (MTb) can spread to other organs. Extrapulmonary tuberculosis (EPTb) represents an increasing proportion of all tuberculosis cases. We present two cases of EPTb.

Case Presentation Summary: Case 1 is a 7-month-old previously healthy girl, who presented with fever without focus, a chest radiograph showing a right medium lobe opacity, and pleocytosis of the CSF collected on lumbar puncture. On the fourth day after admission, because of fever persistence and somnolence, a brain CT was performed, showing obstructive hydrocephaly. On the seventh day, a bronchofibroscopy was done, and a right medium lobe bronchium granuloma was discovered, that prompted a presumptive diagnosis of Tuberculous Meningitis, and the beginning of quadruple antituberculous therapy (RHZE) and Dexamethasone. The diagnosis was confirmed by MRI and identification of MTb in bronchial secretions. Case 2 is a 15-year-old girl with Jacobsen Syndrome, that presented with abdominal pain and distension. She had history of tuberculosis contact and had done prophylaxis. An abdominal CT was performed, showing ascites and omental caking, and granulomas were discovered on peritoneal biopsies. These findings, associated with prior history, led to a presumptive diagnosis of peritoneal tuberculosis, and RHZE was started. Later, peritoneal fluid cultures became positive for MTb. In both cases, the immunization schedule was updated, including vaccination with BCG. The two girls’ clinical status improved under antituberculous therapy.

Learning Points/Discussion: Despite a decrease in incidence rates in Portugal, infection by MTb remains a common diagnosis. This agent must be considered even in the absence of signs of pulmonary infection, due to the high rates of morbidity and mortality associated with EPTb. These two cases show how important a high degree of clinical suspicion is.
Title of Case(s): Congenital Cytomegalovirus – Neuroimaging And Treatment Controversies In Two Case Reports

Background: Congenital cytomegalovirus (cCMV) is one of the major infectious causes of sensorineural hearing loss and neurodevelopmental abnormalities in infants. Despite its clinical importance, questions remain regarding neuroimaging modalities and therapeutic strategies for infected neonates and mothers.

Case Presentation Summary: Case 1. A medical physician (Gravida I) experienced mononucleosis-like symptoms at 20 weeks of gestation. At 34 weeks, serum immunoassay was positive for CMV IgM and IgG with low avidity antibodies and valaciclovir was initiated. Mild calcifications on thalamoperforating vessels were observed by brain ultrasound on day one postpartum. Posterior ultrasounds were considered normal. cCMV was established on day 15 of life by positive polymerase chain reaction (PCR) on urine and saliva samples. At two months of age, brain magnetic resonance imaging (MRI) was normal. No postnatal antiviral therapy was performed. At one year of age, this infant remains without auditory or neurodevelopmental impairment.

Case 2. A dental assistant (Gravida III Para I) was diagnosed with primary CMV-infection at 17 weeks of gestation. At 23 weeks, amniotic fluid revealed positive CMV-DNA and treatment with valaciclovir was initiated. Fetal MRI at 33 weeks of gestation detected intracranial cysts. On day one of life, cCMV was established by PCR on urine/blood samples and cranial ultrasound was considered normal. On day 10, T2-weighted MRI showed occipital pseudocysts and frontoparietal white matter areas of high signal intensity. This patient was treated with oral valganciclovir (six-month treatment course). At eight months of age, brainstem evoked response audiometry showed normal hearing threshold levels (30dB).

Learning Points/Discussion: The pediatrician plays an important role in the anticipatory management of cCMV. It is essential to know prenatal/neonatal clinical clues and the algorithm assessment after diagnosis, considering there are therapeutic options implying better prognosis. Due to viral latency, long-term multidisciplinary assessment is mandatory.