Background The definition for sepsis was updated (Sepsis-3) to improve the sensitivity of identifying patients at risk for poor clinical outcomes, which was lacking with SIRS criteria. Our objective was to evaluate the predictive value of Sepsis-3 vs SIRS criteria for mortality in patients with Enterobacteriacae (EB) infections. Methods This was a retrospective cohort study of all admitted patients with EB infection between Jun 2015-Oct 2017. Patients were excluded if: <18yo, received effective therapy <48 hours, antibiotic therapy not started within 48 hr from 1st culture date, polymicrobial culture, and full medical chart unavailable for review. Medical charts were reviewed to evaluate for the number of criteria met for Sepsis-3 and SIRS at the onset of infection. The primary outcome was 30-day mortality. Secondary outcomes were hospital length of stay (LOS) and clinical success. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of Sepsis-3 vs SIRS criteria to predict 30-day mortality were calculated and compared. Results 259 patients met inclusion criteria; median age was 56 years old, 45% were male, and 72% were Hispanic. Median Charlson Comorbidity Index score was 3. The most common infectious diagnosis was UTI (38%) and pneumonia (25%). Overall, mortality was 15%. Patients who met sepsis-3 criteria (125/255, 49%) had higher mortality rate (22%) compared to patients who did not meet sepsis-3 criteria (8%, p=0.003). Sepsis-3 positive patients also had significantly longer LOS (15.5 days vs 6 days, p=0.0019) and lower rate of clinical success (89% vs 69%, p<0.0001). However, SIRS criteria did not differentiate mortality rate (SIRS positive: 24/173, 14% vs SIRS negative: 15/85, 18%, p=0.5), hospital LOS (SIRS positive median 8 days vs SIRS negative 11days, p=0.7), or clinical success (SIRS positive: 134/173, 77% vs SIRS negative: 70/85, 82%, p=0.4). Sepsis-3 criteria had higher sensitivity (71.8%, 95%CI: 56.2-83.5), specificity (55.1%, 95%CI: 48.4-61.6), PPV (22.4%, 95%CI: 15.9-30.5), and NPV (91.5%, 95%CI: 85.5-95.2) for mortality prediction compared to SIRS criteria (sensitivity 61.5%, 95%CI: 45.9-75.1; specificity 31.9%. 95%CI 26.1-38.4; PPV 13.9%, 95%CI: 9.5-19.8; NPV 82.4%, 95%CI: 72.9-89%). Conclusion Sepsis-3 criteria has better predictive value than SIRS criteria in identifying patients at risk for mortality from EB infections. Sepsis-3 shows promise to be a more sensitive tool to use at bedside that SIRS in identifying those who warrant early aggressive management.
Abstract Title:

Primary Author Block:
A. P. Gould1, C. Drennan2, O. Hill2, P. Bookstaver2, J. A. Justo2, J. Kohn1, M. N. Al-Hasan1; 1Palmetto Hlth.Richland, Columbia, SC, 2South Carolina Coll. of Pharmacy, Columbia, SC

Abstract Body:
Background: Increasing rates of antimicrobial resistance have limited fluoroquinolone (FQ) use for empirical therapy of serious infections, such as bloodstream infections (BSI). However, recent studies have demonstrated low FQ resistance rates in bloodstream isolates of patients without resistance risk factors such as prior antimicrobial use, residence in skilled nursing facilities, or recent ambulatory gastrointestinal or genitourinary procedures. This retrospective matched cohort study examined clinical outcomes in patients receiving empirical FQ or beta-lactam (BL) monotherapy for gram-negative BSI in the absence of risk factors for antimicrobial resistance at initial presentation. Methods: Hospitalized adults with gram-negative BSI from January 1, 2010 to June 30, 2015 at Palmetto Health hospitals in Columbia, SC, USA were identified. Patients without risk factors for antimicrobial resistance receiving empirical FQ were matched to those receiving BL in 1:2 fashion based on age, sex, and bloodstream infection mortality risk score. Multivariable logistic regression was used to examine early treatment failure, defined as mortality or persistence of ≥2 of the following criteria by 96 hours: fever/hypothermia, hypotension, mechanical ventilation, altered mental status, and leukopenia/leukocytosis. Cox proportional hazards regression was used to examine 28-day mortality and hospital length of stay (HLOS). Results: During study period, 74 and 148 patients receiving FQ and BL empirical therapy, respectively, for gram-negative BSI were matched and included in final analysis. Overall, median age was 68 years, 159 (72%) were women, 157 (71%) had community-acquired BSI, and 152 (68%) had urinary source of infection. Empirical antimicrobial therapy was appropriate in 69 (93%) and 145 (98%) patients in FQ and BL groups, respectively. Early treatment failure rates were comparable in FQ and BL groups (12% vs. 16%, respectively, odds ratio 0.70, 95% confidence intervals [CI] 0.30-1.62, p=0.41) as well as 28-day mortality (8.9% vs. 9.7%, respectively, hazards ratio [HR] 0.74, 95% CI 0.26-1.90, p=0.54). Median HLOS was 6.1 days in empirical FQ group and 7.1 days in BL group (HR 0.73, 95% CI 0.54-0.99, p=0.04). Conclusion: In the absence of risk factors for antimicrobial resistance, FQ seem to provide an additional option to BL for empirical therapy of gram-negative BSI. Shorter HLOS in FQ group as compared to BL may be due to smoother transition from intravenous to oral antimicrobial therapy and warrants further investigations.
Abstract Title:
Outstanding Abstract Award: Clinical Prediction Score for Community-Onset Bloodstream Infections Caused by Extended-Spectrum Beta-Lactamase-Producing Escherichia coli and Klebsiella Species
Primary Author Block:
M. Kim1, K-H. Song1, C-J. Kim1, P. Choe2, W. Park2, J. Bang2, E. Kim1, S-W. Park2, N. Kim2, M-d. Oh2, H. Kim1; 1Seoul Natl. Univ. Bundang Hosp., Seongnam, Korea, Republic of, 2Seoul Natl. Univ. Coll. of Med., Seoul, Korea, Republic of
Abstract Body:
Background: The incidence of infections due to extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae has been increasing in the community. This study aimed to identify the predictors and build a prediction score for community-onset bloodstream infections (CO-BSIs) caused by extended-spectrum beta-lactamase (ESBL)-producing Escherichia coli and Klebsiella species. Methods: All CO-BSIs caused by E. coli and Klebsiella species from 2012 to 2015 were included in the study. The study subjects were divided into derivation (BSIs from 2012 to 2014) and validation (BSIs in 2015) cohorts. A prediction score was built based on the multivariate logistic regression model and coefficients using the subjects in the derivation cohort. Results: The study included 886 CO-BSIs (594 and 292 in the derivation and validation cohorts, respectively). Multivariate logistic regression analysis revealed that the independent predictors of CO-BSIs caused by ESBL-producing E. coli and Klebsiella species included (1) identification of ESBL-producing microorganisms from any clinical culture within one year of admission, (2) hospitalisation within one year, (3) antimicrobial treatment with third-generation cephalosporins within 30 days, and (4) the presence of an indwelling urinary catheter at the time of admission. The area under the curve (AUC) of the clinical prediction score was 0.72 (95% confidence interval [CI] 0.67-0.77). When the prediction score was applied to the validation cohort, the AUC was 0.70 (95% CI 0.63-0.77). Conclusions: The results of this study suggest a simple and easy-to-use scoring system to predict CO-BSIs caused by ESBL-producing E. coli and Klebsiella species. We expect this strategic approach will help to improve the clinical outcomes and control broad-spectrum antimicrobial use for the treatment of community-onset infections.
Abstract Title:
Multicenter Evaluation of Ceftolozane-Tazobactam Monotherapy versus Combination Therapy for Multidrug-Resistant Pseudomonas Aeruginosa Infections

Primary Author Block:

Abstract Body:
Background: Combination therapy for Pseudomonas aeruginosa (PA) infections is controversial. Theoretical benefits (synergy, resistance prevention and improved adequacy of empiric therapy) may be mitigated by adverse effects. Ceftolozane-tazobactam (C/T) demonstrates potent in vitro activity against multidrug-resistant (MDR) PA, yet despite high PA susceptibility rates, combination therapy is still frequently utilized. We sought to evaluate efficacy and safety outcomes with C/T monotherapy (C/T-M) vs. C/T combination therapy (C/T-C) for MDR PA infections. Methods: This was a retrospective, multicenter, observational study from 2015 to 2017 in adult patients (≥ 18 y) with MDR PA infections treated with C/T for ≥ 72 h. Combination therapy was defined as receipt of an IV or inhaled aminoglycoside (AMG), polymyxin or fluoroquinolone for ≥ 48 h concomitant with C/T. The primary efficacy outcome was a composite of 30-d mortality and/or 30-d recurrence. The primary safety outcome was nephrotoxicity. Independent predictors of the primary outcomes were sought through multivariable regression analysis. Results: A total of 105 patients were included (68 CT-M, 37 C/T-C including 25 IV, 14 inhaled and 2 both). The most common source of infection was respiratory (63.8%). Median (IQR) time to C/T initiation from culture collection was 3 (2 - 5) d. Baseline clinical and infection characteristics were similar between groups except C/T susceptibility was higher in the CT-M group (98% vs. 71.4%; P = 0.001). An AMG was the most common combination agent (81.1%). On univariate analysis, there was no significant difference between groups in composite failure (CT-M 27.9% vs. CT-C 27.0%; P = 0.920). Nephrotoxicity was significantly higher in the C/T-C group (C/T-M 1.7% vs. C/T-C 14.3%; P = 0.023). Multivariable regression analysis revealed that APACHE II score ≥ 20, (aOR 3.70; 95% CI 1.28 - 10.68), diabetes mellitus (aOR 3.02; 95% CI 1.16 - 7.91), and age ≥ 65 y (aOR 2.72; 95% CI 1.03 - 7.15) were independent predictors of the primary efficacy outcome. Use of vasopressors (aOR 36.29; 95% CI 2.93 - 450.08) and combination IV therapy (aOR 13.73; 95% CI 1.25 - 150.67) were independently associated with nephrotoxicity. Conclusions: The addition of a second active antibiotic was not associated with improved efficacy in patients treated with C/T for MDR PA infections but combination IV therapy was independently associated with nephrotoxicity. Additional research evaluating the benefits and risks of C/T combination therapy for MDR PA is urgently needed.
Abstract Title:
Clinical Characteristics and Outcomes Of Staphylococcus aureus Bacteremia in Neutropenic Patients with Hematologic Diseases: A 10-year Experience of A Tertiary-care Hospital

Primary Author Block:

Abstract Body:
Background: Staphylococcus aureus bacteremia (SAB) is one of serious bacterial infections. However, there are limited data on clinical characteristics and outcomes of SAB in neutropenic patients with hematologic malignancy. Methods: We compared clinical characteristics and outcomes of SAB in neutropenic hematologic patients, in neutropenic solid tumor patients, and in non-neutropenic patients without malignancy, using a prospective cohort of SAB patients at a tertiary-care hospital from 2008 to 2017. Results: Our cohort consisted of 2,613 patients; 64 (2.4%) neutropenic hematologic patients, 24 (0.9%) neutropenic solid tumor patients, and 847 (32.4%) non-neutropenic patients without malignancy. Nosocomial and primary bacteremia were more frequent in neutropenic hematologic patients than in other two groups. There was no significant difference in the incidence of metastatic infections among 3 groups (17.2% vs. 16.7% vs. 20%). Although the removal of eradicable focus was less frequent in neutropenic hematologic patients, crude mortality of this group was not higher than that of other two groups. In particular, neutropenic hematologic patients showed significantly lower 12-week mortality than neutropenic solid tumor patients (15.6% vs. 45.8%; p = 0.003). In the multivariable analysis, independent risk factors for mortality were age, Charson comorbidity score, Pitt bacteremia score, pneumonia, longer duration of bacteremia, and metastatic infection. Conclusion: Our findings suggest that clinical characteristics and outcomes of SAB in neutropenic hematologic patients are not significantly different from those in non-neutropenic patients. Key words: Staphylococcus aureus, bacteremia, neutropenia, hematologic disease
Abstract Title:
A Partition of Toxoplasma gondii Genotypes Across Spatial Gradients and among Host Species, and Decreased Parasite Diversity Towards Anthropized Environment in North America

Primary Author Block:
T. J. Jiang, 37917; The Univ. of Tennessee, Knoxville, TN

Abstract Body:
Previous studies have demonstrated that North American T. gondii populations are clonal and dominated by a few lineages identified as types II, III, and type 12. It has been revealed that type 12 is the dominate genotype in wildlife in North America. Whereas type II is mostly found in domestic animals. To better understand habitat effects on this parasite’s transmission, we compiled and analyzed existing genotypic data from animals across a proximity gradient from anthropized environments to the wilderness in North America. Toxoplasma isolates were divided into three groups: (a) farm-bound animals; (b) from free-roaming animals; and (c) from wildlife. Furthermore, parasite genotype distribution in different animal species was analyzed. The results showed that, the genotypic composition of parasites in wildlife differed from those in farm-bound and free-roaming animals. In addition, parasite genotypes differed among animal host species. We conclude that T. gondii genotype distribution is influenced by the spatial habitat and host species composition, and parasite diversity decreases towards the human environment, suggesting human settlements affect parasite transmission and genotype distribution.
Abstract Title: The use of whole genome sequencing technology to elucidate the genomic variation and epidemiology of Candida glabrata in United States

Primary Author Block: R. M. Welsh, L. Gade, M. Bentz, N. Chow, N. Le, S. Lockhart, A. Litvintseva; CDC, Atlanta, GA

Abstract Body:
Background: Candida glabrata is the second most common causative agent of systemic candidiasis in United States (US). Some strains of C. glabrata are resistant to multiple classes of antifungals, severely limiting treatment options. C. glabrata infections typically occur as a result of autoinfection from endogenous populations present in patient microbial flora. A small fraction of cases are hypothesized to be nosocomially transmitted patient-to-patient, but strain typing is needed to distinguish between the two scenarios. Whole-genome sequencing (WGS) is ideal for the analysis of the molecular epidemiology and phylogeography. Herein, we investigated the utility of WGS to assess transmission of C. glabrata within healthcare facilities.

Methods: We performed WGS using Illumina short-read sequencing technology on 40 US isolates obtained from axilla, nares, and groin skin sites. Skins swabs were collected in order to screen for Candida colonization from multiple facilities, including 19 from facility A and 10 from Facility B. PacBio long-read sequencing technology used to generate a de novo reference genome assembly. SNP variants were identified using GATK and the NASP SNP analysis pipeline. Phylogenies were inferred using a maximum likelihood algorithm.

Results: All isolates had at least 75X sequence coverage. Seven major clades were identified with our phylogenetic analysis. Pairs of isolates from the same patient (n=8) displayed the tightest clustering with an observed relatedness of 0.0038-0.1688 allele sharing distance (ASD) or genetic distance, and the overall range of pairwise relatedness for all isolates (n=41) was 0.0038 - 0.3755 ASD. A subset of isolates collected from different patients at the same facility display similar clustering (0.0041-0.0079 for facility B and 0.0073-0.0074 for facility A).

Facility A included isolates from all seven major clades. Conclusions: Substantial genomic diversity of C. glabrata was observed within isolates collected from a single facility. US isolates did not always cluster by patient, facility, or even state. Continued WGS and phylogenetic analysis may help track the spread of Candida species and improve infection control.
Abstract Title: Detection of Binary Toxin Coding Genes in Clostridioides [Clostridium] difficile Isolates Recovered from a Pediatric Population in Buenos Aires, Argentina.

Primary Author Block: M. L. Maldonado1, D. Cejas2, M. Litterio1, C. Hernandez1, G. Gutkind2, M. Radice2; 1Hosp. de Pediatria Garrahan, Buenos Aires, Argentina, 2Univ. de Buenos Aires, CONICET, Buenos Aires, Argentina

Abstract Body:
Background: The incidence of C. difficile infection (CDI) in hospitalized children have been increasing worldwide. A previous study performed in Argentina in an adult population reported that 21% of toxigenic C. difficile isolates, harboring tcdA and tcdB genes, also presented the binary toxin genes (cdtA/cdtB). However, in our country no data is available about toxigenic C. difficile recovered from stool samples of hospitalized children with acute diarrhea. The aim of this study was to perform the molecular characterization of C. difficile isolates from children with CDI in a Pediatric Hospital in Buenos Aires and to analyze its correlation with clinical outcomes.

Methods: 89 C. difficile isolates were recovered from diarrheal stool samples of hospitalized patients with presumptive CDI, between June 2016 and January 2018 at a Pediatric Hospital. Toxins TcdA/TcdB and C. difficile presence were investigated by enzyme immunoassay (EIA) and by Glutamate Dehydrogenase (GDH) detection, respectively. Susceptibility to metronidazole (MTZ) and vancomycin (VAN) was determined according to CLSI. A multiplex PCR was carried out in order to detect tcdA, tcdB, cdtA and cdtB according to Persson et al, using genomic DNA obtained from C. difficile cultures as template. Results: All samples were positive for GDH and 59/89 samples were TcdA/TcdB positive by EIA. 84/89 isolates were positive for both tcdA/tcdB and 1/89 was tcdA/-tcdB+. Thirty two percent of the tcdA+/tcdB+ isolates were also positive for cdtA/cdtB (27/84). The cdtA/cdtB positive isolates were recovered from 21 patients, 12/21 presented moderate to severe CDI and 8/21 presented at least 1 recurrence episode. From this latter, 2/8 patients received empiric treatment, 2/8 were reinfected with a cdtA-/cdtB- strain and 4/8 were reinfected with a cdtA+/cdtB+ strain. One out of 21 patients died from septic shock. MIC90 (µg/ml) of MTZ and VAN were 0.032 and 0.5, respectively, being the MIC90 for cdtA+/cdtB+ isolates 0.016 and 0.25 for MTZ and VAN, respectively. Conclusions: High incidence rates of cdtA+/cdtB+ isolates were noticed in the analyzed pediatric population when compared with an adult population (32% versus 21%). Our results encourage further studies concerning the molecular typing of these isolates. Disregarding clinical outcomes and the presence of toxins genes all isolates remained susceptible to MTZ and VAN which are first line therapy drugs for CDI.
Abstract Title:
Levels of Inflammatory Mediators among Confirmed N. Meningitidis Positive Meningitis Patients with Varied Amounts of Bacterial DNA and Endotoxin Activity

Primary Author Block:

Abstract Body:
Background: Bacterial meningitis (BM) is a severe infectious disease of the nervous system that needs urgent medical attention. Ethiopia, a country located at the eastern end of the “meningitis belt”, is frequently affected by meningitis epidemics. Objective: Measuring levels of inflammatory mediators among N. meningitidis confirmed positive meningitis patients with varied amounts of bacterial DNA and endotoxin activity. Methods: A prospective case-based study was launched from 2012-2013 on 139 patients clinically diagnosed with BM from three referral level university hospitals in Ethiopia. Sera of 27 Nm confirmed positive patients were evaluated by immunological assays while levels of endotoxin activity in the CSF was measured with limulus amoebocyte lysate (LAL). Result: Age groups of patients confirmed positive for Nm were varying from 2 days to 39 years old. Real time PCR (RT-PCR) detected a total of 27 ctrA gene of N. meningitidis genogroups A (11/27, 40.7%), W-135 (7/27, 26%), C (1/27, 3.7%), X (1/27, 3.7%) and non-groupable (7/27, 26%). Only 23 out of 27 real-time PCR confirmed Nm positive patients, had detectable CSF N. meningitidis (Nm) DNA in the circulation and this group had a median of 8.2 x 105 (range < 2.5 x 102-1.4x107) copies of NmDNA per ml. In 6 out of the 23 (26%) patients matched serum samples, detectable levels of NmDNA was found with median concentration of 2.1 x104 (range 6.4 x103-1.8 x 105) copies per mL. The difference in copies of NmDNA between the CSF and serum was statistically significant (P < 0.05). Significant differences were not observed in the levels of endotoxin activity, NmDNA load and levels of cytokines, chemokines, or MMP-9 in the CSF across the different gender or age groups, or between deceased and surviving patients. No correlations were found between age and endotoxin activity as well as NmDNA, whereas a negative correlation was apparent between age and levels of IL-18 (r=-0.45, P=0.02, n=26). On the other hand, NmDNA copy number was positively correlated with IL-18 (r=0.62, P=0.002, n=23) and MMP-9 (r=0.46, P=0.03, n=23) while negatively correlated with IL-6 (r=-0.45, P=0.03, n=23). Conclusion: the presence of significantly higher
levels of bacteria in the subarachnoid space than in the blood of the 21 Ethiopian meningococcal meningitis patients may have an impact on immune responses and clinical outcomes. Key words: Bacterial meningitis, Endotoxin activity, Cerebrospinal fluid
Abstract Title:
Effect of Virus-like Particle Fusion on the Uptake of Antigens Derived from Neisseria Meningitidis
Primary Author Block:
M. Jibril, J. Derrick, E. Carlsson, S. Aston-Deaville; Univ. of Manchester, Manchester, United Kingdom
Abstract Body:
Neisseria meningitidis is a Gram-negative bacterium and obligate human pathogen, causing meningitis and septicaemia. There have been effective vaccines for serotypes A, C, W135 and Y produced using their capsular polysaccharides (CPS) but with limited impact against serogroup B (MenB). Hepatitis B core antigen (HBCAg) was used as a virus-like particle (VLP) scaffold; using a process of structural design, whole domains from defined meningococcal surface antigens were incorporated into HBCAg, and the fusion proteins expressed, purified and their assembly verified by electron microscopy. Uptake of these VLP-antigen fusion proteins by dendritic cells and macrophages was compared by cell culture and FACS analysis of cell surface markers. HBCAg and HBCAg-antigen fusion VLPs were shown to be both effectively internalized by THP-1-derived macrophages. In the case of dendritic cells, however, differences were noted in the efficiency of uptake of antigen domain alone and the cognate HBCAg-antigen fusion; reasons for this divergence will be discussed.
Abstract Title:
Replicating Single-cycle Adenovirus Vaccine against Clostridium difficile

Primary Author Block:
W. Matchett, M. Barry; Mayo Clinic, Rochester, MN

Abstract Body:
Background: Clostridium difficile (C. difficile) causes nearly 500,000 infections and 30,000 deaths in the U.S. each year. C. difficile is an anaerobic, gram-positive, spore-forming, toxin-producing bacillus that colonizes the large intestine in susceptible individuals. Once colonization has occurred, pathogenic strains release two protein endotoxins, Toxin A (TcdA) and Toxin B (TcdB), that cause colitis that can result in life-threatening disease. Standard C. difficile infection (CDI) therapies utilize antibiotics that are limited by their broad spectrum and can cause further disruption of the intestinal microbiota, which results in a high rate of recurrence. Methods: Vaccines may offer the best opportunity for sustained, long-term protection against C. difficile. Towards this goal, we developed a novel single-cycle adenovirus (SC-Ad) -gene-based vaccine against C. difficile. Unlike common replication-defective Ad vaccines, SC-Ad vectors replicate antigen genes thousands of times to amplify immune responses. However, unlike fully replication-competent Ads, SC-Ad cannot cause dangerous adenovirus infections. Low seroprevalence SC-Ad6 was engineered to express fused and secreted receptor-binding domains (RBDs) from C. difficile’s two endotoxins TcdA and TcdB. Results: Western blot of transduced cells showed the production and secretion of both TcdA and TcdB RBDs. A single intramuscular or intranasal immunization of mice with this SC-Ad vaccine generated TcdA and B binding antibodies that climbed over one half of a year to reciprocal titers above 105 against both toxin A and B. Samples collected 6 months after single immunization had an average reciprocal TcdB neutralizing titer of 185. When mice were challenged with a lethal dose of TcdA 38 weeks after the single vaccination, all animals in the SC-Ad C. difficile vaccine group survived. In contrast, all PBS and control SC-Ad vaccinated animals succumbed to the toxin within 48 hours. When male and female animals were vaccinated a single time with the vaccine, both sexes generated significant Tcd binding reciprocal titers above 10,000 within 6 weeks with somewhat higher titers in females. When these animals were challenged with TcdA, both sexes repelled the toxin. Conclusions: The ability to vaccinate a single time and provoke long-lasting protective antibodies shows promise when compared to benchmark protein vaccines that may require three or more vaccinations. These data suggest that this replicating single-cycle Ad vaccine may have utility as single vaccine against C. difficile.
Session Number: 65
Session Type: Late-Breaker Poster Presentations

Session Title: FRIDAY - CIV Late-breakers
Session Start Date Time: 6/8/2018 11:00:00 AM
Session End Date Time: 6/8/2018 1:00:00 PM
Session Primary Track: Clinical Infections and Vaccines
Abstract Control Number: 7577
Poster Board Number: FRIDAY - CIV LB8

Abstract Title:
Evaluation of Surface Sampling Tools for Recovery of HAI Pathogens and an Ebola Surrogate

Primary Author Block:
M. M. Martinez, L. J. Rose, J. C. Whitworth, J. A. Noble-Wang; Ctr.s For Disease Control and Prevention, Atlanta, GA

Abstract Body:
Background: Environmental surfaces may play a significant role in transmission of healthcare-associated infections (HAI). Surface sampling is helpful to investigate transmission of HAI from the environment, but currently no standard sampling protocol exists, and little is known about the recovery efficiency of sampling tools. A prototype polyurethane foam paddle (PP; Puritan Medical Products) was developed and compared to the Sponge Stick (SS; 3M™). Methods: A. baumannii (AB), vancomycin-resistant E. faecalis (VRE), Methicillin-resistant S. aureus (MRSA), C. difficile (CD) and Pseudomonas bacteriophage phi6 (Φ6, as an Ebola surrogate) were sampled from two healthcare surfaces: stainless steel and textured plastic. Surfaces (50 in2) were inoculated with 104 CFUs/PFUs of organism suspended in a body fluid simulant, dried for 1 hour, and then sampled with SS and PP tools. The organisms were eluted from the sampling tools, cultured, and percent recovery (%R) was calculated. Results: The %R of A. baumannii, VRE, & MRSA was significantly higher (p<0.01) for PP than SS for both surfaces. There was no significant difference between PP and SS in recovery of C. difficile on stainless steel. Regardless of these variations in %R, the overall recovery of all bacteria was within the same order of magnitude. Alternatively, though the %R of Φ6 with SS was greater than with PP (p<0.01) from both surfaces, use of both sampling tools demonstrated an order of magnitude loss (% R at < 5%). Conclusions: The %R varied with organism, surface, and sampling tool. The low %R demonstrates any sampling may underestimate the surface contamination and therefore the potential for transmission from surfaces. This work informs epidemiologists and researchers about the limits and differences between sampling tools, and contributes data for standardizing environmental surface sampling methods for studies and outbreak investigations.
Abstract Title:

Primary Author Block:
A. P. Gould1, C. Drennan2, O. Hill2, P. Bookstaver2, J. A. Justo2, J. Kohn1, M. N. Al-Hasan1; 1Palmetto Hlth.Richland, Columbia, SC, 2South Carolina Coll. of Pharmacy, Columbia, SC

Abstract Body:
Background: Increasing rates of antimicrobial resistance have limited fluoroquinolone (FQ) use for empirical therapy of serious infections, such as bloodstream infections (BSI). However, recent studies have demonstrated low FQ resistance rates in bloodstream isolates of patients without resistance risk factors such as prior antimicrobial use, residence in skilled nursing facilities, or recent ambulatory gastrointestinal or genitourinary procedures. This retrospective matched cohort study examined clinical outcomes in patients receiving empirical FQ or beta-lactam (BL) monotherapy for gram-negative BSI in the absence of risk factors for antimicrobial resistance at initial presentation. Methods: Hospitalized adults with gram-negative BSI from January 1, 2010 to June 30, 2015 at Palmetto Health hospitals in Columbia, SC, USA were identified. Patients without risk factors for antimicrobial resistance receiving empirical FQ were matched to those receiving BL in 1:2 fashion based on age, sex, and bloodstream infection mortality risk score. Multivariable logistic regression was used to examine early treatment failure, defined as mortality or persistence of ≥2 of the following criteria by 96 hours: fever/hypothermia, hypotension, mechanical ventilation, altered mental status, and leukopenia/leukocytosis. Cox proportional hazards regression was used to examine 28-day mortality and hospital length of stay (HLOS). Results: During study period, 74 and 148 patients receiving FQ and BL empirical therapy, respectively, for gram-negative BSI were matched and included in final analysis. Overall, median age was 68 years, 159 (72%) were women, 157 (71%) had community-acquired BSI, and 152 (68%) had urinary source of infection. Empirical antimicrobial therapy was appropriate in 69 (93%) and 145 (98%) patients in FQ and BL groups, respectively. Early treatment failure rates were comparable in FQ and BL groups (12% vs. 16%, respectively, odds ratio 0.70, 95% confidence intervals [CI] 0.30-1.62, p=0.41) as well as 28-day mortality (8.9% vs. 9.7%, respectively, hazards ratio [HR] 0.74, 95% CI 0.26-1.90, p=0.54). Median HLOS was 6.1 days in empirical FQ group and 7.1 days in BL group (HR 0.73, 95% CI 0.54-0.99, p=0.04). Conclusion: In the absence of risk factors for antimicrobial resistance, FQ seem to provide an additional option to BL for empirical therapy of gram-negative BSI. Shorter HLOS in FQ group as compared to BL may be due to smoother transition from intravenous to oral antimicrobial therapy and warrants further investigations.
Abstract Title:
Clinical Impact of Delayed Catheter Removal for Patients with Central Venous Catheter-Related Gram-Negative Bacteremia
Primary Author Block:
Y-M. Lee1, C. Moon2, Y. Kim1, H-J. Lee1, M. Lee1, K-H. Park1; 1Kyung Hee Univ. Hosp., Seoul, Korea, Republic of, 2Busan Paik Hosp., Busan, Korea, Republic of
Abstract Body:
Background: Gram-negative bacteria are increasingly the cause of catheter-related bloodstream infections (CRBSI), which show a rapidly rising prevalence of multidrug-resistant strains. We evaluated the impact of delayed central venous catheter (CVC) removal on clinical outcomes in patients with gram-negative CRBSI. Methods: Between January 2007 and December 2016, patients with gram-negative bacteremia and CVC placement, from two tertiary care hospitals, were retrospectively included. Cases with CVC removal > 3 days after onset of bacteremia or without CVC removal were classified as having delayed CVC removal. Results: A total of 112 patients were included. Of these, 78 had CRBSI (43 definite and 35 probable), and 34 had gram-negative bacteremia from another source (non-CRBSI). The Enterobacteriaceae were less frequent pathogens in patients with CRBSI than in those with non-CRBSI (11.5% vs. 41.3%; P <0.001). Among 72 patients with CRBSI (6 patients who died before day 3 following the onset of bacteremia were excluded from the evaluation of impact of delayed CVC removal), 34 (47.2%) had early CVC removal and 38 (52.8%) had delayed CVC removal. Delayed CVC removal was associated with increased 30-day mortality (40.5% vs. 11.8%; P = 0.01) in patients with gram-negative CRBSI; this was not seen in patients with non-CRBSI (25.0% vs. 14.3%; P >0.99). Delayed CVC removal [OR = 6.8], multidrug-resistant (MDR) gram-negative bacteremia [OR = 6.3], and chronic renal failure [OR = 11.1] were associated with 30-day mortality in patients with CRBSI. The protective effect of early CVC removal on mortality was evident in the MDR group (48.3% vs. 18.2%; P = 0.03), but not in the non-MDR group (11.1% vs. 0%; P = 0.43) (Figure 1). Conclusion: CVCs should be removed early to improve clinical outcomes in patients with gram-negative CRBSI, especially where there is high prevalence of MDR isolates.
Outstanding Abstract Award: Clinical Prediction Score for Community-Onset Bloodstream Infections Caused by Extended-Spectrum Beta-Lactamase-Producing Escherichia coli and Klebsiella Species

Primary Author Block:
M. Kim1, K-H. Song1, C-J. Kim1, P. Choe2, W. Park2, J. Bang2, E. Kim1, S-W. Park2, N. Kim2, M-d. Oh2, H. Kim1; 1Seoul Natl. Univ. Bundang Hosp., Seongnam, Korea, Republic of, 2Seoul Natl. Univ. Coll. of Med., Seoul, Korea, Republic of

Abstract Body:
Background: The incidence of infections due to extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae has been increasing in the community. This study aimed to identify the predictors and build a prediction score for community-onset bloodstream infections (CO-BSIs) caused by extended-spectrum beta-lactamase (ESBL)-producing Escherichia coli and Klebsiella species. Methods: All CO-BSIs caused by E. coli and Klebsiella species from 2012 to 2015 were included in the study. The study subjects were divided into derivation (BSIs from 2012 to 2014) and validation (BSIs in 2015) cohorts. A prediction score was built based on the multivariate logistic regression model and coefficients using the subjects in the derivation cohort. Results: The study included 886 CO-BSIs (594 and 292 in the derivation and validation cohorts, respectively). Multivariate logistic regression analysis revealed that the independent predictors of CO-BSIs caused by ESBL-producing E. coli and Klebsiella species included (1) identification of ESBL-producing microorganisms from any clinical culture within one year of admission, (2) hospitalisation within one year, (3) antimicrobial treatment with third-generation cephalosporins within 30 days, and (4) the presence of an indwelling urinary catheter at the time of admission. The area under the curve (AUC) of the clinical prediction score was 0.72 (95% confidence interval [CI] 0.67-0.77). When the prediction score was applied to the validation cohort, the AUC was 0.70 (95% CI 0.63-0.77).

Conclusions: The results of this study suggest a simple and easy-to-use scoring system to predict CO-BSIs caused by ESBL-producing E. coli and Klebsiella species. We expect this strategic approach will help to improve the clinical outcomes and control broad-spectrum antimicrobial use for the treatment of community-onset infections.
Abstract Title:
The Bacteremia of AmpC β-Lactamase-Overproducing Enterobacter Sp: Clinical Characteristics and Susceptibility to Piperacillin-Tazobactam

Primary Author Block:
K. Yamairi, K. Yamada, W. Shibata, H. Namikawa, H. Fujimoto, H. Kakeya; Osaka City Univ. Graduate Sch. of Med., Osaka, Japan

Abstract Body:
Background: AmpC β-lactamase-overproducing Enterobacter sp (AmpC-Enterobacter) is one of the main antimicrobial resistant pathogens. This study aimed to assess the risk factors and appropriate chemotherapy for patients with bacteremia due to AmpC-Enterobacter. Methods: Medical records of patients with Enterobacter sp bacteremia who had been admitted to Osaka City University Hospital between January 2011 and December 2017 were retrospectively reviewed. Patient background, risk factors for AmpC-Enterobacter, and prognosis were evaluated. In addition, regarding the strains of Enterobacter sp between April 2013 and December 2017, susceptibility to piperacillin-tazobactam were also investigated. Results: Ninety-six cases of Enterobacter sp bacteremia were documented in hospitalized patients. Forty-four (45.8%) were caused by AmpC-Enterobacter and 52 (54.2%) were caused by non-AmpC-Enterobacter. Prior exposure to cephalosporins (OR 5.730; 95% CI: 1.560-21.000; P <0.01) and carbapenems (OR 9.770; 95% CI: 2.390-40.000; P <0.01) were identified as independent risk factors for AmpC-Enterobacter. There was a significant difference in the susceptibility to piperacillin-tazobactam between AmpC-Enterobacter and non-AmpC-Enterobacter (51% and 97%; P<0.001). Conclusions: When treating Enterobacter sp bacteremia patients with a history of cephalosporin or carbapenem usage, piperacillin-tazobactam therapy should be selected carefully, with the possibility of AmpC-Enterobacter in mind.
Abstract Title:
Multicenter Evaluation of Ceftolozane-Tazobactam Monotherapy versus Combination Therapy for Multidrug-Resistant Pseudomonas Aeruginosa Infections

Primary Author Block:

Abstract Body:
Background: Combination therapy for Pseudomonas aeruginosa (PA) infections is controversial. Theoretical benefits (synergy, resistance prevention and improved adequacy of empiric therapy) may be mitigated by adverse effects. Ceftolozane-tazobactam (C/T) demonstrates potent in vitro activity against multidrug-resistant (MDR) PA, yet despite high PA susceptibility rates, combination therapy is still frequently utilized. We sought to evaluate efficacy and safety outcomes with C/T monotherapy (C/T-M) vs. C/T combination therapy (C/T-C) for MDR PA infections. Methods: This was a retrospective, multicenter, observational study from 2015 to 2017 in adult patients (≥ 18 y) with MDR PA infections treated with C/T for ≥ 72 h. Combination therapy was defined as receipt of an IV or inhaled aminoglycoside (AMG), polymyxin or fluoroquinolone for ≥ 48 h concurrent with C/T. The primary efficacy outcome was a composite of 30-d mortality and/or 30-d recurrence. The primary safety outcome was nephrotoxicity. Independent predictors of the primary outcomes were sought through multivariable regression analysis. Results: A total of 105 patients were included (68 CT-M, 37 C/T-C including 25 IV, 14 inhaled and 2 both). The most common source of infection was respiratory (63.8%). Median (IQR) time to C/T initiation from culture collection was 3 (2 - 5) d. Baseline clinical and infection characteristics were similar between groups except C/T susceptibility was higher in the CT-M group (98% vs. 71.4%; P = 0.001). An AMG was the most common combination agent (81.1%). On univariate analysis, there was no significant difference between groups in composite failure (CT-M 27.9% vs. CT-C 27.0%; P = 0.920). Nephrotoxicity was significantly higher in the C/T-C group (C/T-M 1.7% vs. C/T-C 14.3%; P = 0.023). Multivariable regression analysis revealed that APACHE II score ≥ 20, (aOR 3.70; 95% CI 1.28 - 10.68), diabetes mellitus (aOR 3.02; 95% CI 1.16 - 7.91), and age ≥ 65 y (aOR 2.72; 95% CI 1.03 - 7.15) were independent predictors of the primary efficacy outcome. Use of vasopressors (aOR 36.29; 95% CI 2.93 - 450.08) and combination IV therapy (aOR 13.73; 95% CI 1.25 - 150.67) were independently associated with nephrotoxicity. Conclusions: The addition of a second active antibiotic was not associated with improved efficacy in patients treated with C/T for MDR PA infections but combination IV therapy was independently associated with nephrotoxicity. Additional research evaluating the benefits and risks of C/T combination therapy for MDR PA is urgently needed.
Abstract Title:
Analysis of Antimicrobial Resistant Escherichia coli, Including A St131 Isolate Producing Ctx-M-15 Esbl, from A Mixed-Use Watershed in Northeast Georgia, Usa

Primary Author Block:
S. Cho1, A. H. T. Nguyen1, L. M. Hiott2, C. R. Jackson2, J. G. Frye2; 1Univ. of Georgia, Athens, GA, 2USDA, Athens, GA

Abstract Body:
Background: Our recent study isolated E. coli from the water samples collected quarterly from the Upper Oconee Watershed in northeast Georgia over a two-year period. Some of these isolates were resistant to antimicrobials used in human and veterinary medicines. Methods: Out of 496 E. coli isolated, 34 isolates with phenotypic resistance to at least one of the 14 drugs tested were analyzed. These isolates were analyzed by pulsed-field gel electrophoresis (PFGE), antimicrobial resistance (AR) gene and plasmid replicon typing (RT), and multilocus sequence typing (MLST). Two ceftriaxone-resistant isolates were further tested for the presence of extended-spectrum beta-lactamase (ESBL) genes. Results: Resistances to the drugs tested were most often associated with the following genes: mphA for azithromycin (2/2; 100.0%), floR for chloramphenicol (1/1; 100.0%), strA and strB for streptomycin (7/8; 87.5%), sul1 and sul2 for sulfisoxazole (8/8; 100.0%), tetA and tetB (25/26; 96.2%) for tetracycline, and dhfr5 and dhfr12 for trimethoprim/sulphamethoxazole (3/3; 100.0%). Three resistance genes, blaCMY, blaCTX, and blaTEM, were present (9/11; 81.8%) in β-lactam-resistant isolates. All five isolates with resistances to ciprofloxacin and nalidixic acid had single, double, or triple point mutations in gyrA and parC genes. Most (28/34; 82.4%) of the E. coli isolates carried plasmids. Of the 34 AR isolates, 29 sequence types (ST), including three ST131 and two new STs were detected. One of the suspected ESBL producers carried the blaCTX-M-15 ESBL gene while the other carried non-ESBL blaCMY-17 gene. The ESBL-producer, which also carried blaTEM-1 gene, was an epidemic ST131. Conclusions: This study identified mechanisms of resistance to commonly used antimicrobials in E. coli isolated from surface water. These E. coli often carried plasmids which may play a role in transmission of AR genes among E. coli in the environment. To our knowledge, this is the first study on the emergence of ESBL-producing E. coli ST131 from environmental water in the U.S. This study confirms the presence of AR and pathogenic E. coli, including highly pathogenic ESBL-producing E. coli, in recreational waters where there is a potential for human exposure.
Session Title: Determination of Esbl Producing Entrobacteriacea from Houseflies At the Various Food Vendor Sites in Some Major Hosp. in Greater Accra Region
Primary Author Block: H. N. A. Blankson1, P. Kwao2, N. Obeng-Nkrumah2; 1Res. Ctr. Borstel, Borstel, Germany, 2Univ. of Ghana, Korle-Bu, Accra, Ghana

Abstract Body:
Background: Houseflies increase the risk of human exposure to food borne pathogens including extended-spectrum beta-lactamase (ESBL). The spread of ESBL producing Enterobacteriaceae in communities has not only been facilitated by direct contact with humans or animal carriers, but also through contacts with insect such as houseflies. This study was designed to determine the occurrence of ESBLs in members of the family of Enterobacteriaceae recovered from houseflies in selected food vendors site in some major hospitals in the Greater Accra Region. Methods: Fly swatter was used to collect flies and then transported to the laboratory in a sterile bag. Pooled flies and food were macerated and homogenized, aseptically in brain heart infusion agar. The suspension was then cultured on MacConkey agar for about 18-24 hours. Bacterial colonies were analyzed phenotypically to identify ESBL producing enterobacteria. The DNA of the identified bacteria was extracted and the ESBL genes PCR amplified. Visualization of genes was done using 2% agarose gel electrophoresis. Results: Of the houseflies, thirty nine (39) Cephalosporin Resistant Enterobacteria (CRE) from 4 different species, mostly Proteus vulgaris and Klebsiella oxytoca, were recovered from 39 of the 60 whole insect homogenate samples. Thirty seven (from 37 different food vending samples) of the 39 CRE had ESBL (n=37), phenotype. All the 37 ESBL phenotypes, harboured ESBL gene with the blaCTX-M being the most predominant ESBL gene (n=37). Of the food samples, nine (9) CRE from 7 different species, mostly Proteus vulgaris and Escherichia coli, were recovered from 9 of the 60 whole food homogenate samples. Nine (from 9 different food vending samples) of the 9 CRE had ESBL (n=9), phenotype. All the 9 ESBL phenotypes, harboured ESBL gene with the blaCTX-M being the most predominant ESBL gene (n=9) also. Conclusions: Overall, 65% and 8% of 60 housefly and food samples respectively had ESBL-producing enterobacteria. The Cefotaximases (CTX-M), largely CTX-M-15 were the predominant ESBL genes in both housefly and food samples. Proper hygeine and sanitation at food vending sites may help reduce the spread of ESBLS.
Abstract Title:
Prostaglandin E2 Enhances Inflammasome Activation and Represses M2 Macrophage Polarization During Infection with Gram-Negative Pathogens

Primary Author Block:
A. Sheppe1, W. Hui1, M. Ross2, M. Edelmann1; 1Univ. of Florida, Gainesville, FL, 2Mississippi State Univ., Mississippi State, MS

Abstract Body:
Cellular metabolites shape the type of immune response, such as inflammatory processes in macrophages. Eicosanoids, including prostaglandins (PGs) and thromboxanes (TxBs), are lipid mediators, some of which have positive while others have adverse effects on inflammation. Certain eicosanoids are suspected to individually act as molecular sensors for recruitment of neutrophils, while others regulate bacterial uptake. In this study, gene expression analyses indicated that several genes involved in eicosanoid biosynthesis, including COX-1, COX-2, and PLA-2 are upregulated in human macrophages infected with Salmonella enterica Typhimurium or Yersinia enterocolitica. By using a targeted metabolomics approach, we found that the eicosanoid precursor arachidonic acid (AA) and its metabolites, including PGF2α, PGE2/PGD2, and TxB2, are secreted into the cell culture medium of human macrophages infected with these Gram-negative pathogenic bacteria. The magnitude of eicosanoid biosynthesis depends on the virulence of Y. enterocolitica and S. Typhimurium strains, albeit in an opposite way in Y. enterocolitica compared to S. Typhimurium infections. PGE2 pretreatment led to an increased upregulation of IL-1β transcription and secretion upon S. Typhimurium as well as Y. enterocolitica infection which indicates an increased effectiveness of inflammasome activation. Trials with combinations of EP2/EP4 PGE2 receptor agonists and antagonists before S. Typhimurium infection revealed that PGE2 signaling in this infection model works primarily through the EP4 receptor. Downstream of EP4 activation, PGE2 enhances inflammasome activation and represses M2 macrophage polarization. Our studies indicate that PGE2 is a potent enhancer of inflammasome during infection in Gram-negative bacteria, and may ultimately play a role in cell survival.
Abstract Title:
Exploring Host Range Specificity of Dictyostelium-Burkholderia Interactions

Primary Author Block:
S. A. Bargiel, S. Rubio, S. DiSalvo; Southern Illinois Univ. Edwardsville, Edwardsville, IL

Abstract Body:
Background Symbiosis is defined as the long-term interaction of two different organisms. Dictyostelium discoideum is a social soil-dwelling amoeba that is used as a model system to investigate a variety of eukaryote-bacteria interactions. We have identified several novel species of Burkholderia bacteria that colonize D. discoideum in the wild. These Burkholderia symbionts can be eliminated from their natural hosts by antibiotic treatment and can colonize new hosts in the lab via co-culturing. Fluorescently labeled Burkholderia can be observed intracellularly in amoeba hosts, both in vegetative amoebae and in reproductive spores. It is still unclear if these symbionts are specialists (only infecting D. discoideum) or generalists (bearing the ability to infect a range of eukaryotic hosts). Here, we investigate the host range of these Burkholderia symbionts with a collection of related slime mold species, including: D. giganteum, D. purpureum, D. mucoroides, and Polysphondylium violaceum. We used a fluorescently labeled representative strain for each Burkholderia symbiont species (B. agricola, B. hayleyei, and B. bonniei). Methods We cultivated each slime mold species on SM/5 agar plates with Klebsiella pneumoniae as a bacterial food source. Cultures are incubated at 21-23 °C for >4 days to allow fruiting bodies to form. To test the ability of each Burkholderia strain to infect the slime mold of interest, we plated 1 x10^5 spores with 200 µL (OD1.5) of a liquid culture of Klebsiella mixed with 5% (by volume) Burkholderia. We analyzed total spore productivity and the percent of spores infected with Burkholderia using flow cytometry and further visualized our results using confocal microscopy. Results Our preliminary results suggest that D. discoideum associated Burkholderia symbionts are predominately specialists as they infect D. discoideum more readily than the other slime molds tested. Interestingly, slime mold fitness, as measured by spore productivity, is both dependent on the Burkholderia species and the susceptibility of the slime mold to infection by the symbiont. These results define the host range of Burkholderia symbionts of Dictyostelium. In addition, they provide new opportunities for future experiments probing the basis for species barriers and for testing conditions which may modify these barriers.
Abstract Title:
Sub-Inhibitory Concentration of Silver Nitrate Decreases Phagocytosis, Attenuates Virulence and Increases Silver Tolerance of Enterobacter Cloacae Subsp. Cloacae Type Strain

Primary Author Block:

Abstract Body:
Background: The type strain of Enterobacter cloacae subsp. cloacae carries plasmid-mediated and inducible sil operon, which encodes the SilCBA efflux system and confers silver tolerance. The aim of this study was to investigate the effects of sub-inhibitory concentration of silver nitrate (AgNO3) in the virulence potential, phagocytic capacity and silver tolerance in E. cloacae subsp. cloacae type strain (ATCC 13047). Methods: Two independent and parallel bacterial inocula were sub-cultured during 12 days, one of this with sub-inhibitory concentrations of AgNO3 increasing daily in 0.025 mM/mL (0.025 - 0.3 mM/mL), representing the treated (test) strain, and the other one without AgNO3, representing the untreated (control) strain. At the end of 12th day, the experiments were performed to compare the strains. Silver tolerance was assessed using two-fold serial (0.025 - 12.8 mM/mL of AgNO3) microtiter broth dilution method to determine the minimal inhibitory concentration (MIC). Cellular Ag accumulation was measure by inductively coupled plasma mass spectrometry, using bacterial cells lysis in 2% of nitric acid solution. In vitro phagocytic capacity was verified in J774.1 mouse macrophage, using resazurin fluorescent units (RFU) and colony forming units (CFU), to determine internalized bacteria after phagocytosis period (4 hours). In addition, nitric oxide (NO) production was also determined using Griess reaction to verify the microbicde activity 24 hours after challenge with bacteria. Besides, in vivo virulence was evaluated in invertebrate Galleria mellonella by artificial infection and evaluated during 96 hours. Results: Different MIC values of AgNO3 for treated strain (0.4 mM/mL) compared to untreated strain (0.05 mM/mL) were detected, corresponding to three dilution increase in the silver tolerance. Cellular Ag accumulation for treated strain (177.5 ng/L) was much higher than untreated strain (3.7 ng/L). Decreased phagocytic capacity and reduced NO production for treated strain (RFU = 6.1 x 106, CFU = 3, and NO = 15.5 μM) compared to untreated strain (RFU = 9.6 x 107, CFU = 37, and NO = 21.9 μM) were detected. On the other hand, treated strain demonstrated attenuated virulence in G. mellonella (90% larvae survival) compared to untreated strain (15% larvae survival) up to 96 hours. Conclusions: The inducible expression of the acquired sil operon in Enterobacter cloacae increases tolerance to silver nitrate and impacts on other biological characteristics, such as decreased phagocytosis and attenuated of virulence.
Abstract Title:
Molecular Insights Into Function and Competitive Inhibition of Pseudomonas Aeruginosa Multiple Virulence Factor Regulator

Primary Author Block:

Abstract Body:
New approaches to antimicrobial drug discovery are urgently needed to combat intractable infections caused by multidrug-resistant bacteria. Multiple virulence factor regulator (MvfR), a Pseudomonas aeruginosa quorum sensing transcription factor, regulates functions important in both acute and persistent infections. Recently identified non-ligand-based benzamine-benzimidazole inhibitors of MvfR suppress both acute and persistent P. aeruginosa infections in mice without perturbing bacterial growth. Here, we elucidate the crystal structure of the MvfR ligand binding domain in complex with one potent BB inhibitor, M64. Structural analysis indicated that M64 binds, like native ligands, to the MvfR hydrophobic cavity. A hydrogen bond and pi interaction were found to be important for MvfR-M64 affinity. Surface plasmon resonance analysis demonstrated that M64 is a competitive inhibitor of MvfR. Moreover, a protein engineering approach revealed that Gln194 and Tyr258 are critical for the interaction between MvfR and M64. Random mutagenesis of the full-length MvfR protein identified a single-amino-acid substitution, I68F, at a DNA binding linker domain that confers M64 insensitivity. In the presence of M64, I68F but not the wild-type MvfR protein retained DNA binding ability. Our findings strongly suggest that M64 promotes conformational change at the DNA binding domain of MvfR and that the I68F mutation may compensate for this change, indicating allosteric inhibition. This work provides critical new insights into the molecular mechanism of MvfR function and inhibition that could aid in the optimization of anti-MvfR compounds and improve our understanding of MvfR regulation.
Abstract Title:
Microbiological Characteristics of A Novel Species Most Closely Related to Bergeyella Cardium As A Pathogen of Infective Endocarditis

Primary Author Block:
L-N. Guo, Y. Li, Y-C. Xu; Peking Union Med. Coll. Hosp., Beijing, China

Abstract Body:
Background: The genus Bergeyella, nonfermentative gram-negative bacilli within the family Flavobacteriaceae, is a rare human pathogen. Bergeyella zoohelcum has been known to cause human infections associated with animal bites. Bergeyella cardium was reported as a pathogen of infective endocarditis for the first time in Korea in 2015. In this study, we report the isolation of a bacterial that was genetically most closely related to Bergeyella cardium, from blood culture of a patient with infective endocarditis from China. Methods: A rare case of infective endocarditis caused by a species genetically closely related to Bergeyella cardium is reported. The identification, morphological characteristics and antimicrobial resistance profile of this organism are described. Results: A 24-year-old man was admitted to hospital for intermittent fever (Tmax 39.1°C) with chills and fatigue for six months. Antibiotic therapy doesn’t resolve the problem. Echocardiogram revealed congenital heart disease of patent ductus arteriosus and infective endocarditis was suspected with evidence of aortic regurgitation and multiple vegetations on the pulmonary valve and pulmonary artery wall. The patient had a sheep contact history. Cardiac surgical operation was performed and antibiotic treatment with ceftriaxone for seven weeks. The patient recovered well. Blood culture was positive for some gram-negative aerobic bacillus with irregularly shaped rods after 68 hours of incubation. This fastidious organism grew slowly on sheep blood agar at 35°C with 5% CO2 (Fig.1), was identified initially as Brevundimonas spp. by the Vitek 2 compact, but was finally confirmed as a novel species closest to Bergeyella cardium, with similarity of 98.8% to B. cardium strain 13-07T. The BD Phoenix, Vitek MS and Bruker Biotyper MS failed to identify the isolate. The strain was susceptible to β-lactams and quinolones antibiotics except for Amikacin (24 µg/ml) and Tobramycin (32 µg/ml). Conclusions: Phylogeny analysis revealed this novel species clustered well with B. cardium and other close species of the genus Bergeyella. Further studies should be performed to ascertain the potential of this bacterium to become an emerging cause of infective endocarditis.
Abstract Title:
Evaluation of Sepsis-3 Vs SIRS to Identify Patients At Risk for Mortality in Enterobacteriacae Infections
Primary Author Block:
A. Kang, D. Werge, E. Minejima; Univ. of Southern California Sch. of Pharmacy, Los Angeles, CA
Abstract Body:
Background The definition for sepsis was updated (Sepsis-3) to improve the sensitivity of identifying patients at risk for poor clinical outcomes, which was lacking with SIRS criteria. Our objective was to evaluate the predictive value of Sepsis-3 vs SIRS criteria for mortality in patients with Enterobacteriacae (EB) infections. Methods This was a retrospective cohort study of all admitted patients with EB infection between Jun 2015-Oct 2017. Patients were excluded if: <18yo, received effective therapy <48 hours, antibiotic therapy not started within 48 hr from 1st culture date, polymicrobial culture, and full medical chart unavailable for review. Medical charts were reviewed to evaluate for the number of criteria met for Sepsis-3 and SIRS at the onset of infection. The primary outcome was 30-day mortality. Secondary outcomes were hospital length of stay (LOS) and clinical success. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of Sepsis-3 vs SIRS criteria to predict 30-day mortality were calculated and compared. Results 259 patients met inclusion criteria; median age was 56 years old, 45% were male, and 72% were Hispanic. Median Charlson Comorbidity Index score was 3. The most common infectious diagnosis was UTI (38%) and pneumonia (25%). Overall, mortality was 15%. Patients who met sepsis-3 criteria (125/255, 49%) had higher mortality rate (22%) compared to patients who did not meet sepsis-3 criteria (8%, p=0.003). Sepsis-3 positive patients also had significantly longer LOS (15.5 days vs 6 days, p=0.0019) and lower rate of clinical success (89% vs 69%, p<0.0001). However, SIRS criteria did not differentiate mortality rate (SIRS positive: 24/173, 14% vs SIRS negative: 15/85, 18%, p=0.5), hospital LOS (SIRS positive median 8 days vs SIRS negative 11days, p=0.7), or clinical success (SIRS positive: 134/173, 77% vs SIRS negative: 70/85, 82%, p=0.4). Sepsis-3 criteria had higher sensitivity (71.8%, 95%CI: 56.2-83.5), specificity (55.1%, 95%CI: 48.4-61.6), PPV (22.4%, 95%CI: 15.9-30.5), and NPV (91.5%, 95%CI: 85.5-95.2) for mortality prediction compared to SIRS criteria (sensitivity 61.5%, 95%CI: 45.9-75.1; specificity 31.9%. 95%CI 26.1-38.4; PPV 13.9%, 95%CI: 9.5-19.8; NPV 82.4%, 95%CI: 72.9-89). Conclusion Sepsis-3 criteria has better predictive value than SIRS criteria in identifying patients at risk for mortality from EB infections. Sepsis-3 shows promise to be a more sensitive tool to use at bedside that SIRS in identifying those who warrant early aggressive management.
Abstract Title:
The O Serogroup Epidemiology of Invasive Extraintestinal Escherichia coli Infections: A Systematic Literature Review

Primary Author Block:
P. Hermans1, A. H. J. van den Biggelaar2, J. R. Johnson3, M. J. M. Bonten4, S. Gravenstein5, J. Geurtsen1, J. Poolman1, T. Verstraeten2;  1Janssen Vaccines & Prevention B.V., Leiden, Netherlands, 2P95 Pharmacovigilance and Epidemiology Services, 3001 Heverlee, Belgium, 3Univ. of Minnesota, Minneapolis, MN, 4Julius Ctr., UMC Utrecht, Utrecht, Netherlands, 5Brown Univ. and Providence Veterans Hosp., Providence, RI

Abstract Body:
Background: Extraintestinal pathogenic Escherichia coli (ExPEC), the most common human Gram-negative bacterial pathogen, is a leading cause of invasive infections and cause substantial global mortality. We systematically reviewed the literature to understand the distribution of O serogroups among E. coli isolates from cases of invasive ExPEC disease (IED), both overall and stratified by clinical syndrome, time period, and age group. Methods: A search combining terms for E. coli, invasive disease, and O serogroup was performed in four literature databases (Pubmed, Embase, SciELO, LILACS) to identify peer-reviewed papers published up to March 2017 reporting on IED in Europe, North America, Japan, Australia, and New Zealand. Analysis was restricted to studies reporting O serogroup data for at least 50 isolates. For qualifying studies, reported O serogroups were recorded both overall and for three clinical IED syndromes (bacteremia, urosepsis, and meningitis), three time periods (before 1985, 1985-1999, and 2000 and after), and two age groups (<18 years and ≥18 years). To calculate the prevalence of a particular O serogroup (Ox), the sum of isolates reported to belong to serogroup Ox was divided by the sum of E. coli isolates tested for that serogroup across all studies. Results: The literature search identified 25 qualifying articles, which collectively reported O serogroup data for 4529 clinical isolates from 1954 through 2009. Most studies were conducted before 1985 (n=13), had bacteremia as an outcome (n=14), and included all age groups (n=13). The number of O serogroups investigated per study varied widely. The 12 most prevalent serogroups overall in decreasing order of prevalence were O6, O1, O2, O18, O4, O75, O7, O8, O15, O16, O25, and O9. Some serogroups were more prevalent in certain patient subgroups, such as O1, O18, and O75 among meningitis patients, and O16 and O25 among adults. Of the 4 studies identified since 2000, 3 focused on children. Conclusion: Studies reporting on O serogroups associated with E. coli invasive disease are sparse. A relatively limited number of serogroups accounted for most IED isolates throughout the study period, irrespective of clinical syndrome and age group. The paucity of studies conducted since 2000 warrants that new O serogroup epidemiology studies are needed to guide vaccine development targeting specific O serogroups.
Abstract Title:
Salmonella Typhi Infection among Children in Gadap Town, Karachi

Primary Author Block:
S. Mohsin; Baqai Med. Univ., karachi, Pakistan

Abstract Body:
Background: An increasing frequency of antibiotic resistance of Salmonella Typhi and S.paratyphi species has been reported from all parts of the world principally found in developing countries with poor sanitary conditions. The actual global burden is difficult to determine because many cases are undiagnosed, particularly in young children who may have a nonspecific illness. However, the highest burden of typhoid is reported to occur in children 5-15 years of age. Objectives: To determine the frequency of Salmonella Typhi infection among children in Gadap town, Karachi. Methodology: A total of 275 blood samples were collected from the children up to the age of 14 years with clinical features suggestive of enteric fever who were admitted or visited outpatient department of pediatrics in Fatima hospital, Baqai Medical University, Karachi during the period of August 2014 to September 2015. The samples were processed and identified by biochemical reactions according to recommended guidelines. The susceptibility was also tested by Kirby bauer disc diffusion method using eight different antibiotics. Conclusion: This study indicates that Ceftriaxone and Ciprofloxacin turned out to be the best choice as empiric antibiotic therapy. Out of 29, 17(57%) of S.typhi were found to be resistant with Cefixime which shows its widespread use in children. It is also observed that most of the Salmonella Typhi strains developed multi drug resistance to most of the antibiotic tested. These resistances to numerous antibiotics are developing and this will need further monitoring to ensure it does not escalate to a problem. In cases of children, it is necessary to commence treatment before the results of laboratory antimicrobial sensitivity tests are available. Hence, the right choice of empiric therapy is of importance.
Abstract Title:
Evidence that PscF is the Molecular Target of Phenoxyacetamide Inhibitors of Type III Secretion in P. Aeruginosa

Primary Author Block:

Abstract Body:
Background: The type III secretion system (T3SS) is a clinically important virulence mechanism in Pseudomonas aeruginosa that translocates protein effector toxins into human cells to facilitate the establishment and dissemination of bacterial infection. We previously identified a highly stereo-selective phenoxyacetamide (PhA) series of inhibitors of P. aeruginosa T3SS and demonstrated that mutations selected for resistance to PhA map to the needle protein gene, pscF. Up to 100-200 copies of PscF assemble to form the T3SS needle. Methods: Mutant selection and assays of T3SS-mediated secretion and translocation were done as previously published. Directed mutagenesis of pscF was accomplished with error-prone PCR using the GeneMorph II random mutagenesis kit. Results: We present the following new evidence that supports the genetic finding that PscF is the PhA target: (a) Selected and directed mutants describe a cluster of residues in the assembled PscF needle (based on the cryo-EM/solid state NMR model of the Shigella MxiH needle by Demers et al., 2014) that appear to form a PhA binding site. (b) Addition of PhAs “heals” the type III translocation defects of some PscF mutants. (c) PhA dimers are 30-100-fold more potent than are PhA monomers, consistent with the expected savings in entropy loss required to bind the second half of the dimer to a polymeric substrate containing multiple binding sites. We also discovered that mutations in three PscF residues disrupt regulation of T3SS in Pseudomonas, implicating the needle in T3SS regulation, as has also been reported for Yersinia and Shigella. Finally, we suggest that disruption of T3SS regulation may be the mechanism of action of the PhA series. Conclusions: The cumulative results of genetic, biochemical, and chemical experiments are most consistent with a direct interaction between PhA inhibitors and the T3SS needle.

Primary Author Block:

Abstract Body:
Background: The definition of hypervirulent Klebsiella pneumoniae (hvKp), traditionally regarded as hypermucoviscosity, is controversial, but data based on phenotype (hypermucoviscous) and genetic (aerobactin) background is limited. Methods: A retrospective study was conducted in 175 patients from January 2008 to January 2014 in a tertiary teaching hospital. The detailed clinical and molecular data, containing antimicrobial susceptibility testing, string test, extended-spectrum-β-lactamase (ESBL) production, virulence gene, and multilocus sequence typing, of the hvKp group (defined as hypermucoviscosity and aerobactin positive) were compared with those of classic K. pneumoniae (cKp) isolates. Results: Of 175 K. pneumoniae isolates, 45.7% were hvKp. In pathogen aspect, the presence of K1, K2, magA and rmpA, rmpA2 genes were strongly associated with hvKp (P<0.01). In host aspect, invasive infections (P<0.000), liver abscess (P=0.008), abdominal infection (P=0.002) and sepsis shock (P=0.035) are significantly higher than cKp group. But the urinary infection is less likely occurred with hvKp. Younger and better nutritional status patients frequently infected with hvKp. However, the host inflammatory reaction is severer in hvKp group. Patients with diabetes (odds ratio [OR]=2.548) and digestive diseases (OR=2.196) are more likely to be infected with hvKp. Importantly, the detection of hvKp isolates increased from January 2008 to January 2010, January 2010 to January 2012, and January 2010 to January 2014 (12, 30, and 48 isolates, respectively). Moreover, 16.3% of hvKp isolates produced ESBLs and 20.0% are MDR-hvKp. Multivariate analysis implicated infection occurred in ICU (OR=5.826) and indwelling stomach tube (OR=6.461) as independent risk factors associated with ESBL-hvKp infections. Conclusions: HvKp, especially ESBL-hvKp and MDR-hvKp, is emerging. For in-depth understanding hvKp, host, pathogen and host-pathogen interaction may be the essential element.
Background: Cellulitis and erysipelas are usually considered manifestations of the same condition, a skin infection associated with pain, swelling and systemic symptoms. A variety of antibiotics with a range of treatment durations and routes of administration are suggested in guidelines. To assess the efficacy and safety of antibiotic therapy for non-surgically-acquired cellulitis we undertook a systematic review of antibiotic treatment for cellulitis. Methods: We searched the following databases to June 2016: the Cochrane Skin Group Specialised Register, CENTRAL in The Cochrane Library (2016, Issue 5), MEDLINE (from 1946), Embase (from 1974), and LILACS (from 1982). We searched 5 trials databases, and checked the reference lists of included studies for further references to relevant randomized controlled trials (RCTs). We subsequently searched PubMed and Google Scholar in December 2017 to confirm publication of trials. We selected published RCTs comparing different antibiotics, routes of administration and durations, from which we could extract data on patients with cellulitis. For data collection and analysis, we used RevMan 5.3 and the standard methodological procedures of the Cochrane Collaboration. For dichotomous outcomes, we calculated risk ratio and its 95% confidence interval. We employed a fixed-effect model for analyses. We assessed risk of bias for included studies and created summary of findings tables using GRADE. Results: We included 43 studies with a total of 6229 evaluable participants. Our primary outcome was the proportion cured, improved, recovered or 'symptom free/reduced at end of treatment', as reported by the trial. The outcomes within the trials were variable and makes direct comparisons between trials difficult; there were different lengths of follow up, different criteria for "cure" and intention to treat results as well as per-protocol results. We grouped similar types of drugs together as there was very few trials which compared two identical drugs. Our secondary outcome was any adverse event. Conclusions: The evidence does not support the superiority of any one antibiotic over another. Antibiotics with activity against MRSA do not appear to add benefit. The evidence does not support the use of intravenous antibiotics over oral antibiotics. The trial data does not support a treatment duration of longer than five days, as no trial demonstrated superiority with a longer duration. The limited evidence does not support combination therapy. A standardized set of outcomes is needed for further trials.
Abstract:
Antibiotic Therapy for Cellulitis: Data Extracted from A Multi-Center Clin. Trial
Primary Author Block:
R. Brindle1, O. M. Williams2; 1Univ. of Bristol, Bristol, United Kingdom, 2Univ. Hosp. Bristol, Bristol, United Kingdom
Abstract Body:
Background: There is a lack of consensus on the optimum antibiotic treatment for cellulitis. The available trial data does not demonstrate the superiority of any agent, and there is limited data on the route of administration, or the duration of therapy. What data does exist fails to demonstrate the superiority of intravenous (IV) over oral (PO), or the benefit of courses longer than 5 days. Methods: We used data extracted from a multi-center randomized clinical trial (NCT01876628) of antibiotic therapy for cellulitis to examine outcomes associated with the route (IV or PO) and duration of treatment.
Results: Of the 336 patients with data, 121 patients received some IV therapy, with the remainder only having PO antibiotics. The mean duration of IV antibiotic was 3.4 days, and 6.4 days for PO. The mean duration of individual antibiotic therapy was 7.2 days. The duration of therapy prior to the trial was associated with IV antibiotics within the trial; 31% (80/261) of patients on antibiotics for <24 hours, had some IV therapy compared with 56% (39/70) on antibiotics for ≥24 hours (OR 2.85, 95% CI:1.66 to 4.88, p < 0.00). Those patients with severe cellulitis were more likely to have IV therapy; 30% (61/201) of patients with a baseline affected skin area of ≤ 5% had some IV therapy compared with 45% (58/130) of patients with a baseline affected skin area of >5% (OR 1.85, 95% CI:1.17 to 2.92, p = 0.01). Patients on PO therapy were as likely as those on IV therapy to have improved at Day 5 or to be back to their normal activities at Day 10; 60% (108/179) of patients on oral therapy alone were back to normal activities at Day 10 compared with 48% (48/101) patients who had some IV therapy (OR 0.56, 95% CI:0.36 to 0.97, p = 0.052). There was no association between initial severity and the duration of antibiotic therapy given within the trial; 148 out of 197 (75%) patients with a SIRS score of zero, had antibiotics for > 5 days compared with 105 out of 135 (78%) patients with a SIRS score of 1 or more (OR 1.16, 95% CI:0.69 to 1.95, p = 0. 0.670). There was no association between duration of trial therapy and outcome as measured at Day 10; 130 out of 232 (56%) patients had antibiotics for > 5 days were back to normal activities at Day 10 compared with 26 out of 49 (53%) patients who had antibiotics for 5 days or less (OR1.13, 95% CI: 0.61 to 2.09, p = 0.824). Conclusions: The choice of IV therapy is influenced by prior antibiotics and severity. The trial data fails to provide evidence that IV is superior to PO therapy for those patients with similar severity or that course lengths >5 days result in any benefit at 10 days follow up.
Session Number: 67
Session Type: Poster
Session Number: 67
Session Type: Poster
Session Title: CIV01 - Clinical Studies of Adult Infectious Diseases: Skin, Bone and Joint Infections
Session Start Date Time: 6/8/2018 11:00:00 AM
Session End Date Time: 6/8/2018 1:00:00 PM
Session Primary Track: Clinical Infections and Vaccines
Abstract Control Number: 7085
Poster Board Number: FRIDAY - 688

Abstract Title:
Admission Rate and Length of Stay for Skin Infection Patients in US Hospitals: Use of Oritavancin is Associated with Lower Rates of Hosp. Admission and Shorter Length of Stay

Primary Author Block:

Abstract Body:
Background: When single-dose oritavancin was introduced in 2014 for the treatment of acute bacterial skin and skin structure infection, it was hypothesized that its single-dose formulation may help US hospitals reduce use of inpatient beds through treatment entirely in the outpatient setting and reduction in length of stay (LOS) for admitted patients. This analysis sought to assess the real world impact of oritavancin to US hospitals. Methods: Data were extracted from the Premier Hospital Database for the first full year of oritavancin availability (2015). Hospital admission rates and LOS were assessed for patients receiving oritavancin for skin infection and compared with patients receiving any other intravenous (IV) antibiotic grouped by infection severity (no systemic symptoms, with systemic symptoms, life-threatening infection) and presence of comorbid conditions using Charlson Comorbidity Index score (CCI). Results: There were 208,113 records for patients 18+ with a primary diagnosis of skin infection and administration of IV antibiotic. Among 203 patients who received oritavancin, the average CCI was 1.46; 24.1% patients CCI ≥3; 9.8% life-threatening condition (4.4%) or systemic symptoms (5.4%). 144 (70.9%) oritavancin patients were treated as outpatients. For the 59 patients who were hospitalized (LOS=4.0d), 56 patients received oritavancin after the discharge of hospitalization or at discharge. Compared to patients receiving other IV antibiotics, the patients who received oritavancin had consistently lower admission rates (rate reduction up to 45.4%) across all levels of infection severity and CCI. If admitted, oritavancin patients had shorter LOS (LOS reduction up to 1.8 days) across all severity levels except CCI=1 group. Conclusions: This analysis finds that use of oritavancin avoided hospitalization and shortened length of stay for skin infection patients. As skin infections represent 2% of all US hospital admissions, increased use of oritavancin may represent an opportunity to recover several hundred thousand bed days for use with other patients.
Abstract Title: Economics of Treatment of Skin and Soft Tissue Infections (SSTI) in Us Hospitals
Primary Author Block:
Abstract Body:
Background: While approval of single-dose antibiotics such as oritavancin has enabled an increase in ambulatory treatment of patients with skin and soft tissue infections (SSTI), the majority of patients are still admitted to the hospital. Here, we sought to examine the economic impact of inpatient intravenous (IV) treatment of SSTI to hospitals. Methods: Data from Jan-Dec 2015 were extracted from the Premier Hospital Database. Costs were assessed for all adult inpatients with a primary diagnosis of any SSTI receiving IV therapy. Costs were further stratified by infection type, antibiotic administered, Charlson Comorbidity Index (CCI), presence or absence of systemic symptoms, and payer type. Results: For 115,378 patients with SSTI receiving IV therapy, the average per patient cost was $8,714. Costs (and mean CCI) for patients receiving oritavancin, vancomycin, dalbavancin, or daptomycin were $8,242 (1.81), $8,736 (2.12), $12,448 (1.54), and $16,320 (2.51), respectively. While oritavancin patients had a lower mean CCI score compared to daptomycin or vancomycin patients, a higher proportion of oritavancin patients (13.6%) were treated for life-threatening systemic symptoms vs daptomycin or vancomycin, with 12.4% and 7.2% of patients with life-threatening systemic symptoms, respectively. We found a fairly linear relationship between cost and CCI, with total per patient costs ranging from $6,761 for CCI=0 to $11,506 for CCI=4. Overall costs varied by payer, ranging from $6,455 for self-pay to $9,524 for Medicare patients. Conclusions: This analysis demonstrates that inpatient treatment of SSTI represents a substantial cost burden to hospitals. While costs vary with treatment and disease severity, oritavancin was found to be the least costly IV treatment option, though it was associated with a high proportion of patients with life-threatening systemic symptoms compared to alternative therapies. Outpatient treatment of SSTI, thereby avoiding hospitalization altogether, may represent a further opportunity for hospital cost savings.
Abstract Title:
Increased Platelet Counts: Potential Diagnostic Marker for Osteomyelitis in Patients with Chronic Ulcers?

Primary Author Block:

Abstract Body:
Background: Chronic leg ulcers are a common problem associated with significant morbidity, which is further compounded upon progression to osteomyelitis. Differentially diagnosing between the two is difficult, often requiring pathology and costly imaging studies, but essential for determining appropriate therapy. Elevated c-reactive protein (CRP) and sedimentation rate (ESR) are known to be useful in diagnosing osteomyelitis versus chronic leg ulcer, but are also known to be non-specific. Additionally, reactive thrombocytosis is known to occur with infection. In one small, brief observational study by Schattner A, et al. thrombocytosis was detected more frequently in patients with chronic leg ulcers with osteomyelitis than in those with just chronic leg ulcers. In our study, we looked to expand upon whether platelet counts can help differentiate between osteomyelitis and chronic leg ulcers. Methods: Platelet counts from 213 patients admitted with osteomyelitis versus chronic leg ulcers were obtained via retrospective chart review; levels at baseline and on diagnosis were compared. Patients’ CRP and ESR were examined in a similar fashion. Diagnoses were made via imaging studies, pathology, probe-to-bone tests, and/or clinically by the provider. Results: Although platelet counts on diagnosis were statistically significantly higher in patients diagnosed with osteomyelitis versus chronic leg ulcer (282 x10⁹/L versus 219 x10⁹/L, p<0.001), the difference was deemed to be not clinically relevant. The same was true for the difference in platelet count on diagnosis from their baseline with osteomyelitis versus chronic leg ulcer (26 x10⁹/L versus 5 x10⁹/L, p=0.002). When choosing a cutoff platelet count of >350 x10⁹/L for differentiating osteomyelitis versus chronic leg ulcer, our results showed a sensitivity of 0.24, specificity of 0.93, and positive predictive value of 0.74. Conclusion: In patients presenting with chronic leg ulcers which are concerning for osteomyelitis, a platelet count >350 x10⁹/L is highly specific for aiding in the diagnosis of osteomyelitis versus chronic leg ulcer. Additional laboratory tests such as CRP and ESR, imaging studies, and clinical picture should be used to confirm a diagnosis of osteomyelitis versus chronic leg ulcer. Further trials are warranted to confirm the findings of this study.
Abstract Title:
Microbial Id: A Multiplexed Lab. Diagnostic Method for the Detection of Periprosthetic Joint Infection-Associated Pathogens in Synovial Fluid Samples

Primary Author Block:

Abstract Body:
The detection of pathogens causing periprosthetic joint infections (PJI) is of paramount importance to the medical diagnosis, treatment, and surgical course for affected patients. Microbial culture-based methods of pre-operative synovial fluid samples remain the gold standard in diagnostic microbiology despite several constraints including the propensity to yield false negative results (~50%). The limitations of cultural methods prompted the development of the Synovasure® Microbial ID (MID) Test, a multiplex, bead-based immunometric assay employing anti-microbial polyclonal antibody reagents coupled to MagPlex® microspheres (Luminex) and conjugated to biotin with streptavidin-phycocerythrin (SAPE) as the reporting reagent. This diagnostic method encompasses two microbial panels capable of detecting Staphylococcus, Enterococcus, and Candida (Panel 1) and targeting a less prevalent microbial group in PJI consisting of Streptococcus mitis, Propionibacterium acnes, and Escherichia coli (Panel 2).

This test is intended to be used in conjunction with microbial culture as it may help identify potential organisms in culture negative but infected (culture false negative) samples. Proprietary synovial fluid sample extraction methods consisting of extraction buffer (PBS, hyaluronidase, lysozyme, and Tween 20) treatment, boiling, and centrifugation is employed prior to assay testing. Alpha-defensin is an established biomarker for infection. The combined clinical specificity in α-defensin negative/culture negative samples is >98%. The detection rate of these organisms in α-defensin positive/culture negative samples is >45% (5.5% P. acnes). The overall precision of the panels is 14-21% (%CV). The analytical cutoffs (C50) in the assays are 105 (E. coli), 104 (Staphylococcus sp., S. mitis, P. acnes), 103 (Candida sp.) and 102 (E. faecalis) CFU/ml. Limited cross-reactivity was detected at 106 CFU/ml against a panel including Staphylococcus sp. (8), Candida sp. (4), Streptococcus sp. (2), E. faecalis, P. aeruginosa, E. coli, P. acnes, S. marcescens, and E. cloacae in the P. acnes and S. mitis assays. The E. coli cross-reacted with multiple gram-negative organisms. In Panel 1, some cross-reactivity has been detected between Staphylococcus sp., Candida sp. and Enterococcus which is easily resolved through a data analysis algorithm. This test represents a significant additional tool in the diagnosis of PJI which adds significantly to the information that is obtained from microbial culture.
Abstract Title:
Seratia Odorifera Unusual Bacterium As A Causative Agent for Urinary Tract Infection
Primary Author Block:
S. Azizi; French Med. Inst. For Mothers and Children, Kabul, Afghanistan
Abstract Body:
Background: Urinary tract infection (UTI) is one of the most common infections which have been most extensively studied in the field of clinical practice. Usually, UTI is caused by Escherichia coli and other coliforms and Enterococcus spp. Because of their presence in high numbers on the perineum. In the present study, we describe an unusual high frequency of Seratia odorifera recovered from urine culture of patients at a tertiary care hospital in Kabul. The study evaluated the frequency of S. odorifera as bacterial agent responsible for urinary tract infections and its antimicrobial sensitivity profile.
Materials/Methods: The study was conducted at French Medical Institute for Mothers and Children from June 2013 to May 2017. All patients who were referred to FMIC for their urine culture tests were included in the study. The standard microbiological methods were followed for isolation of uropathogens. Biochemical identification of gram negative bacilli was achieved using API 10S or 20 E (bio Merieux, France). The isolated strains were tested for their susceptibility against commonly used antibiotics and for extended- spectrum β-lactamase (ESBL) production. Results: During the study period, a total of 245 urine samples, which revealed “significant bacteriuria”, yielded the growth of S. odorifera. The result showed that frequency of those isolates was higher (63.3%) in female patients Also majority of such infections (53.3%) occurred in younger patients (≤ 12 years). With regard to antiprogram, S. odorifera showed high resistance to commonly used antibiotics, namely ampicillin, gentamicin, 3rd cephalosporin, fluoroquinolones and co-trimmoxazole. However most of the isolates remained sensitive to Amikacin, Fosfomycin and Nitrofurantoin. Out of all, 49(20%) were ESBL producing strains.
Conclusions: We have noted a high frequency of S. odorifera as a bacterial pathogen causing urinary tract infection, especially in female patients. We suggest that more studies should be done to elucidate the pathogenic role of this bacterium as a causative agent for UTI and to have regular antibiotic susceptibility surveillance.
Abstract Title:
Prognostic Value of Rectal Colonization by Extended-Spectrum Beta-Lactamases Producing Enterobacteriaceae in Patients with Urinary Tract Infections

Primary Author Block:

Abstract Body:
Background: Intestinal colonization by extended-spectrum beta-lactamases producing Enterobacteriaceae (ESBL-EB) has been associated with increased mortality. Prognostic role of rectal colonization by ESBL-EB in patients with urinary tract infection has not been evaluated. The aim of this study was to analyze the impact of concomitant rectal colonization by ESBL-EB on clinical outcomes in patients with urinary tract infections by these microorganisms. Methods: This is an observational and retrospective study. Patients admitted to our hospital between January 2010 and July 2017 with urinary tract infection by ESBL-EB and rectal swab culture performed within 10 days before or after urine culture were included. Repetitive cultures from the same patient were excluded. Several variables were analyzed, including the presence of the same microorganism in urine and rectal swab culture. The primary outcome was mortality at 30 and 90 days. Chi-square test and Fisher’s exact test were used for bivariate analysis. Multivariate analysis was made using Cox regression. Results: 561 urine cultures were positive for ESBL-EB between January 2010 and July 2017. 518 of them did not meet the inclusion criteria. Finally, 43 hospitalized patients were included, with a mean age of 79 years. 52% were female. The most frequent microorganism in urine and rectal swab cultures was Klebsiella spp. 55% of patients had the same microorganism in urine culture and rectal swab culture. Patients with positive rectal swab culture for the same Enterobacteriaceae that causes the urine tract infection had a higher mortality at 90 days (50% vs 15%, p=0.01). Mortality at 30 days was not statistically significative (33% vs 10%, p=0.1). Independent risk factors for mortality at 90 days in multivariate analysis were rectal colonization by the same ESBL-EB (HR 4; IC 90% 1,09-14,6; p=0.03), previous clinical infection by the same ESBL-EB (HR 3,8; IC 95% 1,3-11,1; p=0,01) and chronic renal failure (HR 4; IC 95% 1,3-12,3; p=0,01). Conclusions: Rectal colonization by ESBL-EB is a prognostic factor in hospitalized patients with urinary tract infection by the same microorganism.
Abstract Title:
Treatment Duration of Complicated Urinary Tract Infections by Extended-Spectrum Beta-Lactamases Producing Enterobacteriaceae

Primary Author Block:
J. Álvarez, J. Lamas, F. Maroto, L. González, A. Sanjurjo, J. Bermúdez, I. Rodríguez, M. Fernández, J. de la Fuente; Povisa Hosp., Vigo, Spain

Abstract Body:
Background: Urinary tract infections by extended-spectrum beta-lactamase producing Enterobacteriaceae (ESBL-EB) are a growing problem in our clinical practice. There are no specific studies about optimal antimicrobial treatment duration for complicated urinary tract infections by these microorganisms. The aim of this study was to evaluate the clinical outcome in patients who received short (≤ 7 days) versus long courses (>7 days) of antimicrobial therapy for complicated ESBL-EB urinary tract infections.

Methods: This is a retrospective and observational study. Positive urine cultures for ESBL-EB in our hospital between March 2015 and July 2017 were identified. Exclusion criteria: age under 18 years, asymptomatic bacteriuria, uncomplicated urinary tract infections, recurrences in the first week after the end of treatment, polymicrobial urine cultures, inadequate treatment according to antimicrobial susceptibility results and death before the end of antibiotic treatment. Differences between treatment groups (7 days or less vs more than 7 days) were analyzed according to baseline characteristics, severity of clinical presentation, family of antibiotic used, mortality at 30 days and reinfection by the same ESBL-EB at 30 days. Bivariate analysis was made using Chi square test or Fisher's exact test. Multivariate analysis was performed using Cox regression adjusted for age, sex and comorbidity index. Results: 273 urine cultures were positive for ESBL-EB during the study period. 75 cases were included, 40 in the long treatment group and 35 in the short treatment group. The mean age was 74 years. 57,3% were female. Mean treatment duration in short and long treatment groups was 6,1 and 13,8 days respectively. Proportion of male sex was higher in long treatment group (68,8% vs 31,3%; OR 3; 95% CI 1,1-7,9). There were no other differences in baseline characteristics between groups.

Mortality at 30 days was 5,7% in the short treatment group and 5% in the long treatment group without significant differences (HR 0,8; 95% CI 0,1-6,4; P=0,8). Reinfection by the same ESBL-EB at 30 days was 2,9% in the short treatment group and 5% in the long treatment group, without significant differences (HR 0,7; 95% CI 0,06-8,4; P=0,7). Conclusions: Short courses of antimicrobial treatment seems to be effective for the treatment of complicated urinary tract infections by ESBL-EB. This is an important point in an era of increasing antimicrobial resistance, in order to reduce the overall exposure to antibiotic treatment.
Abstract Title:
Impact of Initial Inappropriate Antibiotic Therapy on Outcome for Outpatient Urinary Tract Infection Due to Fluoroquinolone Non-Susceptible Uropathogens

Primary Author Block:
S. Puttagunta1, V. Gupta2, S. Aronin1, J. Murray2, M. Dunne1; 1Iterum Therapeutics, Old Saybrook, CT, 2Becton, Dickinson, and Company, Franklin Lakes, NJ

Abstract Body:
Background: Urinary tract infection (UTI) is the most common outpatient bacterial infection. Rising resistance rates among gram-negative bacteria have made common oral antibiotics less effective for uncomplicated UTI (uUTI), highlighting the risk of adverse outcome related to initial inappropriate antibiotic therapy (IIAT). There's limited published data quantifying the impact of IIAT in patients with UTI treated in the outpatient setting due to susceptible and non-susceptible Enterobacteriaceae.

Methods: The BD Insights Research Database was queried to evaluate ambulatory antibiotic fill history for patients from 15 U.S. institutions with a positive ambulatory urine culture for an uropathogen. Patients who initially filled a prescription for a fluoroquinolone were further categorized into those with a urine culture positive for a fluoroquinolone-susceptible (QS) versus fluoroquinolone-non-susceptible (QNS) pathogen. Outcome was assessed using two surrogate endpoints: hospital admission and re-prescription within 28 days of initial fluoroquinolone fill. Results: A total of 2,184 ambulatory urine culture episodes with a fluoroquinolone fill were identified in 1,999 patients. Hospitalization data was available for 2,035 of these episodes. 1,576 (72%) had <100,000 CFU/mL and 608 (28%) had <100,000 CFU/mL of an uropathogen identified. The re-prescription rate and rate of all-cause hospitalization within 28 days of the initial fill were significantly higher in the subset of patients with UTI caused by a QNS pathogen, as shown in the Table below.

<table>
<thead>
<tr>
<th>Quinolone Susceptibility</th>
<th>28-day fill Rate</th>
<th>Hospital Admission Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>28-day fill (%)</td>
<td>P value</td>
</tr>
<tr>
<td>Overall</td>
<td>28-day fill (%)</td>
<td>P value</td>
</tr>
<tr>
<td></td>
<td>Admissions</td>
<td>P value</td>
</tr>
<tr>
<td>----------------</td>
<td>------------</td>
<td>---------</td>
</tr>
<tr>
<td>Susceptible</td>
<td>1,216</td>
<td>0.001</td>
</tr>
<tr>
<td>Not susceptible</td>
<td>360</td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>1,576</td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: A considerable proportion of outpatient UTI episodes are due to QNS pathogens. Prescribing ILAT to patients with outpatient UTI due to QNS pathogens is more often associated with a second antibiotic prescription and hospitalization compared with episodes caused by QS strains. These findings highlight the need for novel oral antimicrobial options with activity against QNS uropathogens.
Abstract Title:
Incidence of Urinary Tract Infections among Adolescent and Adult Women in Ogbete Coal Camp, Enugu
Primary Author Block:
E. C. Onwujekwe1, C. C. Ezemba1, A. Agbo2, A. S. Ezemba3; 1Coal City Univ., Emene, Nigeria, 2Coal Camp Hlth.Ctr. Enugu, Enugu, Nigeria, 3Nnamdi Azikiwe Univ. Awka, Anambra State, Nigeria., Enugu, Nigeria
Abstract Body:
This study was to determine the bacteria that are prevalent in UTI’s and the sensitivity of organisms isolated from the urine of adolescent and adult women of 8-51 years old in Ogbete coal camp town in Enugu metropolis, south east Nigeria. A total of 216 individuals, both in and out patients were investigated, 197 women were diagnosed for UTI’s. The microorganisms found responsible for infection were bacteria, fungi, yeast and protozoa. Among the bacteria, two were identified as Gram +ve cocci i.e. Staphylococcus aureus and Staphylococcus saprophyticus, while Gram -ve bacilli were Escherichia coli, Klebsiella, Proteus, Pseudomonas areuginosa. Yeast like fungus Candida albican, protozoan (Trichomonas vaginalis) were also identified using 16S rRNA sequencing. The isolated organism which was prevalent was Staphylococcus aureus (48.2%); followed by Escherichia coli (34.5%). Also, Pseudomonas areuginosa, Proteus and Klebsiella were isolated. Factors responsible for frequent cases of UTI among diagnosed women include shortness of urethra among the females, lack of personal hygiene, sexual intercourse, socio economic challenges in various homes and others. Sensitivity profiles revealed that Augumentin was highly susceptible to Staphylococcus aureus (65%) while Escherichia coli were highly resistant to commonly used drugs such as Ampicillin, and Cloxacillin then Gentamycin was the most active against bacteria isolates.
Trichomonas Vaginalis Virus (Tvv) among Women with Trichomoniasis and Associations with Demographic and Clin. Characteristics

Primary Author Block:

Abstract Body:
Background: Trichomonas vaginalis virus (TVV) is a non-segmented, 4.5-5 kb, double-stranded RNA virus, belonging to the family Totiviridae, that infects the protozoa T. vaginalis. The prevalence of TVV in U.S. T. vaginalis isolates is not well known. It is also unknown if the presence of TVV has important implications for trichomonal virulence and clinical response to therapy. The objectives of this study were to examine the prevalence of TVV in archived T. vaginalis isolates from a randomized controlled T. vaginalis treatment trial (RCT) in HIV-negative women and to examine the association of TVV+ isolates with patient demographic and clinical characteristics. Methods: Archived T. vaginalis isolates from the RCT enrollment visit of 355 HIV-negative women were thawed and subsequently grown in culture. Total RNA from cell pellets was extracted using Trizol reagent (Invitrogen). Contaminating single stranded RNA was precipitated using 4.0M LiCl and centrifugation. dsRNA was then precipitated using isopropanol and ammonium acetate and the pellets were dissolved to obtain a working concentration of dsRNA. Samples were analyzed by electrophoresis on a 1% agarose gel and ethidium bromide staining to visualize a 4.5kb band that was representative of the dsRNA of TVV. Results: Of the 355 T. vaginalis isolates screened, 142 (40.0%) were positive for TVV. Women with TVV+ isolates were relatively older in comparison to women with TVV- isolates (mean age 31.6 years vs. 29.0 years, P< 0.01). Women with TVV+ isolates were as likely to be African American compared to women with TVV- isolates (96.2% vs. 94.4%, P<0.40). There was no association between the presence of pre-treatment genital symptoms and TVV (P<0.77). Of 322 women who returned for their RCT test of cure (TOC) visit, 47 remained persistently positive for T. vaginalis by nucleic acid amplification test (NAAT); 17 (36.2%) of these women were TVV+ at baseline compared to 30 (63.8%) who were TVV- at baseline (P<0.04). Subsequent in vitro testing for metronidazole (MTZ) resistance was performed for 25/47 (53.2%) of isolates from women that failed TOC. Of 10 TVV+ isolates tested, none demonstrated MTZ resistance, while 2/15 TVV- isolates demonstrated mild to moderate MTZ resistance (P<0.23). Conclusions: In one of the largest U.S. studies of T. vaginalis isolates screened for TVV, prevalence was high (40%). However, TVV was not associated with genital symptoms, clinical treatment failure, or MTZ drug resistance. These results suggest that TVV is a commensal to T. vaginalis.
Gentamicin for the Treatment of Gonorrhoea (G-Tog); Minimum Inhibitory Concentration Data versus Clin. Outcome

Primary Author Block:

Abstract Body:
Background: Antimicrobial susceptibility testing is used to predict response to treatment, but very few studies have correlated minimum inhibitory concentration (MIC) to microbiological cure of Neisseria gonorrhoeae (NG) infection. A recent randomised controlled trial in the UK compared gentamicin (GEN) 240 mg plus azithromycin (AZM) 1 g with the current first line treatment of gonorrhoea; ceftriaxone (CRO) 500 mg and AZM 1 g as dual therapy.1 The primary endpoint was clearance of Neisseria gonorrhoeae (NG) using molecular assays two weeks post treatment. Primary outcome data were available for 598 participants randomised to receive CRO/AZM (n=306) or GEN/AZM (n=292). To further investigate the relationship of the MIC data with clinical outcome, MIC analysis was performed on NG isolates from participants who were also culture positive before they received treatment and from those who failed treatment. Methods: Viable NG cultures were available from 280 participants; 264 cleared infection, of whom 143 received CRO/AZM and 121 received GEN/AZM. Four and twelve isolates were available from participants who did not clear infection in the CRO/AZM and GEN/AZM arms, respectively. MICs were determined by Etests on GC agar base with 1% Vitox. The MIC geometric means of AZM, CRO and GEN were compared using linear regression according to treatment received and NG clearance. Results: Within the isolates from participants who received GEN/AZM, the AZM MIC geometric mean ratio was 2.0 (95% confidence interval 1.2-3.4, p=0.007) for those who cleared infection versus those who did not clear infection. No other comparisons were found to be statistically significant. Conclusion: Resistance breakpoints for GEN have not been determined and our data highlight the difficulty in establishing a breakpoint as we found no correlation between MICs and clinical outcome; range 1-8 mg/L vs. 4 mg/L in the clearance and non-clearance groups, respectively. Due to the association of higher AZM MICs with treatment failure in the GEN/AZM arm, it is possible that AZM 1 g failed to provide microbiological cure when GEN treatment failed. However this should be interpreted with due caution as it is based on small sample size. Nonetheless, we should examine the role of 1 g AZM in dual therapy, which is in widespread use to delay the emergence of resistance to CRO. The absence of correlation between clinical outcome and MICs of CRO and AZM for isolates from participants who received CRO/AZM raises the possibility of re-infection rather than treatment failure, although the numbers were small.
Abstract Title:
Delivery of Viral Protein E2 Via A Cell-Penetrating Peptide Adapter for the Treatment of Human Papillomavirus-Mediated Cervical Cancer

Primary Author Block:
J. C. LeCher, R. L. Dickson, J. L. McMurry; Kennesaw State Univ., Kennesaw, GA

Abstract Body:
Human papillomavirus (HPV) is the causative agent of cervical cancer, the 2nd cause of cancer-related deaths in women worldwide. Cervical cancer arises due to the integration of genes encoding two viral oncoproteins, E6 & E7, into the host genome and subsequent loss of the gene encoding for viral regulatory protein E2. E2 functions to directly inhibit the activity of E6 & E7. Unregulated production of E6 & E7 promotes carcinogenesis and high levels of E6 & E7 are correlated to high grade cervical disease and development of high-risk cervical carcinomas. Given E2’s regulatory role, studies have aimed at reintroducing E2 to halt cancer progression. Stable transfection of E2 into cervical cancer cells leads to both senescence and apoptosis. However, due to limitations of performing gene transfection in vivo, E2 has yet to achieve therapeutic usefulness. We developed an efficient cell-penetrating peptide (CPP) adaptor system that readily delivers protein into living cells using a high-affinity, reversible coupling. Standard CPP protein delivery relies on linking a protein cargo directly to the CPP, but CPPs get caught up in endosomes upon cellular entry and are targeted for degradation. Our methodology overcomes these issues. Using our system, we delivered E2 protein into cervical cancer cells to induce senescence and apoptosis. E2 constructs showed rapid, reversible binding kinetics with our CPP adapter system. Intracellular delivery and localization of fluorescently labeled E2 were analyzed via confocal microscopy by generating Z-stack projections. E2 was readily delivered into living cells and localized to mitotic spindles, a known role for endogenous E2. To test for senescence/apoptosis, we delivered E2 into cells every 24 hours over the course of 3 days at different cell-to-peptide ratios. In the low cell-to-peptide ratio group, there was a 28% reduction in metabolic activity and no evidence of cellular proliferation. E2-treated cells showed changes in cellular morphology consistent with senescence. Further, this phenotype was retained long-term with no evidence of cellular proliferation. Next, we performed similar experiments at high cell-to-peptide ratios. Cells showed a rapid loss of metabolic activity by day 4 (<75%) and apoptosis was microscopically evident as early as 24-hours post treatment. Cell death was confirmed by measuring cytosolic leakage over the 3-day treatment. These data confirm the utility of our adaptor system for the delivery of viral E2 protein into living cells for the induction of senescence and/or apoptosis.
Abstract Title:
Diarrheal Illnesses Trigger C. Difficile Colonization in the Human Gut

Primary Author Block:
D. VanInsberghe, B. J. Varian, S. Erdman, M. Polz; Massachusetts Inst. of Technology, Cambridge, MA

Abstract Body:
Background: Clostridium difficile infections have become increasingly treatable in recent years, but their incidence and overall burden on healthcare systems continues to rise (1). Although it is widely held that C. difficile is an antibiotic and hospital associated pathogen, only a few antibiotics carry an elevated relative risk for infection and at most one third of infections can be attributed to transmission within a hospital (2,3). As well, it is common for adults to be asymptomatically colonized by C. difficile, but very little is known about the risk factors for becoming a carrier, or the timescales where people remain carriers. Methods: We searched human microbiome surveys to form a hypothesis about C. difficile colonization dynamics before testing it using a mouse model. Results: After identifying blooms of C. difficile in human gut microbiome studies following Salmonella and Vibrio cholerae infections, we used a mouse model to test if disturbances in general trigger C. difficile colonization. This study showed that as mice ingested increasing amounts of laxatives while being exposed to C. difficile spores, more mice experienced blooms of C. difficile in their feces, while control groups experience none. Conclusions: Our results suggest that colonization becomes likely if people are exposed to C. difficile spores in the days following acute disturbances - where antibiotics and hospitals are common examples of large disturbances and locations with a high burden of exposure. Consequently, the period of recovery from diarrheal illnesses and laxative use could be an important window of intervention for preventing transmission and lowering the incidence of infection and asymptomatic carriage. Further, the temporal variability of C. difficile abundance in the gut highlights that single time-point testing is insufficient to determine carriage. Significance: Here we show that C. difficile colonization requires a prior gut disturbance, initiates following a delay during recovery, and can persist asymptomatically long after full recovery.
Session Number: 69
Session Type: Poster
Session Title: CIV02 - Infection Prevention and Control: Clostridium difficile
Session Start Date Time: 6/8/2018 11:00:00 AM
Session End Date Time: 6/8/2018 1:00:00 PM
Session Primary Track: Clinical Infections and Vaccines
Abstract Control Number: 62
Poster Board Number: FRIDAY - 701

Abstract Title:
Prevalence and Risk Factors for Asymptomatic Colonization With Clostridium Difficile Among Hospitalized Patients
Primary Author Block:
P. Patel1, R. Singh2, M. Vernon1, D. Schora1, C. Wang1, L. Peterson1, K. Singh1; 1NorthShore Univ. Hlth.System, Evanston, IL, 2Parkview Regional Med. Ctr., Fort Wayne, IN
Abstract Body:
Background: C.difficile (Cdif) is one of the most common healthcare-associated infections in the United States. Patients who carry toxigenic Cdif represent a potential reservoir for hospital transmission and identification of such patients could be used as a targeted infection control intervention. The aims of our study were to assess the burden of asymptomatic Cdif carriage and identify risk factors for colonization. Methods: Adult inpatients admitted at two NorthShore University HealthSystem, IL hospitals between July 2016 and March 2017 were eligible for the study. A double-headed pre-moistened rayon peri-rectal swab (BBL) was collected and tested using the cobas® Cdif Test (Roche) or Xpert® Cdif/Epi (Cepheid) real-time PCR. Culture was performed for all real-time PCR positive samples using cycloserine-cefoxitin-fructose agar with horse blood and taurocholate (Anaerobe Systems). Patient demographics and risk factors for Cdif colonization were collected using a standardized form. Binary logistic regression was used to predict association of Cdif colonization with potential risk factors. A multivariable logistic regression model of risk factors was fitted from univariate risk factors at p-value <0.25 using a stepwise regression method (SAS v9.3). Results: There were 2,024 patients enrolled in the study and 172 (8.5%) were real-time PCR positive for toxigenic Cdif. A subset of 147 Cdif positive and negative patients were analyzed for Cdif risk factors. On univariate analysis, risk factors for Cdif colonization were recent hospitalization past 2 months (p<0.01), ICU stay past 6 months (p=0.01), LTCF stay past 6 months (p<0.01), use of enteral feeding tube (p=0.04), steroid therapy (p=0.02), PPI use (p<0.01), H2-blocker use (p=0.01), prior antibiotic use last 6 months (p<0.01) and prior Cdif (p<0.01). In addition, the Karnofsky score for Cdif colonized patients was significantly lower than non-colonized patients (46 versus 57, p<0.01). On multivariable analysis, independent predictors of Cdif colonization were prior Cdif infection or colonization (OR, 3.97; 95% CI, 1.79-8.8), hospitalization past 2 months (OR, 1.97; 95% CI, 1.17-3.32) and lower Karnofsky score (OR, 0.98; 95% CI, 0.96-0.99). Conclusions: We found that 8.5% of new admissions were asymptotically colonized with Cdif. Patients with a prior history of Cdif or recent hospitalization could be targeted for surveillance to prevent Cdif transmission.
Abstract Title:
Performance of A Clostridium Difficile Prediction Tool for Admission Surveillance to Reduce Hosp. Acquired C. Difficile Infection
Primary Author Block:
D. Schora, M. Vernon, K. Singh, S. Zelencic, L. R. Peterson; NorthShore Univ. Hlth.System, Evanston, IL
Abstract Body:
Background: Clostridium difficile (Cdif) infection (CDI) is problematic. To reduce CDI rates, we employ 5 standard infection prevention practices. Despite these efforts, our CDI rates fell short of target at 6.8/10,000 patient days in 2017. As a result, we implemented a program of targeted Cdif surveillance and placed all asymptomatic carriers under contact precautions. A targeted, risk-based screening approach minimizes testing and maximizes colonization detection. Methods: A Cdif admission screening pilot program was performed for 6 months at 2 hospitals. All new admissions had a peri-rectal sample collected and tested for Cdif by real-time PCR. From the pilot data, risk factors for Cdif colonization were derived using a multivariable regression model (SAS v9.3) and built into an algorithm in our electronic medical record system (Epic). A control set of non-risk patients were also tested to validate the algorithm. The risk-based surveillance program was implemented 8/1/17. Results: The rate of asymptomatic Cdif colonization was 8.5% during the pilot. On multivariate analysis, independent predictors of Cdif colonization were prior Cdif infection or colonization and hospitalization in the past 2 months. On univariate analysis, admission from a long-term facility was also a significant risk factor for Cdiff carriage. Together, these 3 risk factors captured 80% of at risk patients. From 8/1/17, patients who met any of these 3 risk factors had a rectal sample collected for Cdif RT-PCR using the cobas® Cdif Test (Roche). In the first 5 months of the program, 4477 patients were tested, including 640 controls. Patients with risk factors had an average Cdif colonization rate of 9% (Graph 1). Control patients averaged < 1% positivity rate for Cdif. Conclusion: The algorithm is performing as expected. A reduction in CDI rates will prove the effectiveness of this surveillance program and will be monitored. <br />

Graph 1. Percent Positive Risk Patients with C.difficile on Admission<br />

![Graph](http://files.abstractsonline.com/CTRL/48/4/013/ece/d13/4f2/2a8/100/efe/6a9/e0c/5c/g5600_1.jpg)
Abstract Title:
Use of the Architect Multigent Vancomycin Assay As A Vancomycin Detection Method from Rectal Swabs & Application in Patients with Recurrent Clostridium Difficile Infection (Rcdi)

Primary Author Block:
S. Hota1, R. Jin2, M. Kissoon2, P. Yip1, S. M. Poutanen2; 1Univ. Hlth.Network, Toronto, ON, Canada, 2Univ. Hlth.Network/Sinai Hlth.System Dept. of Microbiol., Toronto, ON, Canada

Abstract Body:
Background: Fecal microbiota transplantation (FMT) is useful to treat patients with rCDI. Residual stool vancomycin may negatively impact FMT efficacy. Bowel lavage pre-FMT may reduce stool vancomycin levels. This study evaluated the ability of the MULTIGENT Vancomycin Assay (MVA) (Abbott Diagnostics, Ontario) to detect vancomycin from rectal eSwabs™ (Copan, Italy) and applied it to measure stool vancomycin levels in rCDI patients undergoing FMT before and after PICO-SALAX® as bowel preparation.

Methods: The MVA was evaluated with simulated rectal eSwabs™ taken from donated stools spiked with vancomycin to determine limit of detection (LOD) and uncertainty of measurement (UM). eSwabs™ were vortexed, and 0.5 mL of associated transport medium was filtered using a 0.45 µm filter and analyzed. Eight rCDI patients’ rectal eSwabs™ pre- and post-PICO-SALAX® were tested using the assay; all patients were asked to stop taking oral vancomycin treatment 48 hours prior to their scheduled FMT.

Results: An average of 0.099g of stool was shown to be released from each eSwab™ into 1 mL of transport medium. UM for eSwab™ release was 20.5%. MVA eSwab™ vancomycin LOD was 1.2 mg/L corresponding to 12.12μg vancomycin/g stool (10.08-15.25μg/g). UM for vancomycin detection was determined to be 25.3% taking variability in rectal swab collection technique, storage conditions and hold times, and variability within and between runs into account. Two of the 8 patients had undetectable vancomycin in their pre- and post-PICO-SALAX® rectal eSwabs™. The remaining six patients had drops in their vancomycin levels from an average of 44.0 μg/g of stool to an average of 4.9 μg/g (Figure).

Conclusion: MVA can be used to detect vancomycin levels from rectal eSwabs™. PICO-SALAX® is able to reduce but not necessarily eliminate stool vancomycin levels in rCDI patients.

<a href="http://files.abstractsonline.com/CTRL/3d/d/45f/c18/04c/479/3b6/073/e20/060/a43/94/g7312_1.png" target='_blank' address=no ><img src="http://files.abstractsonline.com/CTRL/3d/d/45f/c18/04c/479/3b6/073/e20/060/a43/94/g7312_1.png" alt="" border="0" width="600" height="279" /></a>
Abstract Title:
Clostridium Difficile Toxin Testing Affects the Treatment Decision
Primary Author Block:
S. E. Hoover, J. Zhao; Sanford Res., Sioux Falls, SD
Abstract Body:
Background: The availability of sensitive nucleic acid based-tests (NAT) for Clostridium difficile has led to the concept of “overdiagnosis,” which holds that patients with positive NAT but negative toxin enzyme immunoassays (EIA) may not have true disease or require treatment. In March 2016, our institution changed its testing algorithm to a 2-step procedure using PCR as a screening test, followed by EIA on samples testing positive by PCR. Education was provided to clinicians that PCR-positive, toxin-negative patients might not have clinically relevant C. difficile illness. Methods: We conducted a retrospective cohort study using administrative data on all inpatients over 1 year of age who had one or more tests for C. difficile during their stay. Patients were classified as PCR+/Tox+, PCR+/Tox-, or PCR-. We collected data including patient characteristics, medication use, treatment for C. difficile, readmission, and mortality. Results: 83% of PCR+/Tox+ patients received oral or IV metronidazole, oral vancomycin, or oral fidaxomicin after the C. difficile test was performed, contrasting with 53% of PCR+/Tox- patients and 16% of PCR- patients (p<0.001). Deaths occurred in 10 (16%) of PCR+/Tox+ patients, 33 (18%) of PCR+/Tox- patients, and 149 (9%) of PCR- patients. The difference was statistically significant only between the PCR+ and PCR- patients, without regard to toxin result (p<0.001). Age, sex, number of days from admission to test, source of admission, use of antibiotics, laxatives, or acid suppressing medications, admission WBC count and admission creatinine did not predict a positive C. difficile toxin result. Treatment of C. difficile and length of stay did not predict death or readmission within 30 days. Conclusion: Patients who were PCR and toxin positive were more likely to be treated for C. difficile than were those who were PCR positive and toxin negative. Neither treatment of C. difficile nor length of stay predicted death or readmission within 30 days. In our cohort, therefore, the decision to treat or not treat patients who were PCR-positive and toxin-negative did not have a measurable effect on readmission or mortality, to the extent that these rare outcomes were present in this study.
Abstract Title:
A Non-027 and Non-078 Binary Toxin Positive Clostridium Difficile Plays A Notable Pathogenicity

Primary Author Block:
C. Li; Xiangya Hosp. Central South Univ., Changsha, China

Abstract Body:
Background: Clostridium difficile strains expressing the binary toxin (CDT), is generally found in C. difficile 027 (ST1) and/or 078 (ST11) in clinic associated with severe C. difficile infection (CDI). However, we recently reported a CDI case infected with binary toxin-positive non-027, non-078 C. difficile LC693 that is associated with severe diarrhea in China. We aimed to compare the virulence factors and pathogenicity of C. difficile LC693 with those of C. difficile RT20291 and CD630. Methods: The toxin production was measured by conventional ELISA assay and commercial Kits. The pathogenicity in vivo was evaluated in the mouse model of CDI. The sporulation capacity was measured by sporulation rate assay. The early step of germination was performed by monitoring the initiation of spore germination and Ca-DPA release. The motility was performed by swimming plate assay and Electron microscopy was performed to examine the presence/absence of flagellar structures on the surface of C. difficile. Biofilm formation was evaluated by measuring the biofilm biomass of C. difficile strains in 96-wells plate. The spore adhesion to human gut epithelial cells was also performed. Results: The TcdA production of LC693 was lower than both R20291 and CD630. But the TcdB production of LC693 was higher than CD630 and lower than R20291. LC693 had a highest sporulation rate compared with R20291 and CD630 and showed a fast germination rate (64%) within 8min at the early step of germination. However R20291 was showed a more fast completed DPA release in 30min. LC693 exhibited a notable motility in swimming plate, and carries abundant flagellar on its surface which was demonstrated by Electron microscopy. LC693 developed a robust biofilm formation capacity and a high adherence ability on human gut epithelial cells. Finally, in a mouse mode of CDI, LC693 displayed a high pathogenicity.

Conclusion: These findings highlight the pathogenicity of binary toxin positive non-027 and non-078 C. difficile strains. Though, the virulence was lower than 027 strains, however it has a high spore formation rate which attribute to a high transmission capacity in hospital environment. More strict prevention and control measures should be performed in hospital to curb transmission between different patients.
Abstract Title:
Molecular Epidemiological Analysis of Clostridium Difficile That Caused An Outbreak in A Japanese Hospital

Primary Author Block:
Y. Nukui, Y. Aiso, T. Chino, R. Saito, C. Tani, J. Nakajima, K. Sonobe, S. Tohda, R. Koike; Tokyo Med. and Dental Univ., Tokyo, Japan

Abstract Body:
Background: Clostridium difficile is an important cause of antibiotic-associated diarrhea and one of the most common healthcare-associated infections. This study investigated the molecular epidemiology and risk analysis of an outbreak of C. difficile infection in a Japanese hospital. Methods: From June to November 2016, we analyzed sixteen non-repetitive C. difficile strains (fourteen from patients and two from the environment) isolated in the surgical unit of the Tokyo Medical and Dental University Hospital. Multilocus sequence typing and multiplex polymerase chain reaction were performed to determine the genetic relatedness and detect the toxin genes. Results: Thirteen toxigenic strains (81.3%) (including ten tcdA-positive, tcdB-positive, and cdtA/cdtB-negative strains (A+B+CDT-), and three A+B-CDT- strains) and three (18.7%) non-toxigenic strains were classified into seven sequence types. Of these, sequence type (ST) 17 (50.0%) was the most predominant, followed by ST15 and ST3 (12.5% each). Risk factor analysis of this outbreak showed that using diaper, gastric tube and cefmetazole were significant (p = 0.017, 0.017, 0.015, respectively) risk factors. C. difficile was isolated in the bathroom and bed rails around the patients. Therefore, environmentally-mediated horizontal transmission was also suspected. The outbreak was promptly ended by standard and contact precaution and environmental cleaning. Conclusion: ST17, the major strain of C. difficile identified in this outbreak, has been reported around the world, especially in Asia and Europe. In addition, ST17 was most frequently isolated in our hospital from 2012 to 2013 (Kuwata et al. Eur J Clin Microbiol Infect Dis 2015; 34: 763-72). Finally, the prompt epidemiological analysis may have been efficient in instituting the appropriate infection control protocols to end the outbreak.
Molecular Epidemiology of Clostridium Difficile Infections in A Tertiary Care Hosp. Using Shotgun Metagenomics on Fecal Samples

Primary Author Block:

Abstract Body:
Background: Clostridium difficile infections (CDI) have emerged as a major cause of hospital acquired infections. Infection control strategies focus on contact isolation of cases, intensive terminal cleaning of rooms and reducing antimicrobial use. We used shotgun metagenomics on fecal samples to describe molecular epidemiology of CDI in a tertiary care center. Methods: Microbial DNA was extracted from fecal samples which tested positive for C. difficile using standard testing. Whole genome sequencing (WGS) was performed using Illumina Next Seq. In house bioinformatics pipeline was developed. Sequenced strains were plotted phylogenetically against 669 C. difficile isolates with publicly available sequences. Resfinder and Plasmidfinder tools were used to look for antimicrobial resistance genes and plasmids in the samples. Results: Microbial DNA was extracted from fecal samples from 36 discrete patients with CDI. WGS was performed in 20 samples. Using standard epidemiological criteria, 6 infections were considered community onset (CO), 6 were cancer infusion center onset (ICO) and 8 were hospital onset (HO). 80% of patients were admitted to the hospital, with an average length of stay of 11.4+ _8.8 days. 60% of patients had recent antibiotic usage, 90% were on proton pump inhibitors and 30% were on chemotherapy. Severe CDI was seen in 35% cases, 20% had recurrent CDI. On genotyping, 8 strains were closely clustered (Figure 1). Toxin A and B genes were detected in all samples. Resistance genes to multiple antimicrobial classes (>3) was seen in all samples, including 8 cases with no recent antibiotic use. Plasmids associated with antimicrobial resistance were detected in 13 samples.

Conclusions: Shotgun metagenomics is an effective tool for WGS of Clostridium difficile, bypassing the need for traditional culture methods. This can be utilized an effective tool for real time outbreak investigations and to elucidate transmission patterns of CDI in a nosocomial setting.
Abstract Title:
Emerging Hypervirulent Epidemic Clostridium Difficile Strain of St37 Type (Toxin A-B+) Pose A Potential Threaten in China

Primary Author Block:
C. Li; Xiangya Hosp. Central South Univ., Changsha, China

Abstract Body:
Object: Clostridium difficile strains of ST37 type (RT017) are most frequently isolated epidemic isolates in China. We aimed to compare major virulence factors of an epidemic C. difficile isolate of ST37 type from China with those of C. difficile RT20291 and CD630. Methods: The first hypervirulent XY-06 (ST37, A-B+) C. difficile strain was isolated from ICU hospitalized patient in China. The toxin production was measured by conventional ELISA assay and commercial Kits. Cytotoxic effects of the strains on cultured cells were assessed by cell rounding assays. The pathogenicity in vivo was evaluated in mouse model of C. difficile infection (CDI). The resistance of the strain to antimicrobial agents was performed by micro-dilution assay. The spore adherence effects on human gut epithelial cells was performed by adherence assay. Genome of XY-06 strain was sequenced, and the entire toxin gene PaLoc was compared with 027 and CD630 strains. Results: C. difficile XY-06 produced much more TcdB, adhered stronger to gut epithelial cells, in comparison with C. difficile RT20291 and CD630. In a mouse model of CDI, strain XY-06 was more virulent than strain CD603, and was comparable to strain RT20291. No sizable resistance to antibiotics tested was detected. In addition, biofilm formation, sporulation, germination and motility of this strain was also evaluated, in comparison with RT20291 and CD530, and no remarkable differences were noticed. Conclusion: These findings highlight the potential threaten of epidemic strains ST37 in China.
Abstract Title:
Inactivation of Clostridium Difficile Spores in Carpeting and Upholstery to Prevent Recurrent Community-Acquired Infection

Primary Author Block:
M. J. Sadowsky1, R. Erickson1, M. J. Hamilton1, M. Hoo1, T. Kaiser1, K. Fryxell1, A. Khoruts2; 1Univ. of Minnesota, Saint Paul, MN, 2Univ. of Minnesota, Minneapolis, MN

Abstract Body:
Clostridium difficile is the most commonly reported hospital and community-acquired gastrointestinal infection. Spores produced by this bacterium survive long term in the environment and are actively shed from asymptomatic carriers, as well as those with active disease. Shed spores can be transmitted from the environment to susceptible individuals, germinate in the host’s GI tract, and subsequently cause disease and recurrent infections. In this study we describe the development and use of a method to recover and enumerate C. difficile spores from carpet and textile surfaces. Furthermore, we use this method to determine the concentration and contact time requirements for Virasept®, a known sporicidal solution, containing hydrogen peroxide and peroxyacetic acid as active ingredients, to markedly reduce numbers of C. difficile spores in carpet and fabric models. More importantly, while Virasept® treatment of carpet and upholstery killed spores, it did not damage or bleach carpet or fabric fibers. After a 30 min contact time, Virasept applied at a volume of a volume of ~ 75 ml m⁻² of carpet (or 51.2 ml m⁻² upholstery fabric) resulted in a 3 log reduction in germination of applied spores (a ~99.9% decrease) isolated from five different Clostridium difficile strains, representing several pulsed-field gel electrophoresis (Nap) biotypes. Results of this study allow us to propose a robust regimen for the practical treatment of carpeting and upholstery fabric that can be used in hospitals, nursing care facilities, and residential homes to prevent community- and environment-acquired reinfection and recurrence of CDI in susceptible individuals.
**Session Number:** 69  
**Session Type:** Poster

**Session Number:** 69  
**Session Type:** Poster

**Session Title:** CIV02 - Infection Prevention and Control: Clostridium difficile  
**Session Start Date Time:** 6/8/2018 11:00:00 AM  
**Session End Date Time:** 6/8/2018 1:00:00 PM  
**Session Primary Track:** Clinical Infections and Vaccines  
**Abstract Control Number:** 5242  
**Poster Board Number:** FRIDAY - 710

**Abstract Title:**  
Prevalence of Clostridium Difficile Infection and History of Antibiotic Use among Diarrhea-Presenting Patients in Kenya

**Primary Author Block:**  
M. O. Oyaro1, K. P. Plants2, D. Bishoff2, P. Malonza1, C. S. Gontier1, H. L. DuPont2, C. Darkoh2; 1Univ. of Nairobi, Nairobi, Kenya, 2Univ. of Texas Hlth.Sci. Ctr., Sch. of Publ. Hlth., Houston, TX

**Abstract Body:**

Clostridium difficile infection (CDI) is the most common cause of antibiotic- and diarrhea-associated morbidity and mortality worldwide. Previous antibiotic therapy is a major risk factor for CDI. Most of the studies to date have dealt with CDI in industrialized countries, and little is known about the epidemiology of CDI in developing countries, especially in Africa. The aim of this study was to determine the prevalence of CDI from a cross-section of consecutively seen, randomly enrolled, patients presenting with acute diarrhea to the Kenyatta National Hospital and Kisii Teaching and Referral Hospital in Kenya from May-July, 2017. After signing an informed consent, stool samples were collected and demographic data, medical history, prior antibiotic use, and HIV status was recorded. C. difficile was detected and confirmed using C. difficile-specific culture and PCR on stool samples. Toxins in the culture supernatant of isolated C. difficile colonies was determined using the Cdifftox activity assay. Statistical analysis was performed using Stata. The average age of the patients enrolled was 35.5 yrs (range 3-86 yrs), of which 59% were males (average age 34 yrs) and 41% were females (average age 37 yrs). Out of 105 patient stools tested, 98 (93.3%) were positive for C. difficile by culture. PCR analysis showed 98.9% of the C. difficile-positive stools contain the C. difficile-specific genes, tcdA, tcdB, or tcdC. The data also revealed that 81% of the C. difficile-positive stools showed 18-bp deletion in the tcdC gene that is associated with hypervirulent C. difficile strains. Isolates from all of the PCR-confirmed samples produced active toxins. Both male and female patients had similar prevalence of C. difficile. Majority of the patients (84.8%) reported over-the-counter antibiotic use in the last 30 days before the hospital visit. Among the C. difficile-infected patients, the prevalence of CDI and history of antibiotic use in the last 30 days preceding the diarrhea was 86.7%. All of the HIV-positive patients were C. difficile positive. The study results confirm a very high prevalence of C. difficile in Kenya, which may be attributed to unregulated use of antibiotics in the population. Additional study of the importance of CDI in patients presenting with diarrhea in other African countries are needed.
Abstract Title:
Determination of the Optimal Duration and Conditions of Long-Term Storage of Fecal Filtrate Samples Used for Fecal Microbiota Transplants (FMT)

Primary Author Block:
M. Kissoon1, A. Paterson1, B. M. Willey1, S. Hota2, S. M. Poutanen1; 1Univ. Hlth.Network/Sinai Hlth.Syst Dept. of Microbiol., Toronto, ON, Canada, 2Univ. Hlth.Network, Toronto, ON, Canada

Abstract Body:
Background: FMT is a useful treatment option for patients with recurrent Clostridium difficile infection. Frozen FMT filtrate is an efficient way to store samples. Little data exist showing the stability of frozen filtrate. Our group previously showed that optimal bacterial viability is achieved after 12M storage if filtrate is stored at -80°C with 10%-glycerol. The purpose of this study was to determine whether viability is maintained after 24M of storage. Methods: 4g of fresh stool from anonymous donors (n=2) was homogenized with both 40mL 0.9N-sterile saline and 40 mL 0.9N-sterile saline containing 10%-glycerol. The resulting filtrate was frozen at -20°C and at -80°C in 1.8mL aliquots. At baseline and after 7, 9, 12, 18, and 24M storage, 100μL of filtrate was plated onto anaerobic and aerobic agars and streaked using the Isoplator (Vista Technology). Semi-quantitative growth was recorded by two blinded readers. Loss of microbial growth (LMG) was determined as the difference between bacterial growth at each time-point compared to baseline. Results: At 7, 9, 12, 18, and 24M, fecal filtrate stored at -20°C without 10%-glycerol had the greatest loss of microbial growth (34%, 43%, 30%, 33%, and 45% loss, respectively) followed by filtrate stored at -20°C with glycerol (12%, 15%, 28%, 19%, and 21% loss) then filtrate stored at 80°C without glycerol (13%, 14%, 11%, 5%, and 6% loss). Fecal filtrate stored at -80°C with 10%-glycerol had the least loss of microbial growth (1%, 6%, 5%, 1%, and 2% loss). Conclusions: FMT filtrate is associated with optimal bacterial viability if stored at -80°C with 10%-glycerol, with no significant reduction in viability after storage for 24M. Viability is significantly impacted when fecal filtrate are stored at -20°C without cryo-protectant.
Abstract Title:
Comparative Effectiveness of Early-Targeted Use of Fidaxomicin versus Oral Vancomycin among Hospitalized Veterans’ Affairs Patients with Infections Due to Clostridium Difficile

Primary Author Block:
D. Morgansen1, N. Stornelli2, V. Shah1, C. Lowry1, N. Patel2, T. Lodise2; 1Samuel S. Stratton VA Med. Ctr., Albany, NY, 2Albany Coll. of Pharmacy & Hlth.Sci., Albany, NY

Abstract Body:
Background: The objective of this study was to compare real-world effectiveness outcomes (mortality and recurrence) between hospitalized patients who received regimens containing early-targeted fidaxomicin or oral vancomycin. Methods: A retrospective cohort study was performed among hospitalized patients receiving care in the Upstate New York Healthcare Administration from 5/2000 until 7/2014 with CDI. Inclusion criteria were: 1) age ≥ 18 years, 2) positive C. difficile stool sample (first episode), 3) ≥3 loose stools in past 24 hours or ileus with other causes of diarrhea ruled out, 4) use of fidaxomicin or oral vancomycin-containing regimen (≥48h) within 5d of a positive C. difficile stool sample. Data collected from medical records included demographics, comorbidities, medication history, hospitalization course, vital status, recurrence, lab findings and Hines severity score. Outcomes were: 1) Mortality at 30- and 60-d post C. difficile sample positivity, 2) Recurrent CDI infection within 60 days of completion of initial CDI treatment, 3) Composite failure (60d mortality or CDI recurrence). Results: There were 34 fidaxomicin and 156 oral vancomycin patients that met inclusion criteria. Mean ± standard deviation (SD) age was comparable between fidaxomicin (75.5 ± 9.8 years) and oral vancomycin (73.2 ± 11.7 years). For each study outcome, the following was observed between recipients of oral vancomycin and fidaxomicin: 30-day mortality (21.2% vs 14.1%, p = 0.48), 60-day mortality (28.2% vs 14.7%, p = 0.13), recurrence (22.4% vs 11.8%, p = 0.24) and composite failure (42.9% vs 26.5%, p = 0.09). These differences were greatest in patients ≥75 years (Figure) and those with an elevated Hines severity score. Conclusions: Compared to oral vancomycin, fidaxomicin-containing regimens were associated with lower mortality at 60-days and a composite of 60-d mortality/recurrence among patients ≥ 75 years.
Abstract Title:
The Association and Prevalence of Fetal Growth Retardation in Maternal Infections: A Systematic Review and Meta-Analysis

Primary Author Block:

Abstract Body:
Introduction: Intrauterine growth retardation (IUGR) is a major cause of neonatal morbidity and mortality. Infectious etiologies are estimated to be responsible for 5 – 10% of all growth-restricted fetuses. In this study, we aim to assess the association between maternal infections and IUGR rates and to specify the infections that carry the highest risk for developing IUGR. Methods: We searched nine databases including PubMed for relevant publications. Original articles reporting on intrauterine growth restriction (IUGR) caused by bacterial, viral or parasitic infections during pregnancy were included. We calculated the prevalence of IUGR in infected mothers according to the type and site of infection (placental vs. peripheral). We also assessed the impact of maternal infections on the IUGR rates. Meta-regression analysis was used to verify the dependency of the outcome measures. The National Institutes of Health tool was used to assess the quality of included articles. Begg’s funnel plot and Egger’s regression test were used to assessing for publication bias. Results: From a total of 5,697 articles screened against our criteria, we finally included 64 articles with 8323696 patients for meta-analysis. The pooled event rate for IUGR in infected mothers, including all infections, was 11.7% (95% CI, 10.3-13.2). Sixteen studies reported an estimated CMV event rate of 23.2 (95% CI, 16.3-30.2). HIV was reported in twenty-five studies estimating an event rate of 11.8% (95% CI, 9.3-14.4). Other infections, taken together, provided an estimated event rate of 7.1% (CI, 5.2-9) in a total of twenty-three studies. Placental infections were found to carry a higher risk for IUGR when compared to peripheral infections, with events rates of 21.5% (CI 95%, 16.1-26.9) and 10% (CI 95%, 0.08 – 0.12), respectively. We also found a statistically significant difference in the IUGR prevalence between infected pregnancies and healthy controls (OR = 1.79, CI 95% 1.62-1.97, p-value < 0.001). The results were also statistically significant between the two groups when we investigated the effect of HIV, CMV, Syphilis, and Malaria individually. Conclusions: There is a highly significant increase in the IUGR rates among infected mothers
overall and at the level of every single type of infections separately. CMV maternal infection, followed by HIV, carries the highest risk for developing IUGR. The incidence of IUGR varies based on the site of infection; placental infections carry a higher risk for IUGR as compared to peripheral infections.
Women’s Autonomy and the Vaccination Status of Children Aged 1 - 4 Years in Afghanistan, 2015

L. Shenton1, A. Wagner1, M. Mubarak2, B. Carlson1, M. Boulton1; 1Univ. of Michigan, Ann Arbor, MI, 2Kabul Univ. of Med. Sci., Kabul, Afghanistan

Introduction: Childhood mortality in Afghanistan decreased by 50% between 1990 and 2015, due in part to the government’s strengthened commitment to providing pediatric immunization services. Although improved, immunization coverage has remained low with only 65% of children receiving the third dose of Diphtheria-Pertussis-Tetanus (DPT3) according to WHO estimates. This study aims to calculate the proportion of Afghan children aged 1-4 years who were fully vaccinated, under-vaccinated, or non-vaccinated and identify predictors related to the family’s sociodemographic status and to maternal autonomy.

Methods: Data from the 2015 Afghanistan Demographic and Health Survey was used to calculate the proportion of children who were fully vaccinated (i.e. received all recommended vaccines), under-vaccinated (i.e. received some but not all), and non-vaccination (i.e. did not receive any vaccines) according to WHO guidelines. A multivariable multinomial logistic regression model generated odds ratios for under-vaccination and non-vaccination versus full vaccination, and examined associations between independent factors and full vaccination status.

Results: We found 40.6% of children were fully vaccinated, 42.4% under-vaccinated, and 17% non-vaccinated. Large disparities exist in immunization coverage among provinces and between urban and rural, secure and insecure regions. Birthing in a government institution (vs. non-institutional setting), a higher number of antenatal care visits, and a visit to a health facility in the past 12 months were all associated with increased odds of full immunization. Factors related to maternal autonomy including maternal decision-making and maternal attitudes towards beating were also significantly associated with vaccination status.

Conclusion: More than half of children in Afghanistan are under-vaccinated or non-vaccinated, leaving millions of children unnecessarily at risk for vaccine-preventable diseases. Engagement with community and religious leaders to create programs that increase women’s autonomy and expand access to institutional delivery could lead to downstream increases in vaccination coverage. Moreover, the awareness campaigns through media may also play an important role in order to convince the families to vaccinate their children.

Keywords: vaccination coverage, Afghanistan, maternal autonomy, healthcare, education
Abstract:
Trends of Vaccine-Preventable Diseases in Afghanistan from the Disease Early Warning System, 2009-2015

Primary Author Block:
A. Wagner1, M. Mubarak2, L. Johnson1, J. Porth1, J. Yousif1, M. Boulton1; 1Univ. of Michigan, Ann Arbor, MI, 2Kabul Univ. of Med. Sci., Kabul, Afghanistan

Abstract Body:
Background: Afghanistan's public health system was neglected during decades of military and civil conflict, and trends in infectious disease occurrence remain poorly characterized. This study examines cyclical and long-term trends of six vaccine-preventable diseases: pneumonia, diarrhea, meningitis, typhoid, measles, and acute viral hepatitis. Methods: Using weekly data collected between 2009 and 2015 through Afghanistan's Disease Early Warning System, we calculated monthly case counts, and fit a Poisson regression with a Fourier transformation for seasonal cycles and dummy variables for year. Results: We found the greatest incidence of diarrhea and typhoid in the summer, pneumonia in the winter, and measles in the late spring. Meningitis and acute viral hepatitis did not demonstrate substantial seasonality. Rates of pneumonia and diarrhea were constant across years whereas rates of meningitis, typhoid, and acute viral hepatitis decreased. Measles incidence increased in 2015.

Conclusions: Communicable disease reporting systems can guide public health operations such as the implementation of new vaccines, and permit evaluation of health interventions. For example, measles supplementary immunization activities in Afghanistan have not slowed long-term transmission of the disease, but decreases in typhoid fever and acute viral hepatitis are probably tied to improvements in sanitation in the country.
Host Response Classifier Accurately Discriminates between Bacterial and Viral Etiologies of Globally Important Pathogens


Background: Globalizations and growing antimicrobial resistant pathogens create unique challenges. Diagnostics that are agile, fast, and field-deployable are needed to respond to these challenges. Host response classifiers are poised to fill this diagnostic void. The host response is an attractive target for the classification of infection as we recently demonstrated through the development of a host gene expression signature that discriminates bacterial, viral, and non-infectious disease. We now present the application of this signature to a febrile Duke and Sri Lankan cohort representative of global pathogens.

Methods: We investigated the performance characteristics of a previously developed host response signature for bacterial vs. viral vs. noninfectious illness applied to patients in a global cohort. Total RNA was extracted and RNAseq performed from samples representing acute bacterial, acute viral, and non-infectious illness. Genes from the existing acute respiratory classifiers were mapped to transcripts and a data set was formed consisting of all mapped transcripts expressed in the RNAseq data. Regularized regression (lasso) was used to predict viral, bacterial, and noninfectious illness. Models were trained to predict each class in the presence of the other two classes. Accuracy was estimated through repeated 5-fold cross-validation. Predicted probabilities were used to calculate the area under the receiver operator characteristic curves (AUC).

RESULTS: After mapping our existing bacterial/viral classifier onto the RNA sequencing data, we observed high classification accuracy: bacterial vs. non-bacterial AUC 0.86, viral vs. non-viral AUC 0.88. After correction for batch effects, we did not observe large performance variability based on RIN score, pathogen, or other specific factors. The model will be validated using a global cohort that encompassed a larger array of pathogens and geographic sites.

DISCUSSION: Diagnostics that identify infection class are essential to inform the management of infectious disease. This work reveals the host transcriptional response accurately discriminates bacterial and viral infections for patients around the world with a variety of endemic infections. Further refinement of the transcriptional classifiers for global pathogens, as well as integrating proteomic and metabolomic analytes, will expand the ability of host response diagnostics to inform decisions about infectious disease management including resource allocation, quarantine, and treatment.
Abstract Title:
Increasing Incidence of Active HCV Super Infection in HBsAg Positive Patients in Pakistan
Primary Author Block:
B. A. Khan1, S. Khan2, J. Qazi3; 1Univ. of Karachi, Karachi, Pakistan, 2Dow Univ. of Hlth.Sci., Karachi, Pakistan, 3Quaid-i-Azam Univ., Islamabad, Pakistan
Abstract Body:
Introduction: Hepatitis C Virus (HCV) & Hepatitis B virus (HBV) infections are triggering the global health alarm as more than 350 million peoples are infected with HBV and more than 170 million are infected with HCV. Personnel’s infected with these viruses are at high risk for developing serious liver complications such as liver cirrhosis and hepatocellular carcinoma (HCC). They are collectively responsible for millions of fatalities every year. Pakistan is among the highly endemic countries for these hepatitis viruses as 3-5% of the peoples are reported to be sero-positive for HBsAg and 6-8% are found to be sero-positive for anti-HCV antibody. Since HBV & HCV share the similar transmission route therefore the chances of acquiring the super infection is high in these endemic regions. Co-infection or super infection of these hepatitis viruses is a serious health concern as it alters the disease pathogenesis and prognosis thus making it more severe, lethal & difficult to manage. Therefore, the frequency of active super infection in endemic areas should be evaluated. Objective: This study was conducted to assess the prevalence of active HCV super infection in HBsAg Positive patients in Pakistan. Methodology: A total of 190 HBsAg positive serum samples were collected from all four provinces of Pakistan. In these 190 samples, 113 samples were from males and 77 samples were from females. Total RNA was extracted from these samples and screened for presence of active HCV infection by real-time PCR. Results: The results demonstrate the overall prevalence of active HCV infection to be 7.4%. The highest incident rate for HCV infection are from the province of Sindh with the infection frequency of 10%. Province of Punjab comes afterward with the infection frequency of 8% followed by 6% from the province of Baluchistan as well as 3.3% from the province of Khyber Pakhtunkhwa (KP). Male gender and age group (41 to 60) was found to be more predominant with HCV. Conclusions: This study reports the high prevalence of active HCV super infection in HBsAg positive patients specially from the province of Sindh. Which could result in more severe liver diseases hence, special attention is required towards the management and treatment of patients dually-infected with these viruses. HBV/HCV is significantly boosting in our population, therefore government & other international authorities should focus on this emerging health security issue & should take immediate preventive measures to control the spread of infection.
Risk of Developing Liver Disease in Hev-Hiv-Seropositive Individuals in Nepal

Primary Author Block:
B. P. Gupta1, K. D. Manandhar1, R. Kurmi2; 1Tribhuvan Univ., Kathmandu, Nepal, 2Bhawani Hosp., Birgunj, Nepal

Abstract Body:
Background: Hepatitis E virus (HEV) infection is endemic in certain areas of the world such as Nepal. In this setting, HEV infection in immunocompromised patients could contribute to liver disease as the virus could induce a differential liver-specific immune response. In this regard, some studies in Spain have shown an association between HEV seroprevalence and cirrhosis among HIV-infected patients. In this study we aimed to address if HIV-infected individuals co-infected with HEV have differential degrees of liver fibrosis in an endemic area for the virus. Methods: We prospectively evaluated 200 HIV-infected individuals on antiretroviral therapy, in a clinic in rural Nepal between 2016 and 2017. Serum samples were collected and clinical information obtained concomitantly. Samples were analyzed for multiple components of a variety of liver fibrosis scores (AST, ALT, platelets, albumin, cytokeratin-18), as well as CD4 counts. HEV IgG was measured by ELISA using a Wantai kit. Statistical analyses were performed using Wilcoxon score methods. Results: The median age of patients was 31 years (IQR 14-40) and 61% were males. Forty-three percent of patients (N:87) were positive for HEV-IgG. The average CD4 count was 551/mm3 in those HEV-positive and 674/mm3 in those HEV-negative (p=0.3). We found no association between consumption of of boiled or filtered water, food predilection or presence of gastrointestinal symptoms and HEV seroprevalence. We found a significant association between HEV-seropositivity and elevated Fib4 and NAFLD fibrosis scores: median Fib4 score 1.31 vs 0.87 for HEV-positive and -negative respectively (p<0.001) and median NAFLD fibrosis score of -1.88 vs -2.43 for HEV-positive and -negative respectively (p=0.01). APRI scores were similar among both groups (0.31 vs 0.32 respectively). Interestingly, in a subset of 80 patients, we found no correlation among CK-18 levels and HEV seropositivity. However there was no association between CK-18 and BMI, CD4 counts or the presence of diabetes. Conclusions: We found higher Fib4 and NAFLD fibrosis scores among HIV/HEV positive individuals, suggesting an increased liver fibrosis profile among this group. Further studies using other fibrosis markers such as liver biopsy or liver stiffness measurements should be performed.
Abstract Title:
Molecular Phylogeny & Prevalence of Emerging Hepatitis Delta Virus (Hdv) in Pakistan
Primary Author Block:
N. Maqsood, B. A. Khan, S. Khan; Dow Univ. of Hlth.Sci., Karachi, Pakistan
Abstract Body:
Background: Hepatitis delta virus (HDV) is a negative sense RNA sub satellite virus which requires HBsAg for its transmission and causes chronic viral hepatitis. Its super-infection in HBV infected individuals progress to cirrhosis, hepatocellular carcinoma and liver failure. Furthermore, response to therapeutics is also peculiar and less satisfactory in these patients. Pakistan is among the high HBV endemic countries however the reliable data on HDV active infection and its molecular phylogeny in not available from this region. Therefore, this study was conducted to determine the prevalence of active HDV super infection, its genotype and molecular phylogeny in HBsAg positive patients in Pakistan. Methods: A total of 190 HBsAg samples were collected from all four provinces of Pakistan. In these 190 samples, 113 samples were from males and 77 samples were from females. Total RNA was extracted from these samples and screened for presence of active HDV by RT-PCR. HDV genotyping was performed by using PCR-RFLP method. Partial HDAg fragment from 24 HDV positive samples were amplified and sequenced for phylogenetic reconstruction along with other reference sequences from GenBank. Results:The results demonstrate the overall prevalence of active HDV infection to be 24.7%. The highest incident rate for HDV were from the Sindh with the infection frequency of 35% followed by 24% from Punjab, 20% from Baluchistan as well as 13.3% from Khyber Pakhtunkhwa respectively. Male gender and age group 21 to 40 years was found to be more infected with HDV. All of the 47 HDV positive samples were found to be HDV-genotype I which was further confirmed by phylogenetic analysis which revealed that all the sequences from this study belongs to clade I including three sequences closely related to geographical distant isolates from Turkey and Italy Conclusions: This study reports the high prevalence of active HDV infection in HBsAg positive patients specially from the province of Sindh. Phylogenetic analysis revealed that the current circulating HDV strains have high genetic diversity and multiple origin of spread. Therefore, government & other international authorities should focus on this emerging pathogen & should take immediate preventive measures to control the spread of infection.
Abstract Title:
Diagnosis of Chagas Disease by Detecting Species-Specific Satellite Repeat DNA from Filtered Human Urine Samples

Primary Author Block:
M. Price; Marquette Univ., Milwaukee, WI

Abstract Body:
Chagas disease is a blood parasitic disease caused by Trypanosoma cruzi (genus Trypanosoma), which spreads across the Americas. The disease has infected almost eight million people with millions more at risk and is often missed due to lack of sensitive diagnostic tests. The classic parasitological and immunological tests often fail in the acute phase due to asymptomatic nature of infection and in the chronic phase due to low levels of trypanosomes in the blood. If control strategies are to succeed, there must be a sensitive and specific diagnostic test. Recently, better diagnostics have developed for Chagas detection, where polymerase chain reaction (PCR) was used on blood samples from infected individuals. For this study, our objective was to demonstrate the effectiveness of detecting T. cruzi specific repeat DNA fragment via PCR from urine sediment captured on filter papers after filtration, showing the possible detection of T. cruzi over classical methods of detection. Urine samples were collected from volunteers free of prior infection and divided into 30ml volume of 15 samples. They were spiked with three different concentrations (high, medium and low) of T. cruzi (three strains: T. cruzi CL, T. cruzi Dm28c, and T. cruzi G) and two African strains: T. brucei and T. rhodesiense genomic DNA to test the efficacy of detection of repeat satellite T. cruzi DNA. Three sets of primers were used. Our approach only detected repeat satellite DNA specific for T. cruzi strains, but not for African strains. A serial dilution was also performed on T. cruzi samples to detect all three sets of primer sensitivity. One set of primer constantly detected repeat satellite DNA for all T. cruzi strains ranging from 70 pg/µl to 175 fg/µl. We were able to demonstrate the feasibility of identifying T. cruzi specific satellite DNA from filtered urine samples by sensitive and specific PCR assay. Besides evidence of increased sensitivity and specificity of primers, our approach can be used to explore Chagas prevalence in endemic areas, especially in the acute phase.
Abstract Title:
Epidemiological Characteristics of Risk Factors of Human Brucellosis in Azerbaijan (2012-2016)

Primary Author Block:
N. Ustun, R. Ismayilova, R. Abdullayev; Republican Anti-Plague Station, Baku, Azerbaijan

Abstract Body:
Brucellosis is usually transmitted to humans by consumption of unpasteurized milk or through direct contact with infected animals. The aim of this study was to identify risk factors for brucellosis among humans in Azerbaijan. Data set of all human brucellosis cases from 2012 to 2016 in Azerbaijan was obtained from the Electronic Integrated Disease Surveillance System (EIDSS). Suspected cases of human brucellosis were confirmed by Rose Bengal, Huddleston and the Wright serum agglutination tests. Age, gender, date, location of cases, contact with animals and their products were analysed using the Analysis Visualization Report module of EIDSS and Epi Info 7.0. During the 5-year period, a total of 1516 laboratory confirmed brucellosis cases were reported. Between 2012 -2014, new brucellosis cases ranged from 2.4 to 3/100,000 population. In 2015 there were 3.2 cases / 100,000, and in 2016, 4.1 cases / 100,000. The majority of the cases were reported during February - July. The age group of the highest number of cases was 30-59 years. In that age group, the majority were males (68 %). 80 % of all cases were in rural areas. 51 % reported consumption of unpasteurized milk and dairy products, consumption of undercooked meat accounted for 14% , assistance in animal birth was 24% , contacts with sick animals was 10% , potential laboratory or other occupational exposure was 1% . Consumption of unpasteurized milk products was identified as the most significant source of human brucellosis infections in Azerbaijan. It suggests that brucellosis spreads among farm animals and that home-made milk products are not pasteurized. Health education programs should be increased, and veterinary control should be improved. Vaccination remains the most appropriate control measure in Azerbaijan. Since 2009 the veterinary service has been vaccinating goats and sheep. Perhaps introducing cattle vaccination could reduce the prevalence of animal brucellosis and reduce the risk of transmission to humans.
Abstract Title:
Control of Anthrax Animal Cases Through Risk Based Vaccinations in 2012-2016 Yy in Georgia
Primary Author Block:
L. Avaliani, T. Napetvaridze, Z. Asanishvili; Natl. Food Agency, Tbilisi, Georgia
Abstract Body:
Background: Anthrax is an endemic zoonotic disease in Georgia affecting animal and human health. There is estimated that are more than 2000 anthrax foci in Georgia, but majority of them are not properly registered. Prophylactic vaccination of animals was suspended in 2007-2012. As a result animal disease incidence was raised from 4 confirmed cases (2007 Y) in up to 36 confirmed case in 2012 Y. Due to the progressive number of Anthrax animal and human cases National Food Agency made a decision to reintroduce vaccination campaign in animals. Methods: The goal of these activities was to reduce incidence of the disease in animals and therefore in humans through yearly risk based fully free of charge vaccination campaigns. Yearly spring vaccination campaign was initiated in 2012 with revaccination of youth in autumn. One Health Approach was used in order to determine villages at risk. Villages with animal and human cases (foci) records and high risk area (seasonal migrated animals and animals in villages located at seasonal migration routes). Estimated number of holdings large & small ruminants and horses was determined. Specific written guidelines including biosecurity and vaccination protocols were created for contracted specialists. In addition mapping of Anthrax foci was performed in 2014 through Cooperative Biological Engagement Program (CBEP) funded project TAP7 - “Identification and Mapping of Anthrax foci in Georgia”. Together with Geo-mapping and photographing of traced foci a soil samples were collected in order to define existed risks of reintroduction of outbreaks in historical infected areas. Results: In 2012-2016 in total about 3,235,229 animals (1,571,933 large, 1,645,660 small ruminants and 17,636 horses) were vaccinated/revaccinated. As a result of control activities incidence of the disease in 2016 was decreased 2 times in animals and 5.3 times in humans compare with 2012. A total of 1,825 soil samples were collected from 302 select foci sites, 25 foci sites were positive for Bac. Anthracis. Conclusions: Historical foci sites presents constant threat of reintroduction of disease outbreak in animals. Successful control of Anthrax and reduction of animal and human cases is feasible through the risk based vaccination of animals in infected villages. Future plans: National Food Agency plans to continue risk based vaccination in animals. NFA also plans to establish program for mass disinfection of foci sites followed by soil sample collection in order to access success of the disinfection activities.
Detection of Schistosoma Mansoni and S. Haematobium from Single Filtered Urine Samples from Sch. Children after Mda in Zambia

Primary Author Block:
M. J. Hessler1, A. Cyrs1, S. C. Krenzke1, E. Mahmoud1, C. Sikasunge2, J. Mwansa2, N. Lodh1;
1Marquette Univ., Milwaukee, WI, 2Univ. of Zambia, Lusaka, Zambia

Abstract Body:
Schistosomiasis is one of the most important Neglected Tropical Diseases (NTDs). In sub Saharan Africa two major human schistosomes namely Schistosoma mansoni and S. haematobium often occur sympatrically largely affecting children. In the age group of 6-15 year’s infection prevalence and intensity peaks, which associated with growth delays, delayed cognition, poor school performance and a negative effect on the overall growth and quality of a child’s life. World Health Organization (WHO) is urging member states to regularly treat at least 75% and up to 100%, of all school-aged children at risk of morbidity. We have detected S. mansoni and S. haematobium parasite specific small repeat DNA fragment from filtered urine on filter paper by polymerase chain reaction (PCR). In this study we are testing urine samples obtained from Zambian school children after mass drug administration (MDA) to compare between existing diagnostic tests and PCR amplification of parasite DNA from urine. We have assessed 111 samples for the above-mentioned schistosome species by amplifying species-specific DNA fragment from single urine sample. Our approach detected eight times more positive cases (total 77) than by Kato-Katz (KK: 9) for S. mansoni and six times more (total 72) than by hematuria (11) for S. haematobium and even more than urine filtration (77 compared to only 6). All of the samples were detected with 100% sensitivity and specificity devoid of any cross amplification. The same pattern was observed when stratified for age group and sex specific analysis. In addition, 69 individuals (62%) were co-infected by both parasites. We have demonstrated a significantly higher prevalence of both species after MDA than indicated by the classical examination of urine or stool and also the maintenance of infection reservoir. Our approach of detecting low prevalence multi schistosome infection is an effective means to detect low intensity infection and would enhance the effectiveness of surveillance and MDA control programs of schistosomiasis.
Abstract Title:
Cholera in Haiti: Seven Years Later
Primary Author Block:
Abstract Body:
Introduction: In January 2010, a massive earthquake devastated Haiti. This was followed in October 2010 by a massive cholera outbreak. Since then, and over the past 7 years, thousands of cholera cases and deaths have been documented throughout Haiti. After much controversy, scientific investigations traced the source of the cholera outbreak to a Nepalese United Nation Peacekeeping camp in Haiti. Cholera had not occurred in Haiti before 2010. This report describes recent progress in cholera control efforts in Haiti. Methods: Cases were defined as any case of acute, profuse, watery diarrhea, with or without vomiting occurring in a department of Haiti affected by cholera. Data was obtained from the National Cholera Surveillance System which includes public and private-public institutions. Results: Table 1: The national number of Cholera cases in Haiti reported by the National Cholera Surveillance System per year:

<table>
<thead>
<tr>
<th>Year</th>
<th>National number of Cholera cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>185,210</td>
</tr>
<tr>
<td>2011</td>
<td>351,839</td>
</tr>
<tr>
<td>2012</td>
<td>101,354</td>
</tr>
<tr>
<td>2013</td>
<td>58,917</td>
</tr>
<tr>
<td>2014</td>
<td>46,038</td>
</tr>
<tr>
<td>2015</td>
<td>41,905</td>
</tr>
<tr>
<td>2016</td>
<td>29,078</td>
</tr>
<tr>
<td>2017</td>
<td>13,680</td>
</tr>
<tr>
<td>Total</td>
<td>828,021</td>
</tr>
</tbody>
</table>

The cholera incidence rate was 18 per 1000 (18/1000) residents in 2010, with a peak in 2011 at 34/1000 residents, and a drop in the rate to 1/1000 residents in 2017. Cholera deaths were highest in year 2010 at 2.2/100 cases, and lowest in year 2017 at 1/100 cases. Three of the 10 departments of Haiti, including Artibonite, Centre, and Ouest, together have reported more than 67% of the cholera cases per year, except in year 2016 (61.19%). Cholera control interventions have included efforts from national and international partners in combating the outbreak, including implementing alert/response system, campaigns to promote sanitation and hygiene, and oral...
cholera vaccine campaigns. Conclusion: Considerable progress has been made to control the outbreak of cholera in Haiti, despite significant challenges related to funding, water and sanitation infrastructure, and widespread poverty. These efforts can serve as a model for the control of cholera in other resource-limited countries. Eradication of cholera from Haiti remains a difficult-to-reach goal.
Toxigenic Vibrio Cholerae O1 in Vegetables and Fish Raised in Wastewater Irrigated Fields and Stabilization Ponds During A Non-Cholera Outbreak Period in Tanzania

Abstract Body:
Background: Cholera, one of the world's deadliest infectious diseases, remains rampant and frequent in Tanzania and thus hinders existing control measures. The present study was undertaken to evaluate the occurrence of toxigenic Vibrio cholerae O1 in wastewater, fish and vegetables during a non-outbreak period in Morogoro, Tanzania. Methods: From October 2014 to February 2015, 60 wastewater samples, 60 fish samples from sewage stabilization ponds and 60 wastewater irrigated vegetable samples were collected. Samples were cultured for identification of V. cholerae using conventional bacteriological methods. Isolates were confirmed as V. cholerae by detection of the outer membrane protein gene (ompW) using polymerase chain reaction (PCR). Isolates were further tested for antibiotic susceptibility and presence of virulence genes including, cholera enterotoxin gene (ctx), the toxin co-regulated pilus gene (tcpA) and the haemolysin gene (hlyA). Results: The prevalence of V. cholerae in wastewater, vegetables and fish was 36.7, 21.7 and 23.3 %, respectively. Two isolates from fish gills were V. cholerae O1 and tested positive for ctx and tcpA. One of these contained in addition the hlyA gene while five isolates from fish intestines tested positive for tcpA. All V. cholerae isolates were resistant to ampicillin, amoxicillin and some to tetracycline, but sensitive to gentamicin, chloramphenicol, and ciprofloxacin. Conclusions: Our results show that toxigenic and drug-resistant V. cholerae O1 species are present and persist in aquatic environments during a non-cholera outbreak period. This is of public health importance and shows that such environments may be important as reservoirs and in the transmission of V. cholerae O1.
Helicobacter Pylori Infection & Type 2 Diabetes Mellitus in Lithuania

Primary Author Block:
D. Janulaityte - Gunther; Lithuanian Univ. of Hlth.Sci. (LSMU), Kaunas, Lithuania

Abstract Body:
Background: Helicobacter pylori (H. pylori) is known as the most common gastrointestinal bacterial infection worldwide. It has been proposed as a causative agent of gastritis & peptic ulcer disease & a risk factor of gastric cancer. Several reports have shown the association of H. pylori & extragastric diseases. There is no scientific data on prevalence of H. pylori infection in Type 2 diabetes mellitus exists in Lithuania. The aim of this study was to determine the association between H. pylori infection & Type 2 diabetes mellitus in Lithuania. Objectives: to determine the frequency of H. pylori infection in diabetic & non-diabetic patients; to determine possible relationship of H. pylori with diabetic complications; to determine the prevalence of H. pylori infection in Type 2 diabetes mellitus & its relation with glycated hemoglobin (HbA1c) & serum lipid profile.

Methods: The study was conducted at the Hospital of Lithuanian University of Health Sciences. The study included 71 Type 2 diabetes mellitus patients & seventy one non-diabetic subjects. The study was carried out by using rapid immunochromatographic test. Patient’s medical history has been used to collect the data of HbA1c, serum lipid profile & diabetic complications. SPSS 22.0 used for statistical analysis.

Results: There were forty (56,3%) patients with Type 2 diabetes mellitus & 37 (52,1%) of non-diabetic patients infected with H. pylori. No significant difference (p>0.05) has been found between these two groups. The diabetic complications - retinopathy, nephropathy and neuropathy has been detected in 13 (46,4%), 7 (58,3%) & 15 (51,7%) H. pylori-positive Type 2 diabetes mellitus patients as compared to H. pylori-negative diabetic patients: fifteen (53,6%), 5 (41,7%) & 14 (48,3%). But this difference failed to reach statistical significance (p>0.05). High levels of triglycerides & HbA1c have been detected in H. pylori-positive patients (twenty one (72,4%) and 32 (65,3%) as compared to H. pylori-negative patients with Type 2 diabetes mellitus: eight (27,6%) & 17 (34,7%). The difference between these groups was statistically significant (p<0.05).

Conclusions: There is no association between H. pylori infection & Type 2 diabetes mellitus has been found in this study in Lithuania. The link between H. pylori infection & Type 2 diabetes mellitus complications has not been established. Presence of H. pylori infection significantly correlated with the higher levels of triglycerides & HbA1c.
Phyto-Chemicals; A Novel Approach against Helicobacter Pylori

A. Rehman; Univ. of the Punjab, Lahore, Pakistan

Background: Helicobacter pylori is a gram-negative, flagellated bacterium and a close relative of Campylobacter spp. This gastric maniac is capable to reside peptic mucosa and leads to development of peptic ulcer. A lengthy therapeutic procedure of 7-14 days comprising of multiple antibiotics is required to eliminate Helicobacter pylori. The chromosomal encoded resistance against antibiotics is making cure of Helicobacter pylori difficult day by day. In this study, the objectives were set to determine antimicrobial susceptibility, Exo-Poly Saccharide (EPS) production, existence of complex bacterial biofilms and assessment of therapeutic potential of various phytochemicals against H. pylori and associated microbes in peptic ulcer. Moreover, in-silico tools of bioinformatics were also employed to determine therapeutic capacity of synthetic and natural compounds against H. pylori. Methods: Microbes were isolated from peptic biopsy samples by using Columbia blood agar, followed with identification by bio-chemical testing. The antibiotic susceptibility profiling of isolates was conducted by employing disc diffusion method. For estimation of biofilm formation ability and EPS production, standard motility, adherence and EPS production tests were used. Moreover, microtiter plate assay was employed to determine inhibitory effect of Honey and ethanolic/methanolic extracts of Black Caraway (Nigella sativa seeds). Furthermore, standard docking procedures were employed for in-silico studies. Results: From 5 biopsies, 15 strains were isolated among which one isolate was biochemically identified as Helicobacter pylori. All isolates were resistant to Metronidazole and Amoxicillin. Majority of isolates were sensitive to Clarithromycin and Levofoxacin. Surprisingly, the isolates showed sensitivity against Honey and Nigella sativa at lower concentrations of 2mg/ml and 1mg/ml respectively. Moreover, the ethanolic and methanolic extracts of Nigella sativa significantly reduced biofilm formation and EPS production of isolated bacteria. In-silico studies revealed that many synthetic and natural compounds were able to block active site of key enzyme urease, which could ultimately lead to elimination of Helicobacter pylori. Conclusions: The increasing antibiotic resistance is demanding scientific world to develop novel therapeutics to deal with pathogens like Helicobacter pylori. Phytochemicals are a broad avenue to tackle with shrinking window of available antibiotics requirement of potential therapeutics.
Session Number: 70
Session Type: Poster
Session Number: 70
Session Type: Poster
Session Title: CIV03 - Global Health: Epidemiology and Diagnostics
Session Start Date Time: 6/8/2018 11:00:00 AM
Session End Date Time: 6/8/2018 1:00:00 PM
Session Primary Track: Clinical Infections and Vaccines
Abstract Control Number: 5052
Poster Board Number: FRIDAY - 732

Abstract Title:
Enteric Infections, Caused by Nag-Vibrios 2016 - 2017 in Azerbaijan

Primary Author Block:
S. Ibrahimova, R. Ismailova, R. Abdullayev; Republic Anti-Plague Station, Baku, Azerbaijan

Abstract Body:
Background: V. cholerae is the causative agent of water-borne cholera, and persists in the environment between disease outbreaks. In Azerbaijan, non-agglutinable vibrios (NAG-vibrio) are the main strains causing cholera-like symptoms in humans. Continuous monitoring of infection and disease flow will provide information to devise strategies to fight disease and reduce burden on health personnel and resources. Samples were tested for NAG-vibrio at the Republican Anti-Plague Station (RAPS), Baku.

Methods: Strain isolation and identification of V. cholerae serogroups remain as the gold standard for cholera diagnosis, where suspected samples are cultured and tested for classical cholera and cholera El-Tor using a type-specific O cholera serum agglutination assay. Negative cholera samples are still tested for NAG-vibrio and other cholera-like vibrios as per standard operating procedures and guidance from “Instructions and Guidelines for Laboratory, Clinical Diagnosis, Prevention and Treatment of Infections in Humans” (Ministry of Health, Azerbaijan, 2010, Laboratory Diagnostics of Especially Dangerous Pathogens, 2013) and regulation N64 for sample collection and testing (Ministry of Health, Azerbaijan). Abundance and distribution of environmental V. cholerae were assessed in sentinel sites along public recreational areas in water sources (e.g., beach, potable and waste water). NAG-vibrios are based on biochemical properties following Heiberg’s classification of 7 distinct NAG-vibrio groups (I through VII). Active and passive surveillance provided descriptive epidemiological data. Results: From a total of 24308 samples, 605 samples were environmental (2%) and 23703 were of human origin (98%). Testing of 605 environmental water samples identified 138 NAG-vibrio positive samples (23%). The 23703 human samples originated from either enteric infection (55%), food poisoning (2.7%), and from control groups (41%). One percent of food poisoning samples was NAG-vibrio positive (n=7). Two of 7 NAG-vibrio-positive samples belonged to groups I and II, and the 3 remaining samples to groups III, IV and VII, respectively. V. cholerae prevalence showed temporal fluctuation in environmental samples (i.e., 2015: 23%; 2016: 19%; 1st half of 2017: 35%) and an increase in humans (2015: 0.01%; 2016: 0.02%; 1st half of 2017: 0.09%), with 29% of human samples co-localizing with environmental samples. Conclusions: Knowledge from such data is critical to build efficacious counter-epidemic and sanitary measures for cholera prevention.
Local Population Density As A Risk Factor for Enteric Infection in the Mapsan Trial

T. Sumner, J. Knee, J. Brown; Georgia Inst. of Technology, Atlanta, GA

By 2050, 56% of Africans will live in urban areas. 65% of current urban residents live in informal settlements characterized by high population density, poverty, lack of basic services, and poor sanitary conditions. Enteric infection risk might be higher in these areas. Mixed evidence regarding whether population density is an effect modifier of the relationship between sanitation conditions and health outcomes like diarrhea and enteric infection. Current study is a controlled before-and-after health impact evaluation of a shared sanitation intervention on children living in densely populated neighborhoods outside of Maputo, Mozambique. Children under 4 years old were enrolled in our study and their health was assessed with stool samples. Stool was analyzed with a multiplex PCR based assay that detects 15 viral, bacterial, and protozoan enteropathogens. They were also analyzed for soil-transmitted helminth infection via Kato-Katz microscopy and droplet digital PCR. Population density was measured using three different methods, the first being a measurement of the area of shared living space (known as compounds) and a count of the number of people in that space, the second using residential rooftop area as a proxy for population, and the third using satellite image complexity as a proxy for population. Infection odds ratios for children in the highest tercile of population density were computed in STATA (reference group: lowest tercile of population density, adjusted for age, sex, poverty, and clustering) for each of the three population density estimations. The bacterial, protozoan and helminth infections we studied did not show a significant association with any population density measure. Local population density does seem to be a risk factor for certain enteric viral infections. Though difficult to measure, local population density could possibly be an important aid in targeting public health interventions.
Abstract Title:
Screening for Bk Virus Post Renal Transplantation

Primary Author Block:

Abstract Body:
Background: Reactivation of BK virus (BKV) post renal transplant increases the risk of BK virus associated nephropathy with the end result of graft loss. The only current method to control viral progression is immunosuppression reduction in patients with detectable BKV. Screening for BKV in either blood or urine is routinely performed at most transplant centers. We compared the outcome of blood and urine BKV screening at two different centers. Methods: We retrospectively reviewed 12 years (2003-2015) of renal transplant records at our center and at a second center. We collected demographic, clinical, and laboratory data on all patients. At our center, BKV screening was routinely performed from 2008 till 2011 (Group 1). From 2011 till 2015, we screened for BKV in urine (Group 2). A positive urine result is followed by blood test for BKV. We analyzed the data from these two time periods separately. The second center screened by blood only (2003-2015) (Group 3). Results: In total, our center had 59 subjects with BK viremia, where 27 of those were detected in the period of screening in blood (4 with nephropathy), and 32 by urine screening (5 with nephropathy). The second center had 133 subjects with BK viremia (14 with nephropathy) in the 12 years of study period where screening was performed in blood. There were no significant differences in demographics and clinical data in the three groups. The median months to viremia differed between the groups screening by blood (Groups 1 and 3) and the group screening by urine (Group 2): 6.39 (Std 16.6) and 6.13 months (Std 19) as compared to 3.21 months (Std 4.6). The median number of screening test and frequency of test (tests/months) sent prior to viremia detection were Group 1 with 2.5 tests, 0.28 (Std 2.6, 0.37), Group 2 with 1 test and 0.16 (Std 2.2, 0.25), and Group 3 with 2 tests and 0.48 (Std 2.4, 0.7). Conclusions: Screening for BKV in either blood or urine is performed at different centers. Comparing the two methods, BK viremia is detected earlier (3.19 months) the Group 3 – the urine screening group as compared to 6.39 and 6.19 months in the blood screening groups. The earlier detection is not accompanied by increased number of tests or increased frequency of test. Earlier detection of viral reactivation may be crucial in prevention of nephropathy.
Late CMV Infection Following Letermovir Prophylaxis in Allogeneic Hematopoietic Stem Cell Transplant Recipients

Abstract Title:
Late CMV Infection Following Letermovir Prophylaxis in Allogeneic Hematopoietic Stem Cell Transplant Recipients

Primary Author Block:
A. Hodowanec, T. Komatsu, M. Singer, F. Smith, T. Valappil, J. O'Rear, J. Murray, D. Birnkrant; Food and Drug Admin., Silver Spring, MD

Abstract Body:
Background: CMV infection is associated with significant morbidity and mortality among hematopoietic stem cell transplant (HSCT) recipients. Letermovir is the only drug approved in the US for CMV prophylaxis in this population. In Trial P001, submitted to FDA to support approval, CMV seropositive recipients of an allogeneic HSCT were randomized 2:1 to receive letermovir or placebo through 14 weeks post-transplant. Letermovir was associated with a significant reduction in the proportion of subjects with clinically significant CMV infection through 24-weeks post-transplant (57/325 [17.5%] vs. 71/170 [41.8%], letermovir vs. placebo) (<u>NEJM</u> 2017;377:2433-2444). However, CMV infection was observed in some subjects after completion of letermovir prophylaxis. The risk factors for late CMV infection and its presentation in HSCT recipients receiving letermovir prophylaxis are incompletely characterized.

Methods: We performed additional analyses of Trial P001 data. Rates of clinically significant CMV infection, defined as CMV viremia (DNAemia) prompting preemptive therapy (PET) or CMV end-organ disease (EOD), occurring from Week 0 to 14 (early) and Week 14 to 24 (late) post-transplant were assessed. Results: Among letermovir-treated subjects, 10% developed late CMV infection (Table 1). Among letermovir-treated subjects with late CMV, 47% had ≥1 baseline factor associated with increased risk for CMV reactivation, and 81% were diagnosed with graft versus host disease (GVHD) prior to or concurrent with late CMV infection. Among letermovir-treated subjects with late CMV infection, 4 had CMV EOD and 6 required rehospitalization for CMV infection. Conclusions: Letermovir represents a marked advancement in the care of HSCT recipients. However, some HSCT recipients may be at risk for late CMV infection, including CMV EOD, following the completion of letermovir prophylaxis at 14 weeks post-transplant. Studies assessing the benefit of a longer duration of prophylaxis are warranted.

### Table 1: Summary of Study P001

<table>
<thead>
<tr>
<th></th>
<th>Letermovir</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 0–14</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Late CMV Infection (Overall) | 25/325
<table>
<thead>
<tr>
<th>Event</th>
<th>Amongst Subjects w/ CMV Infection</th>
<th>Amongst Subjects w/ CMV Infection</th>
<th>Amongst Subjects w/ CMV Infection</th>
<th>Amongst Subjects w/ CMV Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viremia with PET</td>
<td>24/325 (7%)</td>
<td>65/170 (38%)</td>
<td>28/325 (9%)</td>
<td>3/170 (2%)</td>
</tr>
<tr>
<td>EOD</td>
<td>1/325 (&lt;1%)</td>
<td>2/170 (1%)</td>
<td>28/325 (9%)</td>
<td>2/170 (1%)</td>
</tr>
<tr>
<td>Rehospitalization for CMV</td>
<td>2/25 (8%)</td>
<td>10/67 (15%)</td>
<td>6/32 (19%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Amongst Subjects w/ CMV Infection</td>
<td>11/25 (44%)</td>
<td>22/67 (33%)</td>
<td>32/325 (10%)</td>
<td>67/170 (39%)</td>
</tr>
<tr>
<td>≥1 baseline high risk factor</td>
<td>15/32 (47%)</td>
<td>1/4 (25%)</td>
<td>1/4 (25%)</td>
<td>32/325 (10%)</td>
</tr>
<tr>
<td>GVHD</td>
<td>10/25 (40%)</td>
<td>26/32 (81%)</td>
<td>2/4 (50%)</td>
<td>2/4 (50%)</td>
</tr>
</tbody>
</table>
Abstract Title:
Cmv Viremia Detection Differences and Clin. Impact between Commercial Assays
Primary Author Block:
J. E. McKinnon1, Z. Osborn1, N. Janakiraman1, J. Zhou1, L. Samuel1, D. Lucic2, M. Ramesh1, K. Williams1, O. Abreu-Lanfranco1, S. Farhan1, E. Peres1, G. Alangaden1; 1Henry Ford Hosp., Detroit, MI, 2Abbott Molecular, Des Plaines, IL
Abstract Body:
Background: Human Cytomegalovirus (CMV) infection carries significant morbidity and mortality in patients undergoing transplantation (Tx). CMV WHO International Standard along with use of the FDA approved real time PCR assay has improved CMV quantitation and agreement between methods. However, clinical significant differences may still exist. The study compares the two currently approved Roche cobas AmpliPrep/cobas TaqMan CMV test (TM assay) and Abbott Molecular RealTime CMV assay (ART assay) for quantification of CMV viremia in patients receiving allogeneic hematopoietic stem cell transplants (aHSCT). Methods: Prospective CMV positive patients, planned for aHSCT, were consented prior to Tx and followed weekly up 12 weeks post-transplant (PT) and once 3 months PT. Matched paired plasma samples were processed and analyzed per manufacturer instructions, Henry Ford clinical laboratory processed the samples using the TM assay and the McKinnon Research Laboratory processed the paired samples using the ART assay. Parametric and non-parametric analyses were conducted as appropriate. Results: Twenty-two patients enrolled, 2 patients have withdrawn, 5 patients died. Patients received peripheral blood stem cells (20) or Bone marrow (2) with 72.7% receiving myeloablative chemotherapy. In paired samples, quantifiable CMV by TM and ART assays was detected in 10 vs 13 patients respectively. Three patients with quantifiable viremia as high as 8547 IU/mL by ART were missed by TM. ART assay detected CMV viremia in all positive paired TM viremic samples except for one sample with 210 IU/mL in the TM assay, as compared to 25 missed samples by TM (p<0.001). Assays differed in samples with quantifiable CMV viremia, with more frequent detection in the ART assay (p=0.003). Time to quantifiable viremia PT by TM and ART assays was a median of 5.3 vs 3 weeks (p=0.02). CMV viremia tended to persist longer using ART 10.4 vs 8.9 weeks for TM assay (p=0.07). After week 4 PT, ART viremia assay results inversely correlated weight (p=0.001), hematocrit (p=0.003) and lymphocyte counts (p=0.009). The TM assay viremia only correlated with weight loss (p<0.001). Bland-Altman plot shows higher viremia levels quantified using the ART assay (p<0.001). Conclusions: The ART assay is quantifying CMV viremia earlier post-transplant with higher levels and is correlated with weight loss, lymphopenia, low hematocrit as compared to TM assay. Further study is warranted to determine clinical impact of discordant and missed CMV viremia results with these new commercial assays.
Abstract Title:
Evaluation of the Gut Microbiota As A Measure to Examine Success of Fecal Microbiota Transplantation in Solid Organ Transplant Recipients.

Primary Author Block:
A. Kates, D. Shirley, M. Duster, J. Skarlupka, N. Safdar; Univ. of Wisconsin-Madison, Madison, WI

Abstract Body:
Fecal microbiota transplantation (FMT) has become a common treatment for Clostridium difficile infections (CDI). Patients with a history of solid organ transplantation (SOT) are at increased risk of CDI due to immunosuppression and exposure to antibiotics. The effectiveness of FMT in this population is unclear. Here we present a pilot study of FMT use to treat CDI in SOT patients. Patients with CDI were treated with FMT from a universal donor or someone the patient knew and administered via colonoscopy or enema. Stool samples were taken from the patient pre- and post-FMT as well as from the donor. DNA was extracted using a bead-beating protocol. Sequencing of the V4 region was done on the Illumina MiSeq. All analyses were done in R v.3.4.0. Alpha diversity was calculated using the Inverse Simpson’s metric and beta diversity was calculated using the Bray-Curtis dissimilarity matrix and plotted using PCoA. Ten patients were treated with FMT and tested culture positive for C. difficile prior to administration with 8 patients culture negative following administration of FMT. The alpha diversity of the pre-FMT patients was significantly higher than post-FMT (p-value = 0.0103). The PCoA (Figure 1) shows the donor and post-FMT samples cluster together and separate from the pre-FMT samples (p-value=0.003). Pre-FMT, the most prominent phyla belonged to the Proteobacteria and Verrucomicrobia. Following FMT, the Firmicutes and Actinobacteria were the most prevalent mirroring the donors. 48 OTUs were significantly different between the pre-and post-FMT patients (p-values:0.009 to < 0.00001) with an increase in gut commensal organisms in the post-FMT patients. FMT is effective at reducing CDI in SOT patients and restores the gut microbiota to a more diverse state similar to the donor stool. Assessing the patients gut microbiota is useful in determining the effectiveness of FMT in SOT patients.

Figure 1: PCoA of SOT patient and donor stool samples across all time points.<br />

![Image](http://files.abstractsonline.com/CTRL/5b/0/221/cb4/d47/4de/6b2/587/6ec/a21/62e/dc/g7211_2.JPG)
Abstract Title:
Factor Associated with Infectious Complications in Patients Receiving Biologic Agents At the Largest Univ. Hosp. in Thailand
Primary Author Block:
K. Chawalitmongkol, W. Katchamart, P. Koomanachai; Faculty of Med. Siriraj Hosp., Bangkok, Thailand
Abstract Body:
Background: Biologic agents are the recommended options for patients with rheumatologic diseases or inflammatory diseases, who did not respond to standard treatments. There were several studies demonstrated infectious diseases as one of the most common complication. This present study aimed to explore the incidence of infection related to biologic agents used and identify risk factors associated with infectious complication. Method: A 10-year observational study of the patients with biologic agent used, anti-tumor necrosis factors (anti-TNF; infliximab, etanercept), interleukin (IL)-6 receptor monoclonal antibody (tocilizumab), and anti-CD20 (rituximab) were included. The study was performed at Siriraj hospital, the largest University Hospital in Thailand. All patients’ demographic data and characteristics of infection complication were reviewed and analyzed. Results: A total of 186 patients were enrolled (female 60.8%). Mean age (SD) was 53.96 (13.94) years. The indicated diagnosis of the patients who were treated with biologic agents were rheumatoid arthritis (44.6%), psoriasis (25.8%), spondyloarthritis (22.6%), inflammatory bowel disease (1.6%), and others (4.8%). Overall infections were 75 events in 57 patients. The highest proportion of patients developing infections were treated with rituximab (28.9 %), followed by etanercept (27.0 %), infliximab (18.4%), and tocilizumab (16.7 %). Serious infection was 21 events, and most of them (19/21) occurred within the first year after drug initiation. Most of infections were caused by bacterial pathogen while TB was diagnosed in 2 infliximab users. All biologic agents infection incidence rate was 13.46/100 patient-year. The incidence of infection (per 100 patient-year) in anti-TNF; etanercept, infliximab, tocilizumab, and rituximab were 13.78, 12.26, 23.7, and 12.78, respectively. In multivariate analysis which adjusted for age, conventional disease modifying anti-rheumatic drugs, immunosuppressive agents, glucocorticoid, type of biologic agents, and comorbidities, only female gender increased the risk of infection with OR 2.4, 95%CI 1.1-5.6, and p = 0.04. Conclusion: Infections in biologic agent users should be monitored especially in the first year after initiation. The infection screening guideline should be strictly used as clinical practice guideline.
Abstract Title:
Successful Treatment of Chronic Hepatitis C in Renal Transplant Recipients- A Prospective Observational Study

Primary Author Block:
S. Sharma, D. Mukherjee, R. K. Nair; Army Hosp. Res. and Referral, Delhi, India

Abstract Body:
Background: Chronic hepatitis C is associated with deleterious consequences in renal transplant recipients (RTR). Since the introduction of direct antiviral agents (DAA), morbidity of HCV has considerably decreased but still no guidelines have been formulated regarding its use in RTR. Aim: We studied the efficacy and tolerability of DAA in RTR. Methods: This prospective observational study was conducted at Army Hospital Research and Referral, New Delhi from June 2016 to May 2017. Forty five HCV infected RTR with stable graft function were included and treated with DAA with or without Ribavirin. HCV-RNA level was done at 4 weeks for rapid-virological-response (RVR), 12 or 24 weeks for end-treatment-response (ETR) and at 12weeks after completion of therapy for sustained-virological-response (SVR12). Tacrolimus trough level was done 4 weekly by tandem-mass spectrometry. Results: Median time between renal transplantation and the start of anti-HCV therapy was 36 months (1-120months). Majority(66.7%) were infected with genotype3. Baseline median HCV-RNA level was 542648IU/ml (1189-55028534IU/ml). Sofosbuvir-Ribavirin combination (24weeks) was given to 30 patients including 3cirrhotics, Ledipasvir-Sofosbuvir combination to 8patients and Daclatasvir-Sofosbuvir combination to 7patients, including 2cirrhotics. Rapid-Virological-Response was observed in 29 patients treated with Sofosbuvir/Ribavirin, all 8 patients on Sofosbuvir/Ledipasvir and all 7 patients on Sofosbuvir/Daclatasvir. End-Treatment-Response and Sustained-Virological-Response (12weeks) was achieved in all patients irrespective of genotype or treatment regimen. Decrease in mean HCV-RNA level and transaminase level was statistically significant(p<0.01). Ribavirin was significantly associated with anaemia(p=0.032). Conclusions: DAA regimens are well tolerated and highly efficacious. Response to DAA is good irrespective of genotype, drug combination, initial HCV-RNA level, age or sex of patient or graft age. However, Sofosbuvir/Ledipasvir and Sofosbuvir/Daclatasvir combination is preferable.
Abstract Title:
Molecular and Genetic Characterization of Rotavirus Strains among Infants and Children with Acute Gastroenteritis in Bangladesh

Primary Author Block:
S. Dey1, S. F. Sifat2, M. Almamun1, K. Hossain1, T. Mou2, M. Marzan2, A. Parvez2; 1Jahangirnagar Univ., Savar, Dhaka-1342, Bangladesh, 2Jahangirnagar Univ., Dhaka, Bangladesh

Abstract Body:
Background: Viral gastroenteritis has been demonstrated as a major cause of morbidity and mortality among infants and children in developing countries as well as in developed countries. It has been reported that about 3 - 5 billion cases of acute gastroenteritis occur each year in children less than 5 years of age, resulting in nearly 2 million deaths. It causes some combination of diarrhea, vomiting, abdominal pain and cramping. Globally most cases are caused by rotaviruses along with noroviruses, adenoviruses, astroviruses and sapoviruses.

Methods: A total of 220 fecal samples were collected between July 2015 and June 2016 from children below 5 years old with acute gastroenteritis from Chittagong region in Bangladesh were examined for rotavirus by Immunochromatography kit (IP-Rota/Noro) and reverse-transcriptase polymerase chain reaction (RT-PCR). PCR product of specific genes of rotaviruses was selected for sequence analysis. Sequence data were analyzed by Chromas 2.32, BioEdit and other software.

Results: Immunochromatography Kit and reverse-transcriptase polymerase chain reaction (RT-PCR) of all the samples revealed the presence of 94 rotavirus positive samples (42.72%). The immunochromatography kit (IP-Noro/Rota) provides high specificity (100%) and sensitivity (98.90%) as well as good agreement with the reference method RT-PCR for the detection of rotavirus. G2 (62%) was detected at the highest frequency, followed by G8 (15%), G1 (9%), G4 (7%), and G3 (4%). P[8] was the most predominant genotype (58%), followed by P[4] (42%). Phylogenetic analysis revealed that Bangladeshi Rota_BDJU strains clustered closely among each other (98-100% identity at nucleotide level) and displayed highest similarity (99-100%) to previously studied Bangladeshi strains. Eight Rota_BDJU strains had very much similarity with strains of China and Thailand.

Conclusions: We found the highest prevalence (42.72%) of rotavirus infection among Bangladeshi pediatric patients. This study also demonstrated that the IP-Rota/Noro kit proved to be a rapid method for detection of rotavirus directly from stool samples. Data generated from this study will provide crucial information on the burden of the rotavirus disease and genotype distribution in Bangladesh. Such information will not only aid in seeking advocacy for rotavirus vaccine introduction in the country’s national immunization program, but will also help in the evaluation of the efficacy of these vaccines in relation to the rotavirus genotypes in circulation.
Abstract Title:
Mutations Frequency in Epitopes of the Vp8* Subunit of Circulating Rotavirus in Chihuahua, Mexico

Primary Author Block:
M. S. Contreras1, C. I. Romo2, B. Sanchez1, G. Erosa1, F. J. Zavala1, M. C. Delgado1, J. F. Contreras3, E. Guevara4, M. R. Infante1; 1Univ. Autónoma de Chihuahua, Chihuahua, Mexico, 2Univ. del Valle de Mexico, Monterrey, Mexico, 3Univ. Autónoma de Nuevo Leon, Monterrey, Mexico, 4Hosp. Infantil de Especialidades, Chihuahua, Mexico

Abstract Body:
Background: Rotavirus is one of the main causes of gastroenteritis worldwide. Most infections on infants have been presented by rotavirus strains genotype P[8] of the VP4 spicule. In this protein, nine antigenic domains have been identified that induce neutralizing antibodies. Four of these epitopes have been identified in the VP8* subunit (8-1 to 8-4). Due to changes in the vaccination system, there is a need to evaluate the genetic variation of these epitopes in circulating rotavirus strains. Methods: A total of 55 rotavirus-positive stool samples from children under 5 years of age were collected in two hospitals in the city of Chihuahua during 2004 to 2015. The VP8* subunit genotype P[8] of the samples were amplified, cloned and sequenced. The epitopes were compared with the sequence of the vaccine strains. Results: Genetic changes of the strains analyzed were identified in epitope 8-1 (S146G, S190N, N196GDS) and 8-3 (N113TD, D116N, S125R, D133E, N135D) of the VP8* subunit. The analysis in epitopes 8-2 and 8-4 showed no change. Conclusions: These results suggest the continuous monitoring of genetic variations in the main antigenic epitopes in circulating rotavirus strains generated by the pressure induced by rotavirus vaccination.
Abstract Title:
Outstanding Abstract Award: Development and Evaluation of Practical Synthetic Bacterial Flagellin Fusion Constructs Expressing Conserved Protein Fragments of Respiratory Syncytial Virus (RSV)

Primary Author Block:
J. Renfroe1, C. Barlament2, S. Belshazzar3, S. Boyd1, Y. Kwon1, S-M. Kang1, S. Crow1, G. Pierce1
1Georgia State Univ., Atlanta, GA, 2Emergent BioSolutions, Gaithersburg, MD, 3Univ. of Southern California, Los Angeles, CA

Abstract Body:
Background: Salmonella enterica Typhimurium Flagellin monomer FliC is recognized as a bioactive compound used in basic immunological research, vaccine development, and diagnostic assays. In this study, a synthetic version of flagellin incorporating common restriction enzyme sites is used to rapidly model, screen, and predict bioactivity of Respiratory Syncytial Virus (RSV) flagellin fusion constructs and achieve proper epitope conformation of RSV F antigenic site II by use of hypervariable region as a scaffold. This rational vaccine manufacturing approach and platform is aimed to standardize early characterization of vaccine candidates and large-scale production in E. coli, reducing cost of research, development, and manufacturing. Methods: To aid rapid in silico screening of recombinant FliC fusion constructs, we designed a flexible Synthetic FliC platform by incorporating common restriction enzyme sites in hypervariable D3 and N and C terminal regions. Respiratory Syncytial Virus (RSV) protein fragments G (aa 130-230) and F (Palivizumab-binding antigenic site II, aa 253-278) were integrated in five different Synthetic FliC locations and evaluated in silico for epitope conformation and exposure by I-TASSER homology modeling program. Constructs were cloned in an expression vector by PCR, overexpressed in flask and bioreactors, purified by PEG precipitation, 2-phase separation, and affinity chromatography. Endotoxin levels were quantified by 5-point LAL chromogenic endotoxin assay and fusion proteins bioactivity by ELISA and TLR5-specific assay. Results: Bioreactor cultivation yielded 1 kg cell paste, and purified yield resulted in approximately half a million equivalent doses per fermentation run. All FliC-RSV fusion proteins demonstrated TLR5-activation, specific antibody affinity above or equal to whole cell FI-RSV standard, >95% purity as determined by SDS-PAGE, and endotoxin levels acceptable by FDA. Conclusions: Our findings highlight the potential for a scalable, flexible, and cost-effective flagellin platform compatible with rational vaccine design and computer modeling and scaffolding. This platform system has been demonstrated as a modular and adaptable system for addressing complex vaccine design and production scenarios. Future studies will demonstrate multivalent capacity of platform, evaluate modifications of flagellin structure to target specific immune pathways, incorporate greater computational evaluation by 3D modeling, and express other organisms such as P. pastoris.
Epidemiology and Genetic Diversity of Group A Rotavirus in Acute Diarrhea Patients in Pre-Vaccination Era in Himachal Pradesh, India

Primary Author Block:
P. Ray1, S. Gupta1, S. Chaudhary2; 1Jamia Hamdard Univ., New Delhi, India, 2Rajendra Prasad Govt Med. Coll., Tanda, Himachal Pradesh, India

Abstract Body:
Background: Acute gastroenteritis due to Group A rotaviruses remains the leading cause of mortality and morbidity in children in developing countries. India has introduced its indigenous vaccine Rotavac® (monovalent vaccine with G9P[11] combination) in Universal Immunization Programme (UIP) in 2016 in Himachal Pradesh, the first state to launch it. The present study aimed to evaluate the rotavirus strain diversity associated with severe diarrhea prior to vaccine introduction in Himachal Pradesh.

Methods: A total of 487 fecal specimens collected from children (<5 years old) hospitalized with diarrhea RPGMC Tanda, Himachal Pradesh during October 2013 to June 2016 were screened for Group A rotavirus by antigen ELISA. Rotavirus RNA was extracted by TRIZOL method and used to synthesize cDNA by random priming method. G/P typing was performed using hemi-nested and multiplex PCR. Electropherotyping was performed by RNA-PAGE.

Results: In overall, rotavirus was detected in 52.0% (N=487) of diarrheal children and detection rate being highest among 6-11 months age group (44.3%). Rotavirus infected children were found more frequently associated with vomiting as compared to uninfected children.

Rotavirus strains with G12 genotype was found most prevalent (38.1%) followed by G1 (30.9%), G9 (10.3%) and G2 (7.9%). G10 (1.6%) and G4 (0.4%) strains were rarely detected. Among P genotypes, P[6] was the most prevalence (50%) followed by P[8] (25.4%) and P[4] (12.7%). Of note, G3, P[9] and P[11] genotypes were first time detected in Himachal Pradesh. Among G and P combinations, G12P[6] was most prevalent (36.1%). The other common rotavirus strains were G1P[8], G1P[6], G2P[4], and G9P[6] with prevalence of 19.8%, 6.7%, 4.4% and 1.2%, respectively. Interestingly, the present study demonstrates a high incidence (12.7%) of unusual G/P combinations namely G9P[4], G2P[6], G2P[8], G12P[4], G1P[9], G1P[11] and G9P[9]. Strains with G3P[8], G4P[6], G9P[8], G10P[6], G10P[8] and G12P[8] combinations were very rarely detected. Similarly non-typeable rotavirus strains were found less frequently. Interestingly, genomic heterogeneity was observed within G12P[4] rotavirus strains with both long and short electropherotypes.

Conclusions: The present study highlights the rich genetic diversity with emergence of rare rotavirus strains circulating in HP. This pre-vaccination strain data will provide a baseline to compare the post-vaccination data and will help to gauge the impact of vaccine in this region.
Abstract Title:
Rotavirus Disease Burden and Surveillance in Under-Five Children Attending Yangon Children Hospital, Myanmar

Primary Author Block:
H. Thu; Dept. of Med. Res., Yangon, Myanmar

Abstract Body:
Rotavirus gastroenteritis (RVGE) is the leading cause of severe diarrhoea affecting infants and young children. Mortality and severe outcome are more concentrated in developing countries. Diarrhoea is among the priority childhood diseases in Myanmar according to the National Health Plan. The Department of Medical Research (DMR) has carried out surveillance of rotavirus diarrhoea in Yangon Children Hospital with the support of WHO (SEARO) since 2009. The objectives were to raise awareness and contribute data to estimate the burden of rotavirus diarrhea in under-five children, identification of currently circulating rotavirus strains, timely detection of emerging new strains and to help in decision-making for the introduction of rotavirus vaccines. Stool samples not less than 3 mls were collected from diarrhoeic children under 5 years of age admitted with diarrhea to the three medical wards of the Yangon Children Hospital. All the samples collected were tested for the presence of rotavirus antigen by a commercial enzyme immunoassay kit (ProSpecTMRotavirus from OXOID, UK). G and P genotypes were identified by multiplex RT-PCR assay using genotype-specific primers from the Christian Medical College, Vellore, India. A total of 5242 stool samples were tested from the period 2010 to 2017 September and rotavirus positivity ranged from 46% to 56%. Rotavirus diarrhoea was most prevalent in the 6-11 months age group (44.8%) showing a male preponderance in all years. A seasonal variation was seen with high number of cases from November to February with the highest peak occurring in January. Categorization of RVGE cases according to the Vesikari clinical severity scoring system showed that 72 to 82% of cases were severe (score ≥11). A sub-sample of rotavirus positive samples were selected and subjected to G and P genotyping. G and P combinations showed changing profiles for each year. In 2009, G12 was detected for the first time and G12P[8] and G1P[8] combinations were equally distributed. From 2010 to 2012, G12P[8] became the most prevalent genotype (62 to 75.2%). In 2013, G2P[4] was the most detected (73%) which changed to G9P[8] from 2014 to 2016 (31 to 53%). Currently in 2017, the most identified combination is G3P[8] (58%). RVGE is a vaccine preventable disease and while improvements in clinical management in the hospital has contributed to gains in child survival, diarrhoea is still on the top list of priority childhood diseases and rotavirus vaccine introduction in the nationwide childhood immunization programme is being considered for 2019 in Myanmar.
Abstract Title:
Rotavirus-Associated Hosp. Discharge Rates from 2004 to 2015 in Europe

Primary Author Block:
E. Negro-Calduch, T. Verstraeten, T. Cattaert; P-95 Epidemiology and Pharmacovigilance Consulting & Services, Heverlee, Leuven, Belgium

Abstract Body:
Background: Despite enteric viruses, including rotavirus (RV), are the leading cause of acute gastroenteritis (AGE) worldwide, hospitals rarely test for RV or other AGE-associated pathogens, leading to an underestimation of the burden of disease. We aimed to determine rotavirus-associated gastroenteritis (RVGE) hospitalizations in children in a range of European countries and to evaluate the impact of the introduction of RV vaccination into routine immunization schedules.

Methods: Inpatient data with AGE diagnostic codes in primary position were obtained from nationally representative hospital registers of 12 European countries (Austria, Denmark, England, Germany, Hungary, Italy, Lithuania, Poland, Portugal, Romania, Spain & Sweden) for 2004-15. Discharge rates of cause-unspecified AGE hospitalizations attributable to RV were estimated using a statistical model based on the temporal patterns of AGE occurrence [1]. Denominators of incidence were obtained from Eurostat [2].

Results: RV was estimated to cause 35% of all AGE discharges and an annual mean of 82,861 RVGE discharges in children aged 0-4 years in Europe (n=32 countries). RV also caused 19% of all AGE hospitalizations in children aged 5-9 years, 5% in children 10-17 years, and 4% in adult and elderly (>18 years), totaling 29,630 discharges in >5 years old. The mean annual RVGE discharge rate in under 5s was 5.0 discharges/1,000. RVGE discharge rates in under 5s declined in countries that had introduced RV vaccination in either national (Austria and England) or regional (Germany, Italy and Sweden) immunization programs during the study period. Reductions in RVGE hospitalizations in children under 5 years were of 74% in England ((from 3.1 to 0.8/1,000) and 68% in Austria (from 12.5 to 4.0/1,000) compared with the pre-vaccine period. The relative contribution of RV to overall AGE hospitalizations in children <5 years evolved from 50% to 24% in Austria and from 50% to 21% in England. Conclusions: This study illustrates the high burden of rotavirus and the potential impact of vaccination among children 0-4 years in Europe. Further investigation would be needed to assess the impact of universal RV vaccination on older children and adults.
Abstract Title:
Rotavirus Vaccines: Current Prospects and Future Challenges of New Vaccines
Primary Author Block:
N. T. Bukhari1, S. U. Kazmi2; 1NICH, Karachi, Pakistan, 2Dadabhoye Univ. of Higher Ed., Karachi, Pakistan
Abstract Body:
Introduction: Rotavirus is the most common cause of severe infantile diarrhea worldwide and responsible deaths in developing countries. By the accelerated efforts by WHO and other international agencies for the introduction of rotavirus vaccines into global immunization programs has been a high priority to tackle this issue effectively, as Rota virus due to severity of infection in young children and high mortality rate is matter of prime importance. Vaccines and Immunizations can reduce child mortality rate and there is a need to introduce indigenous vaccines as well due to emergence of new Rotavirus strains. Material and method: Stool sample were collected and processed by ELISA method to confirm the presence of Rotavirus. By using primers set against outer G and P antigen molecular identification was done by visualizing bands of specific Bp on gel Results: Rotavirus was found in 6.09% stool samples. Images indicated that Rota virus subtypes, G2P4 (3.0%), G10P4 (0.54%), G9P4 (0.40%), G3P4 (0.27%), were isolated. Oral administration Live attenuated mixture of (0.5ml) these isolated strains was orally introduced in rabbit as animal model, in other set of animals as control available vaccines in market was orally (0.5ml)administered. After seven days blood samples were collected and protein electrophoresis showed immunoglobulin elicitation .experimental group showed spectrum of immunoglobulin quantitatively as well qualitatively as compared to control group. Live attenuated human reassortant strain of rotavirus vaccine has proven highly effective in preventing severe rotavirus diarrhea in animal model and was safe Conclusion: In developing world these vaccines could substantially reduce the number and associated costs of child hospitalizations and clinical visits for acute diarrhea. Simultaneously new vaccines could reduce deaths from diarrhea and improve child survival through introduction of new vaccines if included in childhood immunizations and diarrheal disease control. Aims and Objectives: To establish the burden of life-threatening rotavirus disease and importance of introduction of new rotavirus vaccine, aimed to update the estimated number of deaths in children at national level younger than 5 years due to diarrhea attributable to rotavirus infection.
Session Number: 111
Session Type: Poster Talk
Session Title: Advances and Insights in the Management of Gram-positive Infections
Session Start Date Time: 6/8/2018 12:15:00 PM
Session End Date Time: 6/8/2018 1:15:00 PM
Session Primary Track: Clinical Infections and Vaccines
Abstract Control Number: 9234
Poster Board Number:

Abstract Title:
Moderator
Primary Author Block:
Benjamin Howden; The Univ. of Melbourne and The Royal Melbourne Hosp., Melbourne, Australia
Abstract Body:
Abstract Title:
Outstanding Abstract Award: Evaluation of Vancomycin Or Daptomycin Alone versus Combination with Beta-Lactams in the Treatment of Methicillin-Resistant Staphylococcus aureus Bloodstream Infections (BSI)

Primary Author Block:
N. Sabagha, E. J. Zasowski, T. D. Trinh, A. M. Lagnf, S. Bhatia, M. J. Rybak; Wayne State Univ., Detroit, MI

Abstract Body:
Background: Vancomycin (VAN) has been the antibiotic of choice to treat methicillin-resistant Staphylococcus aureus (MRSA) infections. Despite attempts to optimize VAN therapy over the years, treatment failures for bloodstream infections (BSI) have not improved. Studies have also demonstrated that daptomycin (DAP) use after VAN failure increases the potential for DAP resistance. Combination therapy may address these limitations. We evaluated the impact of combination VAN or DAP with a beta-lactam (BL) on patient outcomes with MRSA BSI. Methods: This is a retrospective cohort study comparing outcomes of patients with MRSA BSI treated with monotherapy or combination therapy. Inclusion criteria: adults with >=1 positive MRSA blood culture initiated with monotherapy or combination therapy <72h after culture collection. Primary outcome: BSI ≥7d. Secondary outcomes: 30d mortality, 60d BSI recurrence, and length of stay. Multivariable logistic regression was conducted to determine the independent predictors of BSI ≥7d. Result: A total of 505 patients were included (140 monotherapy, 365 combination). Mean (SD) age was 60 (16.3) y, 64% males, and 79.2% African-American. Median (IQR) Charlson Comorbidity Index and APACHE II score were 3 (1-5) and 17 (11-22), respectively. The most common sources were: infective endocarditis (IE) 22.8%, skin and soft tissue 20.9%, pneumonia 20.5%, intravenous catheter 19.6%, and bone/joint 15%. Outcomes are presented below:

<table>
<thead>
<tr>
<th></th>
<th>Monotherapy (VAN/DAP) (n=140)</th>
<th>Combination therapy VAN or DAP + BL (n=365)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BSI ≥7d, n (%)</td>
<td>20 (22%)</td>
<td>43 (12%)</td>
<td>0.007</td>
</tr>
<tr>
<td>30d mortality, n (%)</td>
<td>14 (10%)</td>
<td>60 (16%)</td>
<td>0.067</td>
</tr>
<tr>
<td>60d recurrence, n (%)</td>
<td>19 (14%)</td>
<td>33 (9%)</td>
<td>0.170</td>
</tr>
<tr>
<td>Antibiotic switch due to failure, n (%)</td>
<td>21 (15%)</td>
<td>28 (8%)</td>
<td>0.014</td>
</tr>
</tbody>
</table>
In regression, combination therapy was protective (aOR 0.51; 95% CI 0.28 - 0.94), while IE (aOR 4.0; 95% CI 2.4 - 6.7), diabetes with end stage organ damage (aOR, 1.89; 95% CI, 1.1 - 3.0), bone/joint source (aOR 1.97; 95% CI 1.0 - 3.8), and APACHE II score (aOR 1.04; 95% CI 1.0 - 1.1), were associated with BSI >=7d. Conclusion: Combination VAN or DAP with beta-lactam was protective against MRSA BSI >=7 d and may improve patient outcomes with MRSA BSI. Additional studies are needed to confirm these findings.
Adjuvant Azithromycin for Bacteremic Pneumonia Due to Methicillin-Resistant Staphylococcus aureus

Primary Author Block:

Abstract Body:
Background: Bloodstream infection (BSI) secondary to methicillin-resistant Staphylococcus aureus pneumonia (MRSA PNA) complicates 5% to 20% of cases with associated mortality rates up to 6-fold higher than for MRSA PNA without BSI. Macrolides have demonstrated favorable immunomodulatory effects in experimental models and have been associated with improved clinical outcomes in a number of inflammatory lung conditions. Furthermore, sub-inhibitory macrolide concentrations exhibit anti-virulence affects against S. aureus. Objective: To investigate clinical outcomes associated with early azithromycin (AZM) use in patients with MRSA PNA and BSI

Methods: Retrospective, observational cohort study among adult patients with MRSA BSI and PNA admitted to the Detroit Medical Center between 2008 and 2017. Patients with a positive Legionella pneumophila urinary antigen or isolation of an atypical pathogen from a respiratory or blood specimen were excluded. The primary outcome was 30-day mortality among patients who received at least 1 dose of AZM within 48 hours of blood culture collection compared to those who received no AZM. Multivariable logistic regression was conducted to examined the independent association of AZM and 30-day mortality. Results: A total of 87 patients were included (AZM 27 vs. no AZM 60). The majority were male (62.1%) with a mean (± SD) age of 63.2 (± 14) years. A lower proportion of patients in the AZM group were admitted from a skilled-nursing facility / outside hospital (29.6% vs. 55.0%; P = 0.028) or met criteria for hospital-acquired/ventilator-associated PNA (11.1% vs. 43.3%; P = 0.003). However, there were no differences in the median [IQR] Charlson Comorbidity Index (3 [2 - 6] vs. 3 [1 - 5]; P = 0.498) or APACHE II score (28 [22 - 32] vs. 25 [19 - 33]; P = 0.762). Primary MRSA antibiotic treatment was similar in both groups with most (95.0% vs. 92.6%; P = 0.655) receiving initial vancomycin. Thirty-day mortality trended lower among patients in the AZM group (25.9% vs. 45.0%; P = 0.092). On multivariable analysis, APACHE II score greater than 21 was independently associated with increased 30-day mortality (aOR 5.544, 95% CI 1.779 - 17.276; P = 0.003), while receipt of AZM was independently associated with decreased 30-day mortality (aOR 0.314, 95% CI 0.108 - 0.908; P = 0.033). Conclusions: The early use of AZM among patients with MRSA PNA and BSI was independently associated with decreased 30-day mortality. Future studies, including a larger number of patients, are needed to confirm these preliminary findings.
Abstract Title:
Duration of Bacteremia According to Methicillin Resistance and Primary Foci of Infection in Staphylococcus aureus Bacteremia

Primary Author Block:

Abstract Body:
Backgrounds: It is unknown how long Staphylococcus aureus bacteremia (SAB) persists after administration of susceptible antibiotic. We aimed to describe the duration of SAB according to methicillin resistance and primary foci of infection. Methods: Cases of all adult patients with SAB prospectively collected from 15 hospitals in Korea over 9-year period were reviewed. Patients without follow-up blood cultures who survived or who died after two days from the onset of SAB were excluded. The duration of SAB was defined as a number of calendar-day between the date of administration of susceptible antibiotic after first positive blood culture for S. aureus and the last date of positive blood culture. Kaplan-Meier curves for negative conversion rates were plotted and compared using log-rank test. Patients who died during SAB were censored at the time of death. Results: Among 2,239 SAB cases, 1,574 cases were included in the analyses after excluding 49 cases of contamination, 100 of polymicrobial bacteremia, 175 administered with non-susceptible antibiotic, and 341 without follow-up blood cultures. Numbers of methicillin-resistant SAB (MRSAB) and methicillin-susceptible SAB (MSSAB) were 854 (54.3%) and 720 (45.7%), respectively. The duration of MRSAB was longer than that of MSSAB (median [IQR], 1 [0-6] days in MRSAB vs. 1 [0-3] days in MSSAB, P<0.001). The durations of bacteremia in infective endocarditis (median [IQR], 5 [1-11] days in MRSAB, 3 [1-5] days in MSSAB), bone & joint infection (median [IQR], 5 [1-12] days in MRSAB, 1 [1-5] days in MSSAB), and endovascular infection (median [IQR], 2 [1-9] days in MRSAB, 1 [1-4] days in MSSAB) were longer than that of skin & soft tissue infection (median [IQR], 1 [0-5] days in MRSAB, 1 [0-2] days in MSSAB). Conclusions: The durations of SAB are significantly different according to methicillin resistance and primary foci of infection. Treatment failure and persistence of SAB should be defined accounting for those factors.
Prediction Model for Methicillin-Resistant Staphylococcus aureus (MRSA) Bacteremia among Patients with Community-Onset MRSA Skin and Skin-Structure Infections

Primary Author Block:
S. C. J. Jorgensen1, A. M. Lagnf1, S. Bahatia1, S. L. Davis2, M. Rybak1; 1Wayne State Univ., Detroit, MI, 2Henry Ford Hosp., Detroit, MI

Abstract Body:
Background: The emergence, spread and persistence of methicillin-resistant Staphylococcus aureus (MRSA) as a cause of community-onset (CO) acute bacterial skin and skin structure infections (ABSSSI) has resulted in substantial changes to the epidemiology and management of these infections. Although blood stream infection (BSI) was once considered an uncommon complication of CO ABSSSI, evidence suggests the MRSA USA300 clone may have an enhanced propensity to cause invasive infections. The high morbidity and mortality associated with MRSA BSI underscores the need to identify patients at increased risk for this complication. Objective: We sought to construct a MRSA BSI predictive model for patients with CO MRSA ABSSSI based on characteristics readily assessable at the time of initial evaluation. Methods: A multi-center, retrospective, case-control design was used. The population of interest included adult patients satisfying the following criteria: 1.) admitted through the emergency department between 2010 and 2017; 2.) ABSSSI primary diagnosis; 3.) MRSA positive skin specimen collected within 48 hours of admission; and 4.) blood culture collected within 48 hours of admission. Cases were defined as patients who met the above criteria and had MRSA isolated from the index blood culture. Patients with negative or contaminated blood cultures served as controls. Independent risk factors for MRSA BSI were identified through logistic regression analysis. The predictive model was derived using a regression coefficient-based scoring method. Results: A total of 307 patients were included (155 cases, 152 controls). Independent predictors of BSI, in descending order of adjusted odds ratio, were: purulent cellulitis, temperature < 35.6 C or > 38 C, chronic kidney disease, IV drug use, white blood cell count > 11 x 109/L, heart rate > 100 beats/min, body mass index < 25 kg/m2, and non-upper extremity infection site. The area under the receiver operator curve (AUROC) of the final regression model was 0.855 (95% CI 0.813 - 0.893). The AUROC of the weighted coefficient-based BSI-predictive score (BSI-PS) was 0.844 (95% CI 0.801 - 0.887). Using a threshold BSI-PS of ≥ 8 (range 0 to 35) demonstrated 94.1% and 40.1% sensitivity and specificity, respectively. Conclusions: Our findings demonstrate a weighted combination of 8 independent variables readily assessable at the time of initial evaluation can be used to predict, with high discrimination, MRSA BSI among patients hospitalized with CO MRSA ABSSSI. Validation is required before wide-spread clinical use.
Session Number: 111  
Session Type: Poster Talk

Session Title: Advances and Insights in the Management of Gram-positive Infections

Abstract Control Number: 9487  
Poster Board Number: 

Abstract Title:  
Analysis of Prognosis Factors Related with Mortality of Staphylococcus aureus Bacteremia in Our Facility

Primary Author Block:  

Abstract Body:

Background: Staphylococcus aureus is one of the causes of healthcare-associated bacteremia of hospitalized patients in Japan. The mortality of S. aureus bacteremia (SAB) is still higher and it lengthens hospitalization. The mortality rate of SAB indicates 20~30%. 30-day mortality has been analyzed previously. It is reported that SAB is a life-threatening infection with an incidence rate ranging from 20 to 50 cases /100,000 population per year. It has been not clarified what is the reason why the mortality is high in SAB. Methods: This survey was conducted retrospectively. The participants were administered in our facility from Jan. in 2007 to Nov. in 2014. The entry criterion for participating was a single blood culture, which was tested to be positive for Staphylococcus aureus within 48 hours after administration. Factors were analyzed multi-variable quantitatively using logistic regression analysis system. Results:

MRSA Morbidity was 57.9% (73/126) and MSSA was 42.1% (53/126). The most frequent source of SAB was primary bacteremia (80.2%;101/126). It included catheter related infection, febrile neutropenia, and undetected focus of infection. 14 day mortality was 11.1% (14/126). In SAB, independent risk factors were age over 70 y.o. (Odds Ratio (OR) 4.7:95% CI (CI) 1.04-21.13), existence of malignancies (OR 4.5:CI 1.10-17.96), starting day of antibiotics therapy (OR 0.2:CI 0.05-0.79), TTP (Time from taking culture to positive detection) less than 12 hours (OR 4.9:CI 1.18-20.03), the Pitt bacteremia score more than 3 (OR 4.2:CI 1.15-15.31). Between each 2 groups, significant prognostic factors were related to 1) the delay of adequate treatment 2) high severity score. Both diagnosis and proper antibiotics administration on early stage of SAB are very crucial to improve the prognosis. As for proper usage of antibiotics, it should be avoided administering anti-SAB antibiotics to all the patients with SAB. Prophylaxis administrations are not always correct. In addition we need to consider about risk factors such as the period of administration, previous medication and drug sensitivity. Conclusions: Concerned with SAB, 14 day mortality has not been analyzed in previous studies. This time we have shown prognosis factors using 14 day mortality.
Session Number: 152
Session Type: Rapid Fire
Session Number: 152
Session Type: Rapid Fire
Session Title: Vaccine Development
Session Start Date Time: 6/8/2018 3:00:00 PM
Session End Date Time: 6/8/2018 3:45:00 PM
Session Primary Track: Clinical Infections and Vaccines
Abstract Control Number: 9358
Poster Board Number:

Abstract Title:
Moderator
Primary Author Block:
Katie Flanagan; Univ. of Tasmania, Tasmania, Australia
Abstract Body:
Outstanding Abstract Award: Pneumococcal Conjugate Vaccines: Potential Serotypes for Future Formulations

Primary Author Block:
A. R. Golden1, H. J. Adam2, M. Baxter1, I. Martin3, W. Demczuk3, K. A. Nichol2, M. R. Mulvey3, G. G. Zhanel1, Canadian Antimicrobial Resistance Alliance (CARA); 1Univ. of Manitoba, Winnipeg, MB, Canada, 2Diagnostic Services Manitoba, Winnipeg, MB, Canada, 3Natl. Microbiol. Lab., Winnipeg, MB, Canada

Abstract Body:
Background: The serotype distribution of Streptococcus pneumoniae (SPN) is constantly shifting due to vaccine pressure. Despite the addition of key serotypes (3, 19A) to PCV-13 in 2010, serotype replacement is already evident in the pneumococcal population. The purpose of this study was to identify additional SPN serotypes that warrant consideration for inclusion in future conjugate vaccine formulations. Methods: In a collaboration between CARA and NML, invasive SPN isolates were collected from across Canada from 2011-14 as part of the SAVE study. All isolates were serotyped by the Quellung reaction and tested for antimicrobial susceptibilities using CLSI methods. A subset of commonly collected non-PCV-13 serotypes (6C, 8, 9N, 11A, 12F, 15A, 22F, 33F, 35B) were further characterized using MLST and WGS analyses. Results: Serotypes 22F and 33F (already included in a 15-valent vaccine undergoing development in the US) appear to be good choices for inclusion based on our Canadian data; serotype 22F was highly clonal, with almost all isolates sharing relatedness to ST433. This characteristic may contribute to vaccine success for serotype 22F, as similarly clonal vaccine types (e.g., 7F) have rapidly decreased in prevalence following conjugate vaccine use. Serotype 33F demonstrated increasing genetic diversity and MDR, characteristics that are often possessed by successful serotypes. Other serotypes of interest included 35B and 15A. Approximately 40% of 35B were penicillin (PEN)-nonsusceptible, attributed to rapidly expanding ST55B. These isolates possessed PBP1A alterations most commonly seen in 19A-ST320, indicating that, like serotype 19A, 35B may have the capacity to acquire full PEN resistance in the future. Additionally, capsular switch variant 35B-ST156 was identified in Canada; this persistent and successful international clone is associated with PEN resistance and MDR, and has recently increased in prevalence in the US. Serotype 15A was associated with the highest rate of MDR in Canada, attributable to international clone ST63. However, serotype 15A demonstrated an overall decreasing trend from 2011-2014, necessitating future monitoring to determine if prevalence continues to decrease. Conclusion: Based on analysis of Canadian SPN isolates, there are many serotypes that warrant consideration for inclusion in future conjugate vaccines, including 35B and 15A. Continued surveillance is necessary to identify trends moving forward, both within these serotypes and others that may become prevalent.
Session Number: 152  
Session Type: Rapid Fire

Session Title: Vaccine Development  
Session Start Date Time: 6/8/2018 3:00:00 PM  
Session End Date Time: 6/8/2018 3:45:00 PM  
Session Primary Track: Clinical Infections and Vaccines  
Abstract Control Number: 9405  
Poster Board Number:

Abstract Title:
Outstanding Abstract Award: Development and Evaluation of Practical Synthetic Bacterial Flagellin Fusion Constructs Expressing Conserved Protein Fragments of Respiratory Syncytial Virus (Rsv)

Primary Author Block:
J. Renfroe1, C. Barlament2, S. Belshazzar3, S. Boyd1, Y. Kwon1, S-M. Kang1, S. Crow1, G. Pierce1;  
1Georgia State Univ., Atlanta, GA, 2Emergent BioSolutions, Gaithersburg, MD, 3Univ. of Southern California, Los Angeles, CA

Abstract Body:
Background: Salmonella enterica Typhimurium Flagellin monomer FltC is recognized as a bioactive compound used in basic immunological research, vaccine development, and diagnostic assays. In this study, a synthetic version of flagellin incorporating common restriction enzyme sites is used to rapidly model, screen, and predict bioactivity of Respiratory Syncytial Virus (RSV) flagellin fusion constructs and achieve proper epitope conformation of RSV F antigenic site II by use of hypervariable region as a scaffold. This rational vaccine manufacturing approach and platform is aimed to standardize early characterization of vaccine candidates and large-scale production in E. coli, reducing cost of research, development, and manufacturing. Methods: To aid rapid in silico screening of recombinant FltC fusion constructs, we designed a flexible Synthetic FltC platform by incorporating common restriction enzyme sites in hypervariable D3 and N and C terminal regions. Respiratory Syncytial Virus (RSV) protein fragments G (aa 130 - 230) and F (Palivizumab-binding antigenic site II, aa 253 - 278) were integrated in five different Synthetic FltC locations and evaluated in silico for epitope conformation and exposure by I-TASSER homology modeling program. Constructs were cloned in an expression vector by PCR, overexpressed in flask and bioreactors, purified by PEG precipitation, 2-phase separation, and affinity chromatography. Endotoxin levels were quantified by 5-point LAL chromogenic endotoxin assay and fusion proteins bioactivity by ELISA and TLR5-specific assay. Results: Bioreactor cultivation yielded 1 kg cell paste, and purified yield resulted in approximately half a million equivalent doses per fermentation run. All FltC-RSV fusion proteins demonstrated TLR5-activation, specific antibody affinity above or equal to whole cell F1-RSV standard, >95% purity as determined by SDS-PAGE, and endotoxin levels acceptable by FDA. Conclusions: Our findings highlight the potential for a scalable, flexible, and cost-effective flagellin platform compatible with rational vaccine design and computer modeling and scaffolding. This platform system has been demonstrated as a modular and adaptable system for addressing complex vaccine design and production scenarios. Future studies will demonstrate multivalent capacity of platform, evaluate modifications of flagellin structure to target specific immune pathways, incorporate greater computational evaluation by 3D modeling, and express other organisms such as P. pastoris.
Abstract Title:
Improving Protection by Manipulating Bacterial Immunomodulators
Primary Author Block:
M. Cartelle Gestal, L. K. Howard, I. Hamidou Soumana, E. T. Harvill; Univ. of Georgia, Athens, GA
Abstract Body:
Background: Bordetella pertussis and other Bordetella spp. can cause whooping cough and other respiratory diseases in humans and animals. B. pertussis is reemerging, and animal disease continue to circulate despite vaccines being available. A noted failure of these is that they protect against severe symptoms, but not colonization that can allow for transmission. We have recently defined sets of gene regulated by within-host signals that we infer to be involved in manipulation of host immunity. We hypothesized that by disrupting these we are able to interfere with B. bronchiseptica manipulation of the host immune response. Methods: By generating a deletion in bsr using allelic exchange, we performed several studies using C57 mice. Vaccine experiments were performed by challenging mice with the bsr mutant and 60 days after, mice were re-challenged with 50 ul 10^5 CFU of B. bronchiseptica, B. pertussis or B. parapertussis. For the immunology experiments, mice were challenged with 50 ul 10^5 CFU of bsr mutant strain and immune cells were analyzed using flow cytometer. Results: Here we describe how this novel approach to vaccine development can generate sterilizing immunity against multiple Bordetella spp., including all three classical species, B. pertussis, B. parapertussis and B. bronchiseptica. Mice vaccinated with our novel vaccine recruit significantly higher numbers of CD4, CD8, neutrophils and B cells to the lungs, allowing for complete clearance of both the lower respiratory tract and nasal cavity. Conclusions: Our results showed that inhibiting the ability of bacteria to manipulate host immunity confers robust and long-lasting protection against further encounter with the pathogen.
Abstract Title:
Outstanding Abstract Award: PilVax - A Novel Peptide Delivery Platform for the Dev. of Mucosal Vaccine
Primary Author Block:
C. J. Tsai, J. M. Loh, T. K. Proft; The Univ. of Auckland, Auckland, New Zealand, Auckland, New Zealand
Abstract Body:
Background: Vaccines remain the most cost-effective and feasible means of infectious disease control in the community. Vaccine development has evolved from killed or live attenuated microorganisms to well-defined synthetic vaccines based on individual proteins or peptides. However, peptide antigens are usually poorly immunogenic and sensitive to proteolytic degradation, and thus require conjugation to carrier proteins, and administration with potentially toxic adjuvants. Lactic acid bacteria have become promising vehicle for delivering active molecules to mucosal sites. We propose that the group A streptococcus (GAS) pilus structure expressed on the surface of the non-pathogenic surrogate Lactococcus lactis can be an ideal carrier for antigenic peptides. Pili (sing. Pilus) are hair-like protrusions from the cell surface. GAS pilus usually consists of 3 structural proteins that are highly immunogenic.
Methods: We identified several regions within the backbone pilin(Spy0128) of a serotype M1 strain that can be replaced with the model peptide OVA324-339. The modified pilus structure was expressed on the surface of L. lactis. Pili assembly and display were analysed by western blot and quantified by flow cytometry using specific anti-M1_Spy0128 antibodies. Mice were immunised intranasally with the resulting L. lactis live vaccines, and serum, saliva and bronchoalveolar lavage fluid samples were obtained and analysed for Spy0128 and Ova-specific antibodies. Results: Insertion of the Ova324-339 peptide into the βE-βF, the β3-β4 or β9-β10 loop regions of Spy0218 resulted in assembled pili. Intranasal immunisation of mice with the resulting recombinant L. lactis strain produced strong Ova-specific antibody responses in serum and bronchoalveolar fluid. We have further shown that it is possible to insert more than one peptide into the same integration site, and peptide epitopes can be incorporated into structurally similar but antigenically different pilus structure, expanding the versatility of the PilVax platform. Conclusions: The PilVax technology provides a novel system for developing peptide vaccines for mucosal delivery. Other benefits of PilVax include low production costs, as no chemical peptide coupling is required and the modified bacteria can easily be shipped in lyophylised form. Furthermore, no potentially toxic adjuvants are required and the vaccine can be delivered needle-free to a mucosal site. These advantages are highly desired in developing countries, where efficacious vaccines are most needed.
**Abstract Title:**
Production of the Egg Yolk Antibodies Directed against Enterobactin

**Primary Author Block:**
X. Zeng, H. Wang, C. Huang, B. Gillespie, J. Lin; Univ. of Tennessee, Knoxville, TN

**Abstract Body:**
Background: Enterobactin (Ent), a siderophore produced by most members of Enterobacteriaceae, serves as an efficient and significant iron source for Gram-negative pathogens during intestinal colonization. Recent findings strongly support that the Ent-specific antibodies can inhibit Ent utilization, consequently starving Gram-negative pathogens out of iron. Given that passive immunization with specific egg yolk antibodies is emerging as a potential alternative to antibiotics for the treatment and prevention of various diseases, in this study, laying hens were immunized with Ent conjugate vaccines to produce large quantities of hyperimmune egg yolk antibodies.

Methods: Ent was purified from E. coli and subsequently conjugated two carrier proteins, keyhole limpet hemocyanin (KLH) and bovine serum albumin (BSA), respectively. Two immunization trials were performed using different layers and conjugate vaccines. In the first trial, the 35-week old Barred Rock layers (3 birds/group) were immunized with 100 µg of KLH or KLH-Ent conjugate, followed by three booster immunizations every two weeks. In the second trial, two 26-week old Rhode Island Red pullets were immunized with 100 µg of BSA-Ent conjugate vaccine, followed by three booster immunizations every 3-4 weeks. Specific IgY responses in sera and egg yolks collected at select dates were measured using dot blot and ELISA. Selected egg yolks were pooled and subsequently lyophilized for production of egg yolk powder.

Results: The KLH-Ent and BSA-Ent conjugate vaccines were produced using a straightforward and efficient conjugation protocol. Regardless of breed, immunization of layers with specific conjugate vaccine triggered strong immune responses in both serum and egg yolk. Specifically, ELISA analysis indicated serum IgY titer to specific conjugate vaccine increased greatly by the first booster immunization and maintain or further increased through up to 9 weeks post immunization; the specific IgY level in egg yolk was correlated with that in serum. However, the Ent-specific immune response in layers is weaker than that observed in previous rabbit vaccination trials. Large amount of egg yolk powder was prepared for future passive immunization studies.

Conclusions: The Ent conjugate vaccines triggered strong immune response in different breeds of layers. However, the level of anti-Ent specific IgY still needs to be improved upon vaccination in layers.
Session Title: Vaccine Development
Session Start Date Time: 6/8/2018 3:00:00 PM
Session End Date Time: 6/8/2018 3:45:00 PM
Session Primary Track: Clinical Infections and Vaccines
Abstract Control Number: 9429
Poster Board Number:

Abstract Title:
Development of A Technique for Intranasal Delivery of An Influenza Virus Vaccine Candidate
Primary Author Block:
J. Justen1, S. Rose1, H. Wenzel2, G. Sweet1, K. Nelson1; 1MPI Res., Mattawan, MI, 2PATH, Washington, DC

Abstract Body:
Several influenza vaccines are available to prevent seasonal and pandemic influenza, and they include both inactivated vaccines delivered via intramuscular injection and live attenuated influenza vaccines (LAIV) delivered intranasally. Mucosal delivery of LAIV is unique in that a protective local immune response is developed. Proper consideration of animal models for potential prophylactic intervention is a critical component of the preclinical evaluation of mucosal immunization. Ferrets, while not commonly used for toxicology studies, support influenza virus infection, replication, and transmission similar to humans, and thus the intranasal model of vaccination is particularly appropriate to model safety of a LAIV candidate. Ferrets do not have extensive nasal cavities and dose volume may be a limiting factor. Given these issues, an investigation of the planned volume for nasal administration was conducted prior to conducting a multi-dose toxicology study of a LAIV. Ferrets were anesthetized and dyed saline was instilled intranasally. Ferrets were then necropsied to identify extension of dye into the sinus cavities. This pilot study demonstrated 0.5 mL of vaccine could be successfully administered to ferrets and delivered to the appropriate mucosal surfaces. In the toxicology study of the LAIV, serological analysis of treated animals showed seroconversion, demonstrating successful immunization by the developed technique and relevance of this model for intranasal vaccination with a live attenuated influenza virus. Further, microscopic evaluation of multiple nasal sections and the lower respiratory tract did not reveal any treatment related lesions in either the vehicle control or LAIV treated animals.
Abstract Title:
Developing A Novel Broadly Protective Bordetella Vaccine Based on Type III Secretion Sys. Proteins

Primary Author Block:
J. P. Stewart, S. B. Tallapaka, F. J. Martinez-Becerra, Q. Zheng, W. D. Picking, W. L. Picking; Univ. of Kansas, Lawrence, KS

Abstract Body:
There has been a significant reemergence of whooping cough (pertussis) in recent years. While there is an acellular pertussis (aP) vaccine available against the bacterial pathogen Bordetella pertussis, studies have shown that the aP vaccine fails to provide long lasting protection and those who receive it when young can become asymptomatic carriers later in life. The goal of this project is to develop a vaccine that can induce long lasting immunological memory against B. pertussis based on its type III secretion system. The T3SS is found in many gram-negative bacteria and is used to inject effector proteins into host cells. B. pertussis uses its T3SS to aid in colonization of and persistence in the human upper respiratory tract. Because the proteins that make up the Bordetella T3SS are highly conserved within the genus, a vaccine based on T3SS components should be protective against B. pertussis, B. bronchiseptica, and B. parapertussis. To produce a T3SS-based vaccine, we genetically fused two proteins: the T3SS needle tip-associated protein, Bsp22, and one of two translocator proteins, BopB, to produce a recombinant protein 22BF. Mice were vaccinated with 22BF and an adjuvant (double mutant heat-labile toxin or dmLT) on days 0, 14, and 28. On day 56, mice were challenged intranasally with a sublethal dose of B. bronchiseptica. Mice were necropsied and lungs were collected to determine the bacterial burden within the lungs after 3 and 7 days post-infection. Immune organs were then harvested to measure antibody secreting cells. Mice vaccinated with 22BF had greatly reduced weight loss and decreased lung colonization. The vaccinated with 22BF also had higher serum IgG titers against BopB and Bsp22 than did mice vaccinated with either protein (BopB or Bsp22) alone. Vaccination with 22BF also led to higher numbers of antibody secreting cells than did either protein alone. These findings demonstrate proof of concept in a small animal model that the T3SS-based subunit vaccine 22BF can provide protection against Bordetella infection. Future studies will target the use of 22BF in stimulating sterilizing immune against B. pertussis.
Abstract Title:
Development of Mucosal Vaccines to Protect against Pertussis

Primary Author Block:
D. T. Boehm1, J. M. Hall1, T. Y. Wong1, C. B. Blackwood1, E. S. Kilic1, M. P. Gutierrez2, W. Witt1, S. Bradford1, M. E. Varney1, M. Barbier1, F. H. Damron1; 1West Virginia Univ., Morgantown, WV, 2Univ. Natl. de La Plata, La Plata, Argentina

Abstract Body:
The number of pertussis cases in the United States is on the rise, and has recently been classified as the most poorly controlled bacterial vaccine preventable disease in the US. Multiple studies suggest that the protection provided by the acellular pertussis vaccines (aP) wanes quickly. The baboon model of pertussis has shown that aPs do not protect against asymptomatic carriage or transmission. The reemergence of pertussis and inadequate vaccine efficacy creates the need for the development of an improved aP vaccine. In this study, we used the murine immunization and challenge model to systematically evaluate a mucosal pertussis vaccine composed of the DTaP supplemented with a Th1/Th17 adjuvant (IN-caP). Curdlan is a Th1/Th17 skewing adjuvant and may also function to retain the DTaP antigens in the upper airway. The overall immune response was quantified at one and three days post-challenge by measuring: bacterial burden in the airway, immune cell populations in the lung, blood, and nasal cavity lavage, antibody and cytokine production. Mice immunized with IN-caP showed significant decreases in bacterial burden in the respiratory tract compared to naïve mice. IgG antibodies against pertussis toxin were found in both the IP-aP and IN-caP immunized groups. IN-caP immunization significantly reduced pro-inflammatory cytokine levels following challenge compared to whole-cell vaccinated mice, again to levels seen following aP immunization. Likewise, we observed decreased leukocyte levels in the blood and respiratory tract compared to mock-vaccinated and whole-cell immunized and challenged mice. Together these data indicate that IN-caP immunized mice are clearing the challenge infection. Interestingly, we observed increased antigen specific production of IL-17 by splenocytes from IN-caP immunized mice. These findings establish that mucosal aPs can protect against Bp challenge and offer similar protection to IP-aP immunized mice. We aim to translate these pre-clinical efficacy trials into other models and seek to develop a booster intranasal pertussis vaccine.
Session Number: 175
Session Type: Rapid Fire
Session Title: New and Emerging Infections
Session Start Date Time: 6/8/2018 4:30:00 PM
Session End Date Time: 6/8/2018 5:00:00 PM
Session Primary Track: Clinical Infections and Vaccines
Abstract Control Number: 9359
Poster Board Number:

Abstract Title:
Moderator
Primary Author Block:
Benjamin Howden; The Univ. of Melbourne and The Royal Melbourne Hosp., Melbourne, Australia
Abstract Body:
Abstract Title:
Development of Single Dose Vaccines for Emerging Infectious Diseases, Preclinical Data for Novel Ebola, Lassa Fever and Zika Vaccines

Primary Author Block:
F. Guirakhoo, N. McCurley, R. Basu; GeoVax, Inc., Smyrna, GA

Abstract Body:
Background: GeoVax MVA platform technology is built on a 4th generation MVA vector system that is improved for high expression and stable transgenes during manufacture. It has the advantages of being a live replication-competent vector in avian cells for manufacturing, yet replication-deficient in mammalian cells for vaccination, thus inherently safe. Importantly, MVA vaccines elicit protective T cell as well as antibody responses in animals and humans. The MVA platform can be combined with the potent immunogenicity of Virus Like Particles (VLPs) (e.g. MVA-VLP-HIV, -Ebola, -Marburg, -Sudan, and -Lassa fever) or be used to express proteins in their native conformations (e.g. MVA-NS1-ZIKA) enabling vaccines that induce full protection after a single dose. In this work, we present preclinical data for vaccines against Ebola, Lassa fever and Zika and show that a single dose intramuscular (IM) inoculation can protect immunocompetent animals against a lethal challenge. Methods: MVA-VLP vaccines were constructed for Ebola (using VP40 and GP), Lassa fever (Z and GPC) and Zika (NS1, eliminates the risk of Antibody Dependent Enhancement, ADE, of infection associated with other vaccines based on the envelope antigens). Vaccine viruses were characterized in vitro for genetic stability, VLP formation (Electron microscopy), sequencing and WB. Inoculations were done in rodent species (mouse, guinea pigs and hamsters) as well as non-human primates. Immunogenicity (ab response) and T cell responses were determined to assess functionality and correlation of protections. Results: Zika: A single immunization of MVA-NS1 Zika by the IM route provided 100% protection against a lethal challenge dose of a neurovirulent ZIKV delivered directly into the brain. All control animals lost weight and died within 1 week. Efficacy of MVA-VLP Ebola vaccine candidate was determined in Guinea pigs, hamsters and rhesus monkey lethal challenge models (BSL4). A single dose of MVA-VLP-LASV protected mice against a lethal challenge delivered directly into the brain. Discussion: Three different vaccines provided full protection after a single dose against 3 different family of viruses using lethal challenge models. These data demonstrate a broad utility of the platform for vaccine against infectious diseases especially suited to combat epidemic in resource constrained countries.
Abstract Title:
Saffold Virus: A Lesser-Known Emerging Human Cardiovascular in Acute Flaccid Paralysis, India
Primary Author Block:
H. Maan, T. Dhole, J. Singh; Sanjay Gandhi Post-Graduate Inst. of Med. Sci., Lucknow, India
Abstract Body:
Though the wild polioviruses have been eradicated from India, the cases of nonpolio acute flaccid paralysis (NP-AFP) of undefined etiology continues to occur in the region. Saffold viruses (SAFV), a recently discovered member of the Cardiovascular genus belonging to family Picornaviridae had been shown to cause infection of the central nervous system. No studies from India so far have recognized the detection and identification of SAFV. First, sequence independent single primer amplification (SISPA) method was performed on culture supernatants of one stool sample NP-AFP inoculated in green monkey kidney cells and that had produced uncharacterized cytopathic effects. Random PCR amplification products produced as a result of SISPA were subsequently cloned and sequenced, on subsequent sequence analysis revealed 78-85% identity to SAFV encoded proteins. The SAFV presence in NP-AFP sample explored by SISPA technique gave us the opportunity to prospectively detect and characterize SAFV in NP-AFP cases of unknown etiology for SAFV. Thus, a total of 1116 stool samples collected from AFP cases in Uttar Pradesh, India, between May 2015 and June 2017, tested negative for virus isolation by WHO algorithm, were subjected to SAFV screening targeting the 5′ untranslated region (UTR). The viral genotypes were also established by VP1-gene amplification and sequencing. 108 (9.6%) samples tested positive for SAFV detection by 5′UTR assay. The SAFV positive samples for further characterization based on VP1 gene and sequencing revealed identification of 70 SAFV strains in NP-AFP children belonging to seven different genotypes as SAFV-1 (n=6;8.5%), SAFV-2 (n=6;8.5%), SAFV-3 (n=10;14.2%), SAFV-4 (n=23;32.8%), SAFV-5(n=3;4.3%), SAFV-6 (n=7;10%) and SAFV-7 (n=15;21.4%). Co-infection in SAFV positive samples with other viruses such as parechovirus, enterovirus and cosavirus were observed for eight AFP cases. The SAFV infection appeared higher (67.1%) in younger children than 6 years of age, showed the seasonality distribution with the highest rate of isolation between late summer and early fall of winter. The SAFV positive AFP cases were from the different districts of Uttar Pradesh such as: Badaun, Barabanki, Hardoi, Azamgarh, Raibareli, Rampur, Sitapur, Lucknow and Kheri region of the state. This study documents the first report of SAFV detection from India and provides the prevalence of saffold virus with the emergence of SAFV-4 and SAFV-7 as the most common type of SAFV in India.
Abstract Title:
Microbiological Characteristics of A Novel Species Most Closely Related to Bergeyella Cardium As A Pathogen of Infective Endocarditis

Primary Author Block:
L-N. Guo, Y. Li, Y-C. Xu; Peking Union Med. Coll. Hosp., Beijing, China

Abstract Body:
Background: The genus Bergeyella, nonfermentative gram-negative bacilli within the family Flavobacteriaceae, is a rare human pathogen. Bergeyella zoohelcum has been known to cause human infections associated with animal bites. Bergeyella cardium was reported as a pathogen of infective endocarditis for the first time in Korea in 2015. In this study, we report the isolation of a bacterial that was genetically most closely related to Bergeyella cardium, from blood culture of a patient with infective endocarditis from China. Methods: A rare case of infective endocarditis caused by a species genetically closely related to Bergeyella cardium is reported. The identification, morphological characteristics and antimicrobial resistance profile of this organism are described. Results: A 24-year-old man was admitted to hospital for intermittent fever (Tmax 39.1°C) with chills and fatigue for six months. Antibiotic therapy doesn’t resolve the problem. Echocardiogram revealed congenital heart disease of patent ductus arteriosus and infective endocarditis was suspected with evidence of aortic regurgitation and multiple vegetations on the pulmonary valve and pulmonary artery wall. The patient had a sheep contact history. Cardiac surgical operation was performed and antibiotic treatment with ceftriaxone for seven weeks. The patient recovered well. Blood culture was positive for some gram-negative aerobic bacillus with irregularly shaped rods after 68 hours of incubation. This fastidious organism grew slowly on sheep blood agar at 35°C with 5% CO2 (Fig.1), was identified initially as Brevundimonas spp. by the Vitek 2 compact, but was finally confirmed as a novel species closest to Bergeyella cardium, with similarity of 98.8% to B. cardium strain 13-07T. The BD Phoenix, Vitek MS and Bruker Biotyper MS failed to identify the isolate. The strain was susceptible to β-lactams and quinolones antibiotics except for Amikacin (24 µg/ml) and Tobramycin (32 µg/ml). Conclusions: Phylogeny analysis revealed this novel species clustered well with B. cardium and other close species of the genus Bergeyella. Further studies should be performed to ascertain the potential of this bacterium to become an emerging cause of infective endocarditis.
Abstract Title:
Clinical Characteristics and Outcome of Streptococcus Tigurinus Infective Endocarditis

Primary Author Block:

Abstract Body:
Background: Streptococcus tigurinus was firstly described as a new streptococcal species in 2012 being in 2016 considered as Streptococcus oralis subspecies. Since its initial description, it has been documented as a causative agent of infective endocarditis (IE). The objective of the present study was to compare the clinical characteristics of IE caused by S. tigurinus and of other mitis group streptococci (MGS). Methods: Retrospective nationwide study, performed in 10 Spanish hospitals located in 6 different provinces. Clinical IE data were prospectively collected between 2008 and 2016 according to a pre-established protocol. Alpha-hemolytic streptococci isolates were identified by sequencing fragments of their 16s rRNA gene, sodA and groEL genes. Overall, the study included 59 cases of the 240 IE caused by MGS: 14 caused by S. tigurinus and 45 by others MGS (25 S. oralis, 11 S. mitis, 9 other species). All S. tigurinus had been previously identified by phenotypic methods as S. oralis and was found in most hospitals of the study. Statistical analysis: the unpaired t-test or the chi-square test (Fisher’s exact test when appropriate) were used to compare continuous and categorical variables, respectively. All statistical analyses were performed using online GraphPad software. Results: Comparing IE caused by S. tigurinus and other MGS, patients’ median age was 65.2 (SD±17.9) and 57.4 (SD±15.8) years, respectively (p=0.124). There were no relevant statistical clinical differences in EI between both groups (Table). Aortic, mitral or both valves were affected in all but one episode, being vegetations more frequent in the aortic valve. Pseudoaneurysms were only observed in 4 patients with MGS EI, and in-hospital (14% and 9%) and 1-year (14% and 8%) mortalities, were similar in both groups. Table. Clinical characteristics of S. tigurinus and other mitis-groups streptococci (MGS) endocarditis.
<table>
<thead>
<tr>
<th></th>
<th>S. tigurinus (n=14)</th>
<th>Other MGS (n=45)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Data of acquisition</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age in years (average, range)</td>
<td>65.2 (19-87)</td>
<td>57.4 (28-86)</td>
<td>0.124</td>
</tr>
<tr>
<td>Female</td>
<td>6 (43%)</td>
<td>7 (16%)</td>
<td>0.060</td>
</tr>
<tr>
<td>Risk factors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous infective endocarditis</td>
<td>2 (14%)</td>
<td>5 (11%)</td>
<td>0.666</td>
</tr>
<tr>
<td>Heart failure</td>
<td>4 (29%)</td>
<td>3 (7%)</td>
<td></td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aortic</td>
<td>5/12 (42%)</td>
<td>24/44 (55%)</td>
<td>0.523</td>
</tr>
<tr>
<td>Mitral</td>
<td>5/12 (42%)</td>
<td>11/44 (25%)</td>
<td></td>
</tr>
<tr>
<td>Aortic + mitral</td>
<td>2/12 (17%)</td>
<td>7/36 (14%)</td>
<td></td>
</tr>
<tr>
<td>Mitral + tricuspid</td>
<td>0</td>
<td>1/36 (2%)</td>
<td></td>
</tr>
<tr>
<td>Chordae tendinae</td>
<td>0</td>
<td>1/36 (2%)</td>
<td></td>
</tr>
<tr>
<td>Intracardiac complication</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perforation</td>
<td>3 (21%)</td>
<td>20 (44%)</td>
<td></td>
</tr>
<tr>
<td>Vegetations</td>
<td>1 (7%)</td>
<td>2 (14%)</td>
<td></td>
</tr>
<tr>
<td>Pulmonary</td>
<td>5/9 (56%)</td>
<td>5 (11%)</td>
<td></td>
</tr>
<tr>
<td>Aortic</td>
<td>19/36 (42%)</td>
<td>1 (2.67%)</td>
<td></td>
</tr>
<tr>
<td>Mitral</td>
<td>19/36 (42%)</td>
<td>1 (2.67%)</td>
<td></td>
</tr>
<tr>
<td>Aortic + mitral</td>
<td>1/36 (2%)</td>
<td>1/36 (2%)</td>
<td></td>
</tr>
<tr>
<td>Mitral + tricuspid</td>
<td>0</td>
<td>1/36 (2%)</td>
<td></td>
</tr>
<tr>
<td>Condition</td>
<td>Cases</td>
<td>Total</td>
<td>p-value</td>
</tr>
<tr>
<td>------------------------------------------------</td>
<td>-------</td>
<td>-------</td>
<td>----------</td>
</tr>
<tr>
<td>9 (20%) Abscess</td>
<td>1</td>
<td>10.00</td>
<td></td>
</tr>
<tr>
<td>7 (16%) Pseudoaneurysm</td>
<td>1</td>
<td>0.67</td>
<td></td>
</tr>
<tr>
<td>2 (4%) Pseudoaneurysm + perforation</td>
<td>1</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>1 (7%) Clinical course</td>
<td>1</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>1 (14%) Embolism</td>
<td>1</td>
<td>0.48</td>
<td></td>
</tr>
<tr>
<td>11/44 (25%) Embolism + perforation</td>
<td>1</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>5/13 (38%) New heart failure</td>
<td>1</td>
<td>0.48</td>
<td></td>
</tr>
<tr>
<td>16/44 (36%) Persistent bacteremia</td>
<td>1</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>2/44 (5%) Surgery</td>
<td>1</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>1 (64%) Indicated</td>
<td>1</td>
<td>0.36</td>
<td></td>
</tr>
<tr>
<td>1 (14%) Embolism</td>
<td>1</td>
<td>0.48</td>
<td></td>
</tr>
<tr>
<td>6 (43%) Performed</td>
<td>1</td>
<td>0.36</td>
<td></td>
</tr>
<tr>
<td>0.358</td>
<td>1</td>
<td>0.36</td>
<td></td>
</tr>
<tr>
<td>28 (62%) Days hospital stay: average, SD range</td>
<td>1</td>
<td>0.36</td>
<td></td>
</tr>
<tr>
<td>2 (14%) In-hospital mortality (%)</td>
<td>1</td>
<td>0.36</td>
<td></td>
</tr>
<tr>
<td>4 (9%) Recurrence</td>
<td>1</td>
<td>0.36</td>
<td></td>
</tr>
<tr>
<td>3/38 (8%) Recurrence + perforation</td>
<td>1</td>
<td>0.36</td>
<td></td>
</tr>
<tr>
<td>1 (14%) Antibiotic treatment</td>
<td>1</td>
<td>0.36</td>
<td></td>
</tr>
<tr>
<td>1 (14%) Beta-lactams alone</td>
<td>1</td>
<td>0.36</td>
<td></td>
</tr>
<tr>
<td>1 (14%) Beta-lactams + gentamicin</td>
<td>1</td>
<td>0.36</td>
<td></td>
</tr>
<tr>
<td>24 (53%) Other combinations</td>
<td>1</td>
<td>0.36</td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: IE caused by S. tigurinus did not clinically differ from that caused by other MGS. Clinical course and outcomes were in general better than IE described for non-viridans streptococci.
Session Number: 205
Session Type: Poster Talk
Session Title: Resistant Gram-negative Pathogens in the Hospital
Session Start Date Time: 6/9/2018 11:00:00 AM
Session End Date Time: 6/9/2018 12:00:00 PM
Session Primary Track: Clinical Infections and Vaccines
Abstract Control Number: 9235
Poster Board Number:

Abstract Title:
Moderator
Primary Author Block:
Estee Torok; Univ. of Cambridge, Cambridge, United Kingdom
Abstract Body:
Abstract Title:
The Assoc. between Intestinal Enterobacteriaceae Dominance and Subsequent Infection in Hospitalized Patients
Primary Author Block:
K. Rao, Y. Sun, A. Seekatz, C. Bassis, E. Mantlo, M. Bachman; Univ. of Michigan, Ann Arbor, MI
Abstract Body:
The Enterobacteriaceae family of Gram-negative bacteria includes the common nosocomial pathogens Klebsiella pneumoniae, Escherichia coli, and Enterobacter cloacae. Bacterial 16S rRNA gene sequence analysis can assess the proportion of total Enterobacteriaceae among the total gastrointestinal microbiota, and prior studies suggest that domination by Gram-negative bacteria is associated with subsequent bloodstream infection. However, 16S rRNA gene sequencing is too costly and slow to be used in a clinical setting. The objectives of this study were to develop a PCR-based assay that can measure Enterobacteriaceae density, validate it against 16S rRNA gene sequencing, and measure the association between Enterobacteriaceae dominance and subsequent infection. Two quantitative PCR (qPCR) assays were developed that quantify Enterobacteriaceae relative to total bacterial 16S rRNA-encoding genes, and both had good correlation with 16S rRNA sequence analysis (P<.0001). A matched case-control study was then performed comparing patients with bloodstream, urinary tract, or respiratory Enterobacteriaceae infections (n=95) to uninfected patients (n=189). Charts were reviewed and rectal swabs collected upon admission to the ward or ICU were analyzed by sequencing and qPCR. Enterobacteriaceae abundance measured by sequencing was high in both cases and controls (mean=31.1% and 27.5%, respectively; P=.322). After adjustment for patient factors there was a modest association with Enterobacteriaceae dominance (defined as >60%) and subsequent infection, although this varied by assay. Dominance on one of the qPCR assays had a significant association with subsequent infection overall (P=.019), adjusting for albumin levels, central venous catheter presence, and use of pressors and cephalosporins at time of swab collection. There was a borderline association with bloodstream infection (P=.076) when measured by sequencing, adjusting for the same clinical factors. These results demonstrate that using qPCR to measure intestinal dominance by a family of bacteria is feasible, indicate that hospitalized patients have high levels of Enterobacteriaceae colonization overall, and suggest that extreme intestinal dominance may be associated with subsequent infection.
Abstract Title:
Predicting Carbapenem Resistance among Gram-Negative Pathogens in Complicated Urinary Tract Infections

Primary Author Block:

Abstract Body:
Background: Rising antimicrobial resistance increases the risk of exposure to inappropriate empiric treatment. Carbapenem resistance (CR) is a concern in complicated urinary tract infections (cUTI). To facilitate improved empiric antimicrobial targeting in cUTI, we developed a bedside instrument to predict CR. Methods: We developed a predictive model using a 60/40 split cohort approach within the Premier Research database (2009-2016) of 178 US hospitals. We included all hospitalized adult patients with a gram-negative organism in at least one urine culture, who fit our algorithm for cUTI, and were treated with an antibiotic starting on the day of the index culture and continued for <u>3</u> days. CR was defined as any organism with an I or R in the susceptibility category to imipenem, meropenem, ertapenem, or doripenem. Results: Among 25,285 patients with cUTI, 1,357 (5.4%) were CR. The median (IQR) hospital rate of CR was 4.0% (1.6%, 6.6%). Patients with CR were more likely male (63.0% vs. 44.0%, p<0.001), black (18.1% vs. 15.0%, p=0.11), and transferred from an extended care facility (ECF) (13.2% vs. 7.6%, p<0.001) than those with carbapenem-susceptible [CS] organisms. Patients with CR also had higher comorbidity burden than CS (median [IQR] Charlson Comorbidity Index 3 [2, 4] vs. 2 [1, 3], p<0.001). Overall E. coli was the most frequent cUTI organism. Among CR pathogens P. aeruginosa predominated (54.5%), with E. coli accounting for 11.5% of all CR infections. Patients with CR were more likely than CS to have previously received antibiotics (50.3% vs. 26.1%, p<0.001), and grown a CR organism (11.8% vs. 0.9%, p<0.001). In a model assigning weighted points for: admission from ECF (1), history of weight loss (1), early mechanical ventilation (1), age<50 (2), male gender (3), catheter-associated UTI (4), prior antibiotics treatment (4) and prior CR (8), the model exhibited good discrimination (c-statistic 0.721), performing better among hospitals with low rates of CR. Conclusions: In this large US cohort of cUTI hospitalizations, CR occurred in ~5% of all cases. A model including eight easily available factors was able to predict the risk of CR at the onset of infection with good discrimination.
Epidemiological and Microbiome Associations between Klebsiella Pneumoniae And Vancomycin-Resistant Enterococci Colonization in Intensive Care Unit Patients

Primary Author Block:
A. H. Collingwood, F. A. Blostein, A. M. Seekatz, C. E. Wobus, R. Woods, B. Foxman, M. A. Bachman; Univ. of Michigan, Ann Arbor, MI

Abstract Body:
Klebsiella pneumoniae and Vancomycin-resistant Enterococci (VRE) are causes of healthcare-associated infections, and prior colonization has been found to be associated with later infection for both organisms. Screening for VRE intestinal colonization is performed routinely on intensive care unit (ICU) patients in some healthcare systems. K. pneumoniae colonization rates are also high in the ICU population, but the association between VRE and K. pneumoniae colonization is unclear. Identification of patient factors associated with K. pneumoniae colonization, including the association with VRE colonization, could direct screening for K. pneumoniae to vulnerable patient populations who could benefit from infection prevention interventions. We hypothesized that K. pneumoniae and VRE both colonize patients with poorer underlying health, and colonization with VRE influences K. pneumoniae colonization and progression of infection. To test this hypothesis, we performed cohort studies on patients screened for VRE colonization by rectal swab culture over two time periods: July-October, 2014 (n=1,209) and January-May, 2016 (n=1,243). The first rectal swab from the first patient encounter in the time frame was screened for K. pneumoniae, and patient demographics, baseline laboratory data, comorbidities, and outcomes were analyzed. VRE colonization was significantly associated with K. pneumoniae colonization in the 2016 cohort (P=0.0062) and approached significance in the 2014 cohort (P=0.0716). VRE colonization was associated with poorer underlying health and worse health outcomes, but co-colonized patients did not have worse comorbidities or outcomes compared to VRE alone. To identify a biological association between VRE and K. pneumoniae colonization and members of the microbiota, 16S rRNA gene-based analysis was performed. This identified an Enterobacteriaceae operational taxonomic unit that was negatively correlated with colonization by both pathogens. These data indicate that VRE colonization is positively associated with K. pneumoniae, and there are shared microbiota signatures in VRE and K. pneumoniae colonized patients.
Study of Extended Spectrum B-Lactamase Producing Enterobacteriaceae from Healthcare Workers from Different Hosp. in Khartoum State 2016-2017

B. I. E. A. Elzubier, M. B. B. M. Bushra; Univ. of Med. Sci. and Technology, Khartoum, Sudan

Abstract Body:
Background: Extended Spectrum B-Lactamase Producing Enterobacteriaceae (ESBL-PE) is categorized as multidrug resistant organisms and one of the most frequent nosocomial infections (1). As of to date, data on colonization and transmission patterns from Sub Sahara Africa is limited; therefore, our study aimed to estimate the prevalence of extended spectrum B-lactamase producing Enterobacteriaceae faecal carriage among healthcare workers in Khartoum state. Methods: A multi-centered prospective cross sectional study was implemented in nine hospitals in Khartoum state. Faecal samples were collected from 100 healthy a-symptomatic healthcare workers and transported in carry-blair transport media to microbiology laboratory of University of Medical Science and Technology. All samples was cultured in Macconkey agar with crystal violet incubated overnight aerobically at 37°C. Then macroscopic examination of colonies applied, purification of gram’s negative bacilli performed on Macconkey agar with crystal violet for standard biochemical identification including: oxidase production test, kliglar iron agar, citrate utilization test, urease production test, indole test and motility test. Standard antimicrobial susceptibility testing to third generation cephalosporins (Cefixime & Ceftazidime ), Amoxcillin, Ciprofloxacin, Cotrimexazole and Gentamycin performed for all gram’s negative oxidase negative bacilli isolated by kirby- bauer disk diffusion method using Molar Hinton agar media. Resistant isolates to third generation cephalosporin (cefixime or ceftazidime or for both) confirmed positive as extended spectrum B-lactamase producing Enterobacteriaceae by double disk diffusion method (key test) as recommended by clinical laboratory standards institute. Descriptive statistics through the statistical package for social sciences (version 23) was performed. Data were summarized including frequency tables for estimating prevalence. Results: Our results revealed that 6.0 % (n=6) of 100 healthcare workers were ESBL-PE positive. 12 % (21/169) of the total 169 Enterobacteriaceae species isolates were resistant to third generation cephalosporin with respectively 12%(21/169)and 5.6%(11/169) for Cefixime and Ceftazidime. Conclusion: The result observed that extended spectrum B-lactamase producing Enterobacteriaceae colonizes healthcare workers which is a threat for both patients and healthcare givers and arise a public health concern for both patients and healthcare givers towards infection prevention and control.
Abstract Title:
Genetic Analysis of Multi-Species, Plasmid-Mediated Carbapenem-Resistant Enterobacteriaceae Hosp. Outbreak
Primary Author Block:
R. A. Stanton1, J. B. Daniels1, L. Sims2, V. Arora2, A. Laufer Halpin1;  1Ctr.s for Disease Control, Atlanta, GA, 2Kentucky Dept. for Publ. Hlth., Frankfort, KY
Abstract Body:
Carbapenem-resistant Enterobacteriaceae (CRE) are an urgent public health threat, responsible for more than 9,000 healthcare-associated infections and 600 deaths per year. An outbreak of CRE in a primary care hospital in 2017 was investigated using whole genome sequencing to determine the identity and possible source(s) of the carbapenemases found in the patient isolates. Twenty carbapenemase-producing isolates (eighteen Klebsiella pneumoniae and two Escherichia coli) were sequenced, nine of which had one beta-lactamase (bla) gene variant (blaKPC-2), eight had blaKPC-3, and one had blaNDM-1. The phylogeny of the K. pneumoniae isolates revealed they were not clonal, as they included four different sequence types, while the E. coli isolates appeared to be closely related. Long-read sequencing determined that the blaKPC-2 and blaKPC-3 genes were harbored on two distinct plasmids, sharing only 48% homology. The blaKPC-2 gene was found on a 128kb plasmid with IncFIB and IncFII replicons that also included a blaTEM-1A gene. While this plasmid appeared to be largely conserved in the nine K. pneumoniae ST258 isolates containing blaKPC-2, the isolates themselves varied from 0 to >1100 SNPs, suggesting that they were not clonal. The plasmid harboring the blaKPC-3 gene was 164kb, with IncFIA and IncFII replicons, as well as blaOXA-9, blaTEM-1A, and six additional antimicrobial resistance genes. Sequences homologous to this plasmid were found in K. pneumoniae isolates from four different STs (including ST258) and both of the E. coli, suggesting horizontal transfer between unrelated bacteria. The results demonstrate that plasmid-mediated carbapenem resistance can be transferred among unrelated bacteria in a healthcare setting, underscoring the impact more granular laboratory methods, such as whole genome sequencing, can have on the ability of public health institutions to investigate outbreaks due to antibiotic resistant threats.
Session Title:
Altered Antibody Responses in Persons Infected with HIV-1 During Prep

Primary Author Block:
I. K. Parker1, G. Khalil1, M. Martin1, W. Leelawiwat2, S. Vanichseni3, K. Choopanya3, W. Switzer1, J. McNicholl1, A. Hickey1, K. Curtis1; 1CDC, Atlanta, GA, 2Thailand Ministry of Publ. Hlth.-US CDC Collaboration, Nonthaburi, Thailand, 3Bangkok Tenofovir Study Group, Bangkok, Thailand

Abstract Body:
Background: Pre-exposure prophylaxis (PrEP) is an effective HIV prevention tool, though its efficacy is dependent upon adherence. The Bangkok Tenofovir Study (BTS), which evaluated the efficacy of oral tenofovir (TDF) among persons who inject drugs (PWID), demonstrated a 49% reduction in the risk of HIV-1 acquisition in study participants who received PrEP as compared to a placebo. In such studies, it is important to characterize the impact of PrEP on HIV antibody responses in persons who become infected during treatment in order to understand the potential impact on timely diagnosis and treatment. Methods: Longitudinal HIV-1-specific antibody responses were evaluated in 42 participants (placebo=28; PrEP=14) who acquired HIV during the BTS. HIV-1 antibody levels and avidity to three envelope proteins (gp41, gp160, and gp120) were measured in the plasma using a customized Bio-Plex (Bio-Rad) assay. A Kaplan Meier analysis was performed for each biomarker to compare the proportion of study subjects who exceeded an assay threshold between treatment groups. Mixed models were used to identify longitudinal differences in antibody levels and avidity between groups. Results: Overall, among PWID longitudinal antibody levels and avidity were notably lower in the PrEP breakthrough group compared to the placebo group. Kaplan Meier analyses demonstrated a significant difference between treatment groups for all Bio-Plex biomarkers (p<0.05). Longitudinal gp120 antibody levels within the PrEP breakthrough group were significantly decreased compared to the placebo group (mixed model; p<0.05). Conclusion: We document an impact on envelope antibody maturation in PWID study subjects who became infected while receiving PrEP, which has significant implications for HIV diagnosis as PrEP use expands. Delayed maturation of the antibody response to HIV may increase the window of detection for antibody-based tests and impact the estimation of population-based incidence.
Abstract Title:
High Pneumonia Incidence in Adults 18 Years and Older in Goto Island, Japan. Early Results from a Population Based Prospective Study.

Primary Author Block:
T. Miyazaki1, K. Hirono1, S. Kohno2, K. Ichihara2, E. N. Gonzalez3, P. Zhang4, R. Istituriz3, A. Arguedas3, B. Gessner3, L. Jodar3; 1Nagasaki Univ., Nagasaki, Japan, 2Yamaguchi Univ., Yamaguchi, Japan, 3Pfizer, Inc., Collegeville, PA, 4Pfizer, Inc., Collegeville, PA

Abstract Body:
Background: Streptococcus pneumoniae is the most common bacterial pathogen causing community acquired pneumonia. Community onset pneumonia (COP) incidence rises with age, representing an important health problem in an aging society like Japan’s. Methods: We report a 1 year interim analysis of a prospective, active surveillance study enrolling Japanese patients ≥18 years of age residing in the southern part of the Goto Island. Patients with clinical pneumonia confirmed by chest X-ray or CT scan were enrolled. Blood and sputum for culture and urine samples for S. pneumoniae antigen detection (Binax and/or UAD) were collected. If S. pneumoniae was detected, serotyping and antimicrobial testing were performed. Results: 494 patients with COP were included. Mean age was 76.4 (±15.6) years. S. pneumoniae was detected in 79/494 (16%) patients (35/494 from sputum) and PCV13 serotypes in 6% of patients. In-hospital mortality was 6.3%. Incidence rates (IR) of COP cases in Goto Island: Overall: 1,512 cases per 100,000 habitants (519/100,000 in those 18-64; 1,471/100,000 in those 65-79; 4,954/100,000 in those >80); etiology confirmed-S. pneumoniae COP: 243 cases per 100,000 habitants (107/100,000 in those 18-64; 253/100,000 in those 65-79; 692/100,000 in those >80) and etiology-confirmed PCV13-serotype-related COP: 32/100,000 in those 18-64, 126/100,000 in those 65-79 and 219/100,000 in those >80 years of age. Annual COP estimates for Japan: 1,626,995 cases; 261,842 S. pneumoniae cases and 76,727 PCV13-related-serotype cases. Based on a VE of PCV13 against VT-COP of 45.56%, the inclusion of PCV13 in the national immunization program in Japan for adults <u>>>>80>65 years of age could prevent, over 5 years period, 121,430 COP cases and 8,375 COP deaths. Conclusions: In spite of the inclusion (November 2013) of PCV 13 to the pediatric national immunization program (NIP) in Japan, COP incidence remains high in Goto Island, increases with age and in-hospital mortality is considerable. The inclusion of PCV 13 in the NIP in adults in Japan may reduce the burden of disease and related mortality.
Session Number: 237  
Session Type: Late-Breaker Poster Presentations

Abstract Title: Understanding the Emergence of Multidrug Resistant Candida: Using Whole-Genome Sequencing to Determine the Population Structure of Candida haemulonii and Candida duobushaemulonii

Primary Author Block: L. Gade1, D. H. Caceres1, N. A. Chow1, N. Le1, R. Ramos-Castro2, P. Escandón3, M. Dolande4, R. Bernardi5, A. Espinosa-Bode1, S. Vallabhaneni1, S. Lockhart1, A. P. Litvintseva1; 1CDC, Atlanta, GA, 2Inst. Conmemorativo Gorgas de Estudios de La Salud, Panamá, Panama, 3Inst. Natl. de Salud, Bogotá, Colombia, 4Inst. Natl. de Higiene Rafael Rangel, Caracas, Venezuela, Bolivarian Republic of, 5Tel Aviv Sourasky Med. Ctr., Tel Aviv, Israel

Abstract Body:

Background: The recent global emergence of a multidrug resistant yeast, Candida auris has drawn attention to the other species from the same phylogenetic clade, C. haemulonii and C. duobushaemulonii, which are also resistant to several classes of antifungal drugs. C. auris and C. duobushaemulonii are frequently misidentified as C. haemulonii by automated systems. In recent years, the number of infections with C. haemulonii and C. duobushaemulonii has been steadily increasing, raising concerns about the possible emergence of these pathogens as a global health threat. Here, we used whole genome sequencing (WGS) to investigate genetic diversity among clinical isolates of C. haemulonii and C. duobushaemulonii from different geographic regions in order to determine the population structure and the extent of clonality among strains, which correlates with emergence.

Methods: We performed WGS on 28 isolates of C. haemulonii from 5 countries and 47 isolates of C. duobushaemulonii from 4 countries using a combination of Illumina and PacBio platforms. Multiple isolates from the same patients, and strains from patients admitted to the same hospital were included to assess diversity within the same person and healthcare facility. The reference genome assemblies were generated from PacBio reads. When available, limited epidemiological data on the isolates were collected including the geographic region and type or site of the infection.

Results: For both organisms, zero single nucleotide polymorphisms (SNPs) were identified among multiple isolates from the same patient; conversely, hundreds of SNPs were detected among isolates from different patients from the United States, Venezuela, Colombia, Guatemala, Israel and different hospitals in Panama, indicating independent acquisition of the infection. However, clonally related isolates of both C. haemulonii and C. duobushaemulonii, different by less than 50 SNPs were identified in one hospital in Panama, which reported a suspected outbreak of bloodstream infections of C. duobushaemulonii. While most of the global isolates of both species were primarily causing wound infections, the majority of isolates from this Panama hospital were isolated from blood. Conclusions: These results indicate that although we are not yet seeing the widespread global emergence of C. haemulonii and C. duobushaemulonii both species can spread within the healthcare facilities and may potentially cause outbreaks.
Abstract Title:
The Contribution of Respiratory Viruses and Bacteria to Community-acquired Pneumonia in Western Australian Children: A Case-control Study

Primary Author Block:
M. Bhuiyan1, T. Snelling2, R. West3, J. Lang4, T. Rahman1, C. Granland3, M. Borland5, R. Thornton1, L-A. Kirkham1, P. Richmond1, D. Smith4, A. Jaffe6, C. Blyth1; 1Univ. of Western Australia, Perth, Australia, 2Telethon Kids Inst., Perth, Australia, 3Telethon Kids Inst., Perth, Australia, 4PathWest Lab., Perth, Australia, 5Princess Margaret Hosp., Perth, Australia, 6Univ. of New South Wales, Sydney, Australia

Abstract Body:
Introduction: Many respiratory pathogens are detected in respiratory tract of healthy children, making it difficult to understand their contribution to childhood pneumonia. We aimed to assess the contribution of common respiratory viruses and bacteria to pneumonia hospitalisations in Australian children to inform future diagnosis, treatment and preventive strategies. Methods: Children aged <18 years old were recruited in a case-control study in Perth, Western Australia. Cases were children hospitalised with radiologically-confirmed pneumonia; controls were contemporaneous age-group frequency-matched healthy children identified from hospital outpatient clinics and from a local immunisation clinic. A nasopharyngeal swab was collected from cases and controls tested for presence of 14 respiratory viruses and 6 bacteria by polymerase chain reaction. Pathogen density was measured for common pathogens. The frequency of detection of each pathogen in cases and controls was compared; logistic regression was used to calculate the odds ratio (aOR, 95%CI) for each pathogen adjusted for demographic factors, recent antibiotic exposure and co-infection. The pneumonia population attributable fraction (% 95% CI) was estimated for each pathogen. Results: From May 2015 to October 2017, 230 cases and 230 controls were enrolled. At least one virus was identified in 57% of cases and 29% of controls (aOR: 4.7, 2.8 - 7.8) and at least one bacterial species was detected in similar proportions of cases and controls (71% vs 79%; aOR: 0.7, 0.4 - 1.0). Respiratory syncytial virus (RSV), human metapneumovirus (hMPV), influenza and adenovirus were detected more frequently in cases than controls (each with aOR > 10). M. pneumoniae was the only bacteria detected more frequently in cases than controls (aOR 14.5). The density of non-typable H. influenza was detected higher in cases than controls whereas the density for S. pneumoniae was lower in cases and M. catarrhalis, and S. aureus was similar in cases and controls. We estimated that RSV, hMPV, influenza, adenovirus and M. pneumoniae contributed approximately 20% (95% CI: 15 - 26), 10% (6 - 14), 6% (3 - 10), 4% (1 - 7) and 7% (4 - 11) of hospitalisations for childhood pneumonia, respectively. Conclusions: Respiratory viruses, particularly RSV and hMPV, are likely to be major contributors to childhood pneumonia in this highly vaccinated population of Australian children. Effective preventive and treatment strategies targeting viruses are likely to reduce childhood pneumonia burden.
Abstract Title:
Novel multivalent vaccines against Clostridium difficile infection

Primary Author Block:
X. SUN, s. wang; Univ. of South Florida, Tampa, FL

Abstract Body:
Previously, we constructed a recombinant vaccine candidate, designated mTcd138 containing the glucosyltransferase and cysteine proteinase domains of TcdB and the receptor binding domain (RBD) of TcdA. To ensure mTcd138 is atoxic, two point mutations were introduced in the glucosyltransferase domain of TcdB, which essentially eliminates mTcd138 toxicity in vitro and in vivo. The RBD of TcdB has been reported to be highly immunogenic. It was also reported that Salmonella typhimurium flagellin (sFliC) protected mice from death during C. difficile infection (CDI) by significantly delaying C. difficile growth in the gut. sFlic is a known potent adjuvant, and is structurally similar to C. difficile flagellin FliC (cFlic). To generate a vaccine candidate targeting both toxins and C. difficile colonization/growth, we further fused mTcd138 with the RBD of TcdB and sFliC, resulting in Tcd169Fl. Parenteral immunization of mice with Tcd169Fl induced potent immune responses against TcdA, TcdB and sFliC, and provided mice full protection against infection with hyper-virulent C. difficile strains.
Session Number: 237
Session Type: Late-Breaker Poster Presentations
Session Number: 237
Session Type: Late-Breaker Poster Presentations
Session Title: SATURDAY - CIV Late-breakers
Session Start Date Time: 6/9/2018 11:00:00 AM
Session End Date Time: 6/9/2018 1:00:00 PM
Session Primary Track: Clinical Infections and Vaccines
Abstract Control Number: 8020
Poster Board Number: SATURDAY - CIV LB6

Abstract Title:
Intranasal Vaccination with An Adjuvanted Ebola-gp Vaccine Alters the Mouse Gut Microbiota

Primary Author Block:
J. Richardson, M. Sunay, M. Gregory, G. Koroleva, G. Palacios; United States Army Med. Res. Inst. for Infectious Diseases, Frederick, MD

Abstract Body:
The gut microbiota plays an important role in the development and maintenance of a healthy immune system. However, little is known about the interaction between vaccines and vaccine adjuvants and the gut microbiota. To better understand how vaccination impacts the gut microbiota, mice were vaccinated with a plasmid based Ebola-GP vaccine containing a TLR-3 antagonist intranasally, intramuscularly or intramuscularly with a vector control. Mouse gut microbiotas were characterized by 16S rRNA sequencing of fecal samples. Mice vaccinated intranasally, but not intramuscularly, showed a dramatic increase in the proportion of Akkermansia muciniphila. This increase was detected on days 40 and 49 post vaccination (days 19 and 28 post-boost). This alteration in the gut microbiota was correlated with protection from mouse-adapted Ebola, and high serum levels of anti-Ebola-GP IgA and IgG titers. This shows that intranasal vaccination against Ebola can change the gut microbiota composition. Further work is required to clarify the consequences and direct causes of this alteration.
Abstract Title:
OralimmunizationwitharecombinantLactobacillusExpressingck6fusedwithvp2proteinagainstipnvinrainbowtrout(Oncorhynchusmykiss)
Primary Author Block:
M. Liu, K. Duan, W. Shi, X. Hua; Northeast Agricultural Univ., P.R.China, Harbin, China
Abstract Body:
Infectious pancreatic necrosis virus (IPNV) infects wild and cultured salmonid fish, causing high mortality in juvenile trouts and salmons with serious economic losses to salmonid aquaculture. It is ideal that the method of oral immunization prevent the infection of rainbow trout juveniles in IPNV. In the present study, genetically engineered Lactobacillus casei 393 pPG-612-VP2/ L.casei 393 and pPG-612-CK6-VP2/L. casei 393 constitutively expressing VP2 protein of Infectious pancreatic necrosis virus (IPNV) were constructed. Orally administrated the recombinant strains pPG-612-CK6 -VP2/L.casei 393 and pPG-612-VP2/L.casei 393 to juvennile rainbow trouts, the titer of specific IgM and IgT of pPG-612-VP2/L. casei 393 exhibited significant levels. The result demonstrated the recombinants could elicit both local mucosal and systemic immune responses. The proliferation of spleen lymphocytes in trouts immunized with pPG-612-CK6-VP2/ L. casei 393 showed that the recombinant strain could induce a strong cellular immune response. The levels IL-1β, IL-8, CK6, MHC-II, Mx,β- defensin and TNF-1α in spleen and gut suggested that the target molecular chemokine has ability to attract relevant immune cells to participate in the inflammatory response and enhance the function of innate immune response. Additionally, the pPG-612-CK6-VP2/ L. casei 393 induced the expression of cytokines which have the effect of promoting inflammation to drive the differentiation of macrophages, kill medium and target cells. To determine the effectiveness of oral immunization with recombinant strain, trouts were challenged with IPNV. After analyzing by RT- PCR, reduction in viral load caused by pPG-612-CK6-VP2/ L. casei 393 was significantly higher than that of other groups. Thus, the recombinant pPG-612-CK6-VP2/ L. casei 393 is a promising candidate for oral vaccine development against IPNV.
Abstract Title:
Cryptococcal Antigenemia among HIV Infected Patients At A Referral Hospital, Northwest Ethiopia
Primary Author Block:
A. Derbie1, W. Ayalew2, D. Mekonnen1, Y. Mulugeta1; 1Bahir Dar Univ., Bahir Dra, Ethiopia, 2FHRH, Bahir Dra, Ethiopia
Abstract Body:
Background: Cryptococcosis remains as one of a common opportunistic fungal infection among HIV infected patients living in Sub-Saharan Africa, including Ethiopia. The magnitude of the disease at Felege Hiwot Referral Hospital (FHRH) in particular and in Ethiopia at large is not well explored. Methods: A retrospective document review was done on records of 137 HIV infected patients who were attending anti-retroviral treatment (ART) monitoring at the FHRH ART clinic. All HIV positive patients who visited the hospital from 1 Sep to 30 Dec 2016 and had registered data on their sex, age, CD4 count and cryptococcal antigen screening result were included in the study. The cryptococcal antigen (CrAg) detection was done by the IMMY CrAg® LFA (Cryptococcal Antigen Lateral Flow Assay) kit from patient serum as per the manufacturer instruction. All data were entered, cleared, and analyzed using the SPSS v20. Descriptive data analysis and cross tabulation was done to assess factors associated with cryptococcal antigen. Statistical significance was set at p-value less than or equal to 0.05. Results: Most of HIV patients at 75 (54.7%) were females. The median age of the participants was at 32.0 years (ranged: 8-52 years). The mean CD4 count was at 51.8 with SD of 26.3 (range 3-98). The proportion of positive cryptococcal antigen from blood serology test was 11.7% (95% CI: 7.3-18.1%). The IMMY CrAg® LFA result was statically associated with patient sex (p= 0.045). However, it was not found associated with patient age group and the CD4 count (P>0.05) Conclusions: This study provided baseline data on the magnitude of cryptococcal antigenemia among HIV positive patients that is not touched before in the studied area. The results of the study showed this opportunistic fungal infection is an important health problem among HIV patients. Further studies with sound design employing adequate sample size should be considered.
Abstract Title:
Evaluation of Opportunistic Intestinal Protozoan Parasites and Haematological Indices of Patients Living with HIV/AIDS on Antiretroviral Therapy in Nigeria

Primary Author Block:
T. N. Njoku-Obi; Imo State Univ., Owerri, Nigeria

Abstract Body:
Background: Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome (HIV/AIDS) is one of the worst pandemics that has been experienced by humankind. This study was carried out to evaluate the opportunistic intestinal protozoan parasites and haematological indices of people living with HIV/AIDS on antiretroviral therapy in Imo state.

Methods: A total of 520 stool and blood samples were collected in syringes and EDTA bottles. These samples were analyzed using standard parasitological, and haematological techniques. The stool samples were prepared and examined using iodine wet mount for cyst and trophozoite of Entamoeba histolytica and Giardia lamblia. Modified Ziehl-Neelson method was used for Cryptosporidium parvum and Isospora belli for their oocyst, while modified trichrome staining method was used for Microsporidium sp. Standard haematological techniques for pack cell volume, haemoglobin, erythrocyte sedimentation rate and cluster of differentiation (CD4+) cell count were determined.

Result: The stool samples examined on HIV positive patients, 204 (48.5%) were infected with intestinal protozoa parasites. From the control group 3.0% prevalence of parasite infection was observed. The result revealed that significantly higher prevalence of infection was recorded in HIV Pre ART patients (45.0%) than HIV patients on ART (37.2%) (P< 0.05). The overall sex related prevalence of opportunistic intestinal protozoa parasites among HIV patients on ART revealed significantly higher infection rate among females (49.0%) than males (48.1%) (P>0.05). The opportunistic intestinal protozoa parasites isolated in this study were Cryptosporidium parvum, Isospora belli and Microsporidium sp., other intestinal parasitic isolated were Entamoeba histolytica and Giardia lamblia. In this study, the level of CD4+ count was significantly decreased among HIV positive when compared with the HIV negative. Also, CD4+ count increased with the taking of ART. Level of haemoglobin significantly decreased when compared with the control subjects.

Conclusion: This probably indicate that taking of ART by people living with HIV could help them improve their blood percentage Key Words: opportunistic intestinal protozoan parasites, haematological ,patients HIV/AIDS , antiretroviral, therapy
Session Number: 238
Session Type: Poster
Session Title: CIV01 - Clinical Studies of Adult Infectious Diseases: HIV Infection
Session Start Date Time: 6/9/2018 11:00:00 AM
Session End Date Time: 6/9/2018 1:00:00 PM
Session Primary Track: Clinical Infections and Vaccines
Abstract Control Number: 4679
Poster Board Number: SATURDAY - 672

Abstract Title:
Emerging Issues in the Treatment of Hiv-Associated Candidiasis in Nigeria

Primary Author Block:
O. B. Onokala1, F. Oluwasina1, G. Abiaziem2; 1AIDS Hlth.care Fndn. Nigeria, Abuja, Nigeria, 2AIDS Hlth.care Fndn. Nigeria, Makurdi, Nigeria

Abstract Body:
Background: Candidiasis is one of the most common HIV-associated opportunistic infections. The high burden of HIV in Nigeria translates to increased incidences of HIV-associated candidiasis, progressing to candidemia if untreated. The study investigated the issues in the treatment of HIV-associated candidiasis, to provide data for clinical interventions required to reduce its incidence in the Nigerian HIV Programme. Methods: The longitudinal study was conducted at 20 randomly selected HIV treatment facilities in Nigeria, from January 2015 to August 2017. A total of 9,540 HIV-positive patients were routinely screened for candidiasis during their clinic visits, within the period. Patients who tested positive for candidiasis were treated with fluconazole capsules, nystatin suspension, nystatin vaginal pessaries or clotrimazole vaginal pessaries as appropriate. Patients who were transferred out of the facilities were excluded from the study. The patients’ demographic data, baseline and routine CD4 tests values, level of adherence to anti-retroviral therapy (ART), number of recurrent episodes of candidiasis, and candidiasis treatment outcome were documented in the patients’ ART Care Cards and Open Medical Record System. The data were analyzed by descriptive statistical methods. Statistical significance was taken as P <0.05. Results: The results revealed that 4,264 patients (18-72 years, mean age: 31.21, standard deviation ± 9.54) tested positive for candidiasis within the study period. Most of them (3,437) resided in the rural areas and presented with advanced HIV disease, and low CD4 values. Furthermore, 2,621 (61.47%) and 217 (5.09%) female patients tested positive for vaginal candidiasis and vaginal-oral candidiasis co-infection respectively. Female and male patients who tested positive for only oral candidiasis were 722 (16.93%), and 704 (16.51%) respectively. Patients who reported recurrence of vaginal candidiasis (68), oral candidiasis (39) and both (12) exhibited poor adherence to ART, when compared with the patients who did not experience recurrence (P <0.05). However, some recurrent cases of vaginal candidiasis (30), oral candidiasis (2) and both (5) were attributed to drug resistance. Conclusions: Medication adherence counseling at HIV facilities need to be strengthened. Clinical HIV testing should be prioritized in rural areas to reduce the incidence of candidiasis due to undiagnosed advanced HIV disease. Interventions to reduce the incidence of HIV-associated candidiasis should be prioritized for women.
Cervical Intraepithelial Neoplasia Screening and HPV Testing in HIV-Infected Women in Nepal

Primary Author Block:
N. P. Awasthi1, P. Chaudhary2, S. Ghimire1, S. Bhattarai1, N. Shrestha1, B. Dhakal1, R. Rajbhandari1, S. M. Dixit1; 1Ctr. for Molecular Dynamics Nepal, Kathmandu, Nepal, 2Dept. of Hlth.Services, Kathmandu, Nepal

Abstract Body:
Background: Immune-compromised state of the HIV infected patient increases the probability of HPV infection which leads to progression of the cervical cancer. Despite of being high risk group, current pattern and prevalence of HPV infection in the HIV infected women of Nepal still remains unexplored.

Methods: Visual Inspection with Acetic Acid (VIA) and real time PCR-based detection of the 14 different high risk HPV strains were conducted following Colposcopy and biopsy for positive VIA findings. Total 786 HIV infected woman with any CD4 count enrolled in National HIV Program at Sukraraj (Teku) Hospital Clinic and Pokhara were considered for the study. Results: In this study, 331 (42.2%) of the cases showed HPV positive whereas remaining 455 (57.9 %)were negative. Among HPV positive cases, 197 (59.51%) had single HPV strain followed by 65 (19.93%) showing two HPV strains. Similarly, six strains were reported in three of the cases and seven strains of HPV in one case. HPV-16 strain was the most prevalent (32.02% of the cases). Other high risk strains like HPV-18, HPV-52, HPV-58, and HPV-51 were also present in higher number in the positive cases. Younger women (18-24 years) were more likely to be infected with HPV (69.6% of positive cases) than older age (25 years and above) with 31.4% cases. Most of the respondents were identified negative in VIA screening whereas 16.4% of them were reported positive in the screening. About 8% of Women with HIV and AIDS were HPV and VIA positive. Women with HPV and VIA were eleven times more likely to develop cancer than women without (aOR=11.1, 95%CI=6.3, 19.7). Conclusions: The study played vital role in documenting the effectiveness of VIA, establishing routine cervical cancer screening and characterizing HPV sub-strains among HIV positive women in Nepal. These results will be applicable to current efforts to extend HPV vaccine coverage in Nepal.
Abstract Title:
Frequency of Broadly Neutralizing Antibodies in Hiv-1 Chronically Infected Individuals in Ugandan Clades A and D

Primary Author Block:
C. Kintu; Makerere Univ. Kampala, Kampala, Uganda

Abstract Body:
Aim: The study was aimed at assessing frequencies of neutralizing antibodies in individuals affected with the commonest HIV-1 clades A and D in Uganda. Methods: This was a cross-sectional study of 83 HIV-1 chronically infected Anti-Retroviral Therapy (ART) naïve adults who were enrolled from Medical Research Council (MRC) cohort and The AIDS Support Organization (TASO) Clinic in Entebbe. Samples of Plasma were tested for the neutralization activity against a panel of 3 clade A and D viruses using the Neutralization Assays. Neutralization assays were performed using Env pseudovirus viruses in the TZM-bl cell-based assay. Neutralization values were obtained as the plasma dilutions at which virus entry was inhibited by 50% compared to that in the absence of plasma (IC50). A plasma sample was scored as displaying neutralizing activity against a particular virus if at least 50% inhibition of infection was recorded at the lowest plasma dilution tested (1: 20) in at least two independent neutralization assays. Results: Clade A viruses are better neutralized compared to clade D viruses. Individuals whose titers were above 1080 (labeled red required further sample dilution. 51.81% of the participants had their antibody neutralization titers above 40. There was a significant difference between the proportion of clade A viruses neutralized and those of clade D as obtained statistically using the Mann-Whitney test with a p-value < 0.0001. The neutralization titers obtained for the individual clade A viruses Q23.17, Q769.d22 and Q842.d12 were much higher than those for clade D viruses QA013.H1, Q857.B3 and QD435.5B. Conclusion: Generally, the frequency of neutralizing antibodies was found to be much higher in Clade A compared to Clade D. This implies that in case of a vaccine design, emphasis should be put on Clade D subtype since it’s harder to neutralize naturally. List of figures

<table>
<thead>
<tr>
<th>Subtype</th>
<th>% of Viruses neutralised</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Q23.17 286.29</td>
</tr>
<tr>
<td></td>
<td>Q769.d22 40</td>
</tr>
<tr>
<td></td>
<td>Q842.d12 181.38</td>
</tr>
<tr>
<td>D</td>
<td>QA013.H1</td>
</tr>
<tr>
<td></td>
<td>Q857.B3</td>
</tr>
<tr>
<td></td>
<td>QD435.5B</td>
</tr>
<tr>
<td>Row</td>
<td>Column 1</td>
</tr>
<tr>
<td>-----</td>
<td>----------</td>
</tr>
<tr>
<td>1</td>
<td>40</td>
</tr>
<tr>
<td>2</td>
<td>484</td>
</tr>
<tr>
<td>3</td>
<td>159</td>
</tr>
<tr>
<td>4</td>
<td>55.11</td>
</tr>
<tr>
<td>5</td>
<td>57</td>
</tr>
<tr>
<td>6</td>
<td>541</td>
</tr>
<tr>
<td>7</td>
<td>193</td>
</tr>
<tr>
<td>8</td>
<td>61</td>
</tr>
<tr>
<td>9</td>
<td>116</td>
</tr>
<tr>
<td>10</td>
<td>82</td>
</tr>
<tr>
<td>11</td>
<td>505</td>
</tr>
<tr>
<td>12</td>
<td>40</td>
</tr>
<tr>
<td>13</td>
<td>55.11</td>
</tr>
<tr>
<td>14</td>
<td>57</td>
</tr>
<tr>
<td>15</td>
<td>541</td>
</tr>
<tr>
<td>16</td>
<td>193</td>
</tr>
<tr>
<td>17</td>
<td>61</td>
</tr>
<tr>
<td>18</td>
<td>116</td>
</tr>
<tr>
<td>19</td>
<td>82</td>
</tr>
<tr>
<td>20</td>
<td>505</td>
</tr>
<tr>
<td>21</td>
<td>40</td>
</tr>
<tr>
<td>22</td>
<td>55.11</td>
</tr>
<tr>
<td>23</td>
<td>57</td>
</tr>
<tr>
<td>24</td>
<td>541</td>
</tr>
<tr>
<td>25</td>
<td>193</td>
</tr>
<tr>
<td>26</td>
<td>61</td>
</tr>
<tr>
<td>27</td>
<td>116</td>
</tr>
<tr>
<td>28</td>
<td>82</td>
</tr>
<tr>
<td>29</td>
<td>505</td>
</tr>
<tr>
<td>30</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>74</td>
<td>173</td>
</tr>
<tr>
<td>79</td>
<td>173</td>
</tr>
<tr>
<td>124</td>
<td>248</td>
</tr>
<tr>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>74</td>
<td>173</td>
</tr>
<tr>
<td>79</td>
<td>173</td>
</tr>
<tr>
<td>124</td>
<td>248</td>
</tr>
<tr>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>74</td>
<td>173</td>
</tr>
<tr>
<td>79</td>
<td>173</td>
</tr>
<tr>
<td>124</td>
<td>248</td>
</tr>
<tr>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>74</td>
<td>173</td>
</tr>
<tr>
<td>79</td>
<td>173</td>
</tr>
<tr>
<td>124</td>
<td>248</td>
</tr>
<tr>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>74</td>
<td>173</td>
</tr>
<tr>
<td>79</td>
<td>173</td>
</tr>
<tr>
<td>124</td>
<td>248</td>
</tr>
</tbody>
</table>
Table 1: Neutralization titres for six virus Panel

<table>
<thead>
<tr>
<th>Titer Value</th>
<th>% of Virus Neutralized</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40.000</td>
<td>40.001-99.99</td>
</tr>
<tr>
<td>&gt;999.99</td>
<td>100-999.999</td>
</tr>
<tr>
<td>&gt;1000000</td>
<td></td>
</tr>
</tbody>
</table>

Figure 1: Neutralization titres for six virus Panel
Figure 2: (a) Average neutralization titres per clade, (b) Proportion of viruses neutralized per Clade
Figure 3: Total Percentage of individuals that neutralized
Abstract Title:
Mutational Analysis of Foxp3 Gene in Pakistani Hiv Patients
Primary Author Block:
N. N. Hussain; Univ. of the Punjab, Lahore, Pakistan
Abstract Body:
Human immunodeficiency virus (HIV) becomes one of the most severe endemic viruses that advance around the world in a deadly manner. It is a serious issue in Pakistan as well and so far 130,000 HIV cases in Pakistan have been identified by the National AIDS Control Programme. Nuclear transcription factor forkhead box P3 (FOXP3) gene is involved in tolerance mechanism so failure of tolerance can lead to mutations in this gene. The main objective of this project was to analyze the possible mutation especially in FOXP3 gene exon 1 that may clarify the reason of reduction of T regulatory cells (Tregs) due to HIV/AIDS. A total of 25 HIV patients were chosen from the Institute of Public Health on the basis of confirm HIV infection and 25 healthy controls as well. First genomic DNA was extracted from the peripheral blood and then amplified by using specific designed primers. Gradient PCR was performed and the product length was 197 bps which was further analyzed on 1% agarose gel. Sequencing was done through genetic analyzer (3500 ABI). No mutation was observed in FOXP3 gene exon 1 of Pakistani HIV patients. Key words: Human immunodeficiency virus, FOXP3 gene, T regulatory cells, Gradient PCR, mutation
Abstract Title:
Maternal Hiv Infection Influences the Microbiome of Hiv-Exposed Uninfected Infants
Primary Author Block:
S. Beurmann1, N. Ndembali2, J. Jumare1, K. J. Schulze3, A. Shutt1, A. Omoigberale4, C. Cairo1, C. M. Fraser1, M. Charurat1; 1Univ. of Maryland, Baltimore, Baltimore, MD, 2Inst. of Human Virology, Nigeria, Abuja, Nigeria, 3John Hopkins Univ., Baltimore, MD, 4Univ. of Benin Teaching Hosp., Benin City, Nigeria
Abstract Body:
Background: The scale-up of antiretroviral prophylaxis to prevent mother-to-child HIV transmission has dramatically reduced the number of infected infants, which results in an increase in HIV-exposed but uninfected (HEU) children. This population is at risk for early-life developmental abnormalities such as growth faltering, increased morbidities, infant diarrhea, and higher mortality than children born to HIV-uninfected mothers (HUU). Methods: 150 HIV-infected and 150 HIV-uninfected women were recruited from Benin City, Nigeria and followed from 18 weeks of gestation to 18 months post-partum. Microbiota from vaginal, stool, skin, and breastmilk samples collected from the mothers and meconium, stool, and oral swabs collected from their infants were characterized using Illumina HiSeq. Alpha- and beta-diversity statistics and taxonomic compositions were calculated. The longitudinal changes in the infants’ gastrointestinal tract microbial diversity and growth indices were determined and compared between HUU and HEU pairs over a period of 18 months. Results: Less HEU infants were breastfed and the overall antibiotic use in HEU infants was higher when compared to HUU infants. The microbial communities identified in the mothers were consistent, which was independent of HIV infection, whereas HEU and HUU infants exhibited differences. PCoA showed clustering of the different sample types, but did not discriminate between HIV status. The Shannon diversity index was significantly greater in HEU compared to HUU infants (P=0.02), and the weight-for-age z scores (WAZ) were significantly lower in HEU infants (P<0.01). The bacterial community composition of the infants’ meconium and stool changed over time, and correlated to the mother’s HIV status. HUU infants had more abundant populations of Bifidobacteriaceae and Enterococcaceae, whereas HEU infants had more Ruminococcaceae, Pseudomonadaceae, and Enterobacteriaceae in their stools. Conclusions: Maternal HIV infection is associated with changes in the gut microbiome of HEU infants. As one of the largest studies ever to characterize longitudinal maternal-infant microbiota, we provide further insight into the understudied role of the infants’ distorted gut microbiota acquired from HIV-infected mothers and its influence on the children’s growth and development. In addition, it will open new avenues for drug-mediated and probiotic interventions in promoting the health of HEU infants.
Session Number: 238
Session Type: Poster

Session Title: CIV01 - Clinical Studies of Adult Infectious Diseases: HIV Infection
Session Start Date Time: 6/9/2018 11:00:00 AM
Session End Date Time: 6/9/2018 1:00:00 PM
Session Primary Track: Clinical Infections and Vaccines
Abstract Control Number: 4716
Poster Board Number: SATURDAY - 679

Abstract Title:

Primary Author Block:
Z. Woldesonbet1, L. Wassie2, H. Bedimo1, A. Mihret1, Y. Asemamaw1; 1Addis Ababa Univ., Addis Ababa, Ethiopia, 2Armauer Hansen Res. Inst., Addis Ababa, Ethiopia

Abstract Body:
Background: Hepatitis, a highly contagious viral infection, is one of the leading killer diseases globally caused by hepatitis virus. Among the existing viral causes for hepatic failure, hepatitis B virus (HBV) plays a significant role with devastating implications, especially when combined with other viral infections such as human immunodeficiency virus (HIV). Co-infection with hepatitis B virus and HIV leads to increased morbidity and mortality as compared to independent HIV and HBV infections. In this study, we aimed to assess the seroprevalence of HBV and HIV coinfection and associated risk factors among pregnant women in a selected hospital facility around Addis Ababa, Ethiopia. Methods: A total of 215 pregnant women were recruited between July and October 2014 from Tirunesh Beijing General Hospital. A pretested and structured questionnaire was used to collect socio-demographic characteristics and possible risk factors. In addition, 5 ml venous blood was collected and centrifuged to estimate the seroprevalence of HBV and HIV. Descriptive statistics and logistic regression analysis were done and a P value less than 0.05 was considered statistically significant Results: The overall prevalence of hepatitis B virus infection was 13 (6 %). This positivity was different across different age categories: 1 (11.1 %), 3 (4.5 %), 6 (6 %), 1 (3.2 %), and 2 (25 %) among those between 15-19, 20-24, 25-29, 30-34, and 35-39 years, respectively. However, a statistically significant association was not established between age and HBV. Among the total, 9 (4.2 %) of the positive cases were detected among primary school completed. Multivariate analyses indicated that history of abortion (p = 0.003), history of surgery (p = 0.022), and tattooing (p = 0.033) were significantly associated with HBV infection. A total of 9 (4.2 %) women were found to be HIV seropositive, of whom 2 (22.2 %) were co-infected with HBV. Conclusions: We observed a relatively higher seroprevalence of HBV infection among pregnant women in the study area, in which majority of the cases had underlying risk factors for acquiring the infection. Since none of the mothers were vaccinated for HBV, the possibility of perinatal transmission is inevitable. Hence, routine screening and immunization against HBV during pregnancy and health education are highly warranted to alleviate the situation.
Impact of Tenofovir Disoproxil Fumarate on the Survival of Patients Coinfected with Hepatitis B Virus and Human Immunodeficiency Virus: A Retrospective Cohort Study

Primary Author Block:
W-C. Tsai1, W-T. Hsu1, W-D. Liu1, W-H. Sheng1, S-M. Hsieh1, H-Y. Sun1, Y-S. Huang2, K-Y. Lin3, C-C. Hung1, S-C. Chang1; 1Natl. Taiwan Univ. Hosp., Taipei, Taiwan, 2Natl. Taiwan Univ. Hosp. Hsin-Chu Branch, Hsinchu City, Taiwan, 3Natl. Taiwan Univ. Hosp. Ji-Shan Branch, New Taipei City, Taiwan

Abstract Body:
Background: Tenofovir disoproxil fumarate (TDF) is an effective agent against both HBV and HIV, and TDF-containing combination antiretroviral therapy (cART) has been recommended for HIV/HBV-coinfected patients. The impact of introducing TDF into cART on the outcome of HIV/HBV-coinfected patients has rarely been investigated in areas of high endemicity of chronic HBV infection. Methods: We retrospectively reviewed the medical records of the patients who were antiretroviral-naive and newly diagnosed with HIV infection between 2007 and 2015 at a university hospital in Taiwan. The initial presentations at HIV diagnosis, baseline plasma HIV RNA load and CD4 count, concurrent sexually transmitted diseases, serological markers of HBV and HCV, and cART were collected. Four groups of patients were defined, according to the HBV status and the time when TDF was first introduced in Taiwan on 30 June, 2011. The primary outcome was all-cause mortality rate. All patients were followed until death, loss to follow-up, or end of observation, whichever occurred first. Results: During the 9-year study period, 1,723 HIV-infected patients were included, with a median age of 31 years (IQR, 26-39), 97.5% being male and a median baseline CD4 count of 262 cells/μL (IQR, 78-435). 857 patients (49.7%) had CD4 count <200 cells/μL. Overall, 13.3% (229/1723) of the patients had chronic HBV infection: 18.1% (125/692) in the pre-TDF era and 10.1% (104/1031) in the TDF era. The mortality rate was 23.2(95% CI, 12.5-43.1), 15.7(95% CI, 7.0-34.8), 9.6(95% CI, 6.1-15.0), and 8.0(95% CI, 5.5-11.6) deaths per 1000 person-years of follow-up (PYFU) for HBV-positive/pre-TDF, HBV-positive/post-TDF, HBV-negative/pre-TDF, and HBV-negative/post-TDF group. The estimated hazard ratio in multivariate Cox proportional hazards regression analysis for mortality among HBV-positive group compared to HBV-negative group was 2.99(95% CI, 1.30-6.86) in the pre-TDF era and 0.94(95% CI, 0.36-2.43) in post-TDF era, after adjusting for age, sex, risk group for HIV transmission, baseline CD4, HCV infection, presence of opportunistic infections at baseline, and cART initiation. Conclusions: In this country of high HBV endemicity, the difference of short-term survival had decreased among HBV-positive patients compared to HBV-negative patients in the era of TDF-containing cART.
Activity of Debio 1452 on Intracellular Staphylococcus aureus in Osteoblasts In Vitro

Primary Author Block:
V. Dyon-Tafani1, G. Dieppois2, A. Cara1, A. Monteix1, F. Valour3, J. Josse1, T. Ferry3, F. Laurent1; 1Intl. Ctr. for Infectiology Res., Lyon, France, 2Debiopharm Intl. SA, Lausanne, Switzerland, 3Dept. of Infectious Diseases, Lyon, France

Abstract Body:
Background: Debio 1452, a first-in-class inhibitor of bacterial fatty acid synthesis, shows selective antibacterial activity against Staphylococci. Its prodrug Debio 1450 (afabicin) has completed Phase II in acute bacterial skin and skin structure infections and is presently investigated for the treatment of bone and joint infections (BJI). Staphylococcus aureus (SA) BJI are a major public health problem with a therapeutic failure rate remaining high despite surgical management and prolonged antibiotic treatment. The persistence of the infection is partly due to the fact that SA is able to internalize and persist within osteoblasts (OBs), hiding from immune system and antibiotics. The objective of this study was to evaluate in vitro the intracellular activity of Debio 1452 in an SA/OB interaction model. Methods: Our previously published infection model between SA ATCC 29213 and human MG-63 OB was used for the evaluation of Debio 1452 activity. Debio 1452 was added 3h after infection and extracellular bacteria were eliminated using lysostaphin. At 24h post-infection, the number of intracellular SA was assessed by plating. Lactate dehydrogenase and the standard 3-(4,5-Dimethyl-2-thiazolyl)-2,5-diphenyl-2H-tetrazolium bromide was quantified to monitor cytotoxicity and cell proliferation, respectively. Debio 1452 was tested at 4 concentrations ranging from 0.1 to 100x its MIC and vancomycin was used as negative control as it is known to have a limited impact on intracellular bacterial growth. Results: No cytotoxicity and no loss of proliferation were observed on human OB cells in presence of Debio 1452 at all the concentrations tested. While Vancomycin failed to reduce the intracellular SA inoculum, Debio 1452 revealed significant intracellular activity with a dose dependent response across the tested concentrations compared to untreated infected OB (up to -50% at 100xMIC p<0.001). The treatment with Debio 1452 has not induced emergence of resistance in the remaining colonies. Conclusions: The preliminary results show that Debio 1452 has the potential to eradicate intracellular SA in osteoblasts and could be a valuable innovative therapeutic option for the treatment of BJI.
Session Number: 239
Session Type: Poster
Session Title: CIV01 - Clinical Studies of Adult Infectious Diseases: Staphylococcal and Other Gram-positive Infections
Session Start Date Time: 6/9/2018 11:00:00 AM
Session End Date Time: 6/9/2018 1:00:00 PM
Session Primary Track: Clinical Infections and Vaccines
Abstract Control Number: 4227
Poster Board Number: SATURDAY - 683

Abstract Title:
Ceftaroline Fosamil in the Treatment of Meningitis Caused by Methicillin-Resistant Staphylococcus aureus Using Rabbit Model

Primary Author Block:

Abstract Body:
Background: Vancomycin is the only recognized treatment for MRSA meningitis. Its efficacy is limited by poor penetration into central nervous system. Ceftaroline is a cephalosporin with effectiveness against MRSA. Recent reports suggest that it penetrates in both the inflamed and non-inflamed meninges. In this study, we compared the efficacy of Ceftaroline and Vancomycin using a rabbit model of MRSA meningitis. Methods: Rabbits were intracisternally inoculated with 5 X 10^5 CFU of MRSA 252. 16h PI (Post infection), rabbits with meningitis were randomized into three groups (Control [CL] [no treatment], Vancomycin [V] [20 mg/Kg q12H], or Ceftaroline [CF] [40mg/Kg at 0 and 4h to replicate human dose]). CSF (~0.5 ml) was withdrawn every 12h (Tap 1: 16h PI; Tap 2: 28h PI and Tap 3: 40h PI) and assayed for killing of S. aureus by quantitative bacterial counts as well as drug levels in the CSF. The median difference in CFU was calculated using [(Tap Y - Tap X)/Tap X] x 100 to normalize for the baseline CFU for each experimental group. Results: There was no difference in the baseline CFU/ml among the experimental groups (CF: 11700; CL: 6600; V:9900; p=0.55). Median difference (CFU/ml) between tap 2 and tap 1 was significant for all 3 groups (CF: -6220; CL: +900; V: -3060; p<0.0001); the difference between tap 3 and tap 1 did not reach statistical significance (CF: -2100; CL: -2350; V: -1875; p=0.063). Pairwise comparisons of normalized differences (tap2 to tap1) were significant between both the CF vs. CL (CF: -90.6% vs. CL: 46.9%; p<0.0001) and V vs. CL (V: -62.1% vs. CL:46.9%; p=0.0007). Again, these differences did not reach the statistical significance between tap 3 and tap 1 (CF: -91.9% vs. CL -91.5%; p=0.30 and V: -75.0% vs. CL: -91.5%; p=0.14). Finally, when comparing CF and V, the difference in CFU counts was significantly different both between tap 2 and tap 1 (CF: -90.6% vs. V: -62.1%; p=0.0020) as well as tap 3 and tap 1 (CF: -91.9% vs. V: -75.0%; p=0.02). The determination of drugs level in CSF and its correlation with the CFU counts is underway. Conclusions: In this rabbit model of MRSA meningitis, CF exhibited similar efficacy to V. Future work should utilize an animal model more physiologically similar to humans, such as the pig, to determine if these results were specific to the treatment.
Abstract Title:
Antimicrobial Activity of Cannabidiol against Eskape Pathogens: Inhibitory and Bactericidal Activity against Vancomycin-Resistant Enterococcus faecium, Vancomycin-Intermediate Staphylococcus aureus, and Methicillin-Resistant S. Aureus

Primary Author Block:
L. N. Andrade1, J. C. Ferreira1, N. C. Moreira1, A. W. Zuardi2, J. E. C. Hallak2, J. A. S. Crippa2, A. L. C. Darini1; 1USP - Faculdade de Ciências Farmacêuticas de Ribeirão Preto, Ribeirao Preto, Brazil, 2USP - Faculdade de Med. de Ribeirão Preto, Ribeirao Preto, Brazil

Abstract Body:
Background: ESKAPE pathogens such as Enterococcus faecium and Staphylococcus aureus resistant to vancomycin (and/or S. aureus resistant to methicillin); Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter species resistant to carbapenems (and/or Enterobacteriaceae resistant to third-generation cephalosporins) have been considered “global priority pathogens” for research and development of new and effective antibiotic treatments, according to The World Health Organization. The aim of this study was to investigate the antimicrobial activity of the cannabidiol (CBD), a substance from Cannabis sativa, against ESKAPE pathogens and to evaluate the activity of antibiotics combined to CBD, searching for synergistic/antagonistic effects, against those bacteria. Methods: Type-strains, quality control strains, and clinical strains, including Gram-negative bacilli producing carbapenemase and/or extended-spectrum beta-lactamase (e.g. NDM, SPM, KPC, OXA, and/or CTX-M, SHV); vancomycin-resistant E. faecium (VRE, vanB gene); heterogeneous and vancomycin-intermediate S. aureus (hVISA, Mu3; and VISA, Mu50), and methicillin-resistant S. aureus (MRSA, mecA gene) were studied. Broth microdilution method was used to evaluate the antimicrobial activity of the CBD, according to standard procedure. Two-fold serial dilution (256 - 0.5 μg/mL) of ultrapure CBD (99.9%; BSPG-Pharm, UK) was used to investigate the minimal inhibitory concentration (MIC). In addition, minimum bactericidal concentration (MBC) was also verified by subculturing to agar media without antibiotics or CBD. Besides, meropenem, ceftazidime, cefotaxime, vancomycin or methicillin MICs values were determined in the presence of CBD (256 μg/mL or ½ and ¼ of the MIC). Results: CBD showed antimicrobial activity only against Gram-positive pathogens evaluated, MIC = 2 μg/mL for E. faecium and S. aureus strains (and MIC = 4 μg/mL for hVISA/VISA). CBD MIC values for Gram-negative bacilli were > 256 μg/mL, including Escherichia coli strains, additionally studied. CBD showed MBC = 8 μg/mL for E. faecium and MBC = 64 μg/mL for S. aureus strains. There was no MIC/MBC differences among susceptible and resistant strains evaluated as well as no synergistic/antagonistic effects of antibiotics combined with CBD. Conclusions: CBD showed low MIC values only against Gram-positive pathogens evaluated, and MBC values for E. faecium lower than for S. aureus. No synergistic/antagonistic effects of antibiotics combined with CBD were observed.
Abstract Title:
Antimicrobial Photodynamic Therapy with Methylene Blue and Chlorin-E6 in Enterococcus faecalis

Primary Author Block:
L. S. Sampaio, L. M. de Freitas, C. R. Fontana; São Paulo State Univ. - UNESP, Araraquara, Brazil

Abstract Body:
Background: PDT has been used as adjuvant treatment in periodontics, implantodontics and endodontics to try to eliminate the remaining microorganisms after mechanical treatment. The genus Enterococcus is part of the group of gram-positive, facultative anaerobic bacteria, residents of the gastrointestinal tract, vagina and oral cavity. They survive rash environments, including extreme alkaline pH (9.6) and salt concentrations. It is associated with endodontic infections and presents resistance to intracanal drugs. In addition, PDT has been studied to be applied in root canal faults where Enterococcus faecalis is able to survive as a single organism or as a major component of this flora. The aim of this study was to evaluate the effect of irradiation in switched and continuous mode on antimicrobial Photodynamic Therapy with Methylene Blue and Chlorin-E6 in Enterococcus faecalis. Methods: The therapy was performed in Enterococcus faecalis (ATCC 29212) with Methylene Blue (MB) and Chlorin-E6 at concentrations of 12.5; 25; 50; 75 and 100 µg/mL, and 3 light doses at the wavelength of 660nm (red light): 80, 100 and 120 J/cm², for MB and, 30, 45 and 60 J/cm², for Chlorin-E6. A bacteria suspension with approximately 107 cells/mL was incubated with the photosensitizer in the dark for 5 minutes for MB and 10 minutes for Chlorin-E6 for further irradiation in a LED-based system at wavelength of 660 nm (red light). After treatment, serial dilution was performed to approximately 101 cells/mL, plated on blood agar and incubated at 37°C for 48 hours in anaerobiosis for further counting of colony forming units per milliliter (CFU/mL). Results: The results obtained from the comparison of aPDT with switched and continuous mode for Enterococcus faecalis showed that for the MB at 80 J/cm² the switched mode was more efficient, but when the dose was increased to 100 and 120 J/cm² the two modes were effective in cell death. With Chlorin-E6, we observed that with a dose of 30 J/cm² there was no significant bacterial reduction, and with the doses of 45 and 60 J/cm² the switched mode was more efficient. Conclusions: The results showed that aPDT mediated by MB and Chlorin-E6 with red light in switched irradiation was more efficient than continuous irradiation. The hypothesis is that during the period without irradiation allows reoxygenation of the microorganism, thus providing more oxygen for the photosensitizer to convert to singlet oxygen.
Session Title: CIV01 - Clinical Studies of Adult Infectious Diseases: Staphylococcal and Other Gram-positive Infections
Session Start Date Time: 6/9/2018 11:00:00 AM
Session End Date Time: 6/9/2018 1:00:00 PM
Session Primary Track: Clinical Infections and Vaccines
Abstract Control Number: 5778
Poster Board Number: SATURDAY - 686

Abstract Title:

Primary Author Block:
R. Graham, J-M. Balada-Llasat, P. Pancholi; The Ohio State Univ. Wexner Med. Ctr., Columbus, OH

Abstract Body:
Introduction: Staphylococcus aureus (SA) infections are a burden for the health care system. Timely identification of SA and methicillin resistance (MR) facilitates patient management before surgery. The BD MAXTM StaphSR Assay is a fully automated, qualitative, in vitro diagnostic test for the direct detection of SA and MRSA from nasal swab specimens collected from patients at risk of infection due to nasal colonization. Methods: This study evaluated the clinical performance characteristics of the BD MAXTM StaphSR Assay using BDTM Liquid Amies Elution Swab (ESwab) Collection and Transport System. Molecular tests, culture-based identification methods and antimicrobial susceptibility testing were used as the reference standards for comparison. Results: A total of 160 samples were included in the study. The positivity rate for SA was 42% and 49 % for MRSA. According to the reference methods, the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for SA were 100% for all. The sensitivity, specificity, PPV and NPV for MRSA were 96.5%, 100 %, 100 % and 97.2% respectively. The limit of detection (at 95% confidence level) was determined at 5.73 x104 cfu/ml for SA and 1.23x105 cfu/ml for MRSA. Conclusions: the BD MAXTM StaphSR Assay is a sensitive and specific assay for the direct detection of SA and MRSA from nasal ESwab specimens.
Abstract Title:
Prediction Model for Methicillin-Resistant Staphylococcus aureus (MRSA) Bacteremia among Patients with Community-Onset MRSA Skin and Skin-Structure Infections

Primary Author Block:
S. C. J. Jorgensen1, A. M. Lagnf1, S. Bahatia1, S. L. Davis2, M. Rybak1; 1Wayne State Univ., Detroit, MI, 2Henry Ford Hosp., Detroit, MI

Abstract Body:
Background: The emergence, spread and persistence of methicillin-resistant Staphylococcus aureus (MRSA) as a cause of community-onset (CO) acute bacterial skin and skin structure infections (ABSSSI) has resulted in substantial changes to the epidemiology and management of these infections. Although bloodstream infection (BSI) was once considered an uncommon complication of CO ABSSSI, evidence suggests the MRSA USA300 clone may have an enhanced propensity to cause invasive infections. The high morbidity and mortality associated with MRSA BSI underscores the need to identify patients at increased risk for this complication. Objective: We sought to construct a MRSA BSI predictive model for patients with CO MRSA ABSSSI based on characteristics readily assessable at the time of initial evaluation. Methods: A multi-center, retrospective, case-control design was used. The population of interest included adult patients satisfying the following criteria:1.) admitted through the emergency department between 2010 and 2017; 2.) ABSSSI primary diagnosis; 3.) MRSA positive skin specimen collected within 48 hours of admission; and 4.) blood culture collected within 48 hours of admission. Cases were defined as patients who met the above criteria and had MRSA isolated from the index blood culture. Patients with negative or contaminated blood cultures served as controls. Independent risk factors for MRSA BSI were identified through logistic regression analysis. The predictive model was derived using a regression coefficient-based scoring method. Results: A total of 307 patients were included (155 cases, 152 controls). Independent predictors of BSI, in descending order of adjusted odds ratio, were: purulent cellulitis, temperature < 35.6 C or > 38 C, chronic kidney disease, IV drug use, white blood cell count > 11 x 109/L, heart rate > 100 beats/min, body mass index < 25 kg/m2, and non-upper extremity infection site. The area under the receiver operator curve (AUROC) of the final regression model was 0.855 (95% CI 0.813 - 0.893). The AUROC of the weighted coefficient-based BSI-predictive score (BSI-PS) was 0.844 (95% CI 0.801 - 0.887). Using a threshold BSI-PS of ≥ 8 (range 0 to 35) demonstrated 94.1% and 40.1% sensitivity and specificity, respectively. Conclusions: Our findings demonstrate a weighted combination of 8 independent variables readily assessable at the time of initial evaluation can be used to predict, with high discrimination, MRSA BSI among patients hospitalized with CO MRSA ABSSSI. Validation is required before wide-spread clinical use.
Session Number: 239
Session Type: Poster
Session Number: 239
Session Type: Poster
Session Title: CIV01 - Clinical Studies of Adult Infectious Diseases: Staphylococcal and Other Gram-positive Infections
Session Start Date Time: 6/9/2018 11:00:00 AM
Session End Date Time: 6/9/2018 1:00:00 PM
Session Primary Track: Clinical Infections and Vaccines
Abstract Control Number: 5780
Poster Board Number: SATURDAY - 688

Abstract Title:
Analysis of Prognosis Factors Related with Mortality of Staphylococcus aureus Bacteremia in Our Facility

Primary Author Block:

Abstract Body:
Background: Staphylococcus aureus is one of the causes of healthcare-associated bacteremia of hospitalized patients in Japan. The mortality of S. aureus bacteremia (SAB) is still higher and it lengthens hospitalization. The mortality rate of SAB indicates 20~30%. 30-day mortality has been analyzed previously. It is reported that SAB is a life-threatening infection with an incidence rate ranging from 20 to 50 cases /100,000 population per year. It has been not clarified what is the reason why the mortality is high in SAB. Methods: This survey was conducted retrospectively. The participants were administered in our facility from Jan. in 2007 to Nov. in 2014. The entry criterion for participating was a single blood culture, which was tested to be positive for Staphylococcus aureus within 48 hours after administration. Factors were analyzed multi-variable quantitatively using logistic regression analysis system. Results: MRSA Morbidity was 57.9% (73/126) and MSSA was 42.1% (53/126). The most frequent source of SAB was primary bacteremia (80.2%;101/126). It included catheter related infection, febrile neutropenia, and undetected focus of infection. 14 day mortality was 11.1% (14/126). In SAB, independent risk factors were age over 70 y.o. (Odds Ratio (OR) 4.7:95% CI (CI) 1.04-21.13), existence of malignancies (OR 4.5:CI 1.10-17.96), starting day of antibiotics therapy (OR 0.2:CI 0.05-0.79), TTP (Time from taking culture to positive detection) less than 12 hours (OR 4.9:CI 1.18-20.03), the Pitt bacteremia score more than 3 (OR 4.2:CI 1.15-15.31). Between each 2 groups, significant prognostic factors were related to 1) the delay of adequate treatment 2) high severity score. Both diagnosis and proper antibiotics administration on early stage of SAB are very crucial to improve the prognosis. As for proper usage of antibiotics, it should be avoided administering anti-SAB antibiotics to all the patients with SAB. Prophylaxis administrations are not always correct. In addition we need to consider about risk factors such as the period of administration, previous medication and drug sensitivity. Conclusions: Concerned with SAB, 14 day mortality has not been analyzed in previous studies. This time we have shown prognosis factors using 14 day mortality.
Abstract Title:

Primary Author Block:
M. Równicki, K. Szymanek-Majchrzak, A. Młynarczyk, A. Sawicka-Grzelak, G. Młynarczyk; Med. Univ. of Warsaw, Warsaw, Poland

Abstract Body:
Background: The rising use of macrolides and lincosamides has led to an increased resistance to macrolides, lincosamides, streptogramin B (MLSB) in many bacteria and MRSA (mecillin resistant Staphylococcus aureus) are one of the most important. Resistance to MLSB in S. aureus is commonly encoded by erm genes, which can be constitutive MLSB (cMLS\text{B}) or inducible MLSB (iMLS\text{B}). The purpose of this study was to compare the frequency of cMLS\text{B}, iMLS\text{B}, and MS phenotypes as well as the frequency of ermA and ermC genes amongst clinical isolates of MRSA from 2012 and 2014. Methods: A total of 189 isolates of methicillin-resistant S. aureus (MRSA) were collected in 2012 and 2014 in the Department of Microbiology of Clinical Hospital in Warsaw, Poland. The frequency of iMLS\text{B} resistant isolates was determined using D-test. For all erythromycin resistant strains, a PCR reaction was performed for detection of ermA and ermC genes. Results: Among 189 MRSA, 160 were resistant to erythromycin and among them 87 were resistant also to clindamycin (cMLS\text{B} phenotype). iMLS\text{B} and cMLS\text{B} resistance phenotypes had a frequency of 28% and 54% respectively. Among isolates with iMLS\text{B} phenotype, 8 contained ermA gene, 35 isolates ermC gene, and 3 isolates both ermA and ermC genes. In the group of cMLS\text{B} phenotype 53 isolates contained ermA gene, 20 isolates ermC and 13 isolates both genes ermA and ermC. Conclusions: In the current study, cMLS\text{B} was the most frequent phenotype. ermA gene was the most frequent gene found in cMLS\text{B} and ermC in iMLS\text{B}.
Abstract Title:
Outstanding Abstract Award: Incidence of Definite Endocarditis with Staphylococcus aureus Bacteremia among Patients with Both Hematologic and Non-Hematologic Malignancies

Primary Author Block:

Abstract Body:
Background: Staphylococcus aureus bacteremia (SAB) is often complicated with infective endocarditis (IE). Studies show low rates of IE (0%-1.3%) in patients (pts) with hematologic malignancies (HM) possibly due to low platelets and early initiation of antibiotics. Sensitivity of TTE for native valve IE is ~70% vs. 96% for TEE. The utility of TEE among neutropenic patients is unclear. We evaluated incidence of definite IE (def-IE) from SABs in pts with hematologic malignancies (HM) and solid tumors (ST) and reviewed whether hematologic parameters affected incidence of def-IE. Methods: Retrospective review of pts ≥ 18 years with HM and ST who had SAB and echocardiogram (ECHO) within 30 days of their SAB between 1/1/11 to 12/31/16. Positive ECHO was considered diagnostic of def-IE. White blood counts (WBCs) and platelets at time of bacteremia, number of positive blood cultures, Duke’s criteria, and 30-day mortality were evaluated. Data was analyzed using the chi-square or student’s t-test. Results: 129 pts, mean age 55 ± 16 years, 55% males, 62% HM, 30% leukemia, 51% hematopoietic cell transplant recipients, 26% had MRSA. 85/129 had TTEs and 44/129 had TEEs or both. Based on ECHO findings, 11 pts had def-IE (7 HM vs. 4 ST). HM pts: 5 TEEs, 1 TTE, 1 had both, were positive. ST pts: 2 TEEs, 2 both, were positive. Though not significant, incidence of IE was lower in pts with WBCs ≤ 0.5 K/uL (9% vs. 91%, p=0.29), platelets ≤ 50 K/uL (9% vs. 91%, p=0.91). 7/11 had bacteremia for 1 day, 4/11 had bacteremia for 4-5 days. 30-day mortality rate was 11.8% in SAB pts. 30-day mortality was 55% (6/11) in def-IE. Conclusion: Def-IE incidence was higher than expected in HM pts. The majority of HM pts had upfront TEE limiting the comparison to TTE. Though not statistically significant, def-IE incidence was lower in pts with lower WBCs and platelets. TEE should be considered in HM pts in the context of higher than expected rate of def-IE in SAB.
Abstract Title:

Primary Author Block:
T. Okada; Okada Med. Clinic, Brisbane, Australia

Abstract Body:
Background: Based on mainly phenotypic features, the name of motile intracellular Gram-stain-negative coccoid bacteria that are associated in non-Helicobacter and Helicobacter gastropathies have been proposed as Okadaella gastrococcus (ATCC BAA-2258, MT/JULY 2010T ). However, genotypic analysis using 16S rRNA suggests the bacteria could belong to Genus Streptococcus. The bacteria have been demonstrated in the classic gastric carcinogenic cascades and reported among patients with cystic fibrosis and stroke. The aim of this study was to investigate the unidentified coccoid bacteria. Methods: Unidentified coccoid bacteria isolated from gastric biopsy samples of two Japanese males (28 and 43 years old) and strain MT/JULY 2010T were used. Motility was examined by hanging drop test with Indian ink. Gram reaction was tested by standard Gram stain and Favor method. Biochemical characteristics were examined by RapID ANA II, RapID STR, RapID NH, rapid ID 32 A and rapid ID 32 STREP identification systems. Hydrogen peroide (3% and 6%), DNase agar and lead acetate strip were use for catalase, DNase and H2S production, respectively. The determination of 16S rRNA gene phylogeny was performed at TechnoSuruga laboratory. H&E, Diff-Quick and WSS stains were used in the histology examination. Results: Histological examination demonstrated the intracellular coccoid bacteria in the background of H. pylori positive active chronic gastritis. Lactic acid producing unidentified coccoid bacteria were alpha-hemolytic, Gram-stain-variable, facultative anaerobic and motile. Urease, catalase, oxidase and PYR were negative. Arginine aminopeptidase, alanine arylamidase, glutamic acid decarboxylase, DNase and H2S gas were positive. These strains could be differentiated by biochemical characteristics. Two strains were partially vancomycin sensitive. The results of 16S rRNA gene sequencing analysis of these strains were 99.0% closely related with S. parasanguinis. They were found to form a distinctive monophyletic group in the phylogenetic tree. Conclusions: Unidentified coccid bacteria co-exist with H. pylori. The results support that the novel bacteria belong to Genus Streptococcus. A novel species Streptococcus mobilis sp. nov. (S-1,S-2 and S-3) is proposed which should replace the previous name of O. gastrococcus. Whole-genome core sequences and multilocus sequence analysis for taxonomic evaluation are warranted as the bacteria belong to the Mitis group of the genus streptococci.
Abstract Title:
Group B Streptococcus Infection among Pregnant Women and Neonatal Colonization Rate in Patients from A Tertiary Inst. Southwestern Nigeria

Primary Author Block:
T. J. Akinlolu; Obafemi Awolow Univ., Ile-Ife. Osum State, Nigeria

Abstract Body:
This study was carried out to evaluate Group B Streptococcus infection among pregnant women and neonatal colonization rate in patients attending Obafemi Awolowo University Teaching Hospital Complex. It also determined the antibiotic susceptibility pattern, also evaluated GBS status of the subjects using demographic and clinical parameters. These were with a view to provide information on the prevalence of GBS infection in Nigeria. One hundred and seventy samples (170) were collected from consenting mothers and neonute between June 2016 and January 2017. Ninety-Eight (98) GBS isolates were recovered from vaginal, rectum of the pregnant woman at the point of labour and Umbilical cord of the neonate within 24 hrs of birth. Cultures for the isolation and identification of Group B Streptococcus (GBS) were carried out using the Centre for Disease Control (CDC) recommended microbiological methods (Lim broth, Chromogenic agar, Blood agar). The Kirby-Bauer disk-diffusion method was employed to determine antibiograms of GBS isolates in accordance with Clinical and Laboratory Standards institute (CLSI). The presence of resistant genes was examined using Polymerase Chain Reaction (PCR). The result shows that the prevalence rate of GBS maternal and neonatal colonization were 29.4% and 20.6% respectively while 4% of the colonized neonates had nosocomial GBS colonization. There was no significant association between GBS colonization status and age (p >0.05), parity (p >0.05), obstetric risk factors (p >0.05) and sex of neonate. No incidence of GBS infection observed during the study. Resistance to augmentin was observed to be as high as 88.8%, ampicillin (60.2%), penicillin (47%), tetracycline (34.7%), ceftriaxone (19.4%), clindamycin (13.3%), vancomycin (10.2%) and erythromycin (7.1%). One of the 8 representatives of the multidrug resistant isolates harboured tetM gene while other resistant genes examined (tetO and linB) were negative in all MDR isolates. In conclusion, this study established high prevalence of maternal and neonatal GBS colonization among pregnant women and neonates while nosocomial infection was also implicated in GBS colonization among neonates. However, further research is required using larger sample size and multiple centers for adequate extrapolation into the general population.
Abstract Title:
Group B Streptococcal Infections Resistant to Vancomycin? A New Threat

Primary Author Block:

Abstract Body:
Group B Streptococcus (GBS) can be a source of significant invasive infection. Usually, GBS is universally susceptible to penicillins (PCN). There has been an increase of GBS resistant to macrolides and quinolones. Patients with PCN allergy are often treated with vancomycin. There have been only two reported cases of vancomycin resistant (VR) GBS in the US. Only one needed alternate therapy. VR GBS was reported in two Streptococcus agalactiae isolates where a vanG element insertion was noted within a conserved chromosomal site. A 47 year old male with a past medical history of Complex Regional Pain Syndrome type II with history of recurrent MRSA and GBS lower extremities cellulitis infections, was readmitted for lower extremity cellulitis and high fevers. Patient was "allergic to Keflex" and was started empirically on vancomycin. During prior admissions, he responded promptly to vancomycin. While receiving vancomycin he remained febrile, toxic, confused with a flushed facies. His cellulitis worsened, began to spread up towards his groin. Previously his cellulitis had been localized to below the knee. On further questioning, the patient revealed he previously tolerated amoxicillin. Therefore, treatment was switched to ampicillin. The patient’s rash disappeared; his fevers resolved after receiving the second dose of ampicillin. Vancomycin is frequently used in treatment of Streptococcal infections in PCN allergic patients. Laboratories do not normally perform routine susceptibilities to Streptococci. With reports of emerging GBS resistance to vancomycin, we recommend GBS susceptibility testing. E faecalis was believed to be the source of the VanG-I element conferring resistance in S.agalactiae in the 2 reported cases. It is interesting to note, that this patient had a E faecalis UTI during previous admission. Another possible contribution to acquisition of vancomycin resistance by GBS may have been multiple exposures to vancomycin through prior treatments. <a href="http://files.abstractsonline.com/CTRL/d5/4/441/a45/387/474/fbb/dca/3d7/b88/cb7/e5/g3762_1.jpg" target='_blank' address=no >img src="http://files.abstractsonline.com/CTRL/d5/4/441/a45/387/474/fbb/dca/3d7/b88/cb7/e5/g3762_1.jpg" alt="" border="0" width="600" height="534" /></a>
Abstract Title:
Clinical Characteristics and Outcome of Streptococcus Tigurinus Infective Endocarditis

Primary Author Block:

Abstract Body:
Background: Streptococcus tigurinus was firstly described as a new streptococcal species in 2012 being in 2016 considered as Streptococcus oralis subspecies. Since its initial description, it has been documented as a causative agent of infective endocarditis (IE). The objective of the present study was to compare the clinical characteristics of IE caused by S. tigurinus and of by other mitis group streptococci (MGS). Methods: Retrospective nationwide study, performed in 10 Spanish hospitals located in 6 different provinces. Clinical IE data were prospectively collected between 2008 and 2016 according to a pre-established protocol. Alpha-hemolytic streptococci isolates were identified by sequencing fragments of their 16S rRNA gene, sodA and groEL genes. Overall, the study included 59 cases of the 240 IE caused by MGS: 14 caused by S. tigurinus and 45 by others MGS (25 S. oralis, 11 S. mitis, 9 other species). All S. tigurinus had been previously identified by phenotypic methods as S. oralis and was found in most hospitals of the study. Statistical analysis: the unpaired t-test or the chi-square test (Fisher’s exact test when appropriate) were used to compare continuous and categorical variables, respectively. All statistical analyses were performed using online GraphPad software. Results: Comparing IE caused by S. tigurinus and other MGS, patients’ median age was 65.2 (SD±17.9) and 57.4 (SD±15.8) years, respectively (p=0.124). There were no relevant statistical differences in EI between both groups (Table). Aortic, mitral or both valves were affected in all but one episode, being vegetations more frequent in the aortic valve. Pseudoaneurysms were only observed in 4 patients with MGS EI, and in-hospital (14% and 9%) and 1-year (14% and 8%) mortalities, were similar in both groups.
<table>
<thead>
<tr>
<th>S. tigurinus (n=14)</th>
<th>Other MGS (n=45)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Data of acquisition</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age in years (average, range)</td>
<td>65.2 (19-87)</td>
<td>57.4 (28-86)</td>
</tr>
<tr>
<td>Female</td>
<td>6 (43%)</td>
<td>7 (16%)</td>
</tr>
<tr>
<td>Risk factors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous infective endocarditis</td>
<td>2 (14%)</td>
<td>7 (16%)</td>
</tr>
<tr>
<td>Heart failure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>14%</td>
<td>11%</td>
</tr>
<tr>
<td>Aortic valve</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aortic</td>
<td>5/12 (42%)</td>
<td>24/44 (55%)</td>
</tr>
<tr>
<td>Mitral</td>
<td>5/12 (42%)</td>
<td>11/44 (25%)</td>
</tr>
<tr>
<td>Aortic + mitral</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aortic</td>
<td>5/12 (42%)</td>
<td>6/44 (14%)</td>
</tr>
<tr>
<td>Mitral</td>
<td>5/12 (42%)</td>
<td>6/44 (14%)</td>
</tr>
<tr>
<td>Aortic + tricuspid + mitral</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vegetations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mitral</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aortic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mitral + tricuspid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aortic + mitral + tricuspid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aortic + tricuspid + mitral + tricuspid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Condition</td>
<td>S. tigurinus</td>
<td>Other MGS</td>
</tr>
<tr>
<td>---------------------------------</td>
<td>-------------</td>
<td>-----------</td>
</tr>
<tr>
<td>Perforation</td>
<td>9 (20%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Abscess</td>
<td>1 (7%)</td>
<td>0.666</td>
</tr>
<tr>
<td>Pseudoaneurysm</td>
<td>1 (4%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Pseudoaneurysm + perforation</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Clinical course</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Embolism</td>
<td>5/13 (38%)</td>
<td>0.483</td>
</tr>
<tr>
<td>New heart failure</td>
<td>5 (36%)</td>
<td>0.620</td>
</tr>
<tr>
<td>Persistent bacteremia</td>
<td>2/44 (5%)</td>
<td></td>
</tr>
<tr>
<td>Surgery</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Indicated</td>
<td>9 (64%)</td>
<td>0.602</td>
</tr>
<tr>
<td>Days hospital stay: average</td>
<td>28.7 SD± 19.4 (5-74)</td>
<td>33.2 SD± 20.7 (3-106)</td>
</tr>
<tr>
<td>In-hospital mortality (%)</td>
<td>2 (14%)</td>
<td>0.358</td>
</tr>
<tr>
<td>1-year mortalities</td>
<td>2 (14%)</td>
<td>0.620</td>
</tr>
<tr>
<td>Recurrence</td>
<td>2 (14%)</td>
<td>0.602</td>
</tr>
<tr>
<td>Antibiotic treatment</td>
<td>2/38 (5%)</td>
<td>0.114</td>
</tr>
<tr>
<td>Beta-lactams alone</td>
<td>5 (36%)</td>
<td>0.360</td>
</tr>
<tr>
<td>Beta-lactams + gentamicin</td>
<td>5 (36%)</td>
<td>0.360</td>
</tr>
<tr>
<td>Other combinations</td>
<td>4 (29%)</td>
<td>0.738</td>
</tr>
</tbody>
</table>

Conclusions: IE caused by S. tigurinus did not clinically differ from that caused by other MGS. Clinical course and outcomes were in general better than IE described for non-viridans streptococci.
Abstract Title:
Clinical and Bacteriological Characteristics Of Ba813 Harboring Bacillus Cereus in Bloodstream Infection in Hosp. Setting

Primary Author Block:
T. Aoyagi, M. Kawauchi, H. Kanamori, K. Ohsima, M. Yoshida, K. Tokuda, M. kaku; Tohoku Univ., Sendai, Japan

Abstract Body:
Background: Bacillus cereus, contaminant of the hospital environment, causes nosocomial bloodstream infection and develops occasionally central nervous system (CNS) infection. We previously reported that B. cereus strains harboring the gene of Ba813, a specific chromosomal marker of B. anthracis, were isolated from hospital environment and might be associated with nosocomial infection. However, it was unclear whether B. cereus harboring Ba813 affected clinical characteristics. Methods:Fifty three patients with B. cereus bacteremia, including two cases with CNS complication, were enrolled from January 2009 to December 2012. B. cereus isolates were evaluated for the gene presentation of Ba813 and B. anthracis-related and food poisoning-related virulence factors, multilocus sequencing typing (MLST) and biofilm formation. We analyzed clinical characteristics between bacteremia due to B. cereus with and without Ba813. Results: 17 of 53 (32%) B. cereus isolates had the Ba813, and these strains were divided into two different groups by MLST analysis. One group (5/17) in Ba813 (+) B. cereus were closely related to B. anthracis and the highly virulent B. cereus strain 03BB102. However, all of Ba813 (+) B. cereus isolates did not possess B. anthracis-related virulence genes, and showed no difference in the prevalence of the enterotoxin gene compared with Ba813 (−) strains. Although biofilm formation was observed in all B. cereus isolates, its ability was significantly lower in Ba813 (+) B. cereus isolates compared to Ba813 (−) strains. All patients had peripheral or central vascular catheter, but no difference in catheter types was observed between two groups. No significantly differences of 30-days mortality, disease severity, persistent bacteremia, duration of therapy and length of hospital stay were found between Ba813 (+) and Ba813 (−) B. cereus isolates, however, B. cereus obtained from two cases with CNS complication did not possess the Ba813. Conclusions: Inpatients with indwelling vascular catheter is risk for B. cereus bloodstream infection, however, B. cereus harboring Ba813 or B. cereus strains with high formed biofilm may not impact on clinical characteristics and outcome in B. cereus bacteremia.
Abstract Title:
Duration of Bacteremia According to Methicillin Resistance and Primary Foci of Infection in Staphylococcus aureus Bacteremia

Primary Author Block:

Abstract Body:
Backgrounds: It is unknown how long Staphylococcus aureus bacteremia (SAB) persists after an administration of susceptible antibiotic. We aimed to describe the duration of SAB according to methicillin resistance and primary foci of infection. Methods: Cases of all adult patients with SAB prospectively collected from 15 hospitals in Korea over 9-year period were reviewed. Patients without follow-up blood cultures who survived or who died after two days from the onset of SAB were excluded. The duration of SAB was defined as a number of calendar-day between the date of administration of susceptible antibiotic after first positive blood culture for S. aureus and the last date of positive blood culture. Kaplan-Meier curves for negative conversion rates were plotted and compared using log-rank test. Patients who died during SAB were censored at the time of death. Results: Among 2,239 SAB cases, 1,574 cases were included in the analyses after excluding 49 cases of contamination, 100 of polymicrobial bacteremia, 175 administered with non-susceptible antibiotic, and 341 without follow-up blood cultures. Numbers of methicillin-resistant SAB (MRSAB) and methicillin-susceptible SAB (MSSAB) were 854 (54.3%) and 720 (45.7%), respectively. The duration of MRSAB was longer than that of MSSAB (median [IQR], 1 [0-6] days in MRSAB vs. 1 [0-3] days in MSSAB, P<0.001). The durations of bacteremia in infective endocarditis (median [IQR], 5 [1-11] days in MRSAB, 3 [1-5] days in MSSAB), bone & joint infection (median [IQR], 5 [1-12] days in MRSAB, 1 [1-5] days in MSSAB), and endovascular infection (median [IQR], 2 [1-9] days in MRSAB, 1 [1-4] days in MSSAB) were longer than that of skin & soft tissue infection (median [IQR], 1 [0-5] days in MRSAB, 1 [0-2] days in MSSAB). Conclusions: The durations of SAB are significantly different according to methicillin resistance and primary foci of infection. Treatment failure and persistence of SAB should be defined accounting for those factors.
Increased Clindamycin Use in Group A Streptococcus Bacteraemia with No Observed Survival Benefit

Primary Author Block:
O. M. Williams1, A. Cochrane2, R. Brindle3; 1Univ. Hosp. Bristol NHS Fndn. Trust, Bristol, United Kingdom, 2Raigmore Hosp., Inverness, United Kingdom, 3Univ. of Bristol, Bristol, United Kingdom

Abstract Body:
Background: As there are no randomised controlled trials to inform on the use of adjuvant clindamycin in invasive Group A Streptococcal (GAS) disease, decisions to prescribe clindamycin are based on basic scientific and observational data. We therefore sought to determine the extent and nature of clindamycin use in patients with GAS bacteraemia, and analyse the effects of any changes in prescribing practices over time.

Methods: A retrospective case note review was conducted of patients with confirmed GAS bacteraemia from ten hospitals in the South West of England over the period between 2006 and 2011.

Results: In total, 391 cases were identified over the 5 year period. Data from 81 cases was reviewed, of which 38 (46.9%) received clindamycin. Clindamycin use increased significantly over time (p=0.013), with no observed change in 30-day all-cause mortality.

Conclusions: Clindamycin use for GAS bacteraemia increased over time with no observed concomitant change in all-cause 30-day mortality.
Abstract Title:
Outstanding Abstract Award: Evaluation of Vancomycin Or Daptomycin Alone versus Combination with Beta-Lactams in the Treatment of Methicillin-Resistance Staphylococcus aureus Bloodstream Infections (BSI)

Primary Author Block:
N. Sabagha, E. J. Zasowski, T. D. Trinh, A. M. Lagnf, S. Bhatia, M. J. Rybak; Wayne State Univ., Detroit, MI

Abstract Body:
Background: Vancomycin (VAN) has been the antibiotic of choice to treat methicillin-resistant Staphylococcus aureus (MRSA) infections. Despite attempts to optimize VAN therapy over the years, treatment failures for bloodstream infections (BSI) have not improved. Studies have also demonstrated that daptomycin (DAP) use after VAN failure increases the potential for DAP resistance. Combination therapy may address these limitations. We evaluated the impact of combination VAN or DAP with a beta-lactam (BL) on patient outcomes with MRSA BSI. Methods: This is a retrospective cohort study comparing outcomes of patients with MRSA BSI treated with monotherapy or combination therapy. Inclusion criteria: adults with >=1 positive MRSA blood culture initiated with monotherapy or combination therapy <72h after culture collection. Primary outcome: BSI >=7d. Secondary outcomes: 30d mortality, 60d BSI recurrence, and length of stay. Multivariable logistic regression was conducted to determine the independent predictors of BSI ≥7d. Result: A total of 505 patients were included (140 monotherapy, 365 combination). Mean (SD) age was 60 (16.3) y, 64% males, and 79.2% African-American. Median (IQR) Charlson Comorbidity Index and APACHE II score were 3 (1-5) and 17 (11-22), respectively. The most common sources were: infective endocarditis (IE) 22.8%, skin and soft tissue 20.9%, pneumonia 20.5%, intravenous catheter 19.6%, and bone/joint 15%. Outcomes are presented below:

<table>
<thead>
<tr>
<th></th>
<th>Monotherapy (VAN/DAP) (n=140)</th>
<th>Combination therapy VAN or DAP + BL (n=365)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BSI &gt;=7d, n (%)</td>
<td>20 (22%)</td>
<td>43 (12%)</td>
<td>0.007</td>
</tr>
<tr>
<td>30d mortality, n (%)</td>
<td>14 (10%)</td>
<td>16 (16%)</td>
<td>0.067</td>
</tr>
<tr>
<td>Antibiotic switch due to failure, n (%)</td>
<td>21 (15%)</td>
<td>33 (9%)</td>
<td>0.170</td>
</tr>
<tr>
<td>Nephrotoxicity, n (%)</td>
<td>28 (8%)</td>
<td>23 (16%)</td>
<td>51 (14%)</td>
</tr>
<tr>
<td>----------------------</td>
<td>---------</td>
<td>----------</td>
<td>----------</td>
</tr>
<tr>
<td>Length of stay in days, median (IQR)</td>
<td>15 (10-23)</td>
<td>13 (9-19)</td>
<td>0.027</td>
</tr>
</tbody>
</table>

In regression, combination therapy was protective (aOR 0.51; 95% CI 0.28-0.94), while IE (aOR 4.0; 95% CI 2.4-6.7), diabetes with end stage organ damage (aOR, 1.89; 95% CI, 1.1-3.0), bone/joint source (aOR 1.97; 95% CI 1.0-3.8), and APACHE II score (aOR 1.04; 95% CI 1.0-1.1), were associated with BSI >=7d. Conclusion: Combination VAN or DAP with beta-lactam was protective against MRSA BSI >=7 d and may improve patient outcomes with MRSA BSI. Additional studies are needed to confirm these findings.
Abstract Title:
Beta-Lactam versus Fluoroquinolone Therapy for Treatment of Streptococcus Anginosus Group Bacteremia

Primary Author Block:

Abstract Body:
Background The incidence of Streptococcus anginosus (SAG) bacteremia has been increasing at our institution. No guideline recommendations currently exist for treatment of SAG bacteremia. Beta-lactams have historically been the drug of choice due to predictable in vitro susceptibility to these agents. Other agents, such as fluoroquinolones, are active in vitro and have been used for odontogenic infections caused by SAG. Fluoroquinolones have an advantage over beta-lactams because of the excellent bioavailability of oral formulations. However, limited clinical data exist regarding their use in bacteremia. This study’s primary objective was to compare treatment failure in patients with SAG bacteremia who were treated with beta-lactam versus fluoroquinolone therapy. Methods This was a single-center, retrospective study of patients >18 years of age who had at least one positive SAG blood culture and received either beta-lactam or fluoroquinolone therapy. Patients with polymicrobial bacteremia and multiple antibiotics active against SAG were excluded from analysis. The primary outcome was treatment failure: a composite endpoint of recurrence of bacteremia within 30 days of treatment initiation, 30-day readmission from end of therapy for an infectious complication, and in the fluoroquinolone group, a switch back to a beta-lactam antibiotic. Results Thirty-seven patients were evaluated. The hepatobiliary system was the most common identifiable source of SAG bacteremia. The median duration of therapy was 25 days (range, 4 to 58). Treatment failure occurred in 10% of patients (1/10) treated with a fluoroquinolone and 7% of patients (2/27) treated with a beta-lactam. One fluoroquinolone-treated patient and two beta-lactam-treated patients experienced a 30-day readmission for an infectious complication. Two patients in the beta-lactam group died within 30 days of treatment initiation. Conclusion Treatment failure was similar between patients receiving a beta-lactam or a fluoroquinolone for the treatment of S. anginosus group bacteremia. However, a larger study is needed to confirm these findings.
Adjuvant Azithromycin for Bacteremic Pneumonia Due to Methicillin-Resistant Staphylococcus aureus Pneumonia (MRSA PNA) complicates 5% to 20% of cases with associated mortality rates up to 6-fold higher than for MRSA PNA without BSI. Macrolides have demonstrated favorable immunomodulatory effects in experimental models and have been associated with improved clinical outcomes in a number of inflammatory lung conditions. Furthermore, sub-inhibitory macrolide concentrations exhibit anti-virulence effects against S. aureus. Objective: To investigate clinical outcomes associated with early azithromycin (AZM) use in patients with MRSA PNA and BSI Methods: Retrospective, observational cohort study among adult patients with MRSA BSI and PNA admitted to the Detroit Medical Center between 2008 and 2017. Patients with a positive Legionella pneumophila urinary antigen or isolation of an atypical pathogen from a respiratory or blood specimen were excluded. The primary outcome was 30-day mortality among patients who received at least 1 dose of AZM within 48 hours of blood culture collection compared to those who received no AZM. Multivariable logistic regression was conducted to examined the independent association of AZM and 30-day mortality. Results: A total of 87 patients were included (AZM 27 vs. no AZM 60). The majority were male (62.1%) with a mean (± SD) age of 63.2 (± 14) years. A lower proportion of patients in the AZM group were admitted from a skilled-nursing facility or outside hospital (29.6% vs. 55.0%; P = 0.028) or met criteria for hospital-acquired/ventilator-associated PNA (11.1% vs. 43.3%; P = 0.003). However, there were no differences in the median [IQR] Charlson Comorbidity Index (3 [2 - 6] vs. 3 [1 - 5]; P = 0.498) or APACHE II score (28 [22 - 32] vs. 25 [19 - 33]; P = 0.762). Primary MRSA antibiotic treatment was similar in both groups with most (95.0% vs. 92.6%; P = 0.655) receiving initial vancomycin. Thirty-day mortality trended lower among patients in the AZM group (25.9% vs. 45.0%; P = 0.092). On multivariable analysis, APACHE II score greater than 21 was independently associated with increased 30-day mortality (aOR 5.544, 95% CI 1.779 - 17.276; P = 0.003), while receipt of AZM was independently associated with decreased 30-day mortality (aOR 0.314, 95% CI 0.108 - 0.908; P = 0.033). Conclusions: The early use of AZM among patients with MRSA PNA and BSI was independently associated with decreased 30-day mortality. Future studies, including a larger number of patients, are needed to confirm these preliminary findings.
Efficacy of Omadacycline and Linezolid against Characterized Drug Resistant S. Aureus from Combined Phase 3 Absssi Studies

Background: Omadacycline (OMC), a novel aminomethylcycline antibiotic, is in clinical development as a once-daily oral and intravenous monotherapy for community-acquired bacterial pneumonia and acute bacterial skin and skin structure infection (ABSSSI). Here we report the clinical outcomes of OMC or linezolid (LZD) treatment when methicillin-resistant (MRSA) or multidrug-resistant (MDR) S. aureus (SA) was the baseline pathogen in the combined IV/oral and oral only OMC in Acute Skin and Skin Structure Infections Studies (OASIS).

Methods: Isolates were obtained from subjects at the screening visit prior to initiation of antibiotic therapy. MIC testing was conducted by ACM Global Laboratories (Rochester, NY) or Eurofins Central Laboratory (Lancaster, PA) by broth microdilution according to CLSI M100-S25 using custom made frozen panels from Thermo Fisher Scientific (Cleveland, OH). Quality control and interpretation of results (susceptible, intermediate, or resistant) were performed in accordance with CLSIM100-S25. The quality control organism was SA ATCC 29213 and results were all within the recommended ranges.

Isolates of SA were selected for PCR testing based on the initial oxacillin MIC result. All isolates with an oxacillin MIC >2 µg/mL were selected for detection of mecA and pvl genes by multiplex real time PCR.

Results: Antibiotic resistance was common among SA isolates with 61.3% (466/760) resistant to ≥1 antibiotic class, while 35.1% (267/760) were resistant to ≥3 antibiotic classes (MDR). The rate of clinical success at the post-treatment evaluation (PTE) with OMC was 81.0% (111/137) when MDR SA was present, comparable to SA overall at 83.0% (312/376). Clinical success at PTE with LZD occurred in 82.3% (107/130) of subjects when MDR SA was present and 81.3% (312/384) with SA overall. MRSA was identified in 330/1018 subjects (32.4%). Clinical success rates at PTE for subjects with MRSA were high in each treatment arm; OMC 146/173 (84.4%), LZD 128/157 (81.5%). Similar rates were seen with MRSA across infection types with OMC 70/83 (84.3%), 47/59 (79.7%), 29/31 (93.5%) and LZD 69/86 (80.2%), 39/48 (81.3%), 20/23 (87.0%) for wound infection, major abscess, and cellulitis/erysipelas, respectively.

The virulence factor PVL was widespread, present in 89.3% of characterized MRSA isolates. Clinical success rates at PTE for treatment of subjects with PVL+ MRSA were high; OMC 125/148 (84.5%), LZD 112/135 (83.0%).

Conclusions: Successful treatment outcomes were observed with OMC for the majority of S. aureus isolates in ABSSSI, even when MDR or PVL+.
Abstract Title:
Comparative Study for the Rapid Detection and Genotyping of Mtb and Rif / Inh Resistant Mtb Mutants with Gene Flow Hybridization and Conventional Pcr

Primary Author Block:
M. F. Ali1, M. U. Rehman1, R. Ghani2; 1Dadaboy Inst. of Higher Ed., Karachi, Pakistan, 2Rubina Ghani Molecular and Pathological lab, Karachi, Pakistan

Abstract Body:
Introduction: Tuberculosis (TB) is one of the major infectious causes of morbidity and mortality worldwide. Members of the Mycobacterium tuberculosis complex (MTBC) are the most important human pathogens of the genus Mycobacterium. Genetic diseases remain an important cause of ailment, morbidity and death for children and adults. Despite the recent advances of tools for molecular diagnosis such as DNA chips and protein arrays which are capable of analyzing many genes. The availability of a low-cost diagnostic system will make molecular testing cost efficient and become readily available worldwide. Material and Methods: Advances in the field of molecular biology have provided rapid diagnostic tools on clinical specimens (tissue, body fluid, CSF, nodule aspiration and sputum) from weeks to days. Collection of specimens This comparative analysis was carried out in the laboratory. A total of 50 cases presenting to chest OPD in a secondary care hospital were selected and samples including tissue, body fluid, CSF, nodule aspiration and sputum were collected. Patient's selection criteria: Samples of those patients were collected whose chest x-ray showed radiographic consolidations suspicious of pulmonary tuberculosis. The basic screening strategy included AFB smear. After initial investigation for the AFB, the DNA were extracted from all specimens for detecting mycobacterium tuberculosis in these specimens by using PCR, and the significant diagnostic value of PCR were observed by comparing the conventional methods with Gene Flow Hybridization technique. PCR was performed according to the conventional procedure. The amplified product was identified by agarose gel electrophoresis as well as gene flow hybridization technique was used and results were obtained. Results: The new technology use for the diagnosis is” Flow-through‘ the uniqueness of hybridization by directing amplicons towards the DNA probes to form duplexes. In this, we evaluated the Flow-through hybridization system with conventional PCR. Our results show that Flow-through hybridization method produces higher sensitivity in 5 to 15 minutes. Conclusion: Knowledge of the susceptibility patterns of M. tuberculosis isolates is important for the effective management of patients and for disease control. The most potent first-line anti-tuberculous drugs used for standard treatment of TB are isoniazid (INH) and rifampicin (RMP). Second-line drugs used for treatment of MDRTB are more toxic, less effective, and more expensive.
Abstract Title:
The Prognostic Factors among Elderly Patients with Lung Tuberculosis

Primary Author Block:
K. Honjo1, K. Komiya2, S. Uchida1, S. Takikawa1, T. Yoshimatsu1, J. Kadota2; 1Nishibeppu National Hosp., Beppu, Japan, 2Oita Univ., Yufu, Japan

Abstract Body:
Background: Japan is categorized as a country with a middle burden of tuberculosis and elderly patients contribute to the prevalence of the disease as well as tuberculosis-related mortality. Nevertheless the factors that affect the prognosis among elderly patients with tuberculosis have not been fully assessed. The aim of this study was to assess the prognostic factors among elderly patients admitted to a hospital for lung tuberculosis. Methods: We retrospectively investigated 275 elderly patients (>65 years of age) who were admitted to the Nishibeppu National Hospital for bacteriologically-diagnosed lung tuberculosis from January 2013 to December 2015, and analyzed the prognostic factors associated with death from tuberculosis or non-tuberculosis-related death. Results: Fifty-nine patients died (tuberculosis, n=18; non-tuberculosis, n=41). The patients who died were significantly older, and had a lower BMI, poorer performance status (PS), a lower swallowing function, a lower oxygenation level, and lower levels of serum albumin and hemoglobin. A multivariate analysis showed that a low serum albumin level significantly predicted death from tuberculosis, and that a poor PS and low hemoglobin level were significantly associated with non-tuberculosis-related death. While the median survival time until tuberculosis-related death in patients with a lower serum albumin level was shorter than that in other patients ([tuberculosis-related death vs survival] 134: 95%CI 127-142 days vs 149: 95%CI 147-151 days, P<0.001), the median survival time until non-tuberculosis-related death in patients with a poor PS or a lower serum hemoglobin level was shorter than that in other patients ([non-tuberculosis-related death vs survival] 166: 95%CI 156-177 days vs 196: 95%CI 190-202 days, P=0.001, 161: 95%CI 149-173 days vs 194: 95%CI 187-201 days, P<0.001, respectively). Conclusions: These results suggested that there were significantly differences in the prognostic factors for death from tuberculosis (low serum albumin) and non-tuberculosis-related death (poor PS and a low hemoglobin level) among elderly patients with lung tuberculosis.
Abstract Title:
Clinical Features of Tuberculosis Presenting As Fever of Unknown Origin

Primary Author Block:

Abstract Body:
Background: Tuberculosis (TB) is one of the important causes of fever of unknown origin (FUO) in TB endemic areas. Little is known about the clinical features of patients with TB presenting as FUO.

Methods: We retrospectively analyzed patients who were referred as FUO and admitted to three tertiary referral hospitals for 8 years (2010 - 2017), and finally diagnosed as TB. The subjects were grouped into FUO and non-FUO groups in accordance with classic FUO criteria at admission. Clinical variables were compared between the groups. Results: A total of 103 patients were included. Twenty-three (22.3%) patients were eligible for the classic FUO criteria and the remaining 80 (77.7%) patients were classified as non-FUO group. Except for 5 (4.8%) cases of pulmonary TB in non-FUO group, all the other cases (95.2%) were extra-pulmonary TB. Patients in FUO group had more previous history of TB (26.1% vs. 1.3%), longer duration of fever (31 days vs. 6 days), and less localized symptoms and sign (30.4% vs. 71.3%) than those in non-FUO group. There was no significant difference in laboratory, radiologic and microbiological findings. Cross-sectional imaging tests such as CT and MRI provided critical diagnostic clues for TB in both groups. Conclusions: TB presenting as FUO was mainly extrapulmonary TB and the localizing symptoms and signs were less prominent. Active cross-sectional imaging test combined with tissue diagnosis may lead to earlier diagnosis of febrile TB.
HIV/Tuberculosis Patients with Slow Acetylator Genotype Have Increased Urine Levels of Oxidative Stress Markers

Primary Author Block:
I. Zentner1, S. Ravimohan2, J. G. Pasipanodya3, S. Srivastava4, T. Gumbo5, G. P. Bisson6, C. Vinnard1; 1Publ. Hlth.Res. Inst., Newark, NJ, 2Univ. of Pennsylvania, Philadelphia, PA, 3Ctr. For Infectious Diseases Res. & Experimental Therapeutics, Dallas, TX, 4Ctr. for Infectious Diseases Res. & Experimental Therapeutics, Dallas, TX, 5Ctr. for Infectious Diseases Res. and Experimental Therapeutics, Dallas, TX, 6Univ. of Pennsylvania, Philadelphia, PA

Abstract Body:
Background: Tuberculosis patients with slow NAT2 acetylator genotype are more likely to develop hepatotoxicity through unknown mechanisms. Isoniazid and its hydrazine metabolites trigger mitochondrial damage in pre-clinical models. We sought to determine whether isoniazid-treated HIV/tuberculosis patients have an elevated marker of oxidative stress detected in urine, as measured by DNA damage from reactive oxygen species. Methods: We analyzed urine samples collected from a cohort HIV/tuberculosis patients enrolled in a prospective study of isoniazid pharmacokinetics, conducted before starting antiretroviral therapy. NAT2 genotype was determined from whole exome sequencing. Urine levels of 8-hydroxydeguanosine (8-OHdG), a marker of DNA damage, were measured using an ELISA kit and normalized to urine creatinine. For comparison, we also analyzed urine collected from untreated healthy volunteers. We performed multivariate linear regression to measure the adjusted relationship of NAT2 genotype and urinary 8-OHdG levels. Results: Urinary 8-OHdG levels were significantly elevated among 39 HIV/tuberculosis patients compared to 3 healthy volunteers (p<0.01; Figure 1). We observed a significant relationship between NAT2 genotype and urine 8-OHdG levels (p=0.046 by non-parametric test for trend). After adjusting for CD4+ T cell count and tuberculosis treatment duration, we observed a statistically significant increase in urine 8-OHdG levels among slow acetylators compared with rapid acetylators (p=0.023). Conclusions: Urine levels of 8-OHdG, a DNA damage marker related to oxidative stress, were elevated among HIV/tuberculosis patients, and the highest levels were observed among slow acetylators. Future work should examine whether oxidative stress assays could serve as early biomarkers for clinically apparent hepatotoxicity.
Abstract Title:
Recent Increase in Nontuberculous Mycobacterial Infection in Patients with Collagen Diseases in Japan

Primary Author Block:
T. Kitazawa, K. Misu, K. Seo, Y. Yoshino, K. Asako, H. Kikuchi, H. Kono, Y. Ota; Teikyo Univ., Tokyo, Japan

Abstract Body:
Background: Non-tuberculous mycobacterial (NTM) infection is currently a growing health concern due to the globally increasing incidence and the need for prolonged therapy. In patients with collagen diseases, the use of immunosuppressants may lead to an increased risk of NTM infection. However, there were few studies about the recent incidence of NTM infection in patients with collagen diseases. In this study, we investigate the trends of NTM infection in patients with collagen diseases in Japan.

Methods: We enrolled adult patients in whose cultures NTM were isolated from January 2009 to October 2017 in our hospital. By reviewing their medical records, patients with collagen diseases were identified. First NTM isolation date, type of collagen diseases, NTM species, treatment of NTM infection were extracted from the medical data. Results: NTM was isolated in 665 patients during the study period. Among the 665 patients, 32 patients had collagen diseases. The number and the rate of NTM isolates from patients with collagen diseases were increased during the study period; 5 patients from 2009 to 2011 (2.3%), 9 patients from 2012 to 2014 (3.1%), and 18 patients from 2015 to 2017 (6.9%). The proportion of Mycobacterium avium-intracellulare (MAC) to total NTM in patients with collagen diseases was lower than that in non-collagen disease-patients, although not statistical difference (62.5% vs. 72.8% p=0.20). Mycobacteria fortuitum was the most frequent NTM species except for MAC in patients with collagen diseases (Table). Conclusions: Increase in the number of NTM infection in patients with collagen diseases were greater than that of general population. Other NTM species than MAC could be isolated from patients with collagen diseases. 

<table>
<thead>
<tr>
<th>NTM species</th>
<th>Collagen Diseases (%)</th>
<th>Non-collagen diseases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M. avium</td>
<td>62.5%</td>
<td>72.8%</td>
</tr>
</tbody>
</table>

M. avium
<table>
<thead>
<tr>
<th>M. intracellulare</th>
<th>M. gordonae</th>
<th>M. fortuitum</th>
</tr>
</thead>
<tbody>
<tr>
<td>348(52)</td>
<td>13(41)</td>
<td>126(20)</td>
</tr>
<tr>
<td>53(8)</td>
<td>1(1)</td>
<td>54(8)</td>
</tr>
<tr>
<td>13(41)</td>
<td>7(22)</td>
<td>126(20)</td>
</tr>
<tr>
<td>133(20)</td>
<td>1(1)</td>
<td>53(8)</td>
</tr>
<tr>
<td>5(5)</td>
<td>1(1)</td>
<td>54(8)</td>
</tr>
<tr>
<td>34(5)</td>
<td>1(1)</td>
<td>4(13)</td>
</tr>
<tr>
<td>3(3)</td>
<td>1(1)</td>
<td>2(2)</td>
</tr>
<tr>
<td>18(3)</td>
<td>23(3)</td>
<td>38(6)</td>
</tr>
<tr>
<td>-------</td>
<td>-------</td>
<td>-------</td>
</tr>
<tr>
<td>M. abscessus</td>
<td>M. kansasii</td>
<td>M. abscessus</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>47(7)</td>
<td>50(8)</td>
<td>Total</td>
</tr>
<tr>
<td>32(100)</td>
<td>665(100)</td>
<td></td>
</tr>
</tbody>
</table>
Mycobacterium Massiliense Cases Identified from 15 Patients with Progressive Neurodegenerative Disease


M. massiliense is categorized as a separate species from M. abscessus based on differences in the clinical manifestations & drug susceptibilities. There have been a few reports about hospital acquired potential outbreaks of M. massiliense, but it is still unclear whether all cases identified as M. massiliense based on respiratory secretion samples require long-term multi-antibiotic therapy. We isolated M. massiliense from the respiratory tract secretion samples of 15 patients who were ventilator-dependent due to progressive neurodegenerative disease in our hospital between August 2014 and February 2016. All patients complained of respiratory symptoms and had abnormal radiographic findings. The sputum smears were all positive for acid-fast bacilli strains; these isolates were identified as M. massiliense by a multiplex PCR. Fourteen patients were empirically treated for oral bacterial aspiration pneumonia and one patient was observed without antibiotic therapy because they did not show typical radiographic findings of non-tuberculous mycobacterium lung disease. Variable-number tandem repeat (VNTR) typing demonstrated that all M. massiliense isolates were indistinguishable. These results suggested that 15 all patients had the same strain of M. massiliense, indicating the possibility of outbreak in the hospital. Although not all patients received appropriate antibiotics for M. massiliense, their symptoms and radiological abnormalities showed significant improvement. M. massiliense may colonize the respiratory tract & does not always require long-term multi-antibiotic therapy.
Abstract Title:
Activity of Antibiotic Synthesized Nano-Particle Coated Surgical Gloves against Bio Threatening Bacteria in Operation Theaters

Primary Author Block:
S. Sattar1, A. Javid2; 1Fatima Mem. System, Lahore, Pakistan, 2Pakistan Kidney & Liver Inst., Lahore, Pakistan

Abstract Body:
Background: Infection of post surgeries because of surgical gloves is a life-threatening problem now a days. Antibiotic treatment is often unsuccessful due to the formation of MDR on the surface of surgical gloves, and is a contributing factor to bacterial resistance. A promising strategy to combat such infection is Nano Particle coating technology as they emit UV rays with the help of body heat. This study reveals the ideal antibacterial coating of green synthesized silver Nano particles on the surgical gloves used in Operation theaters. Methods: Silver Nano particles were prepared in the lab with the help of antibiotics as reducing agents. Characterization of Nano particles were performed from the CAMB institution Lahore Pakistan. Comparative analysis of antibacterial activity against MRSA were performed between coated silver Nano particles of fifth generation antibiotics and antibiotics alone under controlled temperature. Results: Results indicate silver coated fifth generation antibiotics are far effective for MRSA with increase in zone of inhibition with MIC 0.25-0.5 Ug/ml. Silver coated Ceftaroline fosamil (MIC= 0.25ug/ml), Teicoplanin (MIC= 0.25ug/ml), Vancomycin (MIC= 0.5-2.0ug/ml), Telavcin (MIC= 0.125ug/ml), Dalbavancin (MIC= 0.12ug/ml), Oritavancin (MIC= 0.03ug/ml) were used with control non-coated antibiotic and silver Nano particle. Zone of inhibition for Ceftaroline fosamil, Ceftobiprole, Teicoplanin, Vancomycin, Telavcin, Dalbavancin, Oritavancin were 23mm, 20mm, 27mm, 25mm and 30mm respectively under controlled conditions. Conclusions: With increase in rate of post-surgical infections and MDR against nosocomial infection leaves medical science with no choice but far effective prophylactic measures. Silver coated glove is one step innovation towards post-surgical infection control. Green synthesized silver Nano particles seems a promising application to combat strong bacteria like MRSA. It can also help to reduce rate of Bio-threatening and nosocomial infections.
Needle Stick Injury Reporting among Surgeons in Tertiary Hosp. of Lahore

S. Gillani, D. Sarwar; King Edward Med. Univ. / Mayo Hosp., Lahore Pakistan, Lahore, Pakistan

Background: Needle stick injuries have a fairly common incidence in surgical practice exposing surgeons to an array of transmissible diseases. The aim of the study was to assess the prevalence of needle stick injury, and their reporting among surgeons in tertiary hospital setting. Methods: A cross-sectional study using non probability purposive sampling technique was conducted at various tertiary care hospital of Lahore included Mayo Hospital, Shaikh Zayad Hospital, Jinnah Hospital Sir Ganga Ram Hospital, General Hospital and Children Hospital, Capital of Province Punjab, Pakistan during Jan, 2012 through April, 2012. Our sample size was 935 Surgeons. We selected General and Orthopedics Surgeons included House surgeons (HS), Post-graduate trainee (PGT), teaching cadre from Senior Registrar (SR) and above. We determined the prevalence of needle stick injuries, reporting of NSI, the reasons for not reporting and the reasons for acquired injuries. Results: Out of 935 surgeons, there were 564 (60.2%) males and 371 (39.8%) were females. Among them 509 (54.4%) were resident’s junior surgeons, 290 (31%) were senior consultant surgeons and 136 (14.5%) were house surgeons. Needle stick injury was reported by only 85 (9.1%) participants and 850 (90.9%) chose not to report any authority. The reasons for not reporting were varied; 363 (38.8%) did not report due to unawareness of the existence of a relevant system, 250 (26.7%) did not know whom to report, 86 (9.2%) were not able to spare time to report, 81 (8.7%) were afraid of results, 48 (5.1%) thought that patient was low risk and 107 (11.4%) did not bother. Conclusions: We demonstrated that there was a lack of hospital policy to cater to the reporting of injuries sustained during surgical practice in the tertiary public sector hospitals of Lahore. A dire need for the implementation of a system strategy was observed to educate the healthcare workers and provide a medium to assist the process of reporting so the reporting rates may get better. Key words: Needle stick injury (NSI), Hepatitis B Virus (HBV), Surgeon, Pakistan.
Contamination of Healthcare Linens (HCLs) by Mucorales and Other Moulds: A Multi-Center Study of Freshly Laundered Items Arriving At U.S. Transplant Centers


Background: Several mucormycosis outbreaks have been linked to contaminated HCL. HCL facilities can attain voluntary certification from the Healthcare Laundry Association Council (HLAC) and/or Textile Rental Service Association (TRSA), the latter of which includes some biologic testing. However, there are no U.S government regulations for biologic surveillance of HCL facilities, or accepted definitions of “hygienically clean” HCL. Our objective was to determine culture positivity (cx+) for Mucorales and other moulds on freshly-laundered HCL arriving at U.S. transplant centers. Methods: A dedicated team performed RODAC (25cm²) cx on HCLs immediately upon arrival at 14 U.S. hospitals that care for transplant recipients. The benchmark for hygienically clean HCL was adapted from bacterial recommendations (pathogenic mould cx+ in <10% of items). Results: 64% (9/14) and 29% (4/14) of HCL facilities were HLAC and TRSA-certified, respectively. HCLs at 36% (5/14) and HCL carts at 14% (2/14) of hospitals were unclean upon visual inspection at arrival, with evidence of hair, lint, soilage, or insects. Pathogenic moulds (Mucorales, Aspergillus, Fusarium, dematiaceous, Paecilomyces, Geotrichum) were recovered from HCLs at each center. HCL cx+ was > the 10% benchmark for pathogenic moulds, Aspergillus and Mucorales at 64% (9/14), 29% (4/14) and 14% (2/14) of hospitals, respectively. Percentages of cx+ HCLs at individual hospitals ranged from 4-76%, 0-59%, and 0-24%, respectively. Percentages of cx+ for pathogenic moulds, Mucorales and, to a lesser extent, Aspergillus correlated with highest temperature in the preceding 2 days (p=0.0, 0.038 and 0.12, respectively), but not with other meteorological factors. There was no correlation between either TRSA or HLAC certification and HCL
cleanliness or pathogenic mould contamination. At an HCL facility supplying one hospital, a site of contamination in the laundering process was identified and remediated. Pathogenic mould contamination was reduced from >80% (25% Mucorales) to 3% (0% of Mucorales) of items. Conclusions: HCL contamination with pathogenic moulds exceeded a 10% cx+ benchmark upon arrival at most participating U.S. transplant centers. Aspergillus or Mucorales were recovered commonly. It is possible to reduce mould contamination by targeted remediation in HCL facilities. HLAC and TRSA certification does not assure that HCLs are hygienically clean of moulds. U.S. regulations for biologic surveillance and targets for acceptable mould cx+ of HCLs are needed.
Session Number: 241
Session Type: Poster
Session Number: 241
Session Type: Poster
Session Title: CIV02 - Infection Prevention and Control: Hospital Acquired Infections
Session Start Date Time: 6/9/2018 11:00:00 AM
Session End Date Time: 6/9/2018 1:00:00 PM
Session Primary Track: Clinical Infections and Vaccines
Abstract Control Number: 3698
Poster Board Number: SATURDAY - 711

Abstract Title:
Microbiological Analysis of Hemodialysis Water At the Douala Gen. Hosp. Cameroon

Primary Author Block:
C. Gueguim1, N. Nga1, A. Ragon2, F. Kaze1, H. Gonsu Kamga1; 1Univ. of Yaoundé 1, Yaoundé, Cameroon, 2Div. of Uro-Nephrology Lab., Hosp. of Conception, Marseille, France, Marseille, France

Abstract Body:
Background: Rigorous control of the microbiological quality of water in hemodialysis services is important because the immune system of patients with chronic renal failure is weakened. The objective of this study was to determine the microbiological quality of water for hemodialysis in Nephrology Unit of the Douala Général Hospital in order to improve the disinfection strategy. Methods: Twelve water samples were collected each month at different sites of the hemodialysis circuits A (inlet of filters), B (Outlet of filters / inlet of Reverse Osmosis (RO) device) and C (outlet of the RO device / close to the generator) between November 2015 and February 2016 to be analyzed. The bacteria were isolated after filtration of 100 ml of water at each site through nitrocellulose membrane with 0.45 µm microporosity deposited on the surface of the Tryptone Glucose Extract Agar (TGEA) and then incubated at room temperature (20 to 22°C) for 7 days. After transplanting to different environments, pure bacterial isolates were identified by their cultural characters and marketed biochemical galleries. Results: The colony count was well above the required international standards (>100 CFU / ml), for the hemodialysis water with a percentage of 50% of non-compliance. Among the bacteria identified, seven (07) were Gram-negative bacilli including Pseudomonas fluorescens, and Klebsiella pneumoniae subsp ozenenae, three (03) Gram-positive bacilli all Bacillus sp and three (03) Gram-positive cocci all of coagulase-negative staphylococci. The most frequently isolated bacterial genera were Pseudomonas sp (38,5%), Staphylococcus sp (23%), Bacillus sp (23%) and Klebsiella sp (15,5%). Conclusions: The high bacteriological contamination of the hemodialysis water with the detection of a variety of bacteria shows that the disinfection procedure of the distribution loop is not efficient and cannot prevent the development of a biofilm. A higher frequency of disinfection (almost every week), an increase of the concentration and time of contact of the chlorine disinfection product or the use of peracetic acid and a regular monitoring can contribute to improve the quality of the hemodialysis water at the Douala General Hospital to ensure a better quality of life for patients undergoing this treatment.
Abstract Title:
A Prediction Model for Positive Legionella Cultures in Hosp. Water

Primary Author Block:
B. Decker, M. Kelly, J. Mikolic, J. Walker, C. Clancy; VA Pittsburgh Hlth.care System, Pittsburgh, PA

Abstract Body:
Background: Hospitals devote considerable resources to water system surveillance and remediation for Legionella. Rates of Legionnaires disease (LD) are highest in warm months, and have been linked to relative humidity and precipitation. Our goal was to build and validate a model based on weather and water parameters that predicts positive Legionella cultures (cx+) in our hospital water system. Methods: 1 L water samples from fixtures at 2 campuses were cultured for Legionella on BCYE plates with cysteine as part of infection prevention protocols. Logistic regression and random forest models included daily hospital water measurements (over 14 days (d) prior to cx) and U.S. NOAA weather data (over 7 d). Training and validation used 2014-15 and 2016-17 data, respectively. Models predicted (within 14 d windows): 1) first +cx; 2) subsequent +cx after first +cx. Results: >2000 cxs were performed each year. Data from 1,046 loop-specific d were collected. Overall, 1.8% of cx were + for Legionella. 14.6% (2014-15) and 13.6% (2016-17) of d had a first +cx. 53.6% (2014-15) and 81.2% (2016-17) of subsequent d were cx+. Significant predictors of first +cx were minimum/maximum water chlorine (Cl) concentration (p=0.04, Wilcoxon) and relative humidity (p=0.015). Significant predictors of subsequent +cx were minimum/maximum Cl concentration (ps0.003), relative humidity (p=0.0003), and average 24 hour precipitation (p=0.006). The logistic regression model misclassified 31% and 23% of first +cx and subsequent +cx, respectively. Random forest models built upon 9 parameters had AUCs=1 for predicting first +cx and subsequent +cx using training data. In validation studies, the random forest model for first +cx had sensitivity/specificity of 100%/97% and positive/negative predictive values (PPV/NPV) of 71%/100%. The random forest model for subsequent +cx had sensitivity/specificity of 100%/99.7% and PPV/NPV of 94%/100%. Conclusions: Models using water and weather data were validated as accurate predictors of new Legionella cx+ and subsequent Legionella cx+ within a hospital water system. Most importantly, NPVs for the models were 100%, meaning that no positive Legionella cxs were recovered during periods identified as low-risk. The models are powerful tools for directing resources most efficiently to Legionella surveillance and LD prevention.
Abstract:
Surgical Site Infection Following Cesarean Section in A Gen. Hosp. in Kuwait: Trends and Risk Factors
Primary Author Block:
R. Dhar1, W. AlFouzan1, N. Abdo1, M. Al Fadhli2; 1Farwania Hosp., Sabah Al Nasser, Kuwait, 2Infection Control Directorate, Shuweikh, Kuwait
Abstract Body:
Background: Surgical site infections (SSI) are a significant cause of post-surgical morbidity and mortality. The objectives of this study were to determine the incidence of SSI and identify risk factors for infections following cesarean section (CS). Method: A prospective study of SSI after CS was carried out from January 2014 to December 2016 using the methodology of the American National Nosocomial Infection Surveillance System. Follow-up of women was carried out in the Obstetrics and Gynecology outpatient department for any post-discharge SSI. Suspected SSIs were confirmed clinically by the surgeon and or by culture. Results: During the study period, 7235 CS were performed with infection rate estimated at 2.1% (153/7235), increasing from 1.7% in 2014 to 2.95% in 2016 (p=0.010). The infection rate was 46.7% in women ≤ 30 years as compared to 53.3% in women > 30 years of age (p=0.119). Most of the infections were categorized as superficial (98.0%) and presented more often following emergency (73.7%) than elective CS (26.3%) (p=0.554). Of 148 culture samples from as many women, 112 (75.7%) yielded growth of microorganisms with 42 (37.5%) being multi-drug resistant. Among these the most common microorganism isolated was methicillin-resistant Staphylococcus aureus (80.95%; 34/42). Antibiotics for prophylaxis included cefuroxime alone or in combination with gentamicin and or metronidazole. Women who did not receive prophylactic antibiotics (35.5%) developed SSI more often than those who did (p< 0.0001). SSI appeared following discharge from hospital in 99.3% women, becoming evident within the first 13 days (median 11 days) following surgery with median duration of 40 minutes. Majority of the women (103) had American Society of Anesthesiologists (ASA) score of 1 while the remaining 50 patients had a score of 2. A risk score of 1 was presented by 16 women whereas the rest presented with a risk score of 0 (89.5%). Conclusions: Our study demonstrates that most of SSI following CS are detected only after patient’s discharge from the hospital. Emergency CS and improper prophylaxis, are important risk factors in the development of SSI. In the light of emergence of MDROs there is a need to implement revised prophylactic antibiotic policy as part of antimicrobial stewardship to bring down the SSI rate to zero.
Abstract: The recent studies revealed the relationships of the gut microbiome to many diseases. However, its relationship to antimicrobial therapy remains unknown. In this study, we investigate the influence of antimicrobial prophylaxis in surgery and effect of probiotics on the gut microbiome.

Methods: The patients who underwent spine surgery between July 2016 and October 2017 were included in this study. Thirty-four patients were classified into two groups according to permuted block method: control (n=17) and postoperative administration of drug-resistant lactic acid bacteria for 5 days (treatment group, n=17). The patients received surgery and antimicrobial prophylaxis as usual. The feces of the patients were sampled at preoperation, postoperative day (POD) 5 and 10. The gut microbiome were analyzed by using Ion-PGM system and CLC genomics workbench. Results: There were no significant differences between control and treatment groups in the basic characteristics, such as age, gender, underlying diseases and surgical site. The most administered antimicrobial agents at perioperative period was cefazolin in both groups (n=13 in the control and n=14 in the treatment group, respectively). There were no significant differences in administered antimicrobial agents at perioperative period was cefazolin in both groups (n=13 in the control and n=14 in the treatment group, respectively). There were no significant differences in administered antimicrobial agents between two groups. In the control group, two patients showed soft stool at POD5. A total of 102 samples were analyzed and 9,003 sequences were obtained over all samples (mean 2,082.2 ± 642.9 sequences per sample). The sequences were classified into 1032 operational taxonomic units (OTUs). The changes of the gut microbiome were showed in Figure. In PERMANOVA analysis (weighted UniFrac), the composition of the gut microbiome in POD10 was significantly different between both groups (P=0.021).

Conclusions: The composition of the gut microbiome in the patients who were administered antimicrobial prophylaxis in surgery might be different depending on the administration of probiotics.

<a href="http://files.abstractsonline.com/CCTRL/74/d/da6/1c6/a10/46d/b9c/77b/4ca/417/431/48/g4318_2.png" target="_blank" address=no><img src="http://files.abstractsonline.com/CCTRL/74/d/da6/1c6/a10/46d/b9c/77b/4ca/417/431/48/g4318_2.png" alt="" border="0" width="600" height="606" /></a>
**Session Number: 241**
**Session Type: Poster**

Session Number: 241  
Session Type: Poster  
Session Title: CIV02 - Infection Prevention and Control: Hospital Acquired Infections  
Session Start Date Time: 6/9/2018 11:00:00 AM  
Session End Date Time: 6/9/2018 1:00:00 PM  
Session Primary Track: Clinical Infections and Vaccines  
Abstract Control Number: 4984  
Poster Board Number: SATURDAY - 715

Abstract Title:
Success of A Multifaceted Response to An Outbreak of Legionnaire’S Disease (Ld) At A U.S. VA (Va) Healthcare Sys. in 2011-2012

Primary Author Block:
B. Decker1, P. Harris1, L. Chen2, B. Kreiswirth2, C. Clancy1; 1VA Pittsburgh, Pittsburgh, PA, 2Rutgers Univ., Newark, NJ

Abstract Body:
Background: A 2011-12 LD outbreak at the VA Pittsburgh Healthcare System (VAPHS) involved 22 patients (pts) and caused 6 deaths. Multiple factors contributing to a control-system failure were identified. A multifaceted response was initiated in Nov 2012. Our objective is to report 5 year clinical, environmental and genomic epidemiology follow-up data. Materials/Methods: We retrospectively reviewed clinical, epidemiologic, and water system (WS) surveillance data from Nov 2012-Dec 31, 2017. MiSeq whole genome sequencing (WGS) was performed on 72 Legionella isolates recovered from pts, pts’ homes, VAPHS WS, and the Pittsburgh region in 1982-2016. Phylogenetic trees were constructed based on core genome single nucleotide polymorphisms. Results: VAPHS switched from copper-silver to hyperchlorination WS treatment, and instituted analyzer-chlorination units, daily random biocide level sampling, active monthly WS Legionella surveillance, zero-tolerance WS remediation, mandatory ID consults and Legionella testing for all pts with pneumonia, and a rigorous genomic epidemiology program. WGS revealed that the outbreak was caused by L pneumophila (Lp) subsp. pascullei that evolved through 3 recombinations from an endemic 1982 WS strain. Post-outbreak, 21 cases of LD have been diagnosed, including 12 community and 9 possible healthcare-associated. Etiologies included L. pneumophila (Lp) serogroups 1 (n=17) and 2-14 (n=4). WS Legionella positivity has decreased from 15.5% during the outbreak, to 1.8% post-outbreak. Pt and WS isolates included Lp subsp. pneumophila (5 clades), pascullei (2 clades), and fraseri. WS L. longbeachae were also recovered. VAPHS clades were distinct from publically-available genomes. Outbreak and 1982 Lp pascullei strains have not been detected since Nov. 2012. A Dec. 2012 Lp pascullei pt isolate was distinct from outbreak isolates, but identical to an isolate from the pt’s home. Classical and genomic epidemiology verified that no cases of nosocomial LD have occurred since 2012. Conclusions: A Legionella surveillance and prevention program at a VA healthcare system ended an LD outbreak due to endemic Lp subsp. pascullei, eliminated subsequent nosocomial cases, and significantly reduced WS Legionella positivity. Results have been sustained for 5 years.
Clinical Impact of Reinsertion of Central Venous Catheter for Patients with Central Line-Associated Bloodstream Infection

Primary Author Block:
D. Kim1, Y-M. Lee1, H. Park2, M. Lee1, K-H. Park1; 1Kyung Hee Univ. Hosp., Seoul, Korea, Republic of, 2Asan Med. Ctr., Seoul, Korea, Republic of

Abstract Body:
Background: The reinsertion of central venous catheter (CVC) is often required for the care of critically ill and chronically ill patients in patients with central line-associated bloodstream infection (CLABSI). However, the clinical impact of CVC reinsertion was not clearly determined. We evaluated the impact of CVC reinsertion on clinical outcomes in patients with CLABSI. Methods: Between January 2006 and December 2013, patients who diagnosed with CLABSI (a positive blood culture and a positive catheter tip culture yielding the same species of microorganism) in a tertiary care hospital were retrospectively included. Cases with CVC reinsertion within 3 days after CVC removal were classified as having early CVC reinsertion. Clinical outcomes were defined as 1) persistent bacteremia (> 3 days after CVC removal), 2) in-hospital mortality, 3) length of hospital stay (LOS). When catheters were replaced, the catheters were not changed over a guidewire. Results: A total of 105 patients with CLABSI were enrolled, excluding 2 patients who died before day 3 following the onset of bacteremia. Of these, 53 (50.5%) underwent early CVC reinsertion. The causative pathogens were as follows: 31 cases with coagulase-negative Staphylococcus, 30 with methicillin-resistant S. aureus (MRSA), 22 with gram-negative bacteria, 9 with Candida species, 6 with methicillin-susceptible S. aureus, and 5 with Enterococcus species. The median duration from onset of bacteremia to CVC removal was comparable. Early CVC reinsertion was significantly associated with a higher rate of persistent bacteremia after CVC removal (28.3% vs. 5.8%; P = 0.002), increased in-hospital mortality (35.8% vs. 11.5%; P = 0.03), and median LOS after CLABSI (51 vs. 23 days; P = 0.01) in patients with CLABSI. Early CVC reinsertion [OR = 7.0] and MRSA [OR = 4.6] were associated with persistent bacteremia after CVC removal. Early CVC reinsertion [OR = 5.2], inadequate empirical antibiotic therapy [OR = 14.6], and high Pitt bacteremia score [OR = 4.6] were independent risk factors for in-hospital mortality in patients with CLABSI. Conclusion: The necessity of CVC use should be carefully considered to determine CVC reinsertion in patients with CLABSI, as early CVC reinsertion may have an adverse effect on outcomes.
Abstract Title:
Outstanding Abstract Award: Insecticide Resistance is Not Associated with Malaria Prevalence in Anopheles Gambiae S.L. (Diptera: Culicidae) Mosquitoes in Guinea

Primary Author Block:
E. Collins1, N. M. Vaselli1, M. Sylla2, A. H. Beavogui2, J. Orsborne1, S. Irish3, T. Walker1, L. A. Messenger3; 1London Sch. of Hygiene and Tropical Med., London, United Kingdom, 2Ctr. Natl. de Formation et de Recherche en Santé Rurale de Maferinyah, Maferinyah, Guinea, 3CDC, Atlanta, GA

Abstract Body:
Background: The threat of insecticide resistance across sub-Saharan Africa is anticipated to have severe implications for the continued effectiveness of our repertoire of malaria vector control interventions. However, evidence linking the operational failure of control strategies to the presence of local, resistant mosquito populations is lacking. Methods: In an area of high malaria transmission in Forecariah Prefecture, Guinea, we investigated the impact of insecticide resistance intensity on malaria infection prevalence of Anopheles gambiae s.l. Intensity of resistance to carbamates and pyrethroids was assessed using CDC bottle bioassays and underlying resistance mechanisms investigated using piperonyl butoxide (PBO) based CDC synergist assays. A subset of specimens underwent ovarian dissection to determine parity (a proxy for age) and molecular assays were performed to detect Plasmodium falciparum infection and insecticide resistance genes (Ace-1, kdr and N1575Y). Results: In Forecariah Prefecture, pyrethroid resistance was intense as evidenced by mosquito populations which were not only resistant to ten times the insecticide concentration required to kill susceptible individuals, but were also capable of surviving these doses for up to two hours. Insecticide resistance was not associated with decreased capacity to transmit malaria, with no significant differences observed between P. falciparum oocyst or sporozoite rates among susceptible and resistant vectors (χ2=0.89; p=0.345 and χ2=2.10; p=0.148, respectively). Resistant mosquitoes had significantly lower parity rates, i.e. were younger, than susceptible individuals. However, the small proportion of intensely resistant vectors were more likely to be parous (χ2=4.13; p=0.042 and χ2=4.39; p=0.036, for survivors exposed to five and ten times the diagnostic dose of insecticides respectively). Conclusions: Restoration of mosquito susceptibility to pyrethroids following pre-exposure to PBO and the non-association between N1575Y frequency and vector mortality rate indicate that over-expression of P450 monooxygenases is the predominant mechanism driving pyrethroid resistance. Our findings contrast with a number of laboratory studies reporting reduced fitness in insecticide-resistant vectors and highlight the need for additional studies across a range of areas of differing resistance and malaria transmission intensities.
Abstract Title:

Primary Author Block:

Abstract Body:
Background: Indoor residual spraying (IRS) and long-lasting insecticidal nets (LLINs) remain the cornerstones of malaria vector control. However, the development of widespread insecticide resistance and its implications for operational failure of preventative strategies are of increasing concern. We characterized nationwide insecticide resistance among Anopheles gambiae s.l. populations in Ethiopia between 2012 and 2017, and undertook a genomics approach to elucidate the mechanisms of metabolic resistance to organophosphates and pyrethroids. Methods: Mosquito larvae were sampled from seven regions annually and susceptibility levels to organochlorines, pyrethroids, organophosphates, and carbamates, were assessed using WHO susceptibility tests and CDC bottle bioassays. In select sites, specimens were identified to species-level and resistance mechanisms were investigated using CDC synergist assays based on pre-exposing mosquitoes to piperonyl butoxide (PBO), and by PCR screening for knockdown resistance (kdr). RNA was extracted from survivors of malathion and permethrin bioassays and submitted for Illumina RNA-sequencing. Results: Resistance to DDT and pyrethroids was pervasive across Ethiopia and over time, with average mosquito mortality in 2016 of 35%, 48% and 54% for DDT, permethrin and deltamethrin, respectively. These results are consistent with historic use of DDT for IRS and concomitant increases in net coverage over the last 15 years. Temporal changes in resistance to malathion, bendiocarb, propoxur and pirimiphos-methyl corresponded to implementation of these chemicals according to the national insecticide resistance management policy. By 2016, resistance to the latter two insecticides had emerged, with the potential to jeopardize future long-term effectiveness of local vector control activities. Conclusions: Restoration of mosquito susceptibility to pyrethroids following pre-exposure to PBO, a lack of association between kdr allele frequency and vector mortality rate, and the absence of cross-resistance between insecticides of the same chemical class, support the existence of insecticide-specific metabolic mechanisms. Inter- and intra-class rotation
of different insecticides could be exploited to reduce selection pressures, to safeguard continued efficacy of IRS in Ethiopia. Analysis of RNA-seq data is ongoing to identify and validate candidate genes associated with malathion andpermethrin resistance and develop resistance diagnostic assays for prospective field surveillance.
Abstract Title:
Increasing Ex-Vivo Tolerance of Gambian Plasmodium Falciparum Isolates to Amodiaquine and Lumefantrine, Partners of Artemisinin-Based Combination Therapies

Primary Author Block:
H. Mbye; Univ. of Ghana, Accra, Ghana

Abstract Body:
In vitro drug susceptibility studies complement efficacy trials by assessing the effect of individual components of artemisinin-based combination therapies (ACTs) on parasite survival (Witkowski et al., 2013). These can enable early detection of changes in parasite susceptibility to ACT components before the onset of clinical failure. This is particularly crucial given the need for early warning for resistance or tolerance to ACTs in Africa, as artemisinin-resistant Plasmodium falciparum spreads across South East Asia (World Health Organisation, 2016). The high prevalence of malaria in Africa sees an ever-increasing amount of antimalarial pressure on parasite populations as national malaria control programme scale up efforts to eliminate the disease (World Health Organisation, 2016). In this study, 262 Plasmodium falciparum isolates, collected over 3 transmission seasons as part of therapeutic efficacy studies from the West of The Gambia (2013-2015), were analysed by in vitro methods; 50% inhibitory concentration (IC50) for partner drugs and, ring-stage survival assay (RSA); to determine ex vivo susceptibility to artemisinin-derivatives. Plasmodium falciparum isolates showed increasing tolerance to quinolines (Lumefantrine and Amodiaquine) but remained susceptible to artemisinin derivatives; Artemether and Dihydroartemisinin. However, the RSA results showed growth in 26% (13/50) of isolates from 2015, after exposure to 700nM of Dihydroartemisinin. Increased ring survival positively correlated with IC50 for Sulphadoxine and artemisinin-derivatives but negatively with Lumefantrine and Quinine. Increased Lumefantrine tolerance could be due to selection from Artemether-Lumefantrine; the first-line ACT in The Gambia. With the use of SP for chemoprevention, correlation between Sulphadoxine and increased ring survival against Dihydroartemisinin, calls for continuous and rigorous surveillance to sustain the useful lifespan of currently employed ACTs in Africa.
Session Title: CIV03 - Global Health: Tropical Parasites
Session Start Date Time: 6/9/2018 11:00:00 AM
Session End Date Time: 6/9/2018 1:00:00 PM
Session Primary Track: Clinical Infections and Vaccines
Abstract Control Number: 5633
Poster Board Number: SATURDAY - 720

Abstract Title: Novel Biomarkers to Differentiate Children with P. Falciparum Malaria from Bacterial Bloodstream Infections

Primary Author Block:
N. S. Struck1, M. Zimmermann1, R. Krumkamp1, E. Lorenz1, T. Jacobs1, D. Winter1, J. H. Amuasi2, D. Eibach1, J. May1; 1Bernhard Nocht Inst. for Tropical Med., Hamburg, Germany, 2Kumasi Ctr. for Collaborative Res. in Tropical Med., Kumasi, Ghana

Abstract Body:
Background: Malaria is a major health problem and economic burden in sub-Saharan Africa. Clinical symptoms frequently overlap with pneumonia, typhoid fever, acute bacterial meningitis, and invasive non-typhoid salmonella. Most common diagnostic methods (interpretation of clinical symptoms, blood smear microscopy and rapid diagnostic tests) are unable to identify possible concomitant infections that might mask the true cause of illness. In two different experimental approaches we set out to identify a set of prognostic blood biomarkers that are able to distinguish between a malaria infection requiring treatment and a severe bacterial infection.

Methods: We examined serum samples of 65 children under the age of 5 years that were recruited at the Agogo Presbyterian Hospital in Ghana between 2010 and 2012. 35 children with a malaria-positive slide and at least one symptom characteristic for severe malaria (Dondorp et al., 2011) and 30 children with SIRS (Goldstein, Giroir and Randolph, 2005) and a positive blood culture in the absence of malaria parasites were analysed. Autoantibody expression levels were determined through protein microarrays (ThermoFisherScientific) and 95 different inflammatory cytokines were identified using immunoassay detection kits (Merckmillipore). Principal component analyses were applied to identify covariance in marker expressions and random forest models were calculated to predict patient’s disease status from serum content. Results: Sex was equally distributed within the study group (female: 32; 49%), median age was 2 years (IQR: 1-3). Median parasite count in the malaria group was 181,670 (IQR: 32,692-324,725). Bacterial infections were caused by non-typhoid Salmonella (43%; n=13), Salmonella Typhi (23%; n=7), Streptococcus pneumoniae (17%; n=5), Staphylococcus aureus (10%; n=3), Acinobacter spp. (3%; n=1) and Campylobacter spp. (3%; n=1). While prediction models based on the expression levels of more than 9000 autoantibodies misclassified 5 malaria and 7 bacteraemia cases (82% prediction accuracy), the predictive accuracy based on the profile of cytokines was 94%. Conclusion: Our results showed that a specific set of biomarkers are able to predict a patient’s disease status and that prediction accuracy is higher for cytokines than autoantibodies. These panels open up new possibilities for innovative point-of-care tests, which are urgently needed in malaria endemic regions to guide early treatment decisions.
Session Number: 242  
Session Type: Poster
Session Number: 242  
Session Type: Poster
Session Title: CIV03 - Global Health: Tropical Parasites
Session Start Date Time: 6/9/2018 11:00:00 AM
Session End Date Time: 6/9/2018 1:00:00 PM
Session Primary Track: Clinical Infections and Vaccines
Abstract Control Number: 5457
Poster Board Number: SATURDAY - 722

Abstract Title:
Malaria Co-Infections: A Diagnostic Challenge in Malaria Endemic Regions of Sub-Saharan Africa

Primary Author Block:
D. Eibach1, B. Hogan1, N. Sarpong2, R. Krumkamp1, D. Dekker1, B. Kreuels3, O. Maiga-Ascofaré2, Y. Adu-Sarkodie4, E. Owusu-Dabo2, J. May1; 1Bernhard Nocht Inst. for Tropical Med., Hamburg, Germany, 2Kumasi Ctr. for Collaborative Res. in Tropical Med., Kumasi, Ghana, 3Univ. Med. Ctr. Hamburg Eppendorf, Hamburg, Germany, 4Kwame Nkrumah Univ. of Sci. and Technology, Kumasi, Ghana

Abstract Body:
Background: In sub-Saharan regions with holoendemic malaria transmission clinicians primarily focus on malaria diagnostics. Hence, febrile patients with malaria co-infections might receive treatment for non-causative parasitaemia, while the co-infecting agent remains overlooked. This study aims to determine the burden of malaria co-infections among hospitalised children with severe febrile illness and their association with parasite densities. Methods: Between November 2013 and April 2015 all children (age ≥30 days and ≤15 years) with a temperature ≥ 38.0°C, admitted to the Agogo Presbyterian Hospital in central Ghana were included in the study. Malaria parasitaemia was determined and blood, stool, urine, respiratory and cerebrospinal fluid specimens were screened for parasitic, bacterial and viral pathogens. Associations of Plasmodium densities with other pathogens were calculated. Non-febrile, healthy controls were recruited to analyse associations of febrile disease and parasitaemia. Results: From November 2013 to April 2015 1238 children were enrolled out of 4169 admissions. A clinical/microbiological diagnosis could be made in 1109 (90%) patients, with Plasmodium parasitaemia (n=728 [59%]) being predominant. This was followed by lower respiratory tract infections (n=411 [34%]; most frequent Streptococcus pneumoniae, n=192 [46%]), urinary tract infections (n=218 [18%]; Escherichia coli, n=21 [10%]), gastrointestinal infections (n=210 [17%]; rotavirus, n=32 [33%]) and invasive bloodstream infections (n= 62 [5%]; Salmonella spp., n=47 [75%]). Out of 537 healthy children, 83 (15%) revealed malaria parasites, of which 90% had a parasite count below 12,000/µl. In Plasmodium infected children the frequency of lower respiratory tract-, gastrointestinal- and bloodstream infections increased with decreasing parasite densities. Conclusions: With half of all malaria patients revealing an alternative cause for the fever episode and 15% of healthy children being parasitemic, malaria co-infections play a substantial role in the paediatric population of malaria endemic countries. In a hospital setting, the likelihood of comorbidity with a nonmalarial disease is reversely correlated with increasing blood levels of malaria parasites. Hence, parasite densities provide important information as an indicator for the probability of coinfections, in particular to guide antimicrobial medication.
Abstract Title:
Efficacy of Topical Treatments for Cutaneous Leishmaniasis: A Systematic Review and Network Meta-Analysis

Primary Author Block:
T. Thy1, A. Zayan2, M. Kamel3, A. Ahmed4, T-H. Hoang1, M. Othman4, K. Luu1, S. Nguyen5, A. Haleem6, H. Nasser7, R. Yafi8, O. Mattar9, K. Hirayama10, N. Huy10; 1Univ. of Med. and Pharmacy at Ho Chi Minh City, Ho Chi Minh, Viet Nam, 2Menoufia Univ., Menoufia, Egypt, 3Minia Univ., Minia, Egypt, 4Al-Azhar Univ., Cairo, Egypt, 5Univ. of Sci. and Technology of Hanoi, Ha Noi, Viet Nam, 6Ain Shams Univ., Cairo, Egypt, 7Cairo Univ., Cairo, Egypt, 8Damascus Univ., Damascus, Syrian Arab Republic, 9Kasr Al Ainy Sch. of Med., Cairo, Egypt, 10Nagasaki Univ., Nagasaki, Japan

Abstract Body:
Background: Leishmaniasis is a parasitic disease that is considered to be one of the most neglected tropical diseases presented in more than 90 countries all over the world, especially in poor population. Among all leishmaniasis forms, cutaneous leishmaniasis (CL) is considered the most frequent and dangerous form. It causes lesions on different locations and leads to scars or even severe incapacity. Glucantime has been a standard treatment; however, because of various side effects and inconvenience of applying systemic treatments, topical alternatives have been recommended. There is still no conclusion of the most effective topical treatment for CL, therefore, this systematic review and network meta-analysis was conducted to evaluate the efficacy of all the available topical treatments of CL.

Methods: Searches of nine electronic databases and a manual search were performed to find out clinical trials reporting tropical treatments of CL. Screening and data extraction were completed by three independent reviewers. Risk of bias was assessed using the Cochrane Collaboration’s tool. Complete healing cases were evaluated at three, six, twelve weeks and endpoint. Data were analyzed using network meta-analysis (NMA). Results: We included 41 clinical trials. Among that, 38 articles reported complete healing cases per patients. NMA showed that trichloroacetic acid plus glucantime was the most effective option for treating CL followed by topical herbal extract Z-HE. Compared with a standard treatment of CL, glucantime, a combination of glucantime and a topical treatment such as gel extract of Cassia, imiquimod, yarrow, terbinafine or honey showed more advantages, respectively. Trichloroacetic acid and liposomal amphotericin B were other recommended single topical treatments because of better efficacy than the systemic arm. All topical treatments except ketoconazole and shiunko were indicated to have more efficacy than placebo. Efficacy of some topical arms was reported in three studies using complete healing rate of lesions. Miconazole was better than clotrimazole while Thio-Ben was as effective as systemic glucantime. Results evaluated in different time points brought the same conclusion. Conclusions: Adding topical drugs to systemic treatment brings much more effects and among arms, trichloroacetic acid showed the most significant difference. Monotherapy of topica
treatments such as Z-HE, trichloroacetic acid, liposomal amphotericin B or Thio-Ben is also a good selection.
Abstract Title:
Exploratory, Phase II Controlled Trial of Shiunko Ointment Local Application Twice A Day for 4 Weeks in Ethiopian Patients with Localized Cutaneous Leishmaniasis

Primary Author Block:
O. Ahmed; Armauer Hansen Res. Inst., Addis Ababa, Ethiopia

Abstract Body:
Cutaneous leishmaniasis (CL) is a major tropical skin disease which represents a worldwide public health and social problem in many developing countries including Ethiopia. Study in Peru have showed 46 out of 53 (86.8%) patients had complete cure after local administration of Shiunko for 4 weeks, with complete absence of parasites in lesion biopsy at the end of treatment. The aim of the present study was therefore to evaluate the clinical efficacy and safety of Shiunko ointment when applied on the lesion twice a day for 4 weeks in Ethiopian patients with LCL. Patients were randomized to receive treatment with Shiunko ointment or placebo (n = 20, each), applied on the lesion twice a day for 4 weeks. Clinico-parasitological assessments were performed before treatment, weekly for 4 weeks, and then 4, 8, and 12 weeks after the end of treatment A marked reduction in lesion size was observed on week 16 of treatment in the Shiunko compared with placebo group (69% and 22% reduction, resp.). The overall rate of lesion reduction during the four weeks of treatment was significantly faster in the Shiunko group. Shiunko provided significant effect on wound closure in patients with ulcerated lesion. The clinical efficacy and tolerability of Shiunko were comparable to placebo with regard to its clinicoparasitological response (cure rate and parasitological clearance). Results of this preliminary study may suggest that Shiunko could be useful as adjuvant or as complementary treatment, not as alternatives to current treatment. Its attractive action includes fast lesion healing with a significantly smaller lesion at week 16 of treatment compared with placebo. In addition, its action was promoted in ulcerative lesions.
Session Number: 242
Session Type: Poster
Session Number: 242
Session Type: Poster
Session Title: CIV03 - Global Health: Tropical Parasites
Session Start Date Time: 6/9/2018 11:00:00 AM
Session End Date Time: 6/9/2018 1:00:00 PM
Session Primary Track: Clinical Infections and Vaccines
Abstract Control Number: 5966
Poster Board Number: SATURDAY - 725

Abstract Title:
Comparative Expression of Mir-146a, Mir-21 and Mir-155, and their Correlation with Different Cytokines in Human Neurocysticercosis
Primary Author Block:
Abstract Body:
Neurocysticercosis (NCC) is a central nervous system (CNS) infection caused by Taenia solium larva. NCC outcomes are heterogeneous; may vary from symptomatic (seizure) to asymptomatic for infinite time. Host inflammatory response plays vital role in disease pathogenesis. Symptomatic NCC is associated with Th1 or mixed Th1/Th2 response, whereas asymptomatic NCC with anti-inflammatory response. miRNAs are endogenous small noncoding RNAs of about 22 nucleotides in length that that regulate homeostasis, activation and cell differentiation in immune response against helminths. However, association of miRNAs and cytokines expression are yet to be studied in human NCC. All the individuals were subjected to magnetic resonance imaging (MRI) for the confirmation of cyst lesion in the brain. A total 30 each symptomatic and asymptomatic NCC patients were included in this study. Expression profile of miR-146a, miR-21 and miR-155 was studied by qRT-PCR. Different pro- and anti-inflammatory cytokine levels were determined by ELISA. Serum concentrations of cytokines and miRNAs expressions between different groups were analyzed using one-way ANOVA Bonferroni t test. Correlations were calculated using Pearson's test. P values ≤0.05 were considered significant. Our results showed that, levels of IL-4 and IL-10 were significantly higher in asymptomatic patients compared to symptomatic and control individuals, whereas TNF-alpha, IFN-gamma, IL-1 and IL-2 levels were elevated in symptomatic patients compared to controls and asymptomatic cases. However, we also found higher expression of IL-4 and IL-10 in symptomatic cases compared to controls. Moreover, the expression of miR-146a, miR-21 and miR-155 were significantly higher in symptomatic cases compared to controls and asymptomatic cases, whereas miR-146a expression was also higher in asymptomatic cases compared to controls. Further, we found a positive correlation of miR-146a with IL-4 and IL-10; miR-21 with TNF-alpha and IFN-gamma and miR-155 with TNF-alpha and IL-1 in symptomatic cases. In conclusion, this study identifies the higher miR-146a, miR-21 and miR-155 response along with Th1, Th2 and regulatory cytokine that may contribute to a mixed (Th1/Th2) response in symptomatic NCC, which might be one of the precipitating factors responsible for onset of seizure in human NCC. Keywords: Taenia solium; neurocysticercosis; miRNAs
Abstract Title:
Age Dependency of Force of Infection of Dengue Fever in Adult Population of Lahore, Pakistan

Primary Author Block:

Abstract Body:
Background: Dengue fever (DF) is an important vector borne viral disease worldwide. There have been large epidemics of dengue fever in in Pakistan, the worst being the one that affected Lahore in 2011 and resulted in 14031 confirmed cases and over 250 deaths in Lahore. Though infection is endemic in the Indian subcontinent, the epidemiological data on transmission of dengue virus is considerably lacking in Pakistan. Materials and Methods: Force of infection is defined as the rate at which susceptible individuals acquire an infectious disease. We used a catalytic model to estimate the risk of primary infection or force of infection of DF using age specific distribution of susceptible adults in Lahore during 2012. The catalytic model predicts that the proportion of seronegative individuals declines with increasing age at a constant rate, \( \lambda \), or force of infection. The model used allowed to changes in force of infection for different age groups. This study used the data from a seroprevalence study conducted in 2012 in Lahore. The study aimed to determine the seroprevalence of anti-dengue IgG antibodies in healthy adult population of Lahore (Mahmood et al 2013). Of 274 persons tested, 184 (67.2\%) were positive for anti DF IgG antibodies. Results: The force of infection (FOI) for DF infection seems to be age dependent in the adult population of Lahore as estimates of FOI decline with age. The estimates of FOI vary from 2.8\% (95\% CI; 1.9\%-4\%) per year for individuals aged 55 or over to 4.5\% (95\% CI; 3.4\%-5.9\%) per year for adults aged between 15-34 years. Conclusion: The study shows that there is still a considerable risk of DF infection among adult population of Lahore after 2011 epidemic. Dengue represents a considerable infection burden among adult population of Lahore, with levels of transmission comparable to those in more established epidemics from other parts of Southeast Asia.
Abstract Title:
Av0328-A Synthetic Oligosaccharide-Tetanus Toxoid Conjugate Targeting the Broadly Expressed Microbial Surface Polysaccharide Pnag is Safe and Immunogenic in Humans, Eliciting High Titers of Functional Antibody to Multiple Pathogens

Primary Author Block:

Abstract Body:
A major challenge to vaccine development is the serotype-specificity of antigens, limiting their utility to pathogens expressing target antigens. Poly-N-acetyl glucosamine (PNAG) is a surface polysaccharide produced by almost all major pathogenic bacterial, fungal and protozoan parasites, making it an attractive target for a broad-spectrum vaccine. We conducted a phase 1, dose-escalating study in humans of a GMP-quality conjugate vaccine made by coupling a synthetic pentameric oligosaccharide of β-1,6-linked glucosamines to tetanus toxoid (AV0328). Chemical analysis indicated a highly pure material with a ratio of ~35 oligosaccharides/TT molecule. Doses of 15, 30, 75 or 150 µg of AV0328 with Alum were injected on days 1 and 29 into healthy volunteers ≥18 years old (4 per dose group), reactogenicity recorded, and serum antibody responses at days 29, 57 and 6 months measured by ELISA, complement deposition and opsonic or bactericidal killing assays against 10 different pathogens encompassing multiple capsular serotypes among some of these targets. The vaccine was safe and well tolerated at all doses, eliciting only mild adverse events typical of vaccines and primarily confined to the injection site. The two lowest doses were not immunogenic. Among recipients of the 75 µg dose, 3 of 4 had increased IgG/IgG1 titers and increased deposition of complement component C1q onto PNAG. These sera mediated killing of N. gonorrhoeae, N. meningitidis group B and S. aureus. All 4 recipients of the 150 µg dose responded with increased IgG/IgG1 antibody and C1q deposition titers. Functional antibody responses, defined as a four-fold or greater increase in a bactericidal or opsonic killing titer in an in vitro assay, were achieved against 100% of pathogens tested including: 5 N. gonorrhoeae strains (including multi-resistant strains), 6 N. meningitidis Group B strains, 1 each of N. meningitidis Groups A, B, C, X, and W135, S. pneumoniae (5 Prevnar and 3 non-Prevnar serotypes), 4 S. aureus strains (including MRSA clinical isolates), 2 strains each of E. coli and K. pneumoniae (colistin- and multi-drug resistant strains), 1 strain each of A. baumannii and S. typhi and the fungal pathogens C. albicans and C. neoformans. There was little effect of the second dose on functional titers, which were unchanged at 6 months. No changes in bowel habits indicative of an effect on normal microbial flora were reported. AV0328 is safe and immunogenic in humans leading to a durable functional antibody response potentially protective against a broad-spectrum of microbial pathogens.
Session Title: CIV06 - Vaccines and Immunization Science: General
Session Start Date Time: 6/9/2018 11:00:00 AM
Session End Date Time: 6/9/2018 1:00:00 PM
Session Primary Track: Clinical Infections and Vaccines
Abstract Control Number: 7232
Poster Board Number: SATURDAY - 728

Abstract Title:
Expression, Purification of Recombinant Guinea Pig Cytokines and Chemokines for Monoclonal Antibody Production

Primary Author Block:
N. M. Meyer, T. Gupta, F. D. Quinn; Univ. of Georgia, Athens, GA

Abstract Body:
For nearly a century, the Guinea pig has been one of the most widely used animal infection model systems for studying bacterial, viral and parasitic pathogens. A limitation of the model is the dearth of available immunological reagents, specifically available antibodies targeting cytokines and immune cell markers. Without proper reagents the immune response to infection and protective effects of vaccination using this model cannot be quantified. Our goal is to develop mouse antibodies against Guinea pig cytokines IL-4, IL-8, IL-10, and MCP-1; shown to be crucial in mice and humans for assessing the efficacy of the existing BCG vaccine as well as potential new vaccine candidates. In our study, we used a stable expression system for Guinea pig cytokines IL-10 and MCP-1 in Escherichia coli NovaBlue competent cells, and have confirmed expression via Western blot. We have purified and injected these proteins into mice and have obtained antibodies for use in ELISA testing of vaccines. Developing antibodies to these cytokines known to be important during Mycobacterium tuberculosis infection also could be used in other immunological studies.
Abstract Title:
Polyvalent Adjuvant Combination to Prevent Hosp. Acquired Infections

Primary Author Block:
T. B. Nielsen, B. M. Luna, J. Yan, P. Pantapalangkoor, B. Spellberg; Univ. of Southern California, Los Angeles, CA

Abstract Body:
Background: The rise in antibiotic resistance has made treating infections more difficult, placing a premium on infection prevention. Vaccines possess the potential to not only prevent infections in the individual, but in whole populations. However, traditional vaccines provide vertical (pathogen-specific) infection prevention, whereas a horizontal (pathogen-agnostic) approach enables much broader protection. Methods: While attempting to boost the efficacy of various vaccine proteins targeting Staphylococcus aureus, we discovered that a unique combination of adjuvants improves survival of mice infected with Gram-positive or Gram-negative bacteria without the use of protein antigens. Results: The adjuvant combination provides protection that lasts at least 7 days for Gram-negative bacteria and at least 21 days for S. aureus, with a booster dose pushing protection beyond five weeks. Conclusion: These data support the development of this adjuvant combination as a short-to-intermediate-term, horizontal infection-prevention strategy for patients in healthcare settings who are at risk of being infected by nosocomial pathogens.
Abstract Title:
Antibody Response to Upec-Associated Uti Vaccine Antigens in Target Patient Populations
Primary Author Block:
C. A. Sarkissian Milner, V. DeOrnellas, A. Sintsova, C. Alteri, S. N. Smith, H. L. T. Mobley; Univ. of Michigan, Ann Arbor, MI
Abstract Body:
Urinary tract infection (UTI) is the second most common bacterial infection in humans with uropathogenic Escherichia coli (UPEC) being the major cause of UTI in otherwise healthy individuals. Increasing antibiotic resistance and the morbidity of recurrent infection creates a need for a UTI vaccine. Our laboratory has been developing an experimental vaccine targeting four UPEC outer membrane proteins – IreA, FyuA, IutA, and Hma – to elicit protection against UTI. These vaccine targets, all receptors involved in iron-acquisition, are expressed in humans during UTI. The goal of the present study is to better understand pre-existing antibody responses to our vaccine antigens in our target population and to compare antibody responses and protection elicited in mice immunized with the antigens using various routes and adjuvants. Sera were obtained from 77 cystitis patients at the University Health Service. Serum samples from each patient were analyzed for total IgG and antigen-specific titers by ELISA. Although total IgG was consistent across all patients, we found that antigen-specific IgG titers are related to the prevalence of the gene encoding the antigen in UPEC isolates. Mice were immunized with individual antigens using each of the following routes (subcutaneous, intramuscular, and intranasal) and adjuvants (Alum, Poly-IC, Monophosphoryl Lipid A, and dmLT) and IgG response and protection against UPEC challenge was measured. Although all adjuvants and routes produced antigen-specific IgG, only dmLT via the intranasal route provided significant protection against UPEC challenge. Ongoing measurement and analysis of antibody responses in response to immunization combined with our new understanding of native antibody responses in our target population will inform us as we move forward toward human trials with our experimental UTI vaccine.
Abstract Title:
Development of Vaccines and Therapeutics for Biodefense in Military Biodefense Res. Laboratory
Primary Author Block:
J. Yoo, S. Kim, C-H. Kim, S. Park, D. Song, S. Jeong; Agency for Defense Dev., Daejeon, Korea, Republic of
Abstract Body:
The Military Biodefense Research Laboratory, established in 2013, aims to develop vaccines and
therapeutics using cutting-edge biotechnologies for future biodefense. Currently, the laboratory is
carrying out four projects. The first project, ‘research on spore display vaccine’, is developing vaccines
for biological warfare agents, which are based on Bacillus spores with recombinant antigens on their
surfaces. The second project, ‘research on broad-spectrum antibacterial agent’, is developing
antibacterials which can protect from Gram positive pathogens as well as Gram negative pathogens with
microbe-derived or plant-derived materials. The third project, ‘research on bacteriophage-based
therapeutics’, is developing therapeutics based on pathogen-specific bacteriophages. This project is also
studying potential of phage-derived endolysins for infection treatment. The fourth project, ‘research on
high-throughput protein expression platform’, is developing a rapid production platform for
recombinant proteins and DNA vaccines for urgent emergency situation. All the projects have made
substantial progress so far, and in vivo efficacy tests with animal models are ongoing for many candidate
vaccines and therapeutic agents.
Abstract Title:
An Evaluation of the Protective Immunity of Attenuated Yersinia Pestis Live Vaccine Strains against Lethal Infection by Yersinia Pestis

Primary Author Block:

Abstract Body:
Yersinia pestis (Yp) is the agent of plague and is distributed globally, with many natural foci, e.g., Madagascar and western North America. It is a Tier 1 select agent and a major biothreat. Due to its transmissibility, rapid course, high mortality, and antibiotic resistance potential, vaccines are urgently needed. The two-component (F1 capsule and LcrV) vaccines have been variably effective and are vulnerable to vaccine resistance. Existing live bacterial vaccines are reactogenic and elicit only short-term immunity. Candidate live vaccines have included recombinant Yp, Y. pseudotuberculosis, and Salmonella. We are evaluating Yp candidates for efficacy and safety. Seven attenuated Yp strains available from USAMRIID or kindly provided by R. Curtiss and W. Sun, derived from wild type strains CO92 or KIM6+, were assessed in inbred (BALB/c) and outbred (CD-1) mice. These strains have mutations in virulence-associated genes, i.e., yscN, pspA, pspC, lpxL, tatA, crp, or deletions of the pgm locus and pPst plasmid. One dose was injected subcutaneously (SC) and the mice exposed four weeks later by aerosol or SC to a lethal dose of Yp CO92 or its non-encapsulated virulent derivative C12. Four of the candidates having a single attenuating mutation were withdrawn due to residual virulence. The multiply-attenuated KIM6+ derivative χ10030/pCD1Ap was also lethal for BALB/c mice at doses <u><</u> 106 CFU. The remaining candidates, CO92 pgm pPst-cured (p-p-) and CO92 yscN (YscN) were safe at doses <u><</u>107 CFU. Both protected 100% of BALB/c and CD1 mice exposed SC to <u>></u>200 LD50s of CO92. Strain YscN protected 60% of BALB/c mice exposed SC to C12 despite a high challenge dose (789 LD50s). The two vaccines protected 90-100% of BALB/c mice exposed by aerosol to CO92; however, CD-1 mice were only partially protected, with survivals of 60% (p-p-), and 20% (YscN). Studies on protection afforded by the two candidates against aerosol exposure to C12 are in progress, as are analyses of the humoral and cell-mediated immune responses elicited by the selected Yp vaccines. Future studies will assess a two dose vaccination scheme, determine vaccine and challenge infection kinetics, and initiate nonhuman primates trials. These studies contribute to the growing evidence supporting a live vaccine as an optimal plague countermeasure.
Abstract Title:
An Evaluation of the Protective Immunity of Yersinia Pseudotuberculosis Live Vaccine Strains against Lethal Infection by Yersinia Pestis

Primary Author Block:

Abstract Body:
Yersinia pestis (Yp) is the agent of plague and is distributed globally, with many natural foci, e.g., in Madagascar and western USA. It is a Tier 1 select agent and a major biothreat. Due to its transmissibility, rapid course, high mortality, and antibiotic resistance potential, vaccines are urgently needed. Two-component (F1 capsule and LcrV) vaccines have been variably effective and are vulnerable to vaccine resistance. Current live Yp vaccines are reactogenic and elicit only short-term immunity. Candidate live strains include recombinant Y. pseudotuberculosis (Yptb) strains, which offer several advantages: Yptb is much less virulent than Yp, generally causing a self-limited enteritis, is given orally, could stimulate cross-immunity to Yp, and may be more readily accepted. We tested three Yptb strains (kindly provided by R. Curtiss and W. Sun) in inbred (BALB/c) and outbred (CD-1) mouse models of plague. They harbor attenuating yop gene deletions and systems which enable Yp F1capsule expression or enhance LcrV delivery. One dose was given intragastrically, and the mice exposed four weeks later by aerosol or subcutaneously (SC) to a lethal dose of Yp strain C092 or its non-encapsulated derivative C12. Vaccine safety in BALB/c varied in a non-dose related manner, with survival ranging from 60 – 100% of mice given 0.5 -10x10^8 CFU. However, 90 – 100% of CD-1 mice survived the vaccinations. Based on initial findings, one strain was withdrawn and studies continued with strains Yptb χ10068 and χ10069/pYA5199. These strains protected 80 – 87.5% of BALB/c and 50 – 78% of CD-1 mice exposed SC with 362 or 478 LD50s of CO92, respectively. The vaccines also protected mice against SC challenge with C12; 71-88% of BALB/c survived 789 LD50s, and 70-86% of CD1 mice survived a 26 LD50 challenge. The vaccines protected less well vs. aerosol challenge with CO92; 33 - 38% of BALB/c (9 LD50s) and 10 – 22% of CD-1(26 LD50s) survived. Studies on protection afforded against aerosol exposure to C12 are in progress, as are analyses of the immune responses elicited by the vaccines. Future studies will assess a two dose vaccination scheme, determine vaccine and challenge infection kinetics, and initiate nonhuman primates trials. These studies contribute to the growing evidence supporting a live vaccine as an optimal plague countermeasure.
Abstract Title:
Long-Term Immunogenicity and Safety of Expec4v Vaccine against Extraintestinal Pathogenic Escherichia coli Disease in Healthy Participants

Primary Author Block:

Abstract Body:
Background: Extraintestinal pathogenic Escherichia coli (ExPEC) infection is associated with significant disease burden and hospitalizations. ExPEC4V is a bioconjugate vaccine (with exoprotein A, carrier) containing O-antigen polysaccharides from 4 E.coli serotypes (O1A, O2, O6A, O25B) being developed for prevention of invasive ExPEC disease. Immunogenicity and safety of ExPEC4V were analyzed in a phase-2, double-blind study in adults in stable health. Methods: Participants (≥18 to <50 years) were randomized to 1 of 5 groups (O-antigen µg - O1A:O2:O6A:O25B, 4:4:4:4 [G1]; 4:4:4:8 [G2]; 8:8:8:8 [G3]; 8:8:8:16 [G4]; 16:16:16:16 [G5]), or placebo (ratio 2:2:2:2:1); participants ≥50 years were enrolled in a stepwise, dose-escalating manner. After primary analysis (Day 30), G2, G4 and placebo were selected for Day 360 analysis of immunogenicity (ELISA, opsonophagocytic killing [OPK]), safety and reactogenicity. Results: Of 848 participants, 843 (≥18 to <50 years: 272 [32%]; ≥50 years: 571 [68%]) were vaccinated; 447 completed Day 360 from G2, G4 and placebo. ExPEC4V elicited a durable IgG antibody response against all 4 serotypes through Day 360 in all groups (≥2-fold IgG increase from baseline [BL] in G2 and G4 for Day 15; ≥82% and ≥90%, for Day 360; ≥65% and ≥71%. Maximum titers observed by Day 15 decreased by Day 360 similar to other conjugates. Geometric mean (GM) fold increase from BL in G2 and G4 by serotype for Day 360 was 2.8 and 3.9 (O1A), 6.9 and 8.0 (O2), 3.2 and 4.0 (O6), 3.9 and 4.5 (O25B); GM titers effective concentration rank by serotypes was O2>O1A>O6>O25B. A durable functional antibody response through Day 360 was demonstrated by OPK, with per serotype GM-fold increases for Day 15 from 2.1 to 26.6 and for Day 360 from 1.2 to 12.7. Vaccination-induced antibody titers were highest in G4 and maximum for serotype O2 (participants with ≥2-fold increase from BL in G2 and G4: 83% and 89%, Day 360). A robust correlation was observed between ELISA and OPK assays (r=0.61, Day 15; r=0.48, Day 360). Higher incidence of local and systemic solicited AEs, severity of AEs and late onset AEs was observed with increasing dose and were mostly Grade 1 or 2. One serious AE (trigeminal neuralgia) considered vaccine-related by the investigator occurred in highest dose group. Conclusions: ExPEC4V elicited robust and functional antibody response across all serotypes and doses. The 4:4:4:8 and 8:8:8:16 dose groups were selected for long-term followup to evaluate immunogenicity persistence. No safety signals were observed.
**Session Number:** 243  
**Session Type:** Poster

**Session Number:** 243  
**Session Type:** Poster

**Session Title:** CIV06 - Vaccines and Immunization Science: General

**Session Start Date Time:** 6/9/2018 11:00:00 AM  
**Session End Date Time:** 6/9/2018 1:00:00 PM

**Session Primary Track:** Clinical Infections and Vaccines

**Abstract Control Number:** 5663

**Poster Board Number:** SATURDAY - 735

**Abstract Title:** Preparation of Potent Vaccine against Riemerella Anatipestifer in Ducks

**Primary Author Block:** A. M. El Sawah1, H. M. Soliman1, K. F. Mohamed2, J. El Jakee2; 1Central Lab. for Evaluation of Veterinary Biologics, Cairo, Egypt, 2Faculty of Vet. Med. - Cairo Univ., Cairo, Egypt

**Abstract Body:**

Riemerella anatipestifer (R. a.) is the causative agent of septicemia antiserum exsudative which belongs to the family Flavobacteriaceae of Gram-negative bacteria. It has been a cause of economic loss to duck industry. The aim of this study was isolation, identification, and characterization of the most prevalent isolates of R. a. to prepare R. a. inactivated vaccine using two different adjuvants and evaluating the efficacy of this vaccine in ducks. A total of 190 ducks of Muscovy and Balady breeds suffered from signs of septicemia were examined. Five isolates suspected to be R. a. were detected (2.6%). The biochemical properties of the five isolates suspected were examined using API 20E system. They showed positive results with biochemical tests undergo PCR for confirmation of biochemical results using 16S rRNA specific primers of R. a. species. 4 out of 5 isolates were positive by PCR (80%). Aluminum hydroxide gel adjuvant and Montanide (ISA206) adjuvant inactivated vaccines were prepared from the 4 isolates, then evaluated by purity, sterility test, safety test, potency and challenge tests. The prepared vaccines were safe when given to 7-day old ducks in double doses. A humoral immune response of the vaccinated ducklings was estimated using Passive hemagglutination test (PHA) and ELISA and Indirect fluorescent antibody technique (IFAT). ELISA assay had good specificity and reproducibility than (PHA) and (IFAT) to detect serum antibodies against R. a. in ducks. The peak of antibody titers was at 3rd-week post booster vaccination and 3rd-week post challenge and the induced protection index of 70% to 85% in ducklings against challenge with the homologous R. a. serotypes. The ducks were observed, R. a. was isolated from the dead carcasses. The results of challenge tests showed that higher protection percent (92.9%) using Montanide ISA206 adjuvant inactivated vaccine against R. a. infection than using aluminum hydroxide gel adjuvant inactivated vaccine (80%). 90% of unvaccinated ducks (control) died during 3 weeks observation period. In conclusion, PCR assay can replace the traditional methods for identification of R. a. which are cumbersome and time-consuming. The immunization of young ducklings with inactivated adjuvant bacterin containing 4 local isolates of R. a. vaccination is found to be beneficial for protection from infectious serositis outbreaks. The greater sensitivity of the ELISA is capable of providing a much earlier warning of the onset of infection than either of the other methods.
Abstract Title:
Development of A Broad-Spectrum Vaccine Across Multiple Serotypes of Cryptococcus

Primary Author Block:
Univ. of Texas at San Antonio, San Antonio, TX

Abstract Body:
Cryptococcosis is a fungal disease caused by multiple Cryptococcus serotypes; particularly C. neoformans (serotypes A & D) and C. gattii (serotypes B & C). Cryptococcus causes pulmonary infections that lead to life-threatening meningitis. We showed that mice given an experimental pulmonary inoculation with an IFN-γ producing C. neoformans strain, H99γ, resolve the acute infection and are protected against a subsequent pulmonary challenge with the fully pathogenic H99 strain. We hypothesized that immunization with C. neoformans strain H99γ would elicit protection against challenge with multiple serotypes of Cryptococcus. Consequently, we immunized BALB/c mice with either heat killed H99γ (HKH99γ) or H99γ and later challenged these mice with each Cryptococcus serotype and monitored for survival. We observed significant increases in survival rates of mice immunized with H99γ compared to mice immunized with HKH99γ following challenge with serotypes A, B, and D. Furthermore, we performed western blot analysis on cell wall proteins extracted from each serotype and immunoblotted with sera from H99γ infected mice to identify cross-reactive immunodominant proteins that can be used for diagnostic purposes or as candidates for a subunit vaccine against cryptococcosis. Altogether, we describe a model system that is used to identify antigens that may be incorporated into a vaccine formulation to provide broad-spectrum protection against cryptococcosis.
Abstract:
Mycobacterium bovis BCG osteitis is a rare complication of BCG vaccination typically associated with changes in vaccine strain. The incidence of osteitis due to BCG Tokyo-172 strain, which is shared in Japan, Taiwan and Korea, has been reported to be 2 per million in Japan, but recently Taiwan reported a high incidence of BCG osteitis of 30.1 per million. Despite some case reports of BCG osteitis in Korea, the incidence and clinical presentations are not well investigated. This study aimed to evaluate the clinical characteristics of BCG osteitis in Korea from a single center experience during recent 10 years.

Methods: The study subjects included children diagnosed with BCG osteitis in the Seoul National University Hospital from January 2007 to December 2017. M. bovis BCG was confirmed by multiplex PCR which differentiates M. bovis BCG from other M. tuberculosis complex strains.

Results: BCG coverage of 2007-2016 was estimated >95% and ratio of inoculation route was 69% by multiple puncture and 31% by intradermal. Nineteen cases of BCG osteitis were included. The median age was 15 months (range, 7-33) and 12 (63.1%) were male. Sixteen (88.9%) received BCG Tokyo strain in multiple puncture method and three others (11.1%) received Danish or Tokyo strain intradermally. The median age at inoculation was 23.5 days (range, 2-36). Common symptoms were swelling (73.7%), pain (68.4%), and refusal to use the affected limb (52.6%). Fever (≥38.0°C) was accompanied in 21.1%. Patients visited the hospital from 2 to 110 days after the onset of symptoms. The femur (41.2%), tarsal bone (23.5%), and tibia (11.7%) were most commonly affected. The initial bone x-ray showed demarcated osteolytic lesions (58.5%) and cortical breakages (35.3%). Of the eight affected long bones, abscess lesions were located at the epiphyses on MRI. All underwent surgical drainage. Antituberculosis regimens consisting of isoniazid and rifampicin were continued for median duration of 12 months (range, 12-31). During the follow-up of median of 3.6 years, 33.3% required repeated surgical drainage due to persistent pain and swelling. Most (88.2%) recovered without evident sequelae, two had evident length discrepancy or angular deformity of the affected lesions.

Conclusions: This study found 19 cases of BCG osteitis from a single center during a 10-year period. Clinical characteristics illustrated in this study can be helpful in diagnosing BCG osteitis. Further research is needed to evaluate the relation between strain and dose of BCG and the development of serious adverse reactions.
Abstract Title:
TLR-9 Agonist Augments Immunogenicity and Protective Efficacy of Secretory Antigen Rv3620c of Mycobacteria Tuberculosis H37Rv Against Experimental Murine Tuberculosis

Primary Author Block:
S. Kazmi1, S. M. Faisal1, U. D. Gupta2, O. Mohammad1; 1Aligarh Muslim Univ., Aligarh, India, 2JALMA Leprosy Inst., Agra, India

Abstract Body:
Background: The global control of tuberculosis (TB) presents a continuous health challenge to humans. Major challenges to control the deadly disease is the failure of BCG vaccine to impart protection against Mycobacterium tuberculosis (M. tb) and the emergence of MDR-TB, XDR-TB and TDR-TB have further worsened the problem. Undoubtedly, there is a pressing need for alternative and effective immunization strategies that can overcome the above problems. In general, a Rv3620c/ESXW (region of difference, RD9), the members of early secreted antigenic target-6 (ESAT-6) gene family of M. tb evoke a strong immune response and Toll-like receptor 9 (TLR-9) activation augments both pro-inflammatory and adaptive immune response in the host. It has become beneficial to exploit these facets of TLR-9 signaling therapeutically to boost Rv3620c-specific immuno-stimulatory responses. Methods: 6-8 weeks old female BALB/c mice were immunized subcutaneously with various form of the antigen. On 21 day, the mice were boosted with the same formulation of antigen using the same route of administration. 26 weeks post last booster, 10 BALB/c mice from each group were challenged with virulent M. tb H37Rv through aerosol route. The various immunological parameters evoked upon administration of archaeosome based antigen delivery system comprising T cell antigen, Rv3620c (an ESAT-6 family protein), and TLR-9 agonist has been assessed against experimental murine tuberculosis in BALB/c mice. Results: Keeping the above fact into consideration, we investigated the role of Rv3620c, an early secreted antigenic target protein, in imparting protection against experimental murine tuberculosis. The result of the present study suggested that archaeosome encapsulated Rv3620c (archae-Rv3620) antigen induce strong lymphocyte proliferation, enhanced Th-1 biased response, elevated expression of co-stimulatory markers on both antigen presenting cells and T lymphocytes. The immuno-prophylactic response was further modulated by exposure of the animals to CpG oligodeoxynucleotide (CpG-ODN), a potent TLR-9 agonist, prior to immunization with archae-Rv3620c. Interestingly, pre-treatment with CpG-ODN boosted strong immunological memory as compared to archae-Rv3620c and BCG vaccine. Conclusions: Our result suggests that priming of the immunized animal with TLR-9 agonist followed by immunization with archae-Rv3620c augments immunogenicity and protective efficacy against M.tb and open new vistas in the field of immune-prophylaxis and tuberculosis treatment.
Abstract Title:
Potent Live Attenuated Vaccines against Tuberculosis

Primary Author Block:
A. M. Talaat, C.-w. Wu, C. Hansen; Univ. of Wisconsin-Madison, Madison, WI

Abstract Body:
The current tuberculosis vaccine, M. bovis BCG (BCG), has variable protection levels ranging from 0-80%, depending on the country of application and the genotype of vaccine used. The reductionist approach (depending on a selected list of antigens) for developing tuberculosis vaccines, did not identify any better alternatives to BCG, especially when candidates are tested under clinical setting in countries with high tuberculosis prevalence (e.g. South Africa). Earlier research from our group has identified several M. tuberculosis mutants that were further developed into live attenuated vaccine (LAV) candidates against TB. Our working hypothesis is that potent LAV will induce a broader and more potent memory T-cell response, will be more effective against highly virulent M. tuberculosis clinical isolates, and will be able to counteract the activity of regulatory T cells, three areas in which BCG performs very poorly.

Using a stringent aerosol model of murine challenge, immunization with two candidates (M. tbΔmosR, M. tbΔechA7) significantly reduced the M. tb load in murine tissues. Remarkably, by 60 days post challenge (DPC), no colonization was observed in organs of the ΔmosR-vaccinated mice. Immunologically, flow cytometry of lymphocytes isolated from the lung revealed that ΔechA7 primed a significantly greater CD4+ IFN-γ response than either ΔmosR or BCG. ELISA assays at 60 DPC demonstrated significantly higher M. tuberculosis specific IFN-γ production by splenocytes isolated from mice vaccinated with ΔechA7 compared to the others. Interestingly, by 8 weeks post immunization (WPI), ΔmosR was found only in the spleen of one immunized mice. Another experiment with high and low doses of ΔmosR-LAV did not alter any of the mice health parameters, another testimony of the safety of ΔmosR-LAV. Currently, we are pursuing a strategy based on the construction of a double gene knockout LAV (ΔmosRΔechA7) using a novel vector system developed by our group. In a future project, we will dissect the generated immunity in other models more relevant to human tuberculosis (such as non-human primates), to better prepare for clinical trials.
Session Title: CIV06 - Vaccines and Immunization Science: General
Session Start Date Time: 6/9/2018 11:00:00 AM
Session End Date Time: 6/9/2018 1:00:00 PM
Session Primary Track: Clinical Infections and Vaccines
Abstract Control Number: 3430
Poster Board Number: SATURDAY - 740

Abstract Title:
Anti-Tuberculosis Immune Response Induced in Lungs by Mycobacterium Indicus Pranii Given Via Intranasal Route

Primary Author Block:
A. Gupta; Natl. Inst. of Immunology, New Delhi, India

Abstract Body:
Background: Mycobacterium indicus pranii (MIP), a saprophytic mycobacterium shares significant antigenic repertoire with M. tuberculosis. It has been investigated as a vaccine against tuberculosis in animal models. Immunization with MIP by aerosol route provides significantly higher protection as compared to immunization by subcutaneous (s.c.) route in animal models of tuberculosis. However, mechanism behind differential protection has not been studied. Methods: In this study, using mice model we have evaluated and compared the M.tb specific immune response in lung compartments (airway lumen / lung interstitium) as well as spleen following MIP immunization via nasal (i.n.) and s.c. route. Results: MIP i.n. vaccination resulted in increased seeding of memory T cells (CD4+ and CD8+ T-cells) in the airway lumen. Frequency of CD4+ T cells expressing Th1 migratory marker and activation marker were also high in airway lumen of MIP i.n. group. Significantly high ex vivo secretion of cytokines- IFN-, IL-12, IL-17 and TNF- from cells of airway luminal spaces provides evidence of antigen-specific lung immune response, besides generating systemic immunity comparable to MIP s.c. group. Analysis of T cell response on per cell basis revealed that antigen specific T-cells of MIP i.n. group were functionally superior as higher percentage of these cells simultaneously secreted IFN-gamma, IL-2 and TNF-alpha cytokines as compared to MIP s.c. group. Adoptive transfer of airway luminal T-cells from MIP i.n. group into trachea of naive B6 mice revealed that MIP induced CD8 T-cells play crucial role in providing long term protection. Conclusions: Thus the study demonstrates that MIP intranasal vaccination induces M.tb specific memory T-cells in the airway lumen that results in an early and robust recall response against M.tb infection. Keywords: Airway lumen, Immunization, Mycobacterium indicus pranii, Th1 migratory markers
Abstract Title:
Single Cell Genomic Profiling of Human B Cells that are Responsible for Immune Response against Pneumococcal Polysaccharides in Aging HIV-Negative and HIV-Positive Individuals

Primary Author Block:
M. Happe, D. Samuvel, J. Westerink; Med. Univ. of South Carolina, Charleston, SC

Abstract Body:
Background: The introduction of combined anti-retroviral therapy resulted in a significant improvement of life expectancy of HIV-positive individuals leading to a rapid growth of aging HIV-positive population. Together, aging and HIV infection, increase susceptibility to life-threatening infections caused by Streptococcus pneumoniae. Despite preventative strategies, such as pneumococcal vaccination, it remains a challenge to induce potent and durable immune responses against pneumococcal polysaccharides (PPS) possibly due to poorly characterized perturbations in the B cell compartment of immune system of HIV-positive persons. The goal of this study is to characterize individual cellular changes in IgM memory B cell population that is largely responsible for producing immune responses to PPS, identify variations in inter-cellular gene expression that shape polysaccharide-specific B cell responses, and determine how aging affects these gene expressions. Methods: Blood samples were collected pre- and post-pneumococcal vaccination from healthy and HIV+ individuals ages 21-40 and 50-65 according to guidelines of institutional review board of Medical University of South Carolina. Isolated B cells were used for FACS analysis and sorting. Single-cell qPCR was performed using Fluidigm BiomarkHD instrument. Results: We have shown that the phenotype of polysaccharide specific B cells changes with age from predominantly IgM-memory to switched memory in HIV-negative individuals. However, in aging HIV-positive individuals, it resembles the phenotype of HIV-negative young adults in significantly reduced percentages. Single-cell genomic studies of IgM memory B cells revealed differential expression of genes that play an important role in T-cell independent immune responses (TACI, BAFF-R, CD21, TLR9, AICDA and other), B cell proliferation, and signaling between HIV-positive and HIV-negative persons in all age groups. Furthermore, unbiased clustering analysis identified distinct subgroups within IgM memory B cell population. Conclusions: Together, these data significantly increase our knowledge of the genetic identities of B cells in aging HIV+ individuals uncovering their complexity and diversity and revealing insights into mechanisms underlying B cell dysfunctional phenotype that leads to poor responses to pneumococcal vaccination.
Session Number: 243
Session Type: Poster
Session Number: 243
Session Type: Poster
Session Title: CIV06 - Vaccines and Immunization Science: General
Session Start Date Time: 6/9/2018 11:00:00 AM
Session End Date Time: 6/9/2018 1:00:00 PM
Session Primary Track: Clinical Infections and Vaccines
Abstract Control Number: 5649
Poster Board Number: SATURDAY - 742

Abstract Title:
Immunogenicity of Outer Membrane Vehicles From recombinant Yersinia Pestis
Primary Author Block:
W. Sun; Albany Med. Coll., Albany, NY
Abstract Body:
The lipid A species of Yersinia pestis were variable dependent on temperature. In flea (26oC), Y. pestis produces the hexa-acylated lipid A; while, in mammalian host (37oC), Y. pestis produces the tetra-acylated lipid A to evade surveillance of innate immunity via a weak interaction with host toll-like receptor 4 (TLR4). Our previous work demonstrated that incorporation of the Escherichia coli lpxL gene into Y. pestis KIM6+ allow the recombinant strain to produce hexa-acylated lipid A independent on temperature, and then added the Francisella tularensis lpxE gene encoding lipid A 1- phosphatase on top of the mutant strain to predominantly synthesize 1-dephosphorylated hexa-acylated lipid A (monophosphoryl lipid A, an adjuvant). Outer membrane vesicles (OMVs) are naturally non-replicating, highly immunogenic nanoparticles released from Gram-negative bacteria, and have numerous unique features for vaccine purposes. Based on our previous findings, we hypothesize that the lipid A modification in Y. pestis might affect OMVs productions and the self-adjuvanticity OMVs isolated from these mutants or their derivatives might be used as novel, effective and safe vaccines against plague challenge. The significance of these findings will be discussed. Keyword: Yersinia pestis, Lipid A, OMVs, novel plague vaccine
Outstanding Abstract Award: Pneumococcal Conjugate Vaccines: Potential Serotypes for Future Formulations

Primary Author Block:
A. R. Golden1, H. J. Adam2, M. Baxter1, I. Martin3, W. Demczuk3, K. A. Nichol2, M. R. Mulvey3, G. G. Zhanel1, Canadian Antimicrobial Resistance Alliance (CARA); 1Univ. of Manitoba, Winnipeg, MB, Canada, 2Diagnostic Services Manitoba, Winnipeg, MB, Canada, 3Natl. Microbiol. Lab., Winnipeg, MB, Canada

Abstract Body:
Background: The serotype distribution of Streptococcus pneumoniae (SPN) is constantly shifting due to vaccine pressure. Despite the addition of key serotypes (3, 19A) to PCV-13 in 2010, serotype replacement is already evident in the pneumococcal population. The purpose of this study was to identify additional SPN serotypes that warrant consideration for inclusion in future conjugate vaccine formulations. Methods: In a collaboration between CARA and NML, invasive SPN isolates were collected from across Canada from 2011-14 as part of the SAVE study. All isolates were serotyped by the Quellung reaction and tested for antimicrobial susceptibilities using CLSI methods. A subset of commonly collected non-PCV-13 serotypes (6C, 8, 9N, 11A, 12F, 15A, 22F, 33F, 35B) were further characterized using MLST and WGS analyses. Results: Serotypes 22F and 33F (already included in a 15-valent vaccine undergoing development in the US) appear to be good choices for inclusion based on our Canadian data; serotype 22F was highly clonal, with almost all isolates sharing relatedness to ST433. This characteristic may contribute to vaccine success for serotype 22F, as similarly clonal vaccine types (e.g., 7F) have rapidly decreased in prevalence following conjugate vaccine use. Serotype 33F demonstrated increasing genetic diversity and MDR, characteristics that are often possessed by successful serotypes. Other serotypes of interest included 35B and 15A. Approximately 40% of 35B were penicillin (PEN)-nonsusceptible, attributed to rapidly expanding ST558. These isolates possessed PBP1A alterations most commonly seen in 19A-ST320, indicating that, like serotype 19A, 35B may have the capacity to acquire full PEN resistance in the future. Additionally, capsular switch variant 35B-ST156 was identified in Canada; this persistent and successful international clone is associated with PEN resistance and MDR, and has recently increased in prevalence in the US. Serotype 15A was associated with the highest rate of MDR in Canada, attributable to international clone ST63. However, serotype 15A demonstrated an overall decreasing trend from 2011-2014, necessitating future monitoring to determine if prevalence continues to decrease. Conclusion: Based on analysis of Canadian SPN isolates, there are many serotypes that warrant consideration for inclusion in future conjugate vaccines, including 35B and 15A. Continued surveillance is necessary to identify trends moving forward, both within these serotypes and others that may become prevalent.
A Niosome Formulation Modulates the Th1/Th2 Bias Immune Response in Mice and Also Provides Protection against Anthrax Spore Challenge

H. Gogoi, R. Mani, R. Bhatnagar; Jawaharlal Nehru Univ., New Delhi, India

Anthrax is a zoonosis caused by Bacillus anthracis (BA). Virulence of the pathogen is attributed to an anti-phagocytic poly-gamma-D-glutamic acid capsule and a tri-partite toxin system. Current prophylactic approach involves alum precipitated cell free culture supernatant of an unencapsulated strain (Sterne). However, the vaccination schedule is very lengthy with multiple doses at 0, 2, 4 weeks and 6 months with booster doses at 6 and 12 months, which is followed by yearly boosters. Moreover, this vaccine also suffers from drawbacks like, edema, fatigue, headache, myalgia, nasopharyngitis, erythema at injection site, elicitation of heterogeneous immune response amongst immunized population which raised the requirement for a safer vaccine as well as provide a prolonged immunity against the disease. In this present study, we have investigated the immunogenicity and protective efficacy of a niosomal formulation encapsulating Protective Antigen (PA), the immunodominant protein of BA. Niosomal formulation encapsulating PA (NISV+PA) was prepared from span 60 and cholesterol by reverse phase evaporation method and were evaluated for in-vitro characteristics and immunological studies. Particle characterization using TEM and AFM analysis showed that the niosomal formulation was spherical in shape. The entrapment efficiency was calculated to be 58.5 %. Confocal microscopy and flow cytometry studies showed an enhancement in antigen uptake by niosome as compared to antigen only. In-vitro release assay showed a burst release of antigen within 24 hr followed by a gradual release for 144 hr. Immunological studies showed that PA encapsulated niosome elicited a robust IgG titer. Antibody isotyping and cytokine profile showed that NISV + PA enhanced both Th1 and Th2 response in mice suggesting a mixed Th1/Th2 response. NISV+ PA elicited high levels of anti-inflammatory cytokine IL-10 with low levels of pro-inflammatory cytokine TNF-α, suggesting the anti-inflammatory property of niosome. The niosomal formulations were also able to confer protection against BA infection as compared to only PA. Hence, NISV encapsulated PA was found to be better immunoprophylactic against anthrax.
Emergence of the Multidrug-Resistant Pilliated Serotype 19a-St320 Clone in Brazil: from 1988 to 2015 with Pcv10 in Between

Primary Author Block:
L. M. A. Oliveira, A. R. V. Souza, T. C. A. Pinto, L. M. Teixeira; Univ.e Federal do Rio de Janeiro, Rio de Janeiro, Brazil

Abstract Body:
Streptococcus pneumoniae (Sp) of serogroup 19 stands out as a leading cause of pneumococcal pneumonia worldwide frequently associated with multidrug resistance. This serogroup encompasses serotypes 19A, 19B, 19C and 19F, being serotypes 19A and 19F the most commonly found. Distribution of serotypes varies according to geographical region and it has been modulated by the introduction of pneumococcal conjugate vaccines (PCV). Serotype 19A has been reported as the major emerging serotype after PCV7 introduction; however, its emergence after PCV10 introduction still seems debatable. Brazil is one of the few countries that have adopted PCV10 in the National Immunization Program, since 2010. In this study, 231 serogroup 19 Sp, recovered from diseased patients and asymptomatic nasopharyngeal carriers living in Brazil between 1988 and 2015, were evaluated regarding capsular types (Quellung reaction and PCR), antimicrobial susceptibility profile, genetic diversity by MLST and detection of pilus type 1 (PI-1) and type 2 (PI-2) genes by PCR. Serotype 19F was the most frequent overall (67.5%), followed by serotypes 19A (31.2%), 19B (0.9%) and 19C (0.4%). Nearly 25% of the strains were nonsusceptible to penicillin (PNSP), being this characteristic, as well as multidrug resistance, more frequently associated with serotype 19A strains. PI-1 was detected in 56.7% of the isolates, PI-2 was identified in 19.5% of the strains, and 16.9% harbored PI-1 and PI-2 genes simultaneously. An inversion in the proportions between serotypes 19F and 19A was observed over the period of time included in this study, with increasing numbers of 19A especially after 2010. Likewise, penicillin non-susceptibility, as well as multidrug resistance, increased in the same period. Before PCV10 introduction, ST177 (international clone Portugal19F-21 harboring PI-1) and ST763 (regional clone harboring PI-1 and PI-2) were the most frequent clones among serotype 19F strains, while ST733 (regional clone, nonpilliated) was common within serotype 19A. After 2010, ST177 and ST733 almost disappeared, while ST320, associated with serotype 19A and the presence of PI-1 and PI-2 genes, rapidly emerged. Of note, ST320 was not detected in the pre-PCV10 period. We hypothesize that Brazilian isolates of serotype 19A-ST320 detected after the introduction of PCV10 may have originated from capsular switching events in serotype 19F-ST763, which also led to the acquisition of penicillin resistance, as a result of selective pressure imposed by the national introduction of PCV10.
Lacvax® OmpA, An Oral Mucosal Vaccine Candidate for Shigella

Background: Shigellosis is an acute invasive disease of the lower intestine, which afflicts millions of people worldwide with an estimated one million fatalities per annum. Vaccine is one of the most promising approaches to fight against multidrug-resistant Shigella. Despite extensive research during the last two decades, a vaccine against Shigella is not yet available in the market. Aim & Rationale: To provide a safe, effective and broad-spectrum vaccine against Shigella, we explored food grade bacteria Lactococcus lactis (L. lactis) for the delivery of conserved antigenic protein; Outer membrane protein A (OmpA) to mucosal sites for effective elicitation of systemic and mucosal immunity. Methods: To develop a needle-free oral mucosal vaccine, OmpA was cloned and expressed in food grade L. lactis. Construction of r-L. lactis expressing OmpA (LacVax® OmpA) was confirmed by SDS-PAGE and Western Blot analysis. The immunogenic potential of LacVax® OmpA was ascertained by its oral and nasal administration to Balb/C mice. Results: The significant increase in serum IgG, faecal IgA levels and Th1 dominant response in LacVax® OmpA immunized mice revealed successful activation of humoral and cellular immunity. The immunized animals were also protected from human-like shigellosis when challenged with S. flexneri 2a ATCC 12022. Conclusions: These results demonstrate successful development of a putative vaccine candidate against Shigella. The LacVax® based technology can also be used to develop candidate vaccines against other enteric pathogens which require mucosal immunity for their elimination. Further, the validation of LacVax® OmpA in higher animals in collaboration with Industrial partners is currently in progress.
Abstract:
Over-Expression of Lipid A Deacylase PagL Improves Delivery of Protective Antigens from Attenuated Salmonella Typhi Live Carrier Vaccines Through Mediating Hypervesiculation

Primary Author Block:
T. H. Pham, J. E. Gale; Ctr. for Vaccine Dev., Univ. of Maryland Sch. of Med., Baltimore, MD

Abstract Body:
Mucosally delivered bacterial live carrier vaccines represent a practical and versatile strategy for immunization. To enhance antigen-specific immunity, foreign antigens must be delivered to the immune system and induce protective immune responses, and surface-expressed or secreted antigens are generally more immunogenic than cytoplasmic constructs. Our hypothesis is that by inducing outer membrane vesicle (OMV)-mediated delivery, we can improve delivery of sufficient antigens to immune inductive sides to confer protection against bacterial infections. Here we use of the PhoP/PhoQ-activated gene (pagL) of Salmonella typhimurium as a novel outer membrane protein (OMP) that plays important role in OMV formation and antigen delivery. Over-expression of PagL has been shown to induce prolific formation of OMVs vesicles in Salmonella. Interestingly, PagL is a 3-O-deacylase which converts pro-inflammatory hexa-acylated lipid A into penta-acylated forms, thereby reducing TLR-4 signaling of inflammatory responses. Therefore, recombinant OMVs (rOMVs) exported from Salmonella strains through over-expression of PagL would be expected to be less reactogenic, which would improve the clinical acceptability of these vesicles if purified and used as primary or booster vaccines. We constructed a synthetic pagl gene and inserted it into a low-copy-number expression plasmid pSEC10, replacing the clyA gene to create pPagL. To monitor OMV export, we integrated a cassette encoding the reporter protein ClyA into the guaBA locus of Salmonella Typhi live vector vaccine CVD910 and then introduced pPagL into the resulting strain to create CVD910ΔguaBA::clyA(pPagL). We evaluated the effect of PagL on OMV formation and antigen delivery by measuring the hemolytic activity associated with OMVs delivering hemolytic ClyA. We report that the hemolytic activity was significantly increased when pPagL was introduced into CVD910ΔguaBA::clyA in comparison with controls, suggesting that over-expression of PagL induces excellent export of OMPs via OMVs. Taken together, our results firmly establish the feasibility of developing a novel delivery system that foreign OMPs from bacterial pathogens can be efficiently exported from attenuated S. Typhi-based carrier vaccines via rOMVs through over-expression of PagL to enhance delivery and improve protective efficacy.
Abstract Title:
Deciphering the Salmonella-Host Interaction and Devising Strategies to Prevent Infections

Primary Author Block:
S. Das, S. Das; Natl. Inst. of Cholera and Enteric Diseases, Kolkata, India

Abstract Body:
S. Typhi is a leading cause of blood stream infection in low and middle income countries with an incidence rate of 9.9 to 24.2 million and kills 75,000 to 2,08,000 people annually. Most extensively used vaccine is based on the outer polysaccharide coat of S. Typhi (Vi) and is a T independent antigen. Hence it is incapable of imparting protection to children <2 years of age, an age group which is most affected by the disease. We have identified an immunogenic outer-membrane-protein of S. Typhi, T2544, which is essential for adhesion to host cells and pathogenesis in mouse models. We identified the receptor of T2544 to be a trans-membrane channel protein whose membrane translocation increased upon rT2544 attachment, thereby facilitating adhesion and subsequent internalization of more bacteria. Receptor-T2544 interaction also induced phosphorylation of PI3-K/ Akt. We also found association of autophagy related proteins Rheb, mTOR and Tsc-2 with the receptor upon T2544 attachment. Depletion of these proteins by RNAi drastically impaired the intracellular survival of S. Typhi suggesting the importance of T2544-receptor interaction. Since T2544 is an immunogenic protein we conjugated Vi to T2544 and studied the immunogenicity and protective efficacy of Vi-rT2544. Antibody-dependent-cellular-cytotoxicity assay confirmed the capability of anti Vi-rT2544 antibodies to lyse Salmonella infected cells while ELISPOT assay confirmed the generation of significant number of Vi-rT2544 specific effector and memory B cells. Vi-rT2544 specific cytotoxic T lymphocytes (CTLs) were also detected. Both DCs and T cells produced significant amounts of Th1 cytokines which is essential for combating S. Typhi infections. Immunization of mice with Vi-rT2544 conferred protection against S. Typhi and S. Paratyphi infection, thereby confirming the potential of the molecule to be a candidate vaccine. As interaction of T2544 with its receptor is crucial for S. Typhi pathogenesis, disrupting it may be used as therapeutic strategy to check S. Typhi infection. In summary, the proposed candidate vaccine and inhibitor may serve as alternative approaches to tackle emerging MDR strains of S. Typhi and Paratyphi.
Abstract Title:
The Role of Denitrification Genes in Anaerobic Growth and Virulence of Flavobacterium Columnare

Primary Author Block:

Abstract Body:
Channel catfish aquaculture is the most significant aquaculture industry in the U.S., and it has been widely affected by Flavobacterium columnare. Comparative genomics analyses indicated that the F. columnare genome has unique denitrification genes relative to Flavobacterium psychrophilum, including nasA (nitrate reductase); nirS (nitrite reductase); norB (nitric oxide reductase); and nosZ (nitrous oxide reductase). The current study explores the roles of nasA, nirS, norB, and nosZ in anaerobic growth, nitrate reduction, biofilm formation, and virulence. Four in-frame deletion mutants in virulent F. columnare strain 94-081 were constructed by allelic exchange using pCP29 plasmid. Compared with F. columnare strain 94-081, FcΔnasA, FcΔnirS, and FcΔnosZ strains were not able to grow under anaerobic condition, whereas the growth of FcΔnorB strain was similar to the parent strain (FcWT). When supplied with exogenous nitrate, significantly higher concentration of nitrate was found in FcΔnasA, FcΔnirS, and FcΔnosZ compared to FcWT, indicating that nasA, nirS, and nosZ genes are required for nitrate consumption. In contrast, FcΔnorB and FcWT consumed the available nitrate. There were no significant (P < 0.05) differences in biofilm formation among the four mutants and FcWT at 24 and 96 hours. The nitrite reductase mutant FcΔnirS is highly attenuated (6.67% mortality) in catfish, whereas FcΔnasA (80% mortality), FcΔnorB (86.67% mortality), and FcΔnosZ (100% mortality) had similar virulence to FcWT. These results provide, for the first time, information for genes that enable F. columnare to grow anaerobically using nitrate as an electron acceptor. Furthermore, nirS plays a role in F. columnare virulence, and FcΔnirS strain could be useful as a safe live vaccine if it protects catfish against FcWT infections.
Abstract Title:
Protective Antigen Encapsulated Trimethylchitosan Nanoparticles Protect Mice against Virulent Bacillus anthracis

Primary Author Block:
A. Malik, R. Bhatnagar; Jawaharlal Nehru Univ., Delhi, India

Abstract Body:
Anthrax is an era old deadly disease against which there are only two currently available licensed vaccines named Anthrax Vaccine Adsorbed (AVA) and precipitated (AVP). Though they can provide a protective immunity, their multiple side-effects owing to their ill-defined composition and presence of toxic proteins (LF and EF) of Bacillus anthracis, the causative organism of anthrax, in the vaccine formulation makes their widespread use objectionable. Hence, an anthrax vaccine that contains well-defined and controlled components would be highly desirable. In this context, we have evaluated the potential of various vaccine formulations comprising of Protective antigen (PA) encapsulated trimethylchitosan nanoparticles (TMC-PA) in conjunction with either CpG-C ODN 2395(CpG) or Poly I:C. Each formulation was administered via three different routes, viz., subcutaneous (SC), intramuscular (IM) and intraperitoneal (IP) in female BALB/c mice. Irrespective of the route of immunization, CpG or Poly I:C adjuvanted TMC-PA nanoparticles induced a significantly higher humoral response (total serum IgG and its isotypes viz., IgG1, IgG2a, and IgG2b), compared to their CpG or Poly I:C PA counterparts. This clearly demonstrates the synergistic behavior of CpG and Poly I:C with TMC nanoparticles. The adjuvant potential of TMC nanoparticles could be observed in all the three routes as the TMC-PA nanoparticles by themselves induced IgG titers (1-1.5 x105) significantly higher than both CpG PA and Poly I:C PA groups (2-8x104). The effect of formulations on T-helper (Th) cell development was assessed by quantifying the Th1-dependant (TNF-α, IFN-γ, and IL-2), Th2-dependant (IL-4, IL-6, and IL-10) and Th17-type (IL-17A) cytokines. Adjuvanation with CpG and Poly I:C, the TMC-PA nanoparticles triggered a Th1 skewed immune response, as suggested by an increase in the levels of total IgG2a along with IFN-γ cytokine production. Interestingly, the TMC-PA group showed a Th2 biased immune response. Upon challenge with the Bacillus anthracis Ames strain, CpG and Poly I:C adjuvanted TMC-PA nanoparticles immunized via the SC and IM routes showed the highest protective efficacy of ~83%. Altogether the results suggest that CpG or Poly I:C adjuvanted, PA-loaded TMC nanoparticles could be used as an effective, non-toxic, 2nd generation subunit-vaccine candidate against anthrax.
Abstract Title:
Assessment of the Immunogenicity of Chlamydia-Infection Derived Exosomes

Primary Author Block:
R. S. Russell1, A. Rodriguez1, T. Ahmed1, J. U. Igietseme2, F. O. Eko1; 1Morehouse Sch. of Med., Atlanta, GA, 2CDC, Atlanta, GA

Abstract Body:
Background: Exosomes are extracellular vesicles which package cellular components from donor cells and transport them to recipient cells, thereby serving as vehicles for horizontal transfer of effector molecules between cells. We recently showed that Chlamydia muridarum infection-derived exosomes activate the maturation of dendritic cells in vitro but the in vivo immune function of these exosomes is unknown. The aim of this study was to investigate the ability of Chlamydia infection-derived exosomes to induce an immune response following immunization of mice. Methods: Consequently, female mice were immunized and boosted twice subcutaneously with exosomes isolated from Chlamydia infected epithelial cells and humoral and cell-mediated immune responses were evaluated. Immunized mice were infected intravaginally with live C. muridarum 2 weeks after the last immunization and the level of infection was assessed by enumerating the number of chlamydial inclusion forming units (IFU) from cervicovaginal swabs. Results: Our results showed that exosomes, in combination with Vibrio cholerae ghost as an adjuvant, enhanced the clearance of Chlamydia from the genital tract in immunized mice and significantly enhanced the proliferation of immune T cells following re-stimulation with exosomes in vitro. Furthermore, immunization with exosomes increased the secretion of IFN-γ but not IL-4 upon in vitro stimulation with DCs pulsed with exosomes. Similarly, exosomes significantly increased the proliferation of naïve T cells in vitro, and produced significantly higher amounts of IFN-γ compared to IL-4 following incubation with DCs pulsed in vitro with exosomes. Conclusions: Our findings therefore suggest that infection-derived exosomes are immunogenic and can confer protection against infection by eliciting a Th1 immune response.
Abstract Title:
Variation in the Transient Colonization of Murine Upper Reproductive Tracts Following Transcervical Delivery of Chlamydia Trachomatis Serovars D, E, and L2
Primary Author Block:
K. Walters, M. Sabol-Jones, B. Green, N. A. Fisher; Southern Res., Birmingham, AL
Abstract Body:
Background: Chlamydia trachomatis is the causative agent of Chlamydia, the most common sexually transmitted disease in the United States and the leading infectious cause of blindness globally. While antibiotics are generally effective against symptomatic Chlamydia infection, asymptomatic infections predominate. Often, these asymptomatic infections give rise to debilitating sequelae including pelvic inflammatory disease, ectopic pregnancy, lymphogranuloma venereum, and neonatal infections. Thus, a preventative vaccine is necessary to reduce the morbidity associated with Chlamydia. Since Chlamydia trachomatis does not naturally ascend the upper genital tract (UGT) of mice or other standard laboratory animals, efforts to develop Chlamydia vaccines have been hampered by the lack of an adequate non-clinical animal model with which to evaluate efficacy. However, recent reports indicate that transcervical delivery of infectious elementary bodies (EBs) bypasses the physical barrier of the cervix and allows reproducible colonization of the UGT in mice. In this study, we sought to determine the degree and duration of UGT colonization of three distinct Chlamydia trachomatis serovars associated with human disease. Methods: EBs from Chlamydia trachomatis serovars D, E, and L2 were generated by co-culture with McCoy cells. A non-surgical embryo transfer device was then used to bypass the cervix and deliver EBs directly to the uteri of C57BL/6 mice. At various time points post challenge (between 2 and 18 days), mice were euthanized and bacterial burden in the UGT was measured by quantitative PCR and titration of inclusion forming bodies (IFUs). Results: All three serovars colonized the mouse UGT after transcervical inoculation. The degree of colonization and duration of colonization differed by serovar. Animal-to-animal variation also differed between serovars with serovar E being the most variable. IFU titration was less reliable than qPCR in determining the presence of all three serovars. As expected, treatment with azithromycin reduced the bacterial burden in the UGT. Conclusion: Transcervical delivery of Chlamydia trachomatis elementary bodies allows for transient but reproducible colonization of the murine upper genital tract. This is an important step toward a suitable non-clinical model for evaluation of anti-Chlamydia drugs and vaccines.
Abstract Title:
Novel Whole-Cell Inactivated Neisseria Gonorrhoeae Nanoparticle Vaccine Formulation

Primary Author Block:
S. M. Zughaier1, L. Bajaj2, R. P. Gala2, W. B. Gamal2, M. J. D'Souza2; 1Qatar Univ., Doha, Qatar, 2Mercer Univ., Atlanta, GA

Abstract Body:
Background: Neisseria gonorrhoeae is a strict human pathogen responsible for more than 100 million new sexually transmitted infections worldwide each year. Due to the global emergence of antibiotic resistance, the CDC recently listed N. gonorrhoeae as an urgent threat to public health. No vaccine is available in spite of the huge disease burden and the possibility of untreatable gonorrhea. Aim: The aim of this study is to investigate the immunogenicity of a novel whole-cell based inactivated gonococcal nanovaccine formulation. Methods: The nanotechnology-based vaccine formulation consists of inactivated whole-cell gonococci strain CDC-F62, spray dried and encapsulated into biodegradable cross-linked albumin matrix with sustained slow antigen release. The dry vaccine nanoparticles were then loaded in a dissolvable microneedle skin patch for transdermal delivery. The efficacy of the whole-cell nanovaccine formulation loaded in microneedles was assessed in vivo using 4-6 week old Balb/c mice receiving prime dose followed two booster doses at week 2 and 4. Each dose has 10mg of spray-dried nanoparticles containing 500μg of the antigen. Blood samples were collected prior to dosing and every 2 weeks for 10 weeks. Antibody titers were measured using an ELISA and antigen-specific T lymphocytes were assessed in spleens and lymph nodes. Results: The data demonstrated that whole-cell based gonococcal nanovaccine transdermal administration induced significant increase in antigen-specific IgG antibody titers and antigen-specific CD4 and CD8 T lymphocytes in mice vaccinated with gonococcal nanoparticles loaded in microneedles compared to mice vaccinated subcutaneously with gonococcal antigens in solution or empty microneedles. Significant increase in antigen-specific IgG antibody levels was observed at end of week 2 in groups that received the vaccine compared to the group receiving empty nanoparticles. The advantages of using formalin-fixed whole-cell gonococi that all immunogenic epitopes are covered and preserved from degradation. The spherical shaped micro and nanoparticles are biological mimics of gonococci, therefore present to the immune system as invaders but without the ability to suppress adaptive immunity. Conclusions: The transdermal delivery of a nanoparticle vaccine via a microneedle patch was shown to be an effective system for vaccine delivery. The novel gonorrhea nanovaccine is cheap to produce in a stable dry powder and can be delivered in microneedle skin patch obviating the need for needle use or the cold chain.
Abstract Title:
Deletion of the Major Porin Proteins PorA and PorB from Outer Membrane Vesicle Vaccines Enhances Elicitation of Cross-Protective Antibodies against Serogroup B Neisseria Meningitidis

Primary Author Block:
K. A. Matthias, A. M. Reveille, M. C. Bash; Food and Drug Admin., Silver Spring, MD

Abstract Body:
Of the six meningococcal serogroups most commonly associated with invasive disease (A, B, C, W, X, and Y), only the capsular polysaccharide of serogroup B (MenB) is poorly immunogenic and is not currently utilized in licensed vaccines or those in development. Instead, subcapsular antigens, namely outer membrane proteins (OMPs), are targeted in both recombinant and outer membrane vesicle (OMV) MenB vaccines. The major porin proteins, PorA and PorB, have both been suggested as vaccine candidates, with PorA functioning as the immunodominant surface antigen. However, both porins are highly antigenically variable, and OMV vaccines exhibit diminished efficacy against strains heterologous to the PorA type from which they are produced, suggesting a limited breadth of coverage for PorA- and PorB-specific vaccines. To explore the potential protection afforded by other OMPs, we deleted or genetically modified PorA, PorB, and the structural OMP RmpM from the wild type MenB strain MC58. OMVs were produced from the wild type and mutant strains and used to immunize rabbits, from which sera were collected and tested for MenB binding antibody and bactericidal activity. Although all sera contained antibodies that bound strongly to five different MenB strains in whole cell ELISAs, the protein specificity of these antibodies differed according to immunizing OMV type as determined by western blot analysis. OMVs derived from the parental MC58 wild type strain stimulated a strong anti-PorA response as expected and exhibited limited ability to kill heterologous strains in bactericidal assays. In contrast, sera obtained from rabbits immunized with OMVs isolated from the PorA/PorB double deletion (ΔAB) or the PorA/PorB/RmpM triple deletion (ΔABR) strains were able to kill all strains effectively, suggesting that the enhanced cross-protective responses observed upon deletion of the porin proteins may be a result of immune engagement with OMPs that exhibit low variability.
Enterotoxic Escherichia coli Vaccine Efficacy Evaluation Using A Bioluminescent Reporter Strain in Mice

Primary Author Block:
M. Menchel, K. Navarrete, S. Stibitz, M. Osorio; U.S. FDA, Silver Spring, MD

Abstract Body:
Enterotoxigenic Escherichia coli (ETEC) is a leading cause of travelers' diarrhea and of childhood diarrheal disease in low-income nations. An effective ETEC vaccine, however, does not exist at this time. We address this public health need by demonstrating the feasibility of using inactivated ETEC or Shigella-ETEC hybrid whole cell vaccines to protect against colonization. Previously we demonstrated that these whole cell vaccines induce strong immune responses in mice1. While immunogenicity can be measured by the antibody response against specific antigens, demonstrating the protective efficacy against ETEC infection has been challenging due to a lack of a suitable small animal model. To address this problem, we generated a fully virulent bioluminescent derivative of ETEC H10407 via transposon mutagenesis to introduce a luciferase reporter gene into the genome of ETEC. Mice were challenged with a sub-lethal dose of the bioluminescent ETEC (ETEC-lux) which were visualized using a XenogenTM IVIS imaging system to observe the kinetics of ETEC-lux distribution in the respiratory tract. Clearance of the bacteria, as interpreted by the disappearance of a detectable light signal, was used as a surrogate for protection. We evaluated the usability of this model by intranasally challenging vaccinated and naïve mice with a sub-lethal dose of ETEC-lux and monitoring the clearance kinetics of the reporter strain. At 48 hours post challenge, we could detect quantitative differences in the rate of clearance of the reporter strain in vaccinated mice compared to controls. There was also a clear correlation between clearance of ETEC-lux and the antibody response against ETEC colonization factors such as CFA/I. In an effort to extend the model to a more relevant site of ETEC colonization, we explored the possibility of colonizing the intestinal tract of mice with ETEC-lux, following treatment with streptomycin2. Antibiotic-treated mice received an oral gavage of streptomycin and streptomycin in the drinking water for 48 hours. Mice were then orally challenged with 5x10^8 ETEC-lux and imaged over time to track the intensity and location of ETEC-lux. Mice treated with antibiotics had detectable signal for at least 4 weeks after initial challenge. Here we provide data demonstrating that a mouse gastrointestinal ETEC-lux model has the potential to be used to evaluate the protective efficacy of ETEC vaccine candidates and other novel interventions in a relevant animal system.
Abstract Title:
Characterization and Evaluation of Peptide Conjugate Vaccines for Burkholderia

Primary Author Block:
I. Blanco1, C. Klimko1, J. Shoe1, M. Hunter1, P. Guo2, S-C. Lo2, B. Bachert1, S. Lukomski3, R. Bernhards4, P. Worsham1, C. Cote1, S. Welkos1; 1United States Army Med. Res. Inst. of Infectious Diseases, Frederick, MD, 2Food and Drug Admin., Silver Spring, MD, 3West Virginia Univ., Morgantown, WV, 4Edgewood Chemical Biological Ctr., Aberdeen Proving Ground, MD

Abstract Body:
Burkholderia pseudomallei (Bp) and Burkholderia mallei (Bm) are Tier 1 biothreats and the causes of melioidosis (Bp) and glanders (Bm). The course of melioidosis ranges from acute and rapidly fatal to protracted and chronic; glanders produces a similar disease but occurs primarily in horses. Bp is globally distributed in tropical regions and is highly infectious by aerosol, can produce nonspecific symptoms, and is resistant to many antibiotics. Effective treatment is difficult and no vaccine exists. Several outer surface polysaccharide and protein antigens are promising candidate vaccines, i.e., the capsular polysaccharide (CPS) and lipopolysaccharide (LPS) and the Burkholderia collagen-like cell wall protein (CLP) Bucl-8. Polysaccharides usually induce short term immunity and can be reactogenic. Peptides that mimic immunogenic epitopes of CPS or LPS are potentially safer and more effective vaccines. Peptide mimotopes of CPS and LPS were identified previously by phage library panning, and optimal ones selected based on binding to specific antibodies using ELISA and bio-layer interferometry. The final selected peptides included 3 CPS and 2 LPS mimotopes and a peptide containing a surface exposed epitope of Bucl-8. These six peptides were conjugated to carrier proteins CRM197 and KLH, and the conjugates evaluated using western blot and ELISA. All conjugates were recognized in ELISAs with sera from Bp-infected mice and nonhuman primates having high anti-Bp antibody titers. Vaccinations of mice with the CRM197 conjugates (plus Alhydrogel adjuvant and CpG immunostimulator) produced poor antibody responses in ELISAs with Bp whole cell antigen and no protection. The KLH conjugates elicited slightly greater levels of anti-Bp antibody and immunity. Conjugations of peptides with two novel Bp-derived carrier-like proteins, one of which binds to antigen-presenting cells, produced readily soluble and antigenic constructs, and initial vaccination trials with them are in progress. Our goal is to construct protective peptide vaccines and ultimately to develop a multivalent CPS/LPS/Bucl-8 vaccine that is highly efficacious against Burkholderia.
Abstract Title:
Development and Rapid Screening of A Pneumococcal Monoclonal Antibody Panel Pertinent to Vaccine Manufacturing

Primary Author Block:
L. Lillis1, T. Leader1, R. Schuman2, A. Lees3, J. Corvera4, J. Cabrera4, C. Lyman5, A. Tyler5, M. Alderson1, D. Boyle1; 1PATH, Seattle, WA, 2AIC, LLC, Rockville, MD, 3Fina Biosolutions, Rockville, MD, 4Precision Antibody, Columbia, MD, 5Quansys BioSci.s, Logan, UT

Abstract Body:
Streptococcus pneumoniae associated pneumonia is responsible for killing approximately 500,000 children annually while associated sepsis and meningitis contribute to further deaths and disabilities. Pneumococcal pneumonia is a vaccine preventable disease and so vaccine development is a critical strategy to protect children, particularly those in Africa and Asia where over 90 percent of all pneumococcal deaths occur. Pneumococcal antigen-based conjugate vaccines effective against virulent serogroups are available but are expensive. Several vaccine manufacturers in middle income countries are developing low cost vaccines. To enable this, there is a need to access quality antibodies for candidate vaccine development and to inform on vaccine efficacy in clinical trials. We developed a panel of monoclonal antibodies that are highly specific to each of the 24 most clinically relevant serogroups of S. pneumoniae. An initial panel representing 13 pneumococcal serotypes was expanded to include a total of 24 serotypes. Concurrently we developed a rapid screen to assess the avidity and the specificity of candidate hybridomas in addition to the purified antibodies. The screen used multiplexed planar immunoarrays that host antigens to 14 and 10 pneumococcal serotypes respectively; where each antigen is printed in discrete spots in each well on a microtiter plate. The capsular polysaccharide was also screened. The assays enabled the rapid identification of candidates with high specificity to their respective antigen in addition to an absence of cross reactivity with other serotypes. The resulting purified antibodies were rescreened with the arrays to confirm their quality. We have produced serotype-specific antibodies to the 24 serogroups which will will be offered globally at an affordable price. We envision that these mAbs can assist pneumococcal vaccine development, clinical trials, diagnostic test development and epidemiologic studies.
Abstract Title:
Outstanding Abstract Award: Novel Peptide-Based Fpva Conjugate Vaccine against Pseudomonas aeruginosa Respiratory Infections

Primary Author Block:

Abstract Body:
Pseudomonas aeruginosa is one of the major opportunistic pathogens responsible for hospital-acquired infections associated with high morbidity and mortality. High adaptability and multi-drug resistance make this bacterium a major health concern. Vaccination against P. aeruginosa could provide a solution against these infections. However, despite all the research efforts, there is still no licensed vaccine available. Efficient iron uptake is important for P. aeruginosa to colonize and sustain its growth in the host. To produce a vaccine against P. aeruginosa, we developed a set of synthetic peptides based on one of its major iron acquisition receptor, the ferripyoverdine receptor (FpvA). To increase vaccine immunogenicity, we conjugated the peptide antigens to the keyhole limpet hemocyanin (KLH) as a carrier protein. We used a murine vaccination/infection model to evaluate the effectiveness and immunogenicity of FpvA peptides and KLH-conjugated FpvA peptides vaccines compared to heat-killed P. aeruginosa and adjuvant only vaccinated groups. CD1 mice were intranasally vaccinated at days 1 and 21 with a peptide cocktail adjuvanted with curdlan. Blood samples were collected by facial vein puncture every week after vaccination to measure antibody production over time using ELISA. On day 35, mice were challenged intranasally with 6x10^7 live P. aeruginosa and euthanized 16h post infection. Bacteria were quantified by plating the lung homogenates and nasal washes. Total blood was collected by cardiac puncture and lung cells of each mouse were further analyzed by flow cytometry. Our results indicate that vaccination with FpvA-KLH peptides significantly decreased bacterial burden in nasal cavities and lung. Vaccination with FpvA-KLH but not FpvA peptides also decreased the lung weight compared to the naïve adjuvant-only group, which suggest that FpvA-KLH vaccine reduced inflammation and edema. IgG antibody titers against FpvA were detected in the sera of the FpvA-KLH vaccinated group. The flow cytometry results showed an increase in dendritic cell population in lungs of mice vaccinated with FpvA-KLH compared to those vaccinated with the adjuvant-only. These observations suggest that KLH conjugation increased overall immunogenicity and recognition of the FpvA peptides, and triggered the production of both a humoral and a cellular immune response, which provided protection against P. aeruginosa infection. Overall, our study lays the foundations for a possible iron-based vaccine against P. aeruginosa infections.
Abstract Title:
Human Mabs to Staphylococcus aureus Surface Proteins Mediate Protection Through Fc-Mediated Mechanisms

Primary Author Block:
M. Bennett, N. Kose, E. P. Skaar, J. E. Crowe, Jr.; Vanderbilt Univ., Nashville, TN

Abstract Body:
Nutrient acquisition is important for the survival of all living organisms. Nutrient metals such as iron, manganese and zinc are known to play key roles in cellular metabolism, respiration, and both redox and non-redox catalysis. One particularly well-studied nutrient acquisition system is the iron-regulated surface determinant (Isd) system that scavenges iron from the human host. S. aureus utilizes the cell surface receptors IsdB and IsdH to bind hemoproteins and transfer heme to IsdA, ultimately leading to the transfer of heme-iron across the cell surface. The development of a bacterial system to sequester iron fills a fundamental metabolic requirement for the bacterial pathogen, enabling the acquisition of iron in iron-deplete conditions. The importance of this system in both nutrient acquisition and virulence to S. aureus has been validated in the laboratory, making them promising antibody targets. We hypothesize that the development of monoclonal antibodies (mAbs) specific to iron binding proteins will elucidate the importance of metal acquisition in pathogen growth, metabolism, and virulence. To investigate this further, panels of cross-reactive human mAbs specific to the surface proteins of the Staphylococcal Isd system were isolated. This includes the first panel of fully human IsdA mAbs, as well as three cross-specific mAbs each capable of binding to IsdA, IsdB, and IsdH. Two of the identified IsdA-specific mAbs worked cooperatively in a murine septic model of infection to reduce bacterial burden during staphylococcal infection. This protection was shown to be dependent on Fc-mediated antibody effector functions and not on the heme-blocking ability of the IsdA-mAbs. Future studies that combine iron-blocking Isd antibodies that utilize antibody effector functions in combination with antibodies to other vaccine targets may inflict maximal damage to S. aureus.
Abstract Title:
Deciphering the Mechanisms for Attenuation in A Rifampin-Resistant Mutant of Flavobacterium Columnare Used As A Modified-Live Vaccine against Columnaris Disease

Primary Author Block:
W. Cai, C. R. Arias; Auburn Univ., Auburn, AL

Abstract Body:
Bacterial diseases continue to be one of the top priorities for the aquaculture industry. Channel catfish is the main aquaculture species in the USA and farmers are in desperate need of new technologies to control infectious diseases. Vaccines are widely employed in aquaculture to prevent bacterial infections but their use by the catfish industry is very limited. Our group has patented a modified-live vaccine (a rifampin-resistant mutant) against columnaris disease. We have proved that our vaccine is stable, safe, and effective but the mechanisms that resulted in attenuation remained uncharacterized. To understand the molecular basis for attenuation, we conducted a comparative genomics analysis to identify the specific point mutations. The mutant vaccine strain (Fc1723) and parent virulent strain (FcB27) were sequenced using PacBio RS long-read sequencing platform. De novo genome assembly of filtered reads was performed using PacBio PBcR HGAP 2.3 pipeline with default settings, which yield 8 and 16 contigs with 169 X and 109 X coverage, respectively. For function annotation and comparative genomic analysis, we used the Rapid Annotation using Subsystem Technology (RAST; version 2.0). Sequence-based genome comparison identified 16 single nucleotide polymorphisms (SNP) unique to the mutant. Genes that contained mutations were involved in gliding motility, DNA transcription, toxin secretion, and extracellular protease synthesis. Rifampin is a potent, broad-spectrum antibiotic that functions by inhibiting the β-subunit of prokaryotic DNA-dependent RNA polymerase (RNAP). Comparative genomic analysis of the vaccine strain Fc1723 revealed two point mutations in the RNAP gene as compared to the parent strain. Two point mutations were identified in the gene that codes for the dynein protein, which is the key motor protein for gliding motility and type IX secretion system. We hypothesized that this mutations altered the transport of proteins and extracellular polysaccharides products across the outer membrane. We compared biofilm production between the mutant and the parent strain, and our results showed that the vaccine strain formed biofilm at a significantly lower rate than the parent strain. Changes in the LPS were also noticed between the mutant and the parent strain thus supporting the hypothesis that lack of virulence is due to the inability of the bacteria to secrete virulence factors. Ongoing studies will measure the cytopathic effect of extracellular products on fish cell lines when the attenuated vaccine is compared to the wild type.
Abstract Title:
The Enterobactin Conjugate Vaccine Triggered High Titer of Enterobactin-Specific Antibodies

Primary Author Block:
H. Wang, X. Zeng, B. Gillespie, J. Lin; Univ. of Tennessee, Knoxville, Knoxville, TN

Abstract Body:
Background: Siderophore-mediated high affinity iron acquisition plays a key role for Gram-negative pathogens to survive in the iron-limited niches in host, such as intestine and respiratory tract. Among the known natural siderophores, enterobactin (Ent) has the highest affinity to ferric iron and is an architype for iron acquisition in Gram-negative bacteria. Recent studies support Ent as a promising target for vaccine development to sequester iron from Gram-negative bacteria. In this study, Ent conjugate vaccine was generated and evaluated for inducing specific immune response in rabbits.

Methods: Ent was purified from E. coli and subsequently conjugated to the carrier proteins keyhole limpet hemocyanin (KLH) and bovine serum albumin (BSA), respectively. Two independent immunization trials (two rabbits per trial) were performed using similar vaccination regimen except that an additional 4-week extension was included in one trial. The New Zealand white rabbit was immunized with 100µg of KLH-Ent conjugate vaccine, followed by 3 booster immunizations every 3-4 weeks. General IgG response against KLH-Ent vaccine as well as specific titers of anti-Ent IgG in sera were measured using ELISA. Western and dot blotting were performed to further validate the presence and level of specific IgG directed against Ent. Results: The KLH-Ent and BSA-Ent conjugate vaccines were produced using a straightforward and efficient conjugation protocol. Immunization of rabbits with KLH-Ent conjugate vaccine triggered strong immune responses in sera, which was consistently observed in all four immunized rabbits. Specifically, ELISA analysis indicated serum IgG titers to KLH-Ent conjugate vaccine increased dramatically in all rabbits (512-2048 fold) by 7 weeks postimmunization and were maintained through 14 or 18 weeks postimmunization. Consistently, immunization with the KLH-Ent vaccine dramatically increased the titers of Ent-specific IgG in all rabbits (32-4096 fold), which was further confirmed by western and dot blotting assays. Conclusion: Our Ent conjugate vaccine triggered strong Ent-specific IgG response in rabbits, which opens a new avenue to control Gram-negative pathogens by developing Ent-based immunization strategies.
Evaluation of Recombinant Probiotic Bacterium Lactococcus Lactis As A Model Oral Vaccine against Infectious Disease in Swine

Primary Author Block:
J. Meerak1, K. Somboonsod2; 1Chiang Mai Univ., Faculty of Sci., Muang, Chiang Mai, Thailand, 2Chiang Mai Univ., Faculty of Sci., Muang, Thailand

Abstract Body:
Infectious diseases in swine, which are cause by microorganisms including bacteria, fungi and virus, is one of the major economical loss and public health worldwide. To prevent, many types of vaccines have been introduced since its birth period till adult but depend on pathogen and area. However, vaccination by injection needs an expert and it is not emphasis in tropical countries due to the high cost. To reduce the cost and to innovate an easy to use novel oral vaccine for rancher, we aim to construct a live lactic acid bacterium carrying a model antigen gene, chicken ovalbumin or ova, for determination its immunogenicity in swine. An ova gene was amplified by PCR and inserted to food grade plasmid pNZ8149 under nisin promotor and transformed into Lactococcus lactis NZ3900 which the plasmid was maintained by lactose. Expression of the gene was performed by detection of OVA protein using western blot analysis. The live probiotic vaccine was examined for its efficacy to stimulate swine immune response by weekly oral feeding as a capsule formulated with swine feeds. Three vaccination groups (each N=4) were feeding with L. lactis, L. lactis/ pNZ3900 and L. lactis pNZ- OVA, respectively and the control group was received only PBS. Blood sampling was taken each following week after vaccination for 8 weeks and serum was separated for determination of specific IgG by ELISA. Among these, anti OVA sera were significantly highest in pNZ-OVA group at 6-8 weeks after oral vaccination while other groups were similar to control. This suggested that L. lactis carrying ova gene was able to attach to swine intestinal epithelial cell and OVA was continuously in vivo produced and recognized by antigen presenting cell in small intestine area. In addition, to confirm whether the bacteria were able to survive and multiply at intestine epithelial cell, feces was also collected every week during vaccine feeding and a total DNA was extracted for amplification of ova gene. It was interesting that the bacterium carrying the model antigen gene was able to attach and survive since the first week until 1 month after last vaccination without feeding. Thus, it is possible to apply this oral probiotic vaccine from sucking piglet and prolong till adult. Moreover, to determine microbial population change and relationship of swine microbiome with the vaccine, metagenomic was also investigated using total gDNA extracted from feces of each group and was under experiment.
Abstract Title:
Production of the Egg Yolk Antibodies Directed against Enterobactin

Primary Author Block:
X. Zeng, H. Wang, C. Huang, B. Gillespie, J. Lin; Univ. of Tennessee, Knoxville, TN

Abstract Body:
Background: Enterobactin (Ent), a siderophore produced by most members of Enterobacteriaceae, serves as an efficient and significant iron source for Gram-negative pathogens during intestinal colonization. Recent findings strongly support that the Ent-specific antibodies can inhibit Ent utilization, consequently starving Gram-negative pathogens out of iron. Given that passive immunization with specific egg yolk antibodies is emerging as a potential alternative to antibiotics for the treatment and prevention of various diseases, in this study, laying hens were immunized with Ent conjugate vaccines to produce large quantities of hyperimmune egg yolk antibodies. Methods: Ent was purified from E. coli and subsequently conjugated two carrier proteins, keyhole limpet hemocyanin (KLH) and bovine serum albumin (BSA), respectively. Two immunization trials were performed using different layers and conjugate vaccines. In the first trial, the 35-week old Barred Rock layers (3 birds/group) were immunized with 100 µg of KLH or KLH-Ent conjugate, followed by three booster immunizations every two weeks. In the second trial, two 26-week old Rhode Island Red pullets were immunized with 100 µg of BSA-Ent conjugate vaccine, followed by three booster immunizations every 3-4 weeks. Specific IgY responses in sera and egg yolks collected at select dates were measured using dot blot and ELISA. Selected egg yolks were pooled and subsequently lyophilized for production of egg yolk powder. Results: The KLH-Ent and BSA-Ent conjugate vaccines were produced using a straightforward and efficient conjugation protocol. Regardless of breed, immunization of layers with specific conjugate vaccine triggered strong immune responses in both serum and egg yolk. Specifically, ELISA analysis indicated serum IgY titer to specific conjugate vaccine increased greatly by the first booster immunization and maintain or further increased through up to 9 weeks post immunization; the specific IgY level in egg yolk was correlated with that in serum. However, the Ent-specific immune response in layers is weaker than that observed in previous rabbit vaccination trials. Large amount of egg yolk powder was prepared for future passive immunization studies. Conclusions: The Ent conjugate vaccines triggered strong immune response in different breeds of layers. However, the level of anti-Ent specific IgY still needs to be improved upon vaccination in layers.
Antibody Responses to Hiv Protein and Commensal Bacteria after Treatment with Probiotics in A Rhesus Macaque Vaccination Model

Primary Author Block:
A. B. Wilson1, J. A. Manuzak2, N. R. Klatt2, R. M. Lynch1; 1George Washington Univ., Washington, DC, 2Univ. of Washington, Seattle, WA

Abstract Body:
To date there is no highly effective HIV vaccine, and therefore improving vaccine efficacy is of high importance. HIV preferentially replicates within mucosal tissue, and therefore, boosting mucosal immunity may be one strategy to increase vaccine efficacy. Here we studied the effects of microbiome manipulation on antibody responses to vaccination and infection in a rhesus macaque model, and analyzed responses to commensal strains of bacteria. Male rhesus macaques were divided into treatment groups receiving either daily oral probiotic treatment alone, in conjunction with a DNA (SIV p55 and HIV gp160) plus protein (HIV gp140 trimer) subtype C vaccine, or vaccine alone. Following 26 weeks of treatment, macaques were challenged intra-rectally six weeks later with multiple low doses of subtype C SHIV (SHIV.C.CH505.375H.dCT). Plasma was collected longitudinally throughout treatment course and SHIV infection. Plasma antibody responses were analyzed by indirect ELISA to determine levels of IgG against HIV proteins and 5 bacteria strains. In the first cohort of macaques (n=3 per group), background cross-reactive antibodies to HIV gp41 but not gp120 protein were detectable before vaccination. Microbiome manipulation through probiotic treatment moderately dampened the anti-gp41 and gp120 antibody response to HIV vaccine and early SHIV infection compared to the vaccine alone group. Antibody responses to gram positive bacteria L. plantarum, L. rhamnosus, and B. cereus as well as gram negative A. junii remain stable post-vaccination and infection in the presence or absence of probiotic treatment; however, antibody responses to gram negative E. coli increased in all macaques post-SHIV infection. Our preliminary findings suggest that probiotic treatment may moderately affect the antibody response to HIV vaccination or infection, but does not affect the anti-bacterial response in rhesus macaques. This study is currently ongoing and more animals will be studied to increase the sample size. Whether these changes significantly impact immune responses to HIV must be further explored in future studies.
Session Number: 284
Session Type: Poster Talk
Session Number: 284
Session Type: Poster Talk
Session Title: Clostridium difficile Infection
Session Start Date Time: 6/9/2018 12:15:00 PM
Session End Date Time: 6/9/2018 1:15:00 PM
Session Primary Track: Clinical Infections and Vaccines
Abstract Control Number: 9236
Poster Board Number:

Abstract Title:
Moderator
Primary Author Block:
A. Krishna Rao;

Abstract Body:
Abstract Title:
Performance of A Clostridium Difficile Prediction Tool for Admission Surveillance to Reduce Hosp. Acquired C. Difficile Infection
Primary Author Block:
D. Schora, M. Vernon, K. Singh, S. Zelencic, L. R. Peterson;  NorthShore Univ. Hlth.System, Evanston, IL
Abstract Body:
Background: Clostridium difficile (Cdif) infection (CDI) is problematic. To reduce CDI rates, we employ 5 standard infection prevention practices. Despite these efforts, our CDI rates fell short of target at 6.8/10,000 patient days in 2017. As a result, we implemented a program of targeted Cdif surveillance and placed all asymptomatic carriers under contact precautions. A targeted, risk-based screening approach minimizes testing and maximizes colonization detection. Methods: A Cdif admission screening pilot program was performed for 6 months at 2 hospitals. All new admissions had a peri-rectal sample collected and tested for Cdif by real-time PCR. From the pilot data, risk factors for Cdif colonization were derived using a multivariable regression model (SAS v9.3) and built into an algorithm in our electronic medical record system (Epic). A control set of non-risk patients were also tested to validate the algorithm. The risk-based surveillance program was implemented 8/1/17. Results: The rate of asymptomatic Cdif colonization was 8.5% during the pilot. On multivariate analysis, independent predictors of Cdif colonization were prior Cdif infection or colonization and hospitalization in the past 2 months. On univariate analysis, admission from a long-term facility was also a significant risk factor for Cdif carriage. Together, these 3 risk factors captured 80% of at risk patients. From 8/1/17, patients who met any of these 3 risk factors had a rectal sample collected for Cdif RT-PCR using the cobas® Cdif Test (Roche). In the first 5 months of the program, 4477 patients were tested, including 640 controls. Patients with risk factors had an average Cdif colonization rate of 9% (Graph 1). Control patients averaged < 1% positivity rate for Cdif. Conclusion: The algorithm is performing as expected. A reduction in CDI rates will prove the effectiveness of this surveillance program and will be monitored.
Abstract Title:
Emerging Hypervirulent Epidemic Clostridium Difficile Strain of St37 Type (Toxin A-B+) Pose A Potential Threaten in China

Primary Author Block:
C. Li; Xiangya Hosp. Central South Univ., Changsha, China

Abstract Body:
Object: Clostridium difficile strains of ST37 type (RT017) are most frequently isolated epidemic isolates in China. We aimed to compare major virulence factors of an epidemic C. difficile isolate of ST37 type from China with those of C. difficile RT20291 and CD630. Methods: The first hypervirulent XY-06 (ST37, A-B+) C. difficile strain was isolated from ICU hospitalized patient in China. The toxin production was measured by conventional ELISA assay and commercial Kits. Cytotoxic effects of the strains on cultured cells were assessed by cell rounding assays. The pathogenicity in vivo was evaluated in mouse model of C. difficile infection (CDI). The resistance of the strain to antimicrobial agents was performed by microdilution assay. The spore adherence effects on human gut epithelial cells was performed by adherence assay. Genome of XY-06 strain was sequenced, and the entire toxin gene PaLoc was compared with 027 and CD630 strains. Results: C. difficile XY-06 produced much more TcdB, adhered stronger to gut epithelial cells, in comparison with C. difficile RT20291 and CD630. In a mouse model of CDI, strain XY-06 was more virulent than strain CD603, and was comparable to strain RT20291. No sizable resistance to antibiotics tested was detected. In addition, biofilm formation, sporulation, germination and motility of this strain was also evaluated, in comparison with RT20291 and CD530, and no remarkable differences were noticed. Conclusion: These findings highlight the potential threaten of epidemic strains ST37 in China.
Diarrheal Illnesses Trigger C. Difficile Colonization in the Human Gut

D. VanInsbergh, B. J. Varian, S. Erdman, M. Polz; Massachusetts Inst. of Technology, Cambridge, MA

Background: Clostridium difficile infections have become increasingly treatable in recent years, but their incidence and overall burden on healthcare systems continues to rise (1). Although it is widely held that C. difficile is an antibiotic and hospital associated pathogen, only a few antibiotics carry an elevated relative risk for infection and at most one third of infections can be attributed to transmission within a hospital (2,3). As well, it is common for adults to be asymptptomatically colonized by C. difficile, but very little is known about the risk factors for becoming a carrier, or the timescales where people remain carriers. Methods: We searched human microbiome surveys to form a hypothesis about C. difficile colonization dynamics before testing it using a mouse model. Results: After identifying blooms of C. difficile in human gut microbiome studies following Salmonella and Vibrio cholerae infections, we used a mouse model to test if disturbances in general trigger C. difficile colonization. This study showed that as mice ingested increasing amounts of laxatives while being exposed to C. difficile spores, more mice experienced blooms of C. difficile in their feces, while control groups experience none. Conclusions: Our results suggest that colonization becomes likely if people are exposed to C. difficile spores in the days following acute disturbances - where antibiotics and hospitals are common examples of large disturbances and locations with a high burden of exposure. Consequently, the period of recovery from diarrheal illnesses and laxative use could be an important window of intervention for preventing transmission and lowering the incidence of infection and asymptomatic carriage. Further, the temporal variability of C. difficile abundance in the gut highlights that single time-point testing is insufficient to determine carriage. Significance: Here we show that C. difficile colonization requires a prior gut disturbance, initiates following a delay during recovery, and can persist asymptotically long after full recovery.
Abstract Title:
Clostridium Difficile Toxin Testing Affects the Treatment Decision

Primary Author Block:
S. E. Hoover, J. Zhao; Sanford Res., Sioux Falls, SD

Abstract Body:
Background: The availability of sensitive nucleic acid based-tests (NAT) for Clostridium difficile has led to the concept of “overdiagnosis,” which holds that patients with positive NAT but negative toxin enzyme immunoassays (EIA) may not have true disease or require treatment. In March 2016, our institution changed its testing algorithm to a 2-step procedure using PCR as a screening test, followed by EIA on samples testing positive by PCR. Education was provided to clinicians that PCR-positive, toxin-negative patients might not have clinically relevant C. difficile illness. Methods: We conducted a retrospective cohort study using administrative data on all inpatients over 1 year of age who had one or more tests for C. difficile during their stay. Patients were classified as PCR+/Tox+, PCR+/Tox-, or PCR-. We collected data including patient characteristics, medication use, treatment for C. difficile, readmission, and mortality. Results: 83% of PCR+/Tox+ patients received oral or IV metronidazole, oral vancomycin, or oral fidaxomicin after the C. difficile test was performed, contrasting with 53% of PCR+/Tox- patients and 16% of PCR- patients (p<0.001). Deaths occurred in 10 (16%) of PCR+/Tox+ patients, 33 (18%) of PCR+/Tox- patients, and 149 (9%) of PCR- patients. The difference was statistically significant only between the PCR+ and PCR- patients, without regard to toxin result (p<0.001). Age, sex, number of days from admission to test, source of admission, use of antibiotics, laxatives, or acid suppressing medications, admission WBC count and admission creatinine did not predict a positive C. difficile toxin result. Treatment of C. difficile and length of stay did not predict death or readmission within 30 days. Conclusion: Patients who were PCR and toxin positive were more likely to be treated for C. difficile than those who were PCR positive and toxin negative. Neither treatment of C. difficile nor length of stay predicted death or readmission within 30 days. In our cohort, therefore, the decision to treat or not treat patients who were PCR-positive and toxin-negative did not have a measurable effect on readmission or mortality, to the extent that these rare outcomes were present in this study.
Comparative Effectiveness of Early-Targeted Use of Fidaxomicin versus Oral Vancomycin among Hospitalized Veterans’ Affairs Patients with Infections Due to Clostridium Difficile

Primary Author Block:
D. Morgansen1, N. Stornelli2, V. Shah1, C. Lowry1, N. Patel2, T. Lodise2; 1Samuel S. Stratton VA Med. Ctr., Albany, NY, 2Albany Coll. of Pharmacy & Hlth.Sci., Albany, NY

Abstract Body:
Background: The objective of this study was to compare real-world effectiveness outcomes (mortality and recurrence) between hospitalized patients who received regimens containing early-targeted fidaxomicin or oral vancomycin. Methods: A retrospective cohort study was performed among hospitalized patients receiving care in the Upstate New York Healthcare Administration from 5/2000 until 7/2014 with CDI. Inclusion criteria were: 1) age ≥ 18 years, 2) positive C. difficile stool sample (first episode), 3) >3 loose stools in past 24 hours or ileus with other causes of diarrhea ruled out, 4) use of fidaxomicin or oral vancomycin-containing regimen (≥48h) within 5d of a positive C. difficile stool sample. Data collected from medical records included demographics, comorbidities, medication history, hospitalization course, vital status, recurrence, lab findings and Hines severity score. Outcomes were: 1) Mortality at 30- and 60-d post C. difficile sample positivity, 2) Recurrent CDI infection within 60 days of completion of initial CDI treatment, 3) Composite failure (60d mortality or CDI recurrence). Results: There were 34 fidaxomicin and 156 oral vancomycin patients that met inclusion criteria. Mean ± standard deviation (SD) age was comparable between fidaxomicin (75.5 ± 9.8 years) and oral vancomycin (73.2 ± 11.7 years). For each study outcome, the following was observed between recipients of oral vancomycin and fidaxomicin: 30-day mortality (21.2% vs 14.1%, p = 0.48), 60-day mortality (28.2% vs 14.7%, p = 0.13), recurrence (22.4% vs 11.8%, p = 0.24) and composite failure (42.9% vs 26.5%, p = 0.09). These differences were greatest in patients ≥75 years (Figure) and those with an elevated Hines severity score. Conclusions: Compared to oral vancomycin, fidaxomicin-containing regimens were associated with lower mortality at 60-days and a composite of 60-d mortality/recurrence among patients ≥ 75 years.
Session Number: 289  
Session Type: Rapid Fire

Session Title: Biomarkers in Infectious Diseases
Session Start Date Time: 6/9/2018 1:30:00 PM
Session End Date Time: 6/9/2018 2:15:00 PM
Session Primary Track: Clinical Infections and Vaccines
Abstract Control Number: 9360
Poster Board Number:

Abstract Title: 
Moderator 
Primary Author Block: 
Miriam Laufer; Univ. of Maryland, Baltimore, MD
Abstract Body:
Utility of Procalcitonin for Diagnosis of Sepsis or Lower Respiratory Tract Infections

Primary Author Block:
J. Aslanzadeh, E. Orelup, J. Ross, K. Linder, G. Makowski; Hartford Hosp., Hartford, CT

Abstract Body:
Background: Procalcitonin (PCT), a prohormone of calcitonin, is secreted by a variety of cells in response to proinflammatory stimulation. Detection and monitoring of plasma/serum PCT is useful in the setting of serious sepsis as a syndrome of bacterial infection and bacterial pneumonia. PCT < 0.09 ng/mL can be used to rule out sepsis and/or lower respiratory tract infection. PCT > 0.25 ng/mL suggests increased risk of sepsis or lower respiratory tract infection requiring antibiotic therapy. PCT 0.09-0.25 ng/mL is indeterminate. The aim of this study was to compare diagnostic utility of plasma/serum PCT measured by Elecsys BRAHMS PCT on Cobas 6000/e601 (Roche, Indianapolis, IN) vs traditional culture for predicting bacteremia or lower respiratory tract infection. Methods: A total of 450 medical records were reviewed for patients with concurrent PCT and respiratory or blood culture. Results: Eighty two patients had PCT <0.09 ng/mL. Of these, blood culture on one patient (PCT 0.07 ng/mL) was positive for methicillin-resistant Staphylococcus aureus (MRSA). One hundred twenty eight patients were indeterminate. Of these, blood culture on two patients (PCT 0.19 and 0.24 ng/mL) were positive for MRSA and blood culture on one patient (PCT 0.16 ng/mL) was positive for Candida parapsilosis. Two hundred fifty five patients had PCT >0.25 ng/mL. Fifty three patients had received antibiotic prior to collection of blood cultures. Of the remaining 202 patients, blood cultures were positive on 41 patients. Findings included Gram positive cocci (n=20), Gram negative rods (n=19), Gram positive rod (n=1) and Candida glabrata (n=1). PCT ranged from 0.28-345.24 ng/mL with a median PCT of 2.95 ng/mL. Additionally, respiratory cultures were positive on 14 patients (4 S. aureus, 3 Pseudomonas aeruginosa, 1 Klebsiella pneumoniae, 1 K. oxytoca, 1 E. coli,1 Hemophilus influenzia, 1 Streptococcus pneumoniae and 1 Corynebacterium striatum). PCT ranged from 0.27-128 ng/mL with a median PCT of 0.71 ng/mL. Conclusions: PCT had excellent diagnostic specificity (99.3%) and negative predictive value (98.7%), but substantially lower sensitivity (40.4%) and positive predictive value (27.2%) in predicting bacteremia or lower respiratory tract infection vs traditional blood or respiratory cultures.
Abstract Title: Early Diagnosis of Measles for Better Management and Control of Infection

Primary Author Block:
G. Fatima1, S. Kainat2, S. Kazmi3; 1Civil Hosp., Karachi, Pakistan, 2Civil Hospital, Karachi, Pakistan, 3Dadabhoy Inst. of Higher Ed., Karachi, Pakistan

Abstract Body:
Background: Measles is a highly contagious vaccine preventable viral disease which affects the respiratory system of children under 14 years of age. The disease and is endemic due to improper vaccination and poor living conditions in many countries of the world including Pakistan. Vaccination provides lifelong immunity to the children. This study was designed to know the best laboratory diagnostic test for early diagnosis of measles virus infection to facilitate better management of disease and prevention of its complications like SSPE. Methods: A total of 106 blood samples and nasal secretions were collected in viral transport medium (VTM) and kept at -80°C till tested. from clinically diagnosed cases of measles with history of high grade fever and typical symptoms of measles (running nose, conjunctivitis and rashes), between the age of 2-12 years, visiting Pediatric units of Civil Hospital, Karachi. Measles virus specific IgM antibodies in blood samples by ELISA and measles virus RNA in nasal secretions by real time PCR, and genotyping of virus was also carried out at NIH - Islamabad. Demographic data including age, gender, socioeconomic status, especially vaccination against measles and duration of fever were recorded. Results: Out of 106 blood samples of patients, 48 (45.3%) children exhibited measles specific IgM antibodies. Among measles positive children, 18 children had received measles vaccination. Measles virus RNA was detected in all 106 samples of nasal secretions. Genotype analysis indicated Measles virus genotype B2 as the most prominent causative strain. Among the vaccinated group of 18 children, only 6 (33.3%) were positive for measles IgM, while among the unvaccinated group 42(47.7%) tested positive for measles specific IgM. All measles specific IgM positive children (N=48) had history of fever for three days and more while others had fever of less than three days. Females (52%) were affected slightly more than males (48%). Conclusions: Anti-Measles IgM test can be used for early diagnosis of measles after three days of onset of fever for better management. A negative test does not exclude measles. Measles virus RNA can be detected in nasal secretion irrespective of duration of fever. Measles infection in vaccinated children reflects on the efficacy of vaccines in Pakistan. The poor quality of routine vaccination program plus lack of proper surveillance system are some of the factors responsible for rise in measles cases in Pakistan.
Session Number: 289  
Session Type: Rapid Fire

Session Title: Biomarkers in Infectious Diseases
Session Start Date Time: 6/9/2018 1:30:00 PM  
Session End Date Time: 6/9/2018 2:15:00 PM
Session Primary Track: Clinical Infections and Vaccines
Abstract Control Number: 9415
Poster Board Number:

Abstract Title:
Diagnosis of Neonatal Septicemia; Thinking Beyond Blood Culture

Primary Author Block:
A. Gopang; Pakistan Hlth. Res. Council, Karachi, Pakistan

Abstract Body:
Background: Neonatal sepsis (NS) is a major cause of neonatal admissions to hospital and mortality. This study was conducted to evaluate different methods for rapid and reliable diagnosis of NS with an aim to rationalize the use of antibiotics and stay in Neonatal Intensive Care Unit. Objectives: To compare the different available methods for rapid and reliable diagnosis of neonatal sepsis. Study Design, Settings and Duration: This comparative study was conducted in Emergency Department of National Institute of Child Health (NICH) Karachi for the period of six months. Subjects and Methods: Neonates who were brought to the emergency department of National Institute of Child Health with suspicion of NS were clinically examined. Those, supposed to be septic were included as study population and informed written consent was taken from their parents. After this, 3 ml blood was drawn for complete blood count (CBC), blood culture, C-reactive protein (CRP), polymerase chain reaction (PCR) and neutrophilic ratio. PCR and CRP results were compared with blood culture for specificity, sensitivity, positive and negative predictive values. Results: Out of 129 neonates, 23 (17.82%) were positive for bacterial DNA by PCR method while 42 (32.55%) were positive for infection when tested for C reactive protein marker of the blood. Whereas, only 15 (11.62%) were positive by blood culture. Sensitivity and specificity of PCR were 60% and 88% while positive and negative predictive values were 39% and 94% respectively. Sensitivity and specificity of C reactive protein were 60% and 71% while positive and negative predictive values were 21% and 93% respectively. Conclusion: Our study revealed high specificity and positive predictive values of PCR suggesting that PCR is more reliable, rapid and specific adjunct of blood culture for diagnosis of NS. Key words: Neonatal sepsis, blood culture, PCR, CRP.
Session Title: Biomarkers in Infectious Diseases
Session Start Date Time: 6/9/2018 1:30:00 PM
Session End Date Time: 6/9/2018 2:15:00 PM
Session Primary Track: Clinical Infections and Vaccines
Abstract Control Number: 9431
Poster Board Number:

Abstract Title:
Novel Biomarkers to Differentiate Children with P. Falciparum Malaria from Bacterial Bloodstream Infections

Primary Author Block:
N. S. Struck1, M. Zimmermann1, R. Krumkamp1, E. Lorenz1, T. Jacobs1, D. Winter1, J. H. Amuasi2, D. Eibach1, J. May1; 1Bernhard Nocht Inst. for Tropical Med., Hamburg, Germany, 2Kumasi Ctr. for Collaborative Res. in Tropical Med., Kumasi, Ghana

Abstract Body:
Background: Malaria is a major health problem and economic burden in sub-Saharan Africa. Clinical symptoms frequently overlap with pneumonia, typhoid fever, acute bacterial meningitis, and invasive non-typhoid salmonella. Most common diagnostic methods (interpretation of clinical symptoms, blood smear microscopy and rapid diagnostic tests) are unable to identify possible concomitant infections that might mask the true cause of illness. In two different experimental approaches we set out to identify a set of prognostic blood biomarkers that are able to distinguish between a malaria infection requiring treatment and a severe bacterial infection.

Methods: We examined serum samples of 65 children under the age of 5 years that were recruited at the Agogo Presbyterian Hospital in Ghana between 2010 and 2012. 35 children with a malaria-positive slide and at least one symptom characteristic for severe malaria (Dondorp et al., 2011) and 30 children with SIRS (Goldstein, Giroir and Randolph, 2005) and a positive blood culture in the absence of malaria parasites were analysed. Autoantibody expression levels were determined through protein microarrays (ThermoFisherScientific) and 95 different inflammatory cytokines were identified using immunoassay detection kits (Merckmillipore). Principal component analyses were applied to identify covariance in marker expressions and random forest models were calculated to predict patient’s disease status from serum content. Results: Sex was equally distributed within the study group (female: 32; 49%), median age was 2 years (IQR: 1-3). Median parasite count in the malaria group was 181,670 (IQR: 32,692-324,725). Bacterial infections were caused by non-typhoid Salmonella (43%; n=13), Salmonella Typhi (23%; n=7), Streptococcus pneumoniae (17%; n=5), Staphylococcus aureus (10%; n=3), Acinobacter spp. (3%; n=1) and Campylobacter spp. (3%; n=1). While prediction models based on the expression levels of more than 9000 autoantibodies misclassified 5 malaria and 7 bacteraemia cases (82% prediction accuracy), the predictive accuracy based on the profile of cytokines was 94%. Conclusion: Our results showed that a specific set of biomarkers are able to predict a patient’s disease status and that prediction accuracy is higher for cytokines than autoantibodies. These panels open up new possibilities for innovative point-of-care tests, which are urgently needed in malaria endemic regions to guide early treatment decisions.
Abstract Title:
Utility of Procalcitonin to Differentiate between Gram-Positive and Gram-Negative Infections in Pediatric Patients

Primary Author Block:
M. Abadeer1, W. Moore2, A. Chopra3, J. Cies1; 1St. Christopher's Hosp. for Children, Philadelphia, PA, 2The Ctr. for Pediatric Pharmacotherapy, Pottstown, PA, 3NYU Langone Med. Ctr., New York, NY

Abstract Body:
Background: Gram-positive (GP) and gram-negative (GN) bacteria activate different Toll-like receptors signaling pathways resulting in production of different proinflammatory cytokines that stimulate procalcitonin (PCT) release. Adult data suggests median PCT values are higher in GN bloodstream infections (BSI) compared to GP BSI yet there is limited data on whether PCT can differentiate between GP and GN BSI in pediatric patients. The aim of this study was to evaluate whether PCT can discriminate infections caused by GP and GN organisms. Methods: This was a single-center, retrospective medical record review. All patients with documented blood stream infection (BSI) with a single organism and/or meningitis (MEN) from January 2013 to December 2017 were eligible for inclusion. Patients with a documented BSI or MEN and a PCT level were included. During this time period, there was no standard protocol for obtaining PCT levels and patients with polymicrobial infections were excluded. All analyses were performed using IBM SPSS Version 24 (SPSS Inc., Chicago, IL). Results: 44 patients, 27 males and 17 females, with BSI and/or meningitis were included. The median age in the GN group was 9.5 months (IQR 3 months-3.75 years) compared with 9 months (IQR 2 months-4 years) in the GP group, p = 0.85. The median weight was 9.75 kg (IQR 4.7-15.3 kg) in the GN group compared with 7.8 kg (IQR 3.7-16 kg) in the GP group, p = 0.42. The median PRISM score was 14.5 (IQR 9-20.75) in the GN group compared with 15 (IQR 9.5-27.7) in the GP group, p = 0.43. The median PCT in the GN group was 8.11 ng/mL (IQR 1.62-23.95) vs 8.32 ng/mL (IQR 1.26-22.44) in the GP group, p = 0.6 Conclusions: This preliminary pediatric data suggests in the setting of BSI and/or meningitis, the elevation in PCT is similar whether the causative organisms is a GP or GN organism.
Abstract Title:
Cross-Validation of A Standardized Pertussis Multiplex Serological Assay to Quantify Antibodies in Human Dried Blood Spot and Plasma

Primary Author Block:
G. Rajam, E. Kim, S. Park, S. Paulos, D. Patel, A. Jeyachandran, E. Wong, J. Schiffer; CDC, Atlanta, GA

Abstract Body:
Background: CDC has developed and validated a microsphere based multiplex antibody capture assay (MMACA) for the simultaneous quantification of Bordetella pertussis (Bp) antigen specific immunoglobulin G (IgG) in human serum. Considering the logistical limitations in studies involving neonates and infants, dried blood spot (DBS) and plasma are increasingly being used as clinical specimens for serological testing. DBS offers an alternative to serum for rapid and efficient sample collection with fewer on-site equipment requirements and considerably lower storage and transport costs. The purpose of this cross-validation study is to demonstrate the comparability of MMACA to quantify Bp antigen specific IgG in these clinical specimens. Methods: For MMACA, microspheres (Luminex) with distinct fluorescence spectrum were conjugated to five Bp antigens: Pertussis toxin (Pt), Pertactin (Prn), Filamentous Hemaglutinin (Fha), Fimbriae (Fim2/3), and adenylate cyclase toxin (Act) and used to capture Bp antigen specific antibodies in a single serological reaction (5-plex). A panel of 20 paired human DBS/serum samples and 15 paired human plasma/serum samples were tested for Bp antigen specific IgG in two separate experiments. Precision, accuracy and concordance correlation coefficient (CCC) for each Bp antigen was calculated using SAS. Results: The Deming regression of the median anti-Bp antigen specific antibody concentration values in DBS and serum produced a precision of 0.992 - 0.995, an accuracy of 0.995 - 0.998 and a CCC of 0.989 - 0.991 for Bp antigens. Similarly, The Deming regression values in plasma and serum produced a precision of 0.979 - 0.991, an accuracy of 0.992 - 0.999 and a CCC of 0.979 - 0.995 for five different Bp antigens. A CCC ≥ 0.95 is considered to indicate near perfect equivalence. Conclusions: MMACA was successfully cross-validated to quantify anti-Bp antibodies in human DBS and plasma.
Abstract Title:
HIV/Tuberculosis Patients with Slow Acetylator Genotype Have Increased Urine Levels of Oxidative Stress Markers

Primary Author Block:
I. Zentner1, S. Ravimohan2, J. G. Pasipanodya3, S. Srivastava4, T. Gumbo5, G. P. Bisson6, C. Vinnard1; 1Publ. Hlth.Res. Inst., Newark, NJ, 2Univ. of Pennsylvania, Philadelphia, PA, 3Ctr. For Infectious Diseases Res. & Experimental Therapeutics, Dallas, TX, 4Ctr. for Infectious Diseases Res. & Experimental Therapeutics, Dallas, TX, 5Ctr. for Infectious Diseases Res. and Experimental Therapeutics, Dallas, TX, 6Univ. of Pennsylvania, Philadelphia, PA

Abstract Body:
Background: Tuberculosis patients with slow NAT2 acetylator genotype are more likely to develop hepatotoxicity through unknown mechanisms. Isoniazid and its hydrazine metabolites trigger mitochondrial damage in pre-clinical models. We sought to determine whether isoniazid-treated HIV/tuberculosis patients have an elevated marker of oxidative stress detected in urine, as measured by DNA damage from reactive oxygen species. Methods: We analyzed urine samples collected from a cohort HIV/tuberculosis patients enrolled in a prospective study of isoniazid pharmacokinetics, conducted before starting antiretroviral therapy. NAT2 genotype was determined from whole exome sequencing. Urine levels of 8-hydroxydeguanosine (8-OHdG), a marker of DNA damage, were measured using an ELISA kit and normalized to urine creatinine. For comparison, we also analyzed urine collected from untreated healthy volunteers. We performed multivariate linear regression to measure the adjusted relationship of NAT2 genotype and urinary 8-OHdG levels. Results: Urinary 8-OHdG levels were significantly elevated among 39 HIV/tuberculosis patients compared to 3 healthy volunteers (p<0.01; Figure 1). We observed a significant relationship between NAT2 genotype and urine 8-OHdG levels (p=0.046 by non-parametric test for trend). After adjusting for CD4+ T cell count and tuberculosis treatment duration, we observed a statistically significant increase in urine 8-OHdG levels among slow acetylators compared with rapid acetylators (p=0.023). Conclusions: Urine levels of 8-OHdG, a DNA damage marker related to oxidative stress, were elevated among HIV/tuberculosis patients, and the highest levels were observed among slow acetylators. Future work should examine whether oxidative stress assays could serve as early biomarkers for clinically apparent hepatotoxicity.
Increased Platelet Counts: Potential Diagnostic Marker for Osteomyelitis in Patients with Chronic Ulcers?

Primary Author Block:

Abstract Body:
Background: Chronic leg ulcers are a common problem associated with significant morbidity, which is further compounded upon progression to osteomyelitis. Differentially diagnosing between the two is difficult, often requiring pathology and costly imaging studies, but essential for determining appropriate therapy. Elevated c-reactive protein (CRP) and sedimentation rate (ESR) are known to be useful in diagnosing osteomyelitis versus chronic leg ulcer, but are also known to be non-specific. Additionally, reactive thrombocytosis is known to occur with infection. In one small, brief observational study by Schattner A, et al. thrombocytosis was detected more frequently in patients with chronic leg ulcers with osteomyelitis than in those with just chronic leg ulcers. In our study, we looked to expand upon whether platelet counts can help differentiate between osteomyelitis and chronic leg ulcers. Methods: Platelet counts from 213 patients admitted with osteomyelitis versus chronic leg ulcers were obtained via retrospective chart review; levels at baseline and on diagnosis were compared. Patients’ CRP and ESR were examined in a similar fashion. Diagnoses were made via imaging studies, pathology, probe-to-bone tests, and/or clinically by the provider. Results: Although platelet counts on diagnosis were statistically significantly higher in patients diagnosed with osteomyelitis versus chronic leg ulcer (282 x10⁹/L versus 219 x10⁹/L, p<0.001), the difference was deemed to be not clinically relevant. The same was true for the difference in platelet count on diagnosis from their baseline with osteomyelitis versus chronic leg ulcer (26 x10⁹/L versus 5 x10⁹/L, p=0.002). When choosing a cutoff platelet count of >350 x10⁹/L for differentiating osteomyelitis versus chronic leg ulcer, our results showed a sensitivity of 0.24, specificity of 0.93, and positive predictive value of 0.74. Conclusion: In patients presenting with chronic leg ulcers which are concerning for osteomyelitis, a platelet count >350 x10⁹/L is highly specific for aiding in the diagnosis of osteomyelitis versus chronic leg ulcer. Additional laboratory tests such as CRP and ESR, imaging studies, and clinical picture should be used to confirm a diagnosis of osteomyelitis versus chronic leg ulcer. Further trials are warranted to confirm the findings of this study.
Session Number: 348
Session Type: Rapid Fire
Session Title: Probiotics and Microbiome Studies in Clinical Infections
Session Start Date Time: 6/9/2018 4:30:00 PM
Session End Date Time: 6/9/2018 5:00:00 PM
Session Primary Track: Clinical Infections and Vaccines
Abstract Control Number: 9361
Poster Board Number:

Abstract Title:
Moderator
Primary Author Block:
A. Krishna Rao; 1
Abstract Body:
**Abstract Title:**
Influence of Antimicrobial Prophylaxis in Surgery and Effect of Probiotics on the Gut Microbiome: A Randomized Controlled Study

**Background:** The recent studies revealed the relationships of the gut microbiome to many diseases. However, its relationship to antimicrobial therapy remains unknown. In this study, we investigate the influence of antimicrobial prophylaxis in surgery and effect of probiotics on the gut microbiome.

**Methods:** The patients who underwent spine surgery between July 2016 and October 2017 were included in this study. Thirty-four patients were classified into two groups according to permuted block method: control (n=17) and postoperative administration of drug-resistant lactic acid bacteria for 5 days (treatment group, n=17). The patients received surgery and antimicrobial prophylaxis as usual. The feces of the patients were sampled at preoperation, postoperative day (POD) 5 and 10. The gut microbiome were analyzed by using Ion-PGM system and CLC genomics workbench.

**Results:** There were no significant differences between control and treatment groups in the basic characteristics, such as age, gender, underlying diseases and surgical site. The most administered antimicrobial agents at perioperative period was cefazolin in both groups (n=13 in the control and n=14 in the treatment group, respectively). There were no significant differences in administered antimicrobial agents between two groups. In the control group, two patients showed soft stool at POD5. A total of 102 samples were analyzed and 9,003 sequences were obtained over all samples (mean 2,082.2 ± 642.9 sequences per sample). The sequences were classified into 1032 operational taxonomic units (OTUs). The changes of the gut microbiome were showed in Figure. In PERMANOVA analysis (weighted UniFrac), the composition of the gut microbiome in POD10 was significantly different between both groups (P=0.021).

**Conclusions:** The composition of the gut microbiome in the patients who were administered antimicrobial prophylaxis in surgery might be different depending on the administration of probiotics.
Evaluation of the Gut Microbiota As A Measure to Examine Success of Fecal Microbiota Transplantation in Solid Organ Transplant Recipients.

Primary Author Block:
A. Kates, D. Shirley, M. Duster, J. Skarlupka, N. Safdar; Univ. of Wisconsin-Madison, Madison, WI

Abstract Body:
Fecal microbiota transplantation (FMT) has become a common treatment for Clostridium difficile infections (CDI). Patients with a history of solid organ transplantation (SOT) are at increased risk of CDI due to immunosuppression and exposure to antibiotics. The effectiveness of FMT in this population is unclear. Here we present a pilot study of FMT use to treat CDI in SOT patients. Patients with CDI were treated with FMT from a universal donor or someone the patient knew and administered via colonoscopy or enema. Stool samples were taken from the patient pre- and post-FMT as well as from the donor. DNA was extracted using a bead-beating protocol. Sequencing of the V4 region was done on the Illumina MiSeq. All analyses were done in R v.3.4.0. Alpha diversity was calculated using the Inverse Simpson’s metric and beta diversity was calculated using the Bray-Curtis dissimilarity matrix and plotted using PCoA. Ten patients were treated with FMT and tested culture positive for C. difficile prior to administration with 8 patients culture negative following administration of FMT. The alpha diversity of the pre-FMT patients was significantly higher than post-FMT (p-value = 0.0103). The PCoA (Figure 1) shows the donor and post-FMT samples cluster together and separate from the pre-FMT samples (p-value=0.003). Pre-FMT, the most prominent phyla belonged to the Proteobacteria and Verrucomicrobia. Following FMT, the Firmicutes and Actinobacteria were the most prevalent mirroring the donors. 48 OTUs were significantly different between the pre-and post-FMT patients (p-values:0.009 to < 0.00001) with an increase in gut commensal organisms in the post-FMT patients. FMT is effective at reducing CDI in SOT patients and restores the gut microbiota to a more diverse state similar to the donor stool. Assessing the patients gut microbiota is useful in determining the effectiveness of FMT in SOT patients.

Figure 1: PCoA of SOT patient and donor stool samples across all time points.
Abstract Title:
Determination of the Optimal Duration and Conditions of Long-Term Storage of Fecal Filtrate Samples Used for Fecal Microbiota Transplants (FMT)

Primary Author Block:
M. Kissoon1, A. Paterson1, B. M. Willey1, S. Hota2, S. M. Poutanen1; 1Univ. Hlth.Network/Sinai Hlth.System Dept. of Microbiol., Toronto, ON, Canada, 2Univ. Hlth.Network, Toronto, ON, Canada

Abstract Body:
Background: FMT is a useful treatment option for patients with recurrent Clostridium difficile infection. Frozen FMT filtrate is an efficient way to store samples. Little data exist showing the stability of frozen filtrate. Our group previously showed that optimal bacterial viability is achieved after 12M storage if filtrate is stored at -80°C with 10%-glycerol. The purpose of this study was to determine whether viability is maintained after 24M of storage. Methods: 4g of fresh stool from anonymous donors (n=2) was homogenized with both 40mL 0.9N-sterile-saline and 40 mL 0.9N-sterile-saline containing 10%-glycerol. The resulting filtrate was frozen at -20°C and at -80°C in 1.8mL aliquots. At baseline and after 7, 9, 12, 18, and 24M storage, 100μL of filtrate was plated onto anaerobic and aerobic agars and streaked using the Isoplator (Vista Technology). Semi-quantitative growth was recorded by two blinded readers. Loss of microbial growth (LMG) was determined as the difference between bacterial growth at each time-point compared to baseline. Results: At 7, 9, 12, 18, and 24M, fecal filtrate stored at -20°C without 10%-glycerol had the greatest loss of microbial growth (34%, 43%, 30%, 33%, and 45% loss, respectively) followed by filtrate stored at -20°C with glycerol (12%, 15%, 28%, 19%, and 21% loss) then filtrate stored at 80°C without glycerol (13%, 14%, 11%, 5%, and 6% loss). Fecal filtrate stored at -80°C with 10%-glycerol had the least loss of microbial growth (1%, 6%, 5%, 1%, and 2% loss). Conclusions: FMT filtrate is associated with optimal bacterial viability if stored at -80°C with 10%-glycerol, with no significant reduction in viability after storage for 24M. Viability is significantly impacted when fecal filtrate are stored at -20°C without cryo-protectant.
Chronic Otitis Media with Effusion: Microbiome Analysis by QPCR and 16S rRNA Deep Sequencing

Abstract Body:
Background: Acute otitis media is a common condition of childhood. Treatment includes antibiotics, and in case of chronic otitis media with effusion (COME), surgical treatment may be necessary. Bacterial pathogens frequently associated with these conditions are Streptococcus pneumoniae (Sp), Haemophilus influenzae (Hi), and Moraxella catarrhalis (Mc). 16S rRNA deep sequencing has been used to determine the microbiome of different tracts; however, its role in COME has not been widely investigated. Methods: Middle ear fluid (MEF) samples were collected from 75 children less than 5 years old with COME during 2016-2017, with indication for surgical treatment. Fluids were collected during myringotomy to place the ventilation tube. Samples were submitted to nucleic acid extraction for qPCR and 16S rRNA deep sequencing. qPCR was used for specific detection of classic pathogens (Sp, Hi, and Mc) and 16S rRNA deep sequencing was used to assess the microbiome of MEF. Results: qPCR revealed the presence of bacterial pathogens in 67/75 (89.3%) patients. Hi was the most prevalent bacteria found in 59 (78.7%) patients, followed by Sp in 20 (26.7%). Co-infection by Hi and Sp was found in 16 (21.3%). Mc was found in 10 (13.3%), but in 8 patients it was found concomitantly with Hi. Sequencing results confirmed the presence of bacterial DNA in all samples, with >98% concordance with qPCR. Sequencing analysis of MEF revealed the presence of at least 16 genera with ≥ 0.1% mean relative abundance. Conventional pathogens represented <25% of bacterial DNA found in our samples. The most relative abundant genera were Corynebacterium (31%), Haemophilus (17%) Alloiococcus (15%), Propionibacterium (10%), Staphylococcus (9%) and Streptococcus (6%). Other Gram-negative bacilli comprised 5%. Miscellaneous other bacteria, including anaerobes, represented <1%. Conclusions: Although qPCR targeting conventional pathogens associated with COME was positive in 89.3% of patients, sequencing revealed other potential players. In contrast with other studies, our data showed that conventional pathogens represented <25% of bacterial DNA, with >75% of detected DNA belonging to other bacterial genera, especially Corynebacterium, Propionibacterium, Alloiococcus and staphylococci. Results suggest that COME may be the product of the interaction of the host response with a complex bacterial community. Understanding the mutual interaction of this bacterial community may be relevant to better understand the management of children with these conditions.
Intranasal Vaccination with An Adjuvanted Ebola-gp Vaccine Alters the Mouse Gut Microbiota

J. Richardson, M. Sunay, M. Gregory, G. Koroleva, G. Palacios; United States Army Med. Res. Inst. for Infectious Diseases, Frederick, MD

The gut microbiota plays an important role in the development and maintenance of a healthy immune system. However, little is known about the interaction between vaccines and vaccine adjuvants and the gut microbiota. To better understand how vaccination impacts the gut microbiota, mice were vaccinated with a plasmid based Ebola-GP vaccine containing a TLR-3 antagonist intranasally, intramuscularly or intramuscularly with a vector control. Mouse gut microbiotas were characterized by 16S rRNA sequencing of fecal samples. Mice vaccinated intranasally, but not intramuscularly, showed a dramatic increase in the proportion of Akkermansia muciniphila. This increase was detected on days 40 and 49 post vaccination (days 19 and 28 post-boost). This alteration in the gut microbiota was correlated with protection from mouse-adapted Ebola, and high serum levels of anti-Ebola-GP IgA and IgG titers. This shows that intranasal vaccination against Ebola can change the gut microbiota composition. Further work is required to clarify the consequences and direct causes of this alteration.
Session Number: 380  
Session Type: Poster Talk  
Session Title: Studies in Pediatric Infectious Diseases  
Session Start Date Time: 6/10/2018 12:45:00 PM  
Session End Date Time: 6/10/2018 1:35:00 PM  
Session Primary Track: Clinical Infections and Vaccines  
Abstract Control Number: 9356  
Poster Board Number:  

Abstract Title:  
Moderator  
Primary Author Block:  
Miriam Laufer; Univ. of Maryland, Baltimore, MD  
Abstract Body:
Group B Streptococcus Infection among Pregnant Women and Neonatal Colonization Rate in Patients from A Tertiary Inst. Southwestern Nigeria

Primary Author Block:
T. J. Akinlolu; Obafemi Awolowo Univ., Ile-Ife. Osum State, Nigeria

Abstract Body:
This study was carried out to evaluate Group B Streptococcus infection among pregnant women and neonatal colonization rate in patients attending Obafemi Awolowo University Teaching Hospital Complex. It also determined the antibiotic susceptibility pattern, also evaluated GBS status of the subjects using demographic and clinical parameters. These were with a view to provide information on the prevalence of GBS infection in Nigeria. One hundred and seventy samples (170) were collected from consenting mothers and neonate between June 2016 and January 2017. Ninety-Eight (98) GBS isolates were recovered from vaginal, rectum of the pregnant woman at the point of labour and Umbilical cord of the neonate within 24 hrs of birth. Cultures for the isolation and identification of Group B Streptococcus (GBS) were carried out using the Centre for Disease Control (CDC) recommended microbiological methods (Lim broth, Chromogenic agar, Blood agar). The Kirby-Bauer disk-diffusion method was employed to determine antibiograms of GBS isolates in accordance with Clinical and Laboratory Standards institute (CLSI). The presence of resistant genes was examined using Polymerase Chain Reaction (PCR). The result shows that the prevalence rate of GBS maternal and neonatal colonization were 29.4% and 20.6% respectively while 4% of the colonized neonates had nosocomial GBS colonization. There was no significant association between GBS colonization status and age (p >0.05), parity (p >0.05), obstetric risk factors (p >0.05) and sex of neonate. No incidence of GBS infection observed during the study. Resistance to augmentin was observed to be as high as 88.8%, ampicillin (60.2%), penicillin (47%), tetracycline (34.7%), ceftriaxone (19.4%), clindamycin (13.3%), vancomycin (10.2%) and erythromycin (7.1%). One of the 8 representatives of the multidrug resistant isolates harboured tetM gene while other resistant genes examined (tetO and linB) were negative in all MDR isolates. In conclusion, this study established high prevalence of maternal and neonatal GBS colonization among pregnant women and neonates while nosocomial infection was also implicated in GBS colonization among neonates. However, further research is required using larger sample size and multiple centers for adequate extrapolation into the general population.
Association of Intestinal Helminthic Infection, Atopy & Allergic Disorder among Primary Sch. Children

Primary Author Block:
D. D. Abera, A. Tsegaye; Addis Ababa Univ., Addis Ababa, Ethiopia

Abstract Body:
Background: Intestinal helminthic infections have been suggested to play protective role from allergic sensitization & atopic diseases. There is a concern that deworming could increase the prevalence of atopic disease in endemic populations. However, there is inconsistent & little information about the relationship between helminthic infection and allergic disease in the case of deworming set up in Ethiopia

Methods: A cross sectional study was conducted among 526 school children aged 5 to 14 years from three selected government primary schools in Sululta woreda. Information on socio-demographic characteristic, associated risk factors & allergic symptoms were obtained using questionnaire, moreover allergen skin tests to Dermatophagoides pteronyssinus & Blatella germanica (cockroach) were performed to assess atopy status. From all children, fresh stool samples were collected & processed by direct wet mount, Kato-Katz technique & formol-ether concentration technique

Results: Of the total 526 school children 58.2% (306) were females. Overall 24% (n=126/526) had questionnaire based allergic symptoms while 5.1 % (n=27/526) had skin prick test reactivity, 16.9% of them (n=89/526) had intestinal helminthic infection. All helminthic infections were with low intensity level. There was no association between helminthic infection & allergic symptoms (OR=1.30, 95% CI=0.778-2.171, P=0.317). Ascaris lumbricoides infection was positively associated with skin test reactivity (AOR=4.307, 95%CI=1.143-16.222, P=0.031). Atopy was significantly associated with increased allergy symptoms (AOR=2.787, 95%CI=1.253-6.197, P=0.012). Short term deworming had no effect on atopy but has a protective effect on allergic symptom

Conclusions: Low intensity & low prevalence of helminthic infection in our findings may have contributed to the non-significant association of allergy & helminthes infection; however, Ascaris lumbricoides was positively associated with atopy. Further longitudinal study is recommended to examine the mechanism of Ascaris lumbricoides infection for the development of atopy.
Molecular Characterization of Enteroaggregative Escherichia coli Clin. Isolates from Children in Colombia, South America

Primary Author Block:
A. Aldrow1, J. Guerra1, A. Dharia1, A. Farfan2, O. Gomez-Duarte1; 1Univ. at Buffalo, Buffalo, NY, NY, 2Univ. de Santander, Bucaramanga, Cambodia

Abstract Body:
Enteroaggregative E. coli (EAEC) is an enteric pathogen that causes acute diarrheal disease among children and adults worldwide. An important characteristic of EAEC is its heterogeneous nature in terms of virulence gene profile. EAEC typically mediates aggregative adherence (AA) to intestinal cells, biofilm formation on intestinal mucosa and it may secrete enterotoxins. EAEC is divided into typical and atypical EAEC based on the presence or absence of the aggR gene, respectively. The objectives of this study are to identify virulence gene profiles of EAEC clinical isolates from Colombia, to evaluate the genetic relatedness among Colombian EAEC strains, and to quantify the biofilm formation phenotype among all EAEC strains. EAEC clinical isolates from children with and without diarrhea were derived from stool samples of subjects less than 5 years from Colombia (n=109), as part of previously reported IRB-approved childhood diarrhea surveillance studies. Genomic DNA from EAEC clinical isolates and E. coli controls was isolated and processed for multiplex PCR assays for identification of virulence genes. Quantitative biofilm assay was performed using microtiter plates to screen for biofilm formation (BF). Among EAEC cases, aatA, pic, sen, set1A and set1B were the most common virulence genes (71%). The pic gen was statistically associated with EAEC isolated from cases (Fisher test p-value 0.0001). Among EAEC controls, ORF3 (80%), set1A (75%), sen (73%), aggR (71%), aatA (71%) and ORF61 (71%) were the most common virulence genes. Among cases, 69% were typical EAEC and 31% were atypical EAEC. Among controls, 71% were typical EAEC and 29% were atypical EAEC. Quantitative biofilm assay showed similar results for cases and controls. Among the cases, 10% were BF high positive, 38% were BF low positive and 52% were BF negative. Among controls, 8% were BF high positive, 49% were BF low positive and 43% were BF negative. Colombian EAEC clinical isolates are a highly diverse group of strains with respect to virulence genes and BF. The only gene that was statistically associated with EAEC isolated from cases was pic, suggesting that this virulence gene may play a significant role in disease causation in pediatric populations. Further studies are necessary to better understand the role of specific genes, in addition to pic, in EAEC pathogenesis.
Abstract Title:
Rotavirus Disease Burden and Surveillance in Under-Five Children Attending Yangon Children Hospital, Myanmar

Primary Author Block:
H. Thu; Dept. of Med. Res., Yangon, Myanmar

Abstract Body:
Rotavirus gastroenteritis (RVGE) is the leading cause of severe diarrhoea affecting infants and young children. Mortality and severe outcome are more concentrated in developing countries. Diarrhoea is among the priority childhood diseases in Myanmar according to the National Health Plan. The Department of Medical Research (DMR) has carried out surveillance of rotavirus diarrhoea in Yangon Children Hospital with the support of WHO (SEARO) since 2009. The objectives were to raise awareness and contribute data to estimate the burden of rotavirus diarrhea in under-five children, identification of currently circulating rotavirus strains, timely detection of emerging new strains and to help in decision-making for the introduction of rotavirus vaccines. Stool samples not less than 3 mls were collected from diarrhoeic children under 5 years of age admitted with diarrhea to the three medical wards of the Yangon Children Hospital. All the samples collected were tested for the presence of rotavirus antigen by a commercial enzyme immunoassay kit (ProSpecTTMRotavirus from OXOID, UK). G and P genotypes were identified by multiplex RT-PCR assay using genotype-specific primers from the Christian Medical College, Vellore, India. A total of 5242 stool samples were tested from the period 2010 to 2017 September and rotavirus positivity ranged from 46% to 56%. Rotavirus diarrhoea was most prevalent in the 6-11 months age group (44.8%) showing a male preponderance in all years. A seasonal variation was seen with high number of cases from November to February with the highest peak occurring in January. Categorization of RVGE cases according to the Vesikari clinical severity scoring system showed that 72 to 82% of cases were severe (score ≥11). A sub-sample of rotavirus positive samples were selected and subjected to G and P genotyping. G and P combinations showed changing profiles for each year. In 2009, G12 was detected for the first time and G12P[8] and G1P[8] combinations were equally distributed. From 2010 to 2012, G12P[8] became the most prevalent genotype (62 to 75.2%). In 2013, G2P[4] was the most detected (73%) which changed to G9P[8] from 2014 to 2016 (31 to 53%). Currently in 2017, the most identified combination is G3P[8] (58%). RVGE is a vaccine preventable disease and while improvements in clinical management in the hospital has contributed to gains in child survival, diarrhoea is still on the top list of priority childhood diseases and rotavirus vaccine introduction in the nationwide childhood immunization programme is being considered for 2019 in Myanmar.
Abstract Title:
Improvement of Blood Culture Contamination and Positive Rates by Using A Dedicated Phlebotomy Team

Primary Author Block:

Abstract Body:
Background: The introduction of a dedicated phlebotomy team certified for blood collection was highly cost-effective by reducing contamination rate. However, data on its effect on blood volume and true positive rate are limited. Thus, we investigated the effect of implementation of a phlebotomy team replacing intern doctors on blood culture results. Methods: We analyzed all blood cultures obtained from adult inpatients at a 2,700-bed tertiary-care hospital. Blood culture was performed by the interns from Mar 2015 through Feb 2016 and by full-time phlebotomy teams from May 2016 through Apr 2017. During the study period, there were no changes in blood collection method, blood culture tubes, and the application of antisepsis. The same infection control policy was applied over the study period. Blood volume was measured by the BACTECTM FX system using red blood cell metabolism. Contamination among positive results was defined according to CLSI guidelines. Results: A total of 162,489 blood culture sets from 23,483 patients were analyzed, comprising 78,912 blood culture sets during the interns period and 83,577 blood culture sets during the phlebotomy team period. Blood volume was significantly increased from 2.10 ml in the interns period to 5.63 ml in the phlebotomy team period (p<0.001, Table 1). The phlebotomy team had also significantly lower contamination rate (0.45% vs. 0.27%, p<0.001, Table 2) and higher true positive rate than the interns (5.00% vs. 5.86%, p<0.05, Table 3). There was no significant difference in the distribution of isolated microorganisms between the two groups. Increased true positive rates by the phlebotomy team were observed in both gram-positive bacteria and gram-negative bacteria. Conclusions: Our study suggests that the introduction of a dedicated phlebotomy team can increase blood volume and improve blood culture contamination rate and true positive rate.
Abstract Title:
Persistence of Antimicrobial Resistant Bacteria on Hospital Surfaces: Effect of Relative Humidity and Temperature
Primary Author Block:
A. Lyons, L. Rose, J. Noble-Wang; CDC, Atlanta, GA
Abstract Body:
Background: Surfaces in healthcare facilities are thought to be a source of pathogenic bacteria leading to healthcare-associated infections. Daily cleaning of surfaces may not be thorough, allowing organisms to persist long enough for transmission to occur. Previous work has focused on persistence at one temperature (T) and relative humidity (RH) condition (26°C, 57% RH). Here we compare survival of Acinetobacter baumannii and Carbapenemase-producing Klebsiella pneumoniae (KPC) on plastic and steel surfaces for 28 days under two controlled conditions. Methods: Bacteria were prepared in a 20% Artificial Test Soil solution (ATS, Healthmark, Inc.) to simulate body fluids, and 10^6 CFU placed onto 1 cm^2 coupons of stainless steel and plastic. The coupons were held in an environmental chamber at either high temperature/high humidity (T/RH, 26°C, 57% RH) or low T/RH (18°C, 20% RH). Coupons were processed at days 0, 3, 7, 14, 21, and 28. At each time point, 3 coupons were vortexed and sonicated 3 times in 3 mL PBS with 0.02% Tween 80. For each surface material and each microorganism, 2 runs (3 samples each) were completed (n=6 total). Viability was quantified by culture and esterase activity via solid phase cytometry. Results: A. baumannii survived up to 28 days on plastic and steel at both T/RH conditions. A 1 log10 reduction at 18°C, 20% RH was observed from both culture and esterase data. In contrast, at 26°C and 57% RH, KPC demonstrated a 5 log10 and 6 log10 reduction on plastic and steel, respectively, by day 6 as detected by culture, while esterase activity showed a 1 log10 reduction over the 6 days. KPC survived longer at 18°C and 20% RH, with culture demonstrating 1 log10 CFU remaining and esterase activity demonstrating 5 log10 cells remaining on both surfaces after 21 days. Conclusion: Our results suggest that both pathogens survive long enough for potential transfer to occur from surfaces to patients if disinfection practices are not thorough. Results indicate that persistence varies between organisms and can be dependent on temperature and relative humidity. The esterase activity suggests continued persistence (viable but not culturable), though further investigation is necessary to determine if these organisms are still infectious.
Abstract Title:
Discovery of Viral Nucleic Acids from Non-vertebrate Hosts in Children with Fever of Unknown Origins

Primary Author Block:
T. Phan1, J. del Valle Mendoza2, E. Delwart3;  1Indiana Univ. Sch. of Med., Indianapolis, IN, 2Univ. Peruana de Ciencias Aplicadas, Lima, Peru, 3Blood Systems Res. Inst., San Francisco, CA

Abstract Body:
Background: Fever can often remain unexplained despite testing for specific human pathogens. Fever of unknown origin may reflect infections with known but untested pathogens, still uncharacterized and possibly emerging infectious agents. Methods: Serum samples collected from 88 Peruvians with unexplained fever were analyzed for viral sequences using metagenomics. Following enrichment of viral particles-associated nucleic acid, random nucleic acid amplification, deep sequencing and bioinformatics analysis, sequence reads belonging to different viruses was determined. Results: Nucleic acids of anelloviruses, pegivirus A (GBV-C), HIV, Dengue virus, and Oropouche virus were detected. We also characterized from two sera the RNA genomes of partitivirus and dicistrovirus belonging to viral families known to infect fungi or arthropod, respectively. Since very low identities were measured between partitivirus and dicistrovirus and their closest relatives, they can be considered a member of a new species or even a new genus in the family Dicistroviridae and Partitiviridae. Conclusions: The role, if any, of the non-vertebrate infecting viruses detected in serum in inducing fever requires further investigation. Characterization of viral nucleic acids in the sera of a febrile South American population provides a baseline to compare with future virome studies to detect emerging viruses in this region.
Abstract Title:
Development of Vaccines from A to Z, for AIDS and Zika and Many More in Between, Using a Novel MVA Vector Platform Technology
Primary Author Block:
F. Guirakhoo; Geovax, Smyrna, GA
Abstract Body:
Background: GeoVax MVA platform technology is built on a 4th generation MVA vector system that is improved for high expression and stable transgenes during manufacture. It has the advantages of being a live replication-competent vector in avian cells for manufacturing, yet replication-deficient in mammalian cells for vaccination, thus inherently safe. Importantly, MVA vaccines elicit protective T cell as well as antibody responses in animals and humans. The MVA platform can be combined with the potent immunogenicity of Virus Like Particles (VLPs) (e.g. MVA-VLP-HIV, -Ebola, -Marburg, -Sudan, -Lassa fever, -HBV, -HPV, -malaria, -MUC1+ cancers) or be used to express proteins in their native conformations (e.g. MVA-NS1-ZIKA) enabling vaccines that induce full protection after a single dose. In this talk, we present preclinical single dose efficacy data for vaccines against Ebola, Lassa fever and Zika and briefly discuss the pipeline of all other MVA-VLP vaccines in progress. Methods: MVA-VLP vaccines were constructed for Ebola (using VP40 and GP), Lassa fever (Z and GPC) and Zika (NS1, eliminates the risk of Antibody Dependent Enhancement, ADE, of infection associated with other vaccines based on the envelope antigens). Vaccine viruses were characterized in vitro for genetic stability, VLP formation (Electron microscopy), sequencing and WB. Inoculations were done in rodent species (mouse, guinea pigs and hamsters) as well as non-human primates. Immunogenicity (ab response) and T cell responses were determined to assess functionality and correlation of protections. Results: Zika: A single immunization of MVA-NS1 Zika by the IM route provided 100% protection against a lethal challenge dose of a neurovirulent ZIKV delivered directly into the brain. All control animals lost weight and died within 1 week. Efficacy of MVA-VLP Ebola vaccine candidate was determined in Guinea pigs, hamsters and rhesus monkey lethal challenge models (BSL4). A single dose of MVA-VLP-LASV protected mice against a lethal challenge delivered directly into the brain. Discussion: Three different vaccines provided full protection after a single dose against 3 different family of viruses using lethal challenge models. These data demonstrate not only a broad utility of the platform for vaccine against infectious diseases especially suited in resource constrained countries, but also for other indications such a therapeutic vaccine for HBV, a multi-antigen vaccine for malaria and TAA based cancer vaccines.
Session Number: 416
Session Type: Late-Breaker Poster Presentations
Session Number: 416
Session Type: Late-Breaker Poster Presentations
Session Title: SUNDAY - CIV Late-breakers
Session Start Date Time: 6/10/2018 12:45:00 PM
Session End Date Time: 6/10/2018 2:45:00 PM
Session Primary Track: Clinical Infections and Vaccines
Abstract Control Number: 7692
Poster Board Number: SUNDAY - CIV LBS

Abstract Title:
Efficacy of Prokaryotic and Eukaryotic Recombinant Fusion Proteins (m2e-crt) As An Influenza Universal Vaccine in Mice C57bl/6

Primary Author Block:
H. Attaran1, H. Nili2, B. Gholamhossein Goudarzi3; 1Inst. of Zoology, Chinese Academy of Sci., Beijing, China, 2Shiraz Univ., Shiraz, Iran, Islamic Republic of, 3Razi Vaccine and Serum Res. Inst., Tehran, Iran, Islamic Republic of

Abstract Body:
Background: Effective vaccination against influenza viruses remains a challenge as a result of antigenic shift and drift in the viruses. This has led to the search for new vaccine approaches for influenza; specifically, the concept of a “universal vaccine”. Being conserved is an important feature of the M2e protein which makes it a potential candidate for universal vaccine development against influenza A viruses. Carliticulin (CRT) is one of the members in the family of heat shock proteins (molecular chaperons), which are conserved and widely distributed in microorganisms and mammalian cells.
Method: In this paper, for the first time we constructed and expressed M2e-CRT in E.coli and Pichia pastoris. Then we evaluated the immunological responses and virus challenge following injection of M2e-CRT fusion protein, expressed in E. coli and p. pastoris as a recombinant protein vaccine. According to this issue, a prime-boost administration of M2e-CRT by subcutaneous (s.c) route in C57Bl/6 mouse model was done. Result: Based on the results of this study, both fusion proteins induced comparable immunologic responses. Conclusion: Because of easier and cheaper purification in prokaryote system this has led to the conclusion that M2e-CRT fusion protein as a vaccine candidate in prokaryote system compared with eukaryotic is preferred. Key Words: Influenza A virus, M2e-CRT, Recombinant fusion protein, Universal influenza vaccine
Abstract Title:
Edwardsiella ictaluri Strain ΔeseK Produces an Attenuated Effect on Mortality of Enteric Septicemia in the Channel Catfish, Ictalurus punctatus

Primary Author Block:
E. Griggs, R. Thune; Louisiana State Univ., Baton Rouge, LA

Abstract Body:
Background: Edwardsiella ictaluri is a gram-negative bacterium that causes Enteric Septicemia in channel catfish (Ictalurus punctatus). The Type III secretion system (T3SS) encoded in the E. ictaluri genome utilizes effector proteins, such as EseK, to modulate host cell pathogenesis. A preliminary experiment utilizing E. ictaluri T3SS effector mutant strains to infect channel catfish found that exposure to a mutant esseK E. ictaluri (ΔeseK) may confer protection to subsequent exposure to the wild-type (WT). The goal of this study was to evaluate the efficacy of ΔeseK as a vaccine candidate against ESC.

Methods: Twenty-five catfish were added to each of three 20 L challenge tanks per treatment and were vaccinated with ΔeseK at the doses of 1X10^7 cfu/mL, 1X10^6 cfu/mL, and 1X10^5 cfu/mL. This range was chosen because ΔeseK at the dose of 1X10^8 cfu/mL was previously determined to have a high mortality similar to WT. Following the vaccination fish were exposed to WT at 1X10^8 cfu/mL for an efficacy challenge. Results: Mortality to the ΔeseK vaccine doses of 1X10^5 cfu/mL, 1X10^6 cfu/mL, and 1X10^7 cfu/mL was 0% to 6%. Five efficacy challenges were conducted four to eight weeks post vaccination (PV), and significant protection was observed at the ΔeseK 1X10^7 cfu/mL dose that showed 95 to 100% efficacy, but efficacy to WT exposure declined as the vaccine dose decreased. Conclusions/Implications: Vaccination with ΔeseK provides varying levels of protection with ΔeseK 1X10^7 cfu/mL, consistently providing over 95% protection. Mortality following vaccination at some doses, however, raises safety questions that require further investigation.
Abstract Title:
Polymerase Mutations from the Russian Live-Attenuated Influenza Virus (LAIV) Confer a More Robust Temperature-Sensitive Phenotype on H1N1 Influenza A virus than do Those from the U.S LAIV

Primary Author Block:
A. Smith, L. Roberts, L. Rodriguez-Garcia, A. Nogales-Gonzalez, L. Martinez-Sobrido, S. Dewhurst; Univ. of Rochester Sch. of Med. and Dentistry, Rochester, NY

Abstract Body:
The influenza A virus (IAV) infects 10-20% of the world population annually, but current vaccine approaches continue to show poor (50% or less) efficacy. Our long-term goal is therefore to improve the efficacy and safety of Live-Attenuated Influenza Vaccine (LAIV). As a first step, we wish to understand the molecular basis for the attenuation of LAIV - initially by studying how the mutations in the viral RNA-dependent RNA polymerase (RdRp) contribute to the temperature sensitive (ts) phenotype of LAIV. We performed viral minigenome assays in human 293 T cells and A549 lung airway epithelial cells at 33, 37 and 39°C, to assess the functional activity of the viral RdRp, and we also performed virus growth assays at the same temperatures, along with in vivo assays of viral virulence. For these studies, we compared both the U.S (A/Ann Arbor/6/60 [H2N2]) and Russian (A/Leningrad/134/17/57 [H2N2]) LAIVs - by introducing the corresponding polymerase mutations into the genetic backgrounds of the (i) the mouse-adapted A/PR/8/34 [H1N1] virus (PR8) and (ii) the pandemic A/California/04/09 [H1N1] virus (CAL). In minigenome assays, at 39°C, the U.S. LAIV mutations reduced RdRp activity in the PR8 but not the CAL background - whereas the Russian LAIV mutations reduced RdRp activity in both backgrounds by several logs. In viral growth assays, the U.S. LAIV mutations almost completely abrogated the in vitro replication of PR8 at 39°C, but not CAL, whereas the Russian LAIV mutations abrogated replication of both viruses. Finally, in vivo studies in C57BL/6 mice showed that the U.S. LAIV mutations attenuated the virulence of PR8 by 1,000 fold - but reduced the virulence of CAL by only 10 fold. Overall, these data indicate that the Russian LAIV polymerase mutations confer a more strongly ts phenotype on influenza A viruses than do the US LAIV polymerase mutations. Furthermore, they also show that the magnitude of the ts and attenuated phenotype conferred by LAIV mutations is influenced by the genetic background of the influenza virus into which they are introduced. These findings have important implications for the development of new, improved LAIVs.
Utility of Procalcitonin for Diagnosis of Sepsis Or Lower Respiratory Tract Infections

Background: Procalcitonin (PCT), a prohormone of calcitonin, is secreted by a variety of cells in response to proinflammatory stimulation. Detection and monitoring of plasma/serum PCT is useful in the setting of serious sepsis as a syndrome of bacterial infection and bacterial pneumonia. PCT < 0.09 ng/mL can be used to rule out sepsis and/or lower respiratory tract infection. PCT > 0.25 ng/mL suggests increased risk of sepsis or lower respiratory tract infection requiring antibiotic therapy. PCT 0.09-0.25 ng/mL is indeterminate. The aim of this study was to compare diagnostic utility of plasma/serum PCT measured by Elecsys BRAHMS PCT on Cobas 6000/e601 (Roche, Indianapolis, IN) vs traditional culture for predicting bacteremia or lower respiratory tract infection.

Methods: A total of 450 medical records were reviewed for patients with concurrent PCT and respiratory or blood culture.

Results: Eighty two patients had PCT <0.09 ng/mL. Of these, blood culture on one patient (PCT 0.07 ng/mL) was positive for methicillin-resistant Staphylococcus aureus (MRSA). One hundred twenty eight patients were indeterminate. Of these, blood culture on two patients (PCT 0.19 and 0.24 ng/mL) were positive for MRSA and blood culture on one patient (PCT 0.16 ng/mL) was positive for Candida parapsilosis. Two hundred fifty five patients had PCT >0.25 ng/mL. Fifty three patients had received antibiotic prior to collection of blood cultures. Of the remaining 202 patients, blood cultures were positive on 41 patients. Findings included Gram positive cocci (n=20), Gram negative rods (n=19), Gram positive rod (n=1) and Candida glabrata (n=1). PCT ranged from 0.28-345.24 ng/mL with a median PCT of 2.95 ng/mL. Additionally, respiratory cultures were positive on 14 patients (4 S. aureus, 3 Pseudomonas aeruginosa, 1 Klebsiella pneumoniae, 1 K. oxytoca, 1 E. coli, 1 Hemophilus influenza, 1 Streptococcus pneumoniae and 1 Corynebacterium striatum). PCT ranged from 0.27-128 ng/mL with a median PCT of 0.71 ng/mL.

Conclusions: PCT had excellent diagnostic specificity (99.3%) and negative predictive value (98.7%), but substantially lower sensitivity (40.4%) and positive predictive value (27.2%) in predicting bacteremia or lower respiratory tract infection vs traditional blood or respiratory cultures.
Session Number: 417
Session Type: Poster

Session Title: CIV01 - Clinical Studies of Adult Infectious Diseases: Respiratory Tract Infections
Session Start Date Time: 6/10/2018 12:45:00 PM
Session End Date Time: 6/10/2018 2:45:00 PM
Session Primary Track: Clinical Infections and Vaccines
Abstract Control Number: 5353
Poster Board Number: SUNDAY - 671

Abstract Title:
Laboratory Based Surveillance of Pneumococcal Disease to Determine the Serotype Distribution of Streptococcus Pneumoniae in Karachi

Primary Author Block:

Abstract Body:
Background: In Pakistan annually 600,000 cases of pneumococcal infections are reported. Knowledge of pneumococcal serotypes in a population is important for guiding vaccine formulation. This was the first laboratory based surveillance study conducted to determine the serotype distribution of pneumococcal isolates prevalent in the population of Karachi. Methods: The study was conducted at PHRC Research Centre. Clinical isolates of S. pneumoniae from clinical microbiology laboratories of Aga Khan University Hospital Karachi, Liaquat National Hospital Karachi and Ziauddin Hospital Karachi were collected and identification confirmed. Serotyping was done through sequential multiplex PCR method as described by Pai et al and Saha et al to determine the distribution of different pneumococcal serotypes in our population. Results: Total 245 pneumococcal isolates were collected from collaborating laboratories including 155 (63.6%) from hospitalized and 88(35.9%) from non-hospitalized patients. Invasive infections were significantly higher (p-value 0.006) in children <5years while elderly had a high proportion of non-invasive infections. Serogroup 6A/6B/6C/6D (9.2%) was the most commonly isolated serogroup followed by serotype 1(7.9%), 19A (5.8%), 3 (5.8%), 19F (5.4%) while 46 (19.2%) isolates were not type-able by multiplex PCR. Conclusion: Our results suggest that Serogroup 6A/6B/6C/6D is most commonly involved in infections among our population followed by serotype 1 and 19A hence vaccines targeting these serotypes may be effective in our population.

...
Abstract Title:
Profile Global Gene Expression of Streptococcus Pneumoniae Influenced by Haemophilus Influenzae

Primary Author Block:
W. Hong, P. Khampang, J. Kerschner; Med. Coll. of Wisconsin, Milwaukee, WI

Abstract Body:
Streptococcus pneumoniae (Spn) and Haemophilus influenzae are commensals of human upper respiratory tract, which asymptotically colonize 40-60% of health individuals. However, both bacteria can migrate to other niches to cause various diseases including pneumonia, bronchitis, otitis media and sinusitis. Their co-colonization has been verified in the clinical specimens collected from patients with otitis media or sinusitis. Pneumococcal survival, biofilm formation and virulence alter in the presence of H. influenzae in in vitro and in vivo models, indicating the interaction between these two microorganisms plays important roles in their pathogenesis. Spn has competitive advantage over H. influenzae by producing hydrogen peroxide and neuraminidase but how H. influenzae effects pneumococcal activities and what are impacts of this influence on pneumococcal infection have not been defined. We hypothesize that H. influenzae can specifically modulate pneumococcal gene expression to enhance its fitness in polymicrobial infections. To verify the hypothesis, a co-culturing model and RNA-seq analysis were utilized in this study to profile pneumococcal global gene expression in the presence of H. influenzae. The result indicated that expression of up to 22% of pneumococcal gene/open reading frames (ORFs) were significantly changed when co-cultured with H. influenzae (more than 2-fold changes compared to the control). The major up-regulated genes were involved in polysaccharide capsule synthesis, phosphotransferase systems, and ABC transporting systems. Some other up-regulated genes include neuraminidases A and B, choline-binding protein I, and uncharacterized hypothetical proteins. The major down-regulated genes fell to quorum-sensing pathway to decrease competent development, autolysis/fratricide and bacteriocin productions. Down-regulated expressions of gene involved in both competence-stimulating peptide mediated quorum sensing and bacteriocin regulation may be the critical reason resulting in the enhancement of pneumococcal survival and biofilm formation. In summary, co-culturing with H. influenzae enhances pneumococcal survival and biofilm formation by significantly changing pneumococcal gene expressions related to carbohydrate metabolism and peptide-mediated quorum sensing regulation. Future study will be focused on the molecular mechanism facilitating this inter-species interaction and the effects of the interaction on the outcomes of co-infection of the bacteria.
Abstract Title:
Changes in the G Protein Genotypes of Respiratory Syncytial Virus A and B in Korea, 2005-2014

Primary Author Block:
M. Han1, J. Lee1, Y. Choi1, K. Yun1, H. Lee2, E. Choi1, H. Lee1; 1Seoul Natl. Univ. Children’s Hosp., Seoul, Korea, Republic of, 2Seoul Natl. Univ. Bundang Hosp., Seongnam, Korea, Republic of

Abstract Body:
Background: Respiratory syncytial virus (RSV) is a major pathogen causing seasonal epidemics of lower respiratory tract infection in children. The RSV G protein is the major virulence factor and the target of human neutralizing antibodies. Amino acids of the G protein change over time, making its study important for vaccine development. We aimed to explore the molecular epidemiology of the RSV A and B G protein over 10 years in Korea. Methods: Nasopharyngeal aspirates were obtained from children with respiratory symptoms hospitalized at Seoul National University Children’s Hospital from October 2005 to September 2015. RSV were isolated and typed into group A or B by using HEp-2 cells and monoclonal antibodies. The RSV strains were sequenced for the full-length G gene, and the nucleotide (nt) sequences in the second hypervariable region were analyzed to assign the genotype of RSV A and B. The genotypes with the 72- and 60-nt duplication were determined as ON1 in RSV A and BA in RSV B, respectively. Results: During the 10 RSV seasons, 313 RSV isolates were obtained and 253 (80.3%) and 60 (19.2%) were group A and B, respectively. RSV A was the dominant group in all but the 2005/06 and 2010/11 seasons when RSV B predominated. The G gene was sequenced and the isolates were genotyped in 164 (64.8%) of RSV A and 46 (76.7%) of RSV B. In RSV A, genotypes NA1, NA2, GA2, GA5, and ON1 were detected. No single genotype predominated in the 2005/06 season, but NA1 became the dominant circulating genotype from 2007/08 to 2011/12, with a prevalence of 66.7-100%. ON1 was first detected in 2011/12 and rapidly replaced NA1 since, from a prevalence of 11.8% in 2011/12 to 91.7% in 2012/13, and then to 100% in the 2013/14 and 2014/15 seasons. In RSV B, the genotypes GB3, BA7, BA9, and BA10 were identified. Although GB3 was the most common genotype in the 2005/06 season (43.8%), BA9 and BA10 replaced all previously detected genotypes since 2006/07. The most prevalent genotype was BA10 in 2006/07 (100%), BA9 during the 2008/2009-2013/14 seasons (71.4-100%), and BA10 in the latest 2014/15 season (75.0%). Conclusions: The G protein genotypes in RSV A and B changed substantially in Korea during 2005-2014. The genotypes with duplication, ON1 and BA, were introduced in 2011/12 and before the 2005/06 season, respectively, and rapidly became the dominant circulating genotypes of RSV A and B in Korea.
Abstract Title:
Incidence of Hospital-Associated Respiratory Virus Infections: 2016-2017
Primary Author Block:
J. G. Petrie1, A. S. Lauring2, E. T. Martin1, K. S. Kaye2; 1Univ. of Michigan Sch. of Publ. Hlth., Ann Arbor, MI, 2Univ. of Michigan, Ann Arbor, MI
Abstract Body:
Background: Hospital-associated influenza and respiratory syncytial virus (RSV) infections have been frequently described. The incidence of other hospital-associated respiratory virus infections (HA-RVI) is less understood because of limited diagnostic testing. Methods: We examined clinical respiratory virus testing practices and the incidence of HA-RVI in a cohort of patients hospitalized with acute respiratory illness (ARI) broadly defined by ICD-10 diagnostic codes. Results of clinical laboratory testing for 14 different respiratory viruses were used to identify potential HA-RVI, defined as positivity beginning >72 hours following admission. Results: A total of 14,237 individuals had 19,863 inpatient encounters for ARI between July 1, 2016 and June 30, 2017; 45% occurred during the influenza season (December 1 through April 30). Patients of all ages were included (median [IQR]: 59 years [36, 70]), but only 15% were children. Clinical testing was performed during 4,532 (23%) hospitalizations, and ≥1 respiratory virus was identified in 1,712. Testing was more likely to be performed for children than adults (44% vs 19%, p<0.001), and during the influenza season than outside the season (30% vs 17%, p<0.001). A total of 138 HA-RVI were identified >72 hours after admission (0.7% of all ARI hospitalizations, 8.1% of all virus infections), 29% occurring outside of the influenza season. Half of all HA-RVI were identified in adults, but incidence was higher in children (0.4% vs 2.0% of all ARI hospitalizations). The most common HA-RVIs were rhinovirus (n=61, 44%), RSV (n=18, 13%), and influenza A (n=16, 12%), similar to the distribution seen in overall hospital-based testing (Table 1). Conclusion: HA-RVIs were identified in patients of all ages and both during and outside of the influenza season. Further investigation of the clinical outcomes of these infections and evaluation of diagnostic and infection control practices to address HA-RVI are warranted.
Abstract Title:
Underdiagnose of Invasive Pneumococcal Disease (IpD) by Culture: the Case of Empyema

Primary Author Block:
J. J. Picazo de la Garza1, J. Ruiz Contreras1, E. Culebras2, I. Rodriguez Avial2, E. Rios2, M. del Amo3, C. Mendez Diez3, HERACLES GROUP; 1Faculty of Med., Madrid, Spain, 2Hosp. Clinico San Carlos, Madrid, Spain, 3Pfizer, Madrid, Spain

Abstract Body:
Background: The introduction of pneumococcal conjugate vaccines (PCVs) in childhood immunization programs has markedly decreased the incidence of invasive pneumococcal disease (IPD). In the Region of Madrid (Spain), IPD in children <15 years of age has been the target of active surveillance from 2007 to 2016, matching up with the introduction of PCV7 and later on with PCV13 in the Regional Immunization Program. The treatment with antimicrobials prior to the hospitalization may interfere with the culture results. We studied in suspected cases of IPD the PCR results in Culture negative samples. Methods: Clinical forms of IPD and demographic data were prospectively collected from children <15 years of age with laboratory confirmed IPD. When pleural or cerebrospinal fluids from children with meningitis or pleural empyema did not yield positive cultures, samples of these fluids were also sent to the reference laboratory for PCR detection of pneumolysin (ply) and autolysin (lyt) genes. Pneumococci confirmed by PCR were serotyped by real-time PCR assay using the LightCycler SYBR green format analysis, as previously described, detecting serotypes 1, 3, 4, 5, 6, 7F, 14, 19A and 19F. Results: Overall (912 cases), empyema was the most frequent clinical presentation (311; 34.1%) followed by bacteremic pneumonia (250; 27.4%), primary bacteremia (131; 14.4%), meningitis (113; 12.4%) and others (107; 11.7%). In table 1, the results of culture negative and PCR positive samples are indicated by clinical diagnosis.
Since empyema is the most frequently underdiagnosed IPD, we further investigated, and the results are in table 2 demonstrating that 194 cases of Empyema (77.6% of the total) were culture negative and only diagnosed by PCR. Conclusions: The burden of the IPD, and especially of empyema could be underestimated by culture and only detected by PCR. This has an important impact on the effectiveness of the vaccine.
Prevalence and Associated Virulence of Nonencapsulated Streptococcus Pneumoniae among Mississippians

C. Martin, L. McDaniel, J. Bradshaw, H. Pipkins; Univ. of Mississippi Med. Ctr., Jackson, MS

Streptococcus pneumoniae (pneumococcus) is a bacterium that colonizes the human nasopharynx and also causes diseases such as meningitis, otitis media, and pneumonia. Comorbidites such as obesity, diabetes, and chronic obstructive pulmonary disorder (COPD) have been associated with severe illness during pneumococcal infection. Moreover, Mississippi has historically been attributed with the highest prevalence of obesity and diabetes within the United States. Licensed pneumococcal vaccines protect against invasive disease associated with encapsulated strains but elicit no protection against nonencapsulated S. pneumoniae (NESp). Consequently, increased isolation of NESp during disease has occurred following vaccine implementation. The purpose of this study was to define NESp prevalence among Mississippians presenting with disease and determine virulence mechanisms associated with isolated NESp. Pneumococcal clinical isolates were obtained from the UMMC surveillance laboratory from October 2015 to July 2016. Polymerase chain reaction (PCR) was used to classify 35 isolates based on the presence of a conserved capsule gene, cpsA, and three genes associated with NESp virulence: pspK, aliC, and aliD. Antibiotic susceptibility was examined by determining minimum inhibitory concentrations (MICs) using the broth microdilution technique and assigned breakpoints. Bacterial adherence and invasion was investigated using human A549 pulmonary and Detroit 562 pharyngeal epithelial cells. Pneumococcal biofilm production was also assessed. PCR analysis revealed 3 out of 35 isolates (8.6%) were NESp obtained from patients presenting with community-acquired pneumonia. Of the three NESp isolates, two encoded aliD and one encoded pspK. Furthermore, NESp isolates were resistant to multiple classes of antibiotics. NESp strains adhered greater to pharyngeal cells in comparison to pulmonary cells, but these strains did not efficiently invade epithelial cells. Additionally, NESp strains were capable of forming dense biofilms. Altogether, NESp emerging in Mississippi express phenotypes that enhance persistence in a host and result in treatment failures. Additional surveillance will need to be conducted to evaluate the ongoing health threat posed by NESp.
Abstract Title:
Clinical Features of Human Metapneumovirus Pneumonia in Non-Immunocompromised Patients

Primary Author Block:

Abstract Body:
Background: Several studies have reported outbreaks due to human metapneumovirus (hMPV) in long-term care facilities (LTCF) for the elderly, whereas most of these reports are epidemiological studies and do not investigate the clinical features of hMPV pneumonia. Methods: Three independent outbreaks of hMPV occurred at separate LTCF for the intellectually challenged and elderly residents in Okinawa, Japan. During the outbreaks, confirmed cases of hMPV were defined by the detection of virus in clinical respiratory samples using a PCR specific for hMPV and/or the RAT for hMPV. Probable cases were defined by the presence of clinical symptoms (respiratory symptoms and fever more than 37.5 degrees Celsius) compatible with a respiratory infection, during the time period for each outbreak. We retrospectively evaluated the clinical and radiological features of hMPV pneumonia from their medical records. Results: Out of 105 hMPV infections, 49% of patients developed pneumonia. The median age of pneumonia cases was significantly higher than non-pneumonia cases. An elevated white blood cell count and increased levels of C-reactive protein, transaminases and creatine phosphokinase were frequently observed among pneumonia cases. Evaluation of chest imaging revealed proximal bronchial wall thickenings radiating outward from the hilum in most patients. When PCR is considered as the gold standard, the sensitivity of rapid antigen test (RAT) was 58% (7/12). Five patients remained PCR-positive despite having negative RAT results more than 8 days after the onset of symptoms. Conclusions: Pneumonia patients, observed with the above characteristics, should be considered as potential hMPV infected patients and tested with a RAT, within one week after the onset of symptoms, or PCR for prompt diagnosis and infection control.
Antibiotic Resistance in Community Onset Pneumonia: A Stewardship Perspective

Primary Author Block:
A. Farkas1, C. Stavropoulos1, J. Sassine1, J. Matthew1, S. Sirichand1, R. Stern2, G. Mckinley1; 1Mount Sinai West Hosp., NY, NY, 2Univ. of Chicago, Chicago, IL

Abstract Body:
Background: With the growing evidence that patients with community onset pneumonia and recent health care exposure are not equally at high risk for infection with multidrug-resistant (MDR) pathogens, an individualized approach to risk assessment prior to the use of broad-spectrum antibiotics should be considered. Methods: In this retrospective study we reviewed the medical records of 102 adult patients admitted for community-onset pneumonia over a two-year period, before and after the implementation of a stewardship-driven revised risk assessment strategy for MDR pathogens using the drug resistant in pneumonia (DRIP) score; with the primary aim to identify the effects of this intervention on broad-spectrum antibiotic days of therapy (DOT) utilization, and secondarily it’s impact on all cause readmissions and time to clinical improvement. Statistical analyses were carried out using multivariable generalized linear regression models with integrated propensity scores and Cox proportional hazard models. Results: The stewardship intervention resulted in a significant decrease in anti-MRSA (-1.45 days of therapy (DOT), p = 0.007) and antipseudomonal (-2.03 DOT, p < 0.001) antibiotic utilization but was not associated with a significant difference in the odds of readmissions (OR 0.64, 95% CI 0.27; 1.50) or in time to clinical improvement (HR 1.19, 95% CI 0.84; 1.59). Other factors evaluated in the multivariable models, like the Charlson comorbidity score (p <0.05), time to clinical stability (p=0.004), and an interaction term (p = 0.002) were associated with a significant increase in DOT utilization; the DRIP score <u>4 (OR 5.62, 95% CI 2.24; 15.07) and immunosuppression (OR 2.91, 95% CI 1.11; 7.84) impacted readmissions; and an initial serum lactate > 2 mmol/L (HR 0.57, 95% CI 0.39; 0.85) as well as the receipt of an antipseudomonal agent (HR 0.60, 95% CI 0.42; 0.86) effected time to clinical improvement. Conclusions: An individualized MDR risk assessment strategy using a clinical prediction score for community-onset pneumonia have the potential to decreases the utilization of broad-spectrum antibiotics without an increase in adverse clinical outcomes.
Stenotrophomonas Maltophilia Bacteremia with Fatal Hemorrhagic Pneumonia: Clin. and Microbiological Characteristics

Primary Author Block:
S-H. Kim1, J. Oh1, S. Oh1, M. Cha2, C-I. Kang1, K. Huh1, S. Cho1, D. Chung1, K. Peck1; 1Samsung Med. Ctr., Sungkyunkwan Univ. Sch. of Med., Seoul, Korea, Seoul, Korea, Republic of, 2Asia Pacific Fndn. for Infectious Diseases, Seoul, Korea, Republic of

Abstract Body:
Background: Lethal pulmonary hemorrhage has been known as the unique clinical manifestation of Stenotrophomonas maltophilia infection, although catheter-related blood stream infection (CRBSI) is one of the most common clinical presentations of patients with S. maltophilia bacteremia. The purpose of this study is to evaluate clinical and microbiological characteristics of S. maltophilia bacteremia with hemorrhagic pneumonia (HP), compared to those with CRBSI. Methods: Cases with S. maltophilia bacteremia were collected between August 2006 and December 2016 in Samsung Medical Center of Seoul, Korea. HP cases was defined as patient having new lung infiltrate with significant hemorrhage from tracheal aspirates or with hemoptysis, and CRBSI cases was defined by the differential time to positivity criteria. Expression of major virulence-associated genes including encoding type-1 fimbriae (smf1), proteases (StmPr1 and StmPr2), and esterase (Smlt3773) from blood S. maltophilia isolates were investigated, and the phenotypic and genotypic traits of each group were compared. Clinical characteristics and outcomes were also compared in both groups. Results: A total of 31 cases (16 from HP and 15 from CRBSI) were included in the analysis. Cases with HP were fatal, showing significantly higher all-cause mortality compared with those with CRBSI (93.8% vs 20.0%, p<0.001). Twenty-six isolates (83.8%) had ability to form biofilms. Although no significant differences in forming biofilms were found in both groups (81.3% vs 86.6%), isolates from CRBSI exhibited a significantly higher proportion in moderate and strong biofilm formation (moderate: 25.0% vs 33.3%, strong: 6.2% vs 13.3%, respectively, both p<0.05). No significant difference was observed in virulence factors among both groups. When we compared clinical characteristics, prolonged neutropenia (100% vs 73.3%, p=0.04) and thrombocytopenia (93.7% vs 60.0%, p=0.04) were significantly more common in patients with HP than in those with CRBSI. Conclusions: Hemorrhagic pneumonia was significantly associated with thrombocytopenia and neutropenia in patients with S. maltophilia bacteremia, while CRBSI were associated with S. maltophilia isolates producing strong biofilm. Our data suggest that the unique characteristics of microbes and patients contribute to the pathogenesis of these unique clinical manifestations.
Abstract Title:
Community-Acquired Pneumonia in the Elderly (65-84) Vs Very Elderly (85+): Characteristics, Manifestations, and Outcomes

Primary Author Block:
A. Alsatli, S. Blatt, G. Racho, J. Bertrand, J. Steinbrunner; TriHealth., Cincinnati, OH

Abstract Body:
Introduction: Community-acquired pneumonia (CAP) is one of the leading causes of mortality in the elderly. Additionally, the elderly population is increasing and an even more dramatic upward trend in the ‘very elderly’ subgroup is projected over the next several years. This research study was designed to compare characteristics, manifestations and outcomes between the elderly (65-84) and very elderly (85+). Methods: Patients aged 65+ with CAP admitted to Good Samaritan or Bethesda North Hospital from July 2012 to December 2015 were included in the study. Patients who were immunocompromised or had healthcare-associated pneumonia were excluded. CAP was defined as a new or changing pulmonary infiltrate with new or increased cough, fever over 37.8 C, or changes in WBC. Univariate analyses were used to compare the two age groups. Results: Overall, 202 patients (56%) were elderly and 157 patients (44%) were very elderly. The elderly patients had more risk factors compared to the very elderly patients. Seventeen percent of the elderly patients were current smokers compared to only 8% of the very elderly patients (p=0.009). Additionally, 63% of the elderly patients were not vaccinated for pneumonia compared to 50% of the very elderly patients (p=0.03). Over half of the elderly population (53%) had COPD compared to only 27% of the very elderly population (p<0.001). However, the very elderly population had a higher proportion of patients with CHF (40% vs 24%; p=0.001) and dementia (18% vs 5%; p<0.001). In terms of manifestations, the heart rate of the elderly (95.6) was significantly higher than the heart rate of the very elderly (89.5) (p=0.006). Additionally, hematocrit was significantly higher in the elderly group when compared to the very elderly group (38 vs 35; p=0.002). There were no differences in patient outcomes, which included mortality, ICU admission, length of stay, and length of IV therapy, between the elderly and very elderly. Conclusions: The very elderly experienced similar outcomes when compared to the elderly patients with CAP, and besides heart rate and hematocrit, basic clinical findings were the same. The similarity between the two groups suggests evaluation and treatment of CAP does not need to be adjusted for the very elderly, possibly due to the healthier lifestyle that this group maintains.
Abstract Title:
Lefamulin is Non-Inferior to Moxifloxacin in Adults with Community-Acquired Bacterial Pneumonia (Cabp): the Phase 3 Lefamulin Evaluation against Pneumonia (Leap 1) Study

Primary Author Block:

Abstract Body:
Background: Lefamulin is a novel pleuromutilin antibiotic (IV/oral) in development for treating CABP, a leading cause of infection and death. Lefamulin targets key CABP pathogens. Methods: In a multi-center, randomized, double-blind, phase 3 study, CABP patients were randomized to lefamulin 150mg IV Q12 hr or moxifloxacin 400mg IV Q24 hr. Linezolid or placebo was added if MRSA was suspected (Figure). Patients with Patient Outcomes Research Team (PORT) Risk Class III (limit: 75%), IV, or V were eligible. After six IV doses, patients could switch to oral therapy if pre-specified criteria were met. The FDA endpoint was early clinical response (ECR) in the intent-to-treat (ITT) population. EMA co-primary endpoints were investigator assessment of clinical response (IACR) at test of cure in modified ITT (mITT) and clinically evaluable (CE) populations. Results: 551 patients were randomized to lefamulin (n=276) or moxifloxacin (n=275). For the FDA endpoint, lefamulin was non-inferior (12.5% margin) to moxifloxacin (ECR 87.3% vs 90.2%, respectively; difference: -2.9% [95%CI: -8.5,2.8]). For the EMA primary endpoint, lefamulin was also non-inferior (10% margin) to moxifloxacin (IACR: mITT, 81.7% vs 84.2% respectively; difference -2.6 [-8.9,3.9]; CE, 86.9% vs 89.4%; difference -2.5 [-8.4,3.4]). Lefamulin was efficacious regardless of PORT class (ECR rates for PORT III, IV, and V were 89.3% [175/196], 82.9% [63/76], and 75% [3/4] in lefamulin, and 93% [187/201], 81.4% [57/70], and 100% [3/3] in moxifloxacin, respectively; IACR rates in the mITT population for PORT III, IV, and V were 84.0% [163/194], 76.0% [57/75], and 75.0% [3/4] in lefamulin, and 84.0% [168/200], 84.1% [58/69], and 100% [3/3] in moxifloxacin; IACR rates were similar for the CE population. Conclusions: Lefamulin demonstrated non-inferiority for both the FDA and EMA efficacy endpoints vs moxifloxacin. Lefamulin demonstrates promise as a targeted monotherapy for the treatment of CABP in adults.
Lefamulin Demonstrates Favorable Safety and Tolerability in Adults with Community-Acquired Bacterial Pneumonia (Cabp) in the Phase 3 Lefamulin Evaluation against Pneumonia (Leap 1) Study

Primary Author Block:

Abstract Body:
Background: New antibiotics for CABP with a targeted spectrum and improved tolerability are needed. Lefamulin is a novel pleuromutilin antibiotic for IV or oral use in development for treating CABP. Lefamulin binds to a highly conserved region of the ribosomal peptidyl transferase center targeting key CABP pathogens. Methods: In this multi-center, randomized, double-blind phase 3 study, adult patients with CABP (Patient Outcomes Research Team Risk Class ≥III) were randomized to lefamulin 150mg IV Q12 hr or moxifloxacin 400mg IV Q24 hr. Adjunctive linezolid or placebo was added for patients with suspected MRSA infection. After six IV doses, eligible patients could switch to oral therapy, reaching a treatment duration of 7 days. Safety was assessed in patients administered ≥1 dose of study drug.

Results: Lefamulin demonstrated non-inferiority versus moxifloxacin for the FDA and EMA primary efficacy endpoints. Safety and tolerability results are shown in the Figure. Rates of AEs were generally similar between treatment groups. AEs leading to treatment discontinuation or study withdrawal occurred in 8 (2.9%) and 5 (1.8%) vs 12 (4.4%) and 11 (4.0%) patients treated with lefamulin vs moxifloxacin, respectively. More infusion site AEs occurred in the lefamulin arm (infusion site pain, 8 [2.9%] vs 0 [0%]; phlebitis, 6 [2.2%] vs 3 [1.1%]). Lower rates of gastrointestinal (6.6% vs 13.6%), hepatobiliary (0.7% vs 1.5%), and cardiac (2.9% vs 4%) system organ class AEs were reported in the lefamulin arm. Fewer patients on lefamulin than moxifloxacin reported diarrhea (2 [0.7%] vs 21 [7.7%]). No cases of Clostridium difficile infection were reported. Laboratory values, liver function tests and ECG, were similar between groups; no patients met Hy’s Law criteria. Conclusions: In this first phase 3 CABP clinical trial, lefamulin monotherapy treatment of CABP in adults demonstrated a favorable tolerability and safety profile compared to moxifloxacin ±linezolid.
Abstract Title:
Outcomes among Patients with Hospital-Acquired Bacterial Pneumonia Or Ventilator-Associated Bacterial Pneumonia Stratified by Renal Function: Subgroup Analysis from A Phase 3 Study of Ceftazidime-Avibactam

Primary Author Block:
A. Talley1, T. Riccobene1, I. Critchley2, L. Rekeda1, D. Melnick1; 1Allergan plc, Madison, NJ, 2Allergan plc, Irvine, CA

Abstract Body:
Background: The efficacy of ceftazidime-avibactam (CAZ-AVI) for the treatment of hospital-acquired bacterial pneumonia (HABP) or ventilator-associated bacterial pneumonia (VABP) in adults was recently reported based on the results of the Phase 3 REPROVE trial, a randomized, multicenter, double-blind, comparative study. The objective of this subgroup analysis was to determine outcomes among patients by renal function category. Methods: HABP or VABP patients with normal renal function or mild renal impairment (baseline creatinine clearance [CrCL] >50 mL/min) received CAZ-AVI or meropenem administered per the labeled dosing recommendations. Dose adjustments for both drugs were made for patients with moderate to severe renal impairment at baseline (MSRIB; CrCL 16-50 mL/min). A protocol amendment in year 3 (of 4) of the study increased the total daily CAZ-AVI dose for patients with MSRIB by 50%, consistent with the FDA-approved CAZ-AVI dosing recommendations. In this prespecified subgroup analysis, the US-FDA primary endpoint of 28 day all-cause mortality and secondary endpoints of clinical cure at the end of treatment (EOT) and test of cure (TOC) visits in the intent-to-treat population (ITT) were assessed among patient subgroups stratified by renal function and CAZ-AVI dose received. Results: Across all patient subgroups assessed, 28 day all-cause mortality rates were lowest among patients with potential augmented renal clearance (CrCL >150 mL/min; 3.4% and 4.8% for CAZ-AVI and meropenem, respectively), and highest among patients with MSRIB (13.5% and 16.0% for CAZ-AVI and meropenem, respectively); mortality rates were similar for patients with MSRIB receiving the initial (MSRIBorig) or modified (MSRIBnew) CAZ-AVI dose regimens (12.9% and 14.3%, respectively). CAZ-AVI clinical cure rates at the EOT and TOC visits were high and similar to comparator in patients with or without renal impairment; rates at both visits in the CAZ-AVI MSRIBnew subset (85.7% and 71.4%, respectively) were slightly higher than in the MSRIBorig subset (67.7% and 61.3%, respectively). The incidence of adverse events were similar across renal function categories, with a comparable CAZ-AVI safety profile observed between the MSRIBorig and MSRIBnew subsets. Conclusions: In the Phase 3 REPROVE study, outcomes by renal function category were consistent with the overall results for the study, indicating that the FDA-approved CAZ-AVI dose regimens are efficacious and well-tolerated in patients with HABP/VABP and renal impairment or augmented renal clearance.
Outcomes of Current Treatments for Middle East Respiratory Syndrome: A Systematic Review and Meta-Analysis

Primary Author Block:
T. Thy1, M. Morra2, T. Le1, M. Kamel3, A. Ghazy4, A. Altibi5, D. Lu6, V. Nguyen1, M. Mostafa7, S. Ahmed8, S. Elabd9, S. Fathima10, V. Tran11, A. Omrani12, Z. Memish13, K. Hirayama14, N. Huy14; 1Univ. of Med. and Pharmacy at Ho Chi Minh City, Ho Chi Minh, Viet Nam, 2Alazhar Univ., Cairo, Egypt, 3Minia Univ., Minia, Egypt, 4Shebin El-Kom Teaching Hosp., Menofeya, Egypt, 5Univ. of Jordan, Amman, Jordan, 6Pham Ngoc Thach Univ. of Med., Ho Chi Minh, Viet Nam, 7Tanta Univ., Tanta, Egypt, 8Cairo Univ., Giza, Egypt, 9Benha Univ., Benha, Egypt, 10Deccan Coll. of Med. Sci., Univ. of Hlth.and Sci., Hyderabad, India, 11Univ. of California, Los Angeles, CA, 12King Faisal Specialist Hosp. and Res. Ctr., Riyadh, Saudi Arabia, 13Ministry of Hlth., Riyadh., Riyadh, Saudi Arabia, 14Inst. of Tropical Med. (NEKKEN), Leading Graduate Sch. Program, and Graduate Sch. of BioMed. Sci., Nagasaki Univ., Nagasaki, Japan

Abstract Body:
Background: Middle East Respiratory Syndrome (MERS), which is a respiratory disease caused by Middle East Respiratory Syndrome Coronavirus (MERS-CoV). Infected patients suffered from various clinical appearances from asymptomatic to serious acute respiratory distress or death. Currently, there is still no standard cure for MERS and also no vaccine against MERS-CoV. Furthermore, the risk of the outbreak has increased. Therefore, a systematic review and meta-analysis were conducted to evaluate all available treatments for MERS. Methods: A systematic search on ten databases and manual search were handled to retrieve any study giving information of treatments for MERS. Screening and extraction were done by three reviewers. Quality was assessed using CARE statement for case reports and nine metrics tool for nonrandomized studies. Mortality rates were meta-analyzed using STATA software. The classification and regression tree model (CART) was performed to evaluate independent variables that predict fatality results. The mean survival days was calculated for two data sets of Kaplan-Meier survival curves including from hospital admission and from the onset of symptoms to death. Results: Ten case reports, two case series, and four observational studies were included. Among that, the combination of IFN and ribavirin was the most frequent treatment used; however, the mortality rate which was as high as 71% in IFN-treatment group did not change in the only supportive-treatment group. Comparison between three types of IFN brought no statistically significant difference in the fatality. The rate of fatality increased in patients who were older or suffered from the chronic renal disease, hypertension or diabetes mellitus or antiviral admission delay. There was the insignificant difference in mortality rate regarding gender, ribavirin, corticosteroid, oseltamivir, IFN beta 1a, IFN alpha 2b, IFN alpha 2a, congestive heart failure or other comorbidities. CART showed that chronic renal diseases as the best model to predict mortality. Mean of survival days from admission was not significantly different
between groups in contrast of significant difference in mean of survival days from onset of illness. Conclusions: The intervention of antiviral treatment such as the combination of IFN and ribavirin did not bring more effects on mortality rate than supportive-only arms; however, mean of survival days from onset of symptoms in IFN group was longer than supportive-only one. Comorbidities or postponement of antiviral treatment is related to worse outcomes.
**Abstract Title:**
A Novel, Evidence-Based Endpoint for Studies of Hospital-Acquired Bacterial Pneumonia (HABP) and Ventilator-Associated Bacterial Pneumonia (VABP)

**Primary Author Block:**
G. H. Talbot1, A. Das2, S. Cammarata3, J. Powers4, S. Cush5, A. Dane6, M. Wible7, R. Echols8, A. Torres9, T. Fleming10, J. Rex11, J. Loutit12, S. Hoffmann5, FNIH HABP VABP Project Team; 1Talbot Advisors LLC, Anna Maria, FL, 2AdStat, Guerneville, CA, 3Melinta Therapeutics, New haven, CT, 4NIH, Bethesda, MD, 5Fndn. for the NIH, North Bethesda, MD, 6DaneStat Consulting Limited, Cheshire East, United Kingdom, 7Pfizer Inc, Collegeville, PA, 8Infectious Disease Drug Dev. Consulting, LLC, Easton, CT, 9Hosp. Clinic of Barcelona, Barcelona, Spain, 10Univ. of Washington, Seattle, WA, 11F2G Ltd, Manchester, United Kingdom, 12The Med.s Company, San Diego, CA

**Abstract Body:**
Background: The FDA asked the FNIH to provide evidence-based recommendations for use of endpoints other than all-cause mortality (ACM) in non-inferiority (NI) HABP/VABP studies. A major consideration is that a fixed NI margin of 10% is clinically acceptable when the ACM rate is ≥15-20%, but if ACM is <<15%, a 10% margin is less supportable and an odds-ratio analysis approach (or a smaller NI margin) is required, which increases study sample size. Avoiding this issue facilitates study design. Methods: Recent HABP/VABP study datasets (registrational (7) or real-life observational (1)) were analyzed to identify well-defined, reliable endpoints and improve study efficiency for these infections. Results: Mean ACM overall at day 28 post-baseline was ~20%, but varied substantially for ventilated HABP (27.8%) > VABP (18.0%) > non-ventilated HABP (14.5%), with lower ACM in the registrational studies (Table). As an alternative to ACM, a “mortality-plus” endpoint was constructed by combining the study-specific rates of ACM and severe, infection-related, patient-relevant adverse events (e.g., sepsis, septic shock) from the Medical Dictionary for Regulatory Activities (MedDRA) Toxic/Septic Shock Standardized MedDRA Query (SMQ) category. The composite “mortality-plus” rate was 3-10 percentage points higher than that of ACM alone. Conclusions: Since ACM rates vary substantially by infection group, in a given study the proportion of patients in each group influences the overall ACM. If the anticipated ACM rate is so low that sample size would be very large, and ACM would be a meaningfully less influential component of patients’ clinical experience, then a pre-specified “mortality-plus” endpoint using the Toxic/Septic Shock SMQ offers an option that could increase efficiency (hence, a lower study sample size) through the evaluation of a broader range of clinically relevant events. The increased event rate for “mortality plus” would also facilitate evaluation at a time point earlier than 28 days (e.g., 14 days), as well as provide a useful sensitivity analysis option. Table: Example of Point Estimates of ACM and Mortality-Plus Endpoints<br />

**Table:** Example of Point Estimates of ACM and Mortality-Plus Endpoints

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>ACM (%)</th>
<th>Mortality-Plus (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HABP</td>
<td>14.5</td>
<td>17.5</td>
</tr>
<tr>
<td>VABP</td>
<td>18.0</td>
<td>21.0</td>
</tr>
<tr>
<td>Non-VABP</td>
<td>20.0</td>
<td>23.0</td>
</tr>
</tbody>
</table>

*Note: Table data is illustrative and not representative of actual study data.*
<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Endpoint Timing</th>
<th>Study Drug (N=160) %</th>
<th>Comparator (N=160) %</th>
<th>Study Drug (N=63) %</th>
<th>Comparator (N=61) %</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACM</td>
<td>Day 14</td>
<td>9.6</td>
<td>3.1</td>
<td>13.5</td>
<td>11.0</td>
</tr>
<tr>
<td>Mortality-Plus</td>
<td></td>
<td>14.1</td>
<td>6.3</td>
<td>19.8</td>
<td>19.0</td>
</tr>
<tr>
<td></td>
<td>Day 28</td>
<td>13.5</td>
<td>11.0</td>
<td>20.8</td>
<td>20.4</td>
</tr>
<tr>
<td>ACM</td>
<td></td>
<td>11.0</td>
<td>20.8</td>
<td>23.2</td>
<td>19.4</td>
</tr>
<tr>
<td>Mortality-Plus</td>
<td></td>
<td>20.4</td>
<td>19.4</td>
<td>13.5</td>
<td>13.5</td>
</tr>
</tbody>
</table>

ACM: All-cause mortality; nv: non-ventilated; Mortality-plus: ACM plus Toxic/Septic Shock Standardized Query adverse events
Abstract Title:
Tirap-Mediated Transactivation of C-Jun is Critical for Ap-1 Proinflammatory Responses
Primary Author Block:
M. Baig; IIT INDORE, Indore, India
Abstract Body:
Macrophages play pivotal roles in pathogen recognition and elimination, as well as in the maintenance of tissue homeostasis. The inflammatory process is usually tightly regulated, involving both signals that initiate and maintain inflammation and signals that shut the process down. An imbalance between the two signals leaves inflammation unchecked, resulting in cellular and tissue damage. Activation of macrophages by Toll-like and related receptors is characterized by transient activation of AP1-, NF-κB- and IRF-mediated signaling pathways and expression of pro-inflammatory genes. Identifying and targeting important signaling molecule in the cascade is always been a strategy to combat various inflammatory diseases such as asthma, atherosclerosis, rheumatoid arthritis, and even cancer. Our novel finding suggests that c-Jun-TIRAP interaction is essential for c-Jun activation in LPS stimulated macrophages. Activation of c-Jun is directly related to AP1 transcription activity and hence proinflammatory cytokine expression. Therefore disruption of c-Jun-TIRAP complex may be a good strategy to dampen the inflammatory response. Further, structure based design of small molecule or peptide targeting c-Jun-TIRAP interface would be beneficial for therapy in AP1 mediated inflammatory diseases.
Abstract Title:
A Prospective Cohort Study of the Quick Sequential Organ Failure Assessment (Qsofa) Score versus the Systemic Inflammatory Response Syndrome (Sirs) Criteria in the Determination and Prognostication of Sepsis in A Philippine Tertiary Hospital

Primary Author Block:
S. C. Ang, O. V. Ubaldo; The Med. City, Pasig City, Philippines

Abstract Body:
Sepsis and septic shock continue to be two of the major causes of intensive care unit admission, posing a threat to worldwide healthcare leading to significant morbidity and mortality. Diagnosis defined by the SIRS criteria requires fulfillment of 2 out of the 4 criteria that comprise the host response to inflammation. The SIRS criteria was challenged and the operational definition of sepsis was revised into a three-pronged assessment tool labeled by the Sepsis-3 task force as the qSOFA score. Several retrospective studies have been conducted comparing the qSOFA score and SIRS criteria, and researchers have recommended larger prospective studies to validate the qSOFA as a diagnostic tool. We hypothesized that the utilization of the qSOFA score leads to earlier recognition of sepsis, is more sensitive and specific than the SIRS criteria and is predictive of morbidity within the first 48 hours of in-hospital admission. We conducted a prospective study in a tertiary hospital in the Philippines where adult patients 18 years or older, seen at the emergency department (ED) with history and/or physical exam findings suggestive of infection were included in the study. 295 adult patients in the emergency room with suspected infection were included in the study and simultaneously determined their qSOFA score and SIRS criteria. The presence of sepsis was adjudicated by three infectious disease specialists, and outcomes within the first 48 hours were acquired. Sensitivity, specificity, positive predictive and negative predictive values for qSOFA and SIRS were computed using constructed confusion matrices, and overall predictive accuracy was measured by the AUROC. The qSOFA score was specific (95.5%) but poorly sensitive (46.3%) test compared to the SIRS criteria (sensitivity 73.7% and specificity 60%). Both qSOFA and the SIRS criteria significantly co-related with sepsis positivity but the qSOFA score had superior overall predictive accuracy at 70.9% compared to the SIRS criteria. The adjudicators had moderate strength in agreement (Fleiss’ kappa = 0.39) and a percentage agreement of 60%. Based on our findings, we conclude that the qSOFA score is a more accurate predictor of sepsis, but should not be used as a preliminary sepsis screening tool. However, a higher qSOFA score should prompt more assertive diagnostics and earlier interventions in septic patients. We recommend that the SIRS criteria be maintained as a screening tool and to use the qSOFA score simultaneously for timely management.
Abstract Title:
Initial Low Neutrophil/Lymphocyte Ratio is Significantly Associated with 28-Day Mortality in Patients with Severe Sepsis/Septic Shock

Primary Author Block:

Abstract Body:
Background: The neutrophil/lymphocyte ratio (NLR) has been known as a prognostic marker in malignancies and cardiovascular diseases. However, several studies reported conflicting results on the relationship between NLR and mortality in critically ill patients. Therefore, we investigated the relationship between NLR and 28-day mortality in patients with severe sepsis/Septic shock.

Methods: The electronic medical records of patients with severe sepsis/Septic shock admitted at emergency department between June 2010 and January 2016 at a 2400-bed tertiary care hospital in Seoul, Korea, were retrospectively reviewed. The patients were categorized by quartile of initial NLR value. The analysis was performed to identify the relationship between NLR and 28-day mortality.

Results: A total of 797 patients were enrolled. 411 (51.6%) patients were male and the mean age was 65.9 years. All-cause 28-day mortality rate was 12.7% (101/797). According to initial NLR values, patients were categorized into quartiles as follows: less than 6.52, 6.52 to 14.75, 14.75 to 27.12 and more than 27.12. The 28-day mortality rates for the Quartile 1 to Quartile 4 were as follows; 19.1%, 11.6%, 8.0%, and 12% (P=0.009), respectively. In univariate Cox regression analysis, inclusion in Quartile 1, albumin, lactate, C-reactive protein and Sequential Organ Failure Assessment (SOFA) score were a significant prognostic factor for 28-day mortality. In multivariable analysis, albumin (HR 0.391, 95% CI 0.287-0.533, P<0.001), lactate (HR 1.135, 95% CI 1.077-1.196, P<0.001) and SOFA score (HR 1.152, 95% CI 1.077-1.232, P<0.001) were significantly associated with 28-day mortality and the risk of 28-mortality in Quartile 1 was significantly higher compared to Quartile 3 (HR 0.410, 95% CI 0.218-0.770, P=0.007: reference group Quartile 1) and Quartile 4 (HR 0.558, 95% CI 0.319-0.976, P=0.041: reference group Quartile 1).

Conclusions: In our study, initial low NLR value is significantly associated with 28-day mortality in patients with severe sepsis/Septic shock.
Abstract Title:
Efficacy and Safety of Prolonged versus Intermittent Infusion Of beta-Lactam Antibiotics As Empirical Therapy in Patients with Sepsis

Primary Author Block:
S. Hemvimon1, P. Srinithiwat2, P. Koomanachai1, V. Thamlikitkul1, A. Jitmuang1; 1Faculty of Med. Siriraj Hosp., Mahidol Univ., Bangkok, Thailand, 2Panyananthaphikkhu Chonprathan Med. Ctr., Faculty of Med., Srinakharinwirot Univ., Bangkok, Thailand

Abstract Body:
Background: Beta-lactam antibiotics are the cornerstones for empirical treatment of patients with sepsis. There is a controversy over whether intermittent infusion (II) or prolonged infusion (PI) of beta-lactam antibiotics is more preferable. Methods: This prospective cohort study was conducted to determine the efficacy and safety of beta-lactam antibiotics (ceftazidime, cefepime, piperacillin/tazobactam, imipenem, meropenem, and doripenem) administered by II compared with three to four-hour PI regarding attending physicians in hospitalized patients with sepsis between January 2010 to December 2013. Results: Of 219 subjects, 213 were recruited in the study, 109 patients were in II group and 104 patients were in PI group. No significant difference of baseline characteristics between both groups. About 70% of infections from both groups were associated with hospital associated infection. Pneumonia, bacteremia, and urinary tract infection (UTI) were the major foci of sepsis in this study. E. coli mainly came from UTI was the major etiologic pathogen, whereas the causative pathogen was unknown in 49.3%. The 28-day survival was 87.2% in II group and 79.8% in PI group (p = 0.27). The favorable clinical outcomes were 74.3% in II group and 76.9% in PI group (p = 0.11). The complete microbiological response was 62.3% in II group and 63.2% in PI group (p = 0.91). No serious adverse events were observed in both groups. Conclusions: The study found no significant difference of clinical and microbiological outcomes including safety between II and PI of beta-lactams antibiotics for empirical treatment of acutely ill patients with sepsis.
HCV3 Ns5a-Isdr-Pkr Binding-Domain and Response to Interferon Therapy: Mutational Analyses and Prediction of Secondary Structure

M. A. Ashraf, Male, A. Chakravarti, Female, P. Kar, Male; Maulana Azad Med. Coll., New Delhi, India

Background: Hepatitis C Virus (HCV) has emerged as a leading cause of chronic hepatitis, liver cirrhosis and hepatocellular carcinoma worldwide. HCV genotype 3 has been shown most prevalent in India. The current strategy of therapy using pegylated interferon (peg-IFN) plus ribavirin has been found to have higher sustained virological response. Response to therapy varies according to the viral genotype, as well as potential host. The degree of variability of ISDR-PKRBD region in HCV genome has been postulated to predict the response to interferon therapy, although this prediction has been the subject of a long controversy.

Materials: Twenty seven patients of chronic hepatitis who attended OPD and wards of Lok Nayak Hospital, Delhi, India were included in the study. All patients were on peg-IFN-α-2b and ribavirin therapy. The ISDR-PKRBD mutation analysis was done by Sanger sequencing. Results: The patients were infected with HCV3, of them 18 (18/27= 66.67%) responded to therapy and 9 (9/27=33.33%) did not respond. The total number of nucleotide changes in ISDR-PKRBD region was found significantly different between responders and non-responders in HCV 3 (p-value=0.0069). It was found that the mean viral load was significantly different between pre-therapy and post-therapy groups. The secondary structure of ISDR-PKRBD slightly differ when compared with reference secondary structure of ISDR-PKRBD of HCV3 but no clear structural differences were observed between responders and non-responders. Alpha-helix positions were changed in ISDR-PKRBD region of HCV3 patient sequence when compared with the alpha-helix positions of reference sequence of HCV3. Some changes occur in secondary structure of ISDR-PKRBD region when compared with reference secondary structure of ISDR-PKRBD region of HCV3. Conclusion: Number of mutations in ISDR-PKRBD region of HCV3 genome is significantly associated with interferon therapy response. Mutation in ISDR-PKRBD causes changes in secondary structures thereby affecting immunity against the virus and response, to therapy. Hence knowledge of mutations in ISDR-PKRBD and resulting secondary structure changes are instrumental for predicting outcome of therapy, which is indispensable in view of cost and side-effects of antiviral therapy.
Abstract Title:
Prevalence of Pathogenic Bacteria in Blood Cultures of Acute Hbv Patients
Primary Author Block:
D. A. Odaibo; Univ. of Ilorin Teaching Hosp., Ilorin, Nigeria
Abstract Body:
Hepatitis B virus is one of the most common infections worldwide. Screening of common pathogenic bacterial infection that could contribute to complications is important which can help in diagnosing and proper managing of liver infection. Cross sectional study was carried out among subject aged 20-75 years for a period of 6 months. Blood cultures and HBsAg rapid tests were performed on all 122 blood samples collected at Kwara State Civil Service Hospital, Sobi Specialist Hospital, Ilorin General Hospital and Blood bank in Ilorin Metropolis. The screening was carried out among 92 HBsAg(+) patients presented with fever, and 30 healthy (unvaccinated) HBsAg(+) donors from blood bank were used as control. Antibiotic treatment was reported in 46.74% of patient. The prevalence of co-infected bacteria with HBV were E. coli 7(5.7%), S. aureus 7(5.7%), P. aeruginosa 29(23.8%) or K. pneumoniae 12(9.8%). In the control group, 9 samples showed positive bacteria growth (P. aeruginosa). This study revealed percentage of co-infection of HBV with bacteria as 59.8%. The result of this study indicates co-infection of bacterial infection with HBV in febrile patients. Therefore early screening and treatment of HBV infection and concomitant bacterial infection is highly recommended to prevent complications.
Abstract Title:
Decreasing of Burden of Hepatitis B in Azerbaijan Along with Strengthening of the Surveillance Sys. in 2012-2016

Primary Author Block:
S. Gulieva1, Z. Rasulzade2, N. Mursalova3; 1Republican Ctr. of Hygiene and Epidemiology, Baku, Azerbaijan, 2Republican Anti-Plague Station, Baku, Azerbaijan, 3Ministry of Hlth., Baku, Azerbaijan

Abstract Body:
According to WHO 240 million hepatitis B virus carriers are reported worldwide. Hepatitis B is moderately endemic in this country because 2% of adult population (18-60 years) in Azerbaijan is infected. The Electronic Integrated Disease Surveillance System (EIDSS) was officially introduced in the country since 2010 in 86 medical facilities. The objectives of this study were to reveal strong and weak components of the epidemiological surveillance system and develop recommendations for its improvement. The descriptive analysis of Hepatitis B morbidity in 2012-2016 was carried out using data obtained from the EIDSS. Confirmed Hepatitis B was defined as a case with clinical signs, epidemiological links and positive result of ELISA (HBsAg) (sensitivity of method = 99.3%). Evaluation of the surveillance system was conducted by using “Updated Guidelines for Evaluating Public Health Surveillance Systems” (CDC, Atlanta, 2005). Number of new cases of Hepatitis B gradually decreased within last 5 years, from 222 cases in 2012 to 91 cases in 2016. It was observed that men were more frequently infected than women (~60.5% vs 38.7%). The highest percentage of infected people (38.5±0.4% in average) was found in the 30-59 years age group. Hepatitis B surveillance covers the entire population of the country. The standard case definition was applied for identification of cases. Surveillance evaluation revealed that 4 new medical facilities were involved in hepatitis reporting since 2012. Positive Predictive Value (PPV) increased from 0.82 in 2012 to 0.91 in 2016. The high PPV reflects specificity of the case definition and simplicity of the flow of information and reporting. Distribution of tested cases on average has increased by 19.7±1.2% since 2012. The Azerbaijan Ministry of Health carried out mandatory vaccination program among pregnant women and newborns since 2009. Annual screening for Hepatitis B among medical personnel in all medical facilities was implemented in Azerbaijan. Compulsory vaccination of medical personnel was implemented since 2015. The Hepatitis B surveillance system in Azerbaijan has improved in the last 5 years. Due to improving detection of cases, the number of Hepatitis B cases is decreasing. Other contributing factors to decrease might be the implementation of screening and vaccination programs. A periodic evaluation of surveillance was recommended to EIDSS Working Group for monitoring and timely detection of weaknesses, followed by implementation of evidence-based measures for improvement.
Abstract Title:
Adenovirus 36 Infection Increases the Risk for Premenopausal Breast Cancer
Primary Author Block:
J. Mullins, S. Jensen, W. Webley; Univ. of Massachusetts Amherst, Amherst, MA
Abstract Body:
Background: There is a higher risk of breast cancer recurrence and mortality in obese women, despite optimal treatment1,2. Certain viruses have been shown to increase adiposity in animals and subsequent obesity3. While the exact mechanisms involved in infectobesity are not clear, viruses are thought to increase the replication, differentiation, lipid accumulation, and insulin sensitivity in fat cells while reducing leptin secretion. Adv36 is the only human adenovirus to date that has been directly linked with human obesity, however, Adv37 and Adv5 have also been implicated. The current study examines the prevalence of obesogenic adenovirus in mammary epithelial cells and blood from patients undergoing breast biopsy or mammoreduction surgery. Methods: We utilized serotype-specific PCR primers to determine the presence of adenovirus 36 in patient samples obtained from human mammary epithelial cells (HMEC) and buffy coat samples. HMEC were obtained from tissue adjacent to resected breast tumors at the time of biopsy as well as controls undergoing mammoreduction surgeries. 93 women were enrolled in the current study. Results: The average BMI of the patient cohort was 31.1, with an average age of 47.7 years old. Most women had at least one child and there was no significant association between the presence of obesogenic adenovirus and parity. Adv36 DNA was isolated from the breast tissue and blood of 34.4% (32/93) of all HMEC and buffy coat samples. Obese breast cancer patients had an Adv36 DNA prevalence of 69.2%, while patients with a normal BMI had a prevalence of 19.2% and overweight patients had a prevalence of 11.5%. This suggests an association between the prevalence of Adv36 and BMI in this patient cohort. Conclusions: Our data confirms that Adv36 DNA was present more frequently in the breast tissue of breast cancer survivors with higher BMI. These findings support a role for infectobesity in the risk for breast cancer development and suggests that the presence of Adv36 in tissue could be a biomarker of a clinical-metabolic profile, possibly preceding obesity.
Abstract Title:
Genome-Wide Surveillance of Genital Hsv-1 from Multiple Anatomic Sites over Time

Primary Author Block:
M. M. Shipley1, D. W. Renner1, M. Ott2, D. C. Bloom3, D. M. Koelle2, M. L. Szpara1;  
1Pennsylvania State Univ., University Park, PA, 2Univ. of Washington, Seattle, WA, 3Univ. of Florida Coll. of Med., Gainesville, FL

Abstract Body:
Herpes simplex viruses (HSV) cause lifelong infection in the human host, characterized by periodic episodes of mucosal shedding and ulcerative disease, and latent infection of neuronal ganglia. There are two serotypes of HSV: type 1 was historically the cause of oral lesions, and type 2 of genital lesions. However, the prevalence of genital HSV-1 has risen in recent years in high-income countries. Unlike genital HSV-2, which is characterized by frequent outbreaks, genital HSV-1 recurrences are infrequent, even in the first year of infection. There is a small percentage of individuals with genital HSV-1 infection who have a high rate of recurrence beyond the first year of infection. It is presently unknown whether HSV-1 in these individuals differs genetically from other HSV-1 isolates that are successfully controlled by the host immune system, or if the ongoing recurrences represent an innate failure of the immune system. Here we present genomic and in vitro analyses of temporally separated HSV-1 shedding from an HSV-1 seropositive and HIV/HSV-2 seronegative individual who has frequent recurrences of genital HSV-1, even after multiple years of infection. Using oligonucleotide enrichment, we compared viral genomes from uncultured swabs collected on different days and from distinct genital sites. We found a 98.2% viral DNA identity among seven swabs and three viral cultures collected over a five-month period from the same participant. We observed over a four-fold difference in the number of minority variants between lesion, non-lesion sites, and cultured virus samples. This virus appeared distinct in its phylogenetic relationship to other strains, and it contained novel coding variations in 22 viral proteins, including a truncation in the UL11 tegument protein, which is involved in viral egress and spread. Normal T-cell responses in this participant were identified, suggesting that unique viral genomic features may contribute to the recurrent genital infection that this patient experiences. With this new ability to sequence HSV-1 genomes directly from swabs, the next challenges will be to observe how the viral population shifts during transmission between individuals, and during the first year of infection, when an individual’s innate and adaptive immune responses to HSV-1 are first developing.
Session Title: CIV01 - Clinical Studies of Adult Infectious Diseases: Viral and Fungal Infections

Abstract Title:
Detection and Molecular Characterization of Polio Virus Isolates Obtained from Apparently Healthy Children and Sewage in Maiduguri, North Eastern Nigeria

Primary Author Block:
F. Tahir; Abubakar Tafawa Balewa Univ., Bauchi - Nigeria, Bauchi, Nigeria

Abstract Body:
Expanded Programme on Immunization (EPI) is one of the strategic approach of controlling childhood diseases including poliomyelitis. This study was carried out to isolate and characterize polio virus from apparently healthy children and sewage in an effort to complement the Acute Flaccid Paralysis (AFP) surveillance for wild poliovirus in Maiduguri metropolis. Stool and sewage samples were collected and screened for the presence of the virus according to procedures described by WHO Polio Laboratory Manual (2004). Out of 400 stool samples of apparently healthy children assessed, (2.8%) were found to be positive of which 4 (1.9%) were male and 7 (3.8%) were females. Accordingly 263(66%) had vaccination history while 143(36%) had no vaccination against any serotype. None Polio Enterovirus (NPENT) was found to be 34(8.5%) and only 1(0.25%) was wild polio virus (Type 1). The VP1 sequence of the wild isolate NIE-BOS-JRE-16-44C2 was PV1 WEAFB1 orphan virus in cluster N7B, matching the known NIE-BOS-DAM-13-005 and NIE-BOS-BAM-11-012 at 95.8% nt. Out of the 36 litres of Sewage samples from 12 different location, 10(27.8%) were positive for serotype P2 and P3 with P2 having the least 4(40%) and P3 6(60%). Only NPENT was obtained from the sewage samples, distributed as follows; Dalori camp1 and teachers village each with 2(6.7%) followed by Dalori camp2, Gubio camp, Muna custom, Muna Haruna and Farm centre camp each with 1(3.3%). The findings clearly indicates a prevailing immunity gap among children in the IDP camps despite the campaigns using bivalent Oral Polio Vaccine (bOPV), “Sabin -like” strains isolated from some of the settlements establish a good vaccine response and shedding of the virus by the children. Key Words: Poliovirus, Molecular Characterization, Apparently Healthy Children, Sewage, Maiduguri, Nigeria *Correspondent Author
Abstract:
National Trend in the Japanese Distribution of Candida Species Causing Candidemia During 2003-2016: A Report by the Epidemiological Investigation Committee for Human Mycoses in Japan

Primary Author Block:
H. Kakeya, K. Yamada, Y. Kaneko; Osaka City Univ. Graduate Sch. of Med., Osaka, Japan

Abstract Body:
Background: Candida species are a common cause of nosocomial blood stream infections, and candidemia is associated with high mortality rates among adults and neonates. There is limited epidemiological data regarding candidemia in Japan. Therefore, the Epidemiological Investigation Committee for Human Mycoses in Japan performed a retrospective epidemiological survey of candidemia and causative Candida species. Methods: Blood culture results from 2003-2016 were retrospectively evaluated. The data included the center-specific numbers of annual blood cultures, bacterial isolates that included fungi, numbers of fungi, and Candida species. Data were collected from 10 Japanese university hospitals located on all over Japan. Results: A total of 383,699 blood cultures were included. The prevalence of fungi in all cultures and in positive cultures were 0.53 ± 0.08% and 3.72 ± 0.46%, respectively. There was no significant difference in the positive results for fungi when we compared the data from 2003-2009 and 2010-2016. Among the results that were positive for Candida species (N = 2,313), C. albicans was the most common species (39.6%) and was followed by C. parapsilosis (27.6%), C. glabrata (13.0%), C. tropicalis (7.4%), C. krusei (2.9%), and others. And the temporal changes in the five major Candida species’ distributions were analyzed. The frequency of C. albicans was 58% in 2003, approximately 40% during 2004-2011, approximately 30% in 2012 and 2014, and 40% in 2015-2016 (with a temporary increase to 49.5% in 2013). The next most common species were C. parapsilosis and C. glabrata. The frequency of C. parapsilosis was approximately 14% in 2003, approximately 24% during 2005-2009 and 2010-2016 (range: 16.2-29.9%). There was no significant difference in the C. parapsilosis rates for the first and second halves of the study period (22.8% vs 24.1%, P = 0.38). The frequency of C. glabrata was 3.3% in 2003, <10% during 2004-2006, and approximately 15% after 2006 (range: 10.2-22.8%). C. glabrata was significantly more common in the second half of the study period, compared to in the first half (10.5% vs. 14.7%, P = 0.004). The frequency of C. tropicalis remain stable, and C. krusei was significantly less common in the second half of the study period, compared to in the first half (4.1% vs. 2.0%, P =0.003). Conclusions: The frequency of C. albicans was vary in each year in Japan, while that of C. glabrata has increased. Additional surveys are needed to continuously monitor the trends in the distribution of candidemia in Japan.
Abstract Title:
Candida Bloodstream Infections in A Tertiary Hosp. in Ile-Ife, Nigeria

Primary Author Block:

Abstract Body:
Background: Candida species have been shown in the developed world to be important causes of bloodstream infections (BSIs) with high rates of morbidity and mortality, worsened by emergence and increasing prevalence of resistant species of Candida. In spite of an increasing population of immunocompromised patients in Nigeria, such as those with cancers and HIV infection, there is paucity of data on Candida BSIs. Hence, there is a lack of evidence required to develop guidelines for prophylaxis, early detection and treatment of candidaemia. This study set out to determine the role of Candida species as agents of sepsis in immunocompromised patients at a tertiary hospital in, Ile-Ife, Nigeria.

Methods: The study protocol was approved by the Ethics and Research Committee of the hospital. This was a cross sectional study which recruited 210 immunocompromised patients with clinical features of sepsis. Relevant demographic and clinical details were obtained with the aid of a proforma. Twenty millilitres of blood from all eligible patients was cultured using a semi-automated system. Candida species so isolated were identified by microscopy, chromogenic agar and a commercial fermentation and enzyme-based system. The susceptibility of the isolates to antifungals was determined by the broth microdilution method. Data analysis was done with SPSS version 20.

Results: There were 44 positive blood cultures of which eight (3.8%) were candidaemia. The eight were distributed as Candida tropicalis (n=5; 62.5%), C. albicans (n=2; 25%) and C. krusei (n=1; 12.5%). Susceptibility testing showed that 50% of the isolates (2 C. tropicalis, 1 C. albicans and 1 C. krusei) were resistant to fluconazole while 1 C. tropicalis (12.5%) was resistant to voriconazole. There was no resistance to amphotericin B, 5-flucytosine and the echinocandins. Bivariate analysis revealed that oral thrush, prolonged antibiotic use and previous admission were significantly associated with Candida BSI. Furthermore, multivariate analysis revealed that prolonged antibiotic use (OR=0.00; 95%CI= 0.000- 0.058; P=0.004) and previous admission (OR = 0.019; 95%CI = 0.002 - 0.147; P = <0.001) were significantly associated with candidaemia. The crude mortality rate was 50%. Conclusion: Candidaemia represents an important form of BSI and should be sought actively. With high levels of resistance of the isolates to the first line antifungal, there is a need to incorporate species identification and antifungal testing into the routine laboratory processing of invasive Candida isolates in Nigeria.
Abstract Title:

Primary Author Block:

Abstract Body:
Background: Known infectious encephalitic etiologies are overwhelmingly viral and remain a significant health concern in the US. Among sporadic cases, herpes simplex virus (HSV) is the most commonly identified etiologic agent globally, although the US has seen a recent emergence of rare arboviruses and arthropod-borne viruses, such as West Nile fever. Estimates of the economic burden of encephalitis-related hospitalizations exist, but longitudinal data are lacking. Our objective was to examine the longitudinal impact on healthcare resource utilization (HCRU) of herpes simplex encephalitis (HSE) and non-herpetic viral encephalitis within the United States. Methods: Data on patients diagnosed with viral encephalitis between 2000 and 2012 in the US were retrieved from the Truven Health Analytics MarketScan® database. Those with a primary diagnosis of encephalitis from herpetic (HSV-1 and HSV-2) and non-herpetic viral (e.g., West Nile fever, Eastern and Western equine, and St. Louis) etiologies were included in the analysis. Disease prevalence and geographical variability, mortality, length of stay, and accrued healthcare costs were collected for up to 5 years following the initial diagnosis. Results: Among 6205 adult patients (55 ± 17 years; 54.4% female), more non-herpetic encephalitis (60.4%) than HSE (39.6%) cases were recorded, generally concentrated in southern US (33.1%). HSE had lower 5-year survival rates (89.6%) than non-herpetic encephalitis (92.89%), and resulted in longer aggregate stays at the hospital (14 days vs. 4 days). Herpetic encephalitis also accrued 51% higher [P <0.0001, 95% CI (1.36, 1.68)] first year costs than non-herpetic encephalitis, and greater 5-year cumulative median charges ($64,200 vs. $57,134). Conclusions: We have characterized the most updated cohort of viral encephalitis with the lengthiest follow-up in the United States. The health economic impact and associated morbidity and mortality are quantified, indicating a substantial HCRU of viral encephalitis in the US.
Abstract Title:
Dev. of A Potent Chimeric Antigen Receptor for Human Cytomegalovirus Therapy

Primary Author Block:
K. C. Le, A. W. Nguyen, J. A. Maynard; The Univ. of Texas at Austin, Austin, TX

Abstract Body:
Chimeric antigen receptors (CARs) are engineered surface molecules that mimic T-cell receptors and activate a robust T-cell response. CAR development has been mainly limited to cancer therapy, but CARs may also be effective in treating viral infections. Human cytomegalovirus (HCMV), a herpesvirus, infects 50-90% of adults by the age of 50. Normally, HCMV does not cause disease in healthy adults. However, HCMV poses a problem for infants and immunocompromised individuals, causing significant morbidity. Because of this, developing a functional HCMV CAR would be an important T-cell therapy. A major challenge for all CAR therapies is to limit dimerization in the absence of antigen, which can lead to tonic signaling and eventual T-cell exhaustion. In developing a functional HCMV CAR, we aim to create a gB-targeting scFv and optimize for minimal tonic signaling. First, we identified two different gB neutralizing antibodies, 1G2 and SM-5. We then inserted their scFv sequences, along with two controls, anti-CD19 and 4D5 scFvs, into a mammalian expression plasmid and transiently transfected Chinese hamster ovary cells. After 7 days, the culture media was collected for purification. Normalized size exclusion chromatography (SEC) results show that the anti-CD19 does not form large aggregates, while the other scFvs have substantial aggregation peaks. Between the two experimental scFvs, data show that SM-5 had a higher tendency to aggregate than 1G2, suggesting the use of 1G2 for further development. Next, we tested changes such as altered scFv linker length and stabilizing disulfide bonds in 1G2 to reduce multimerization in the absence of antigen. We correlated the aggregation behavior of 1G2, 1G2 variants, and controls as soluble scFvs to the tendency of these scFvs in the full CAR format to inappropriately activate T-cells without gB present. The final product of this work will be an anti-gB CAR with minimal tonic signaling that we will test for HCMV neutralization in later projects.
Abstract Title:
Negative Rapid Influenza Test in Patients of Severe Influenza with Critical Illness

Primary Author Block:
P-Y. Huang1, S-M. Lew2, C-T. Huang1; 1Chang Gung Mem. Hosp., Taoyuan, Taiwan, 2Chang Gung Univ. Coll. of Med., Taoyuan, Taiwan

Abstract Body:
Background: Rapid influenza antigen test (RIAT) is the only available test at the point-of-care settings. Physicians hesitate to dispense antiviral medication upon negative RIAT. Substantial RIAT false negative rate impedes timely medication in a considerable number of patients for whom prompt use may confer a better outcome. This discrepancy has to be obliterated by better understanding of the significance of negative RIAT, especially in severe influenza with critical illness. We propose to define the significance of negative RIAT among patients of severe influenza with critical illness. Methods: In preparedness for novel H1N1 influenza epidemic in 2009, we started to encourage influenza PCR and virus culture at the same time with RIAT. In Intensive Care Units (ICU), all broncho-alveolar lavage (BAL) samples were mandatorily and sputum was sometimes tested for influenza PCR and virus culture. We retrospectively analyzed this prospectively collected cohort of the 10-year period from August 2009 to July 2017.

Results: We have 307 patients with laboratory-confirmed influenza admitted to ICU. RIAT was checked for 259 of the 307 cases and 126 (49%) were RIAT negative. PCR was checked for 99 of the 126 RIAT negative upper respiratory tract (URT) samples and 98 (99%) were PCR positive. Among the 307 cases, 45 (15%) were either with negative results of all URT sample tests (RIAT, PCR or virus culture) or with no URT samples tested. The diagnosis of these 45 cases relied upon tests with lower respiratory tract (LRT) samples. The RIAT negative cases, compared to the RIAT positive, had longer ICU length of stay (LOS) (median 12 vs. 9 d; P<0.99). Antiviral medication was significantly delayed in RIAT negative patients (median 1 vs 0 d; P=0.01). Conclusions: LRT sample tests were crucial for diagnosis of severe influenza with critical illness. Negative RIAT impedes physicians from dispensing antiviral medication. The clinical outcome of RIAT negative critically ill severe influenza was at least equally grave with, if not worse than, those with positive RIAT. Decision-making based on RIAT is strongly discouraged and prompt empiric antiviral medication is justified in severe respiratory infection.
Abstract Title:
Genetic Analysis of Multi-Species, Plasmid-Mediated Carbapenem-Resistant Enterobacteriaceae Hosp. Outbreak

Primary Author Block:
R. A. Stanton1, J. B. Daniels1, L. Sims2, V. Arora2, A. Laufer Halpin1; 1Ctr.s for Disease Control, Atlanta, GA, 2Kentucky Dept. for Publ. Hlth., Frankfort, KY

Abstract Body:
Carbapenem-resistant Enterobacteriaceae (CRE) are an urgent public health threat, responsible for more than 9,000 healthcare-associated infections and 600 deaths per year. An outbreak of CRE in a primary care hospital in 2017 was investigated using whole genome sequencing to determine the identity and possible source(s) of the carbapenemases found in the patient isolates. Twenty carbapenemase-producing isolates (eighteen Klebsiella pneumoniae and two Escherichia coli) were sequenced, nine of which had one beta-lactamase (bla) gene variant (blaKPC-2), eight had blaKPC-3, and one had blaNDM-1. The phylogeny of the K. pneumoniae isolates revealed they were not clonal, as they included four different sequence types, while the E. coli isolates appeared to be closely related. Long-read sequencing determined that the blaKPC-2 and blaKPC-3 genes were harbored on two distinct plasmids, sharing only 48% homology. The blaKPC-2 gene was found on a 128kb plasmid with IncFIB and IncFII replicons that also included a blaTEM-1A gene. While this plasmid appeared to be largely conserved in the nine K. pneumoniae ST258 isolates containing blaKPC-2, the isolates themselves varied from 0 to >1100 SNPs, suggesting that they were not clonal. The plasmid harboring the blaKPC-3 gene was 164kb, with IncFIA and IncFII replicons, as well as blaOXA-9, blaTEM-1A, and six additional antimicrobial resistance genes. Sequences homologous to this plasmid were found in K. pneumoniae isolates from four different STs (including ST258) and both of the E. coli, suggesting horizontal transfer between unrelated bacteria. The results demonstrate that plasmid-mediated carbapenem resistance can be transferred among unrelated bacteria in a healthcare setting, underscoring the impact more granular laboratory methods, such as whole genome sequencing, can have on the ability of public health institutions to investigate outbreaks due to antibiotic resistant threats.
Abstract Title:
Epidemiological and Microbiome Associations between Klebsiella Pneumoniae And Vancomycin-Resistant Enterococci Colonization in Intensive Care Unit Patients

Primary Author Block:
A. H. Collingwood, F. A. Blostein, A. M. Seekatz, C. E. Wobus, R. Woods, B. Foxman, M. A. Bachman;
Univ. of Michigan, Ann Arbor, MI

Abstract Body:
Klebsiella pneumoniae and Vancomycin-resistant Enterococci (VRE) are causes of healthcare-associated infections, and prior colonization has been found to be associated with later infection for both organisms. Screening for VRE intestinal colonization is performed routinely on intensive care unit (ICU) patients in some healthcare systems. K. pneumoniae colonization rates are also high in the ICU population, but the association between VRE and K. pneumoniae colonization is unclear. Identification of patient factors associated with K. pneumoniae colonization, including the association with VRE colonization, could direct screening for K. pneumoniae to vulnerable patient populations who could benefit from infection prevention interventions. We hypothesized that K. pneumoniae and VRE both colonize patients with poorer underlying health, and colonization with VRE influences K. pneumoniae colonization and progression of infection. To test this hypothesis, we performed cohort studies on patients screened for VRE colonization by rectal swab culture over two time periods: July-October, 2014 (n=1,209) and January-May, 2016 (n=1,243). The first rectal swab from the first patient encounter in the time frame was screened for K. pneumoniae, and patient demographics, baseline laboratory data, comorbidities, and outcomes were analyzed. VRE colonization was significantly associated with K. pneumoniae colonization in the 2016 cohort (P=0.0062) and approached significance in the 2014 cohort (P=0.0716). VRE colonization was associated with poorer underlying health and worse health outcomes, but co-colonized patients did not have worse comorbidities or outcomes compared to VRE alone. To identify a biological association between VRE and K. pneumoniae colonization and members of the microbiota, 16S rRNA gene-based analysis was performed. This identified an Enterobacteriaceae operational taxonomic unit that was negatively correlated with colonization by both pathogens. These data indicate that VRE colonization is positively associated with K. pneumoniae, and there are shared microbiota signatures in VRE and K. pneumoniae colonized patients.
The Assoc. between Intestinal Enterobacteriaceae Dominance and Subsequent Infection in Hospitalized Patients

Primary Author Block: K. Rao, Y. Sun, A. Seekatz, C. Bassis, E. Mantlo, M. Bachman; Univ. of Michigan, Ann Arbor, MI

Abstract Body:
The Enterobacteriaceae family of Gram-negative bacteria includes the common nosocomial pathogens Klebsiella pneumoniae, Escherichia coli, and Enterobacter cloacae. Bacterial 16S rRNA gene sequence analysis can assess the proportion of total Enterobacteriaceae among the total gastrointestinal microbiota, and prior studies suggest that domination by Gram-negative bacteria is associated with subsequent bloodstream infection. However, 16S rRNA gene sequencing is too costly and slow to be used in a clinical setting. The objectives of this study were to develop a PCR-based assay that can measure Enterobacteriaceae density, validate it against 16S rRNA gene sequencing, and measure the association between Enterobacteriaceae dominance and subsequent infection. Two quantitative PCR (qPCR) assays were developed that quantify Enterobacteriaceae relative to total bacterial 16S rRNA-encoding genes, and both had good correlation with 16S rRNA sequence analysis (P<.0001). A matched case-control study was then performed comparing patients with bloodstream, urinary tract, or respiratory Enterobacteriaceae infections (n=95) to uninfected patients (n=189). Charts were reviewed and rectal swabs collected upon admission to the ward or ICU were analyzed by sequencing and qPCR. Enterobacteriaceae abundance measured by sequencing was high in both cases and controls (mean=31.1% and 27.5%, respectively; P=.322). After adjustment for patient factors there was a modest association with Enterobacteriaceae dominance (defined as >60%) and subsequent infection, although this varied by assay. Dominance on one of the qPCR assays had a significant association with subsequent infection overall (P=.019), adjusting for albumin levels, central venous catheter presence, and use of pressors and cephalosporins at time of swab collection. There was a borderline association with bloodstream infection (P=.076) when measured by sequencing, adjusting for the same clinical factors. These results demonstrate that using qPCR to measure intestinal dominance by a family of bacteria is feasible, indicate that hospitalized patients have high levels of Enterobacteriaceae colonization overall, and suggest that extreme intestinal dominance may be associated with subsequent infection.
Abstract Title:
Predicting Carbapenem Resistance among Gram-Negative Pathogens in Complicated Urinary Tract Infections
Primary Author Block:
Abstract Body:
Background: Rising antimicrobial resistance increases the risk of exposure to inappropriate empiric treatment. Carbapenem resistance (CR) is a concern in complicated urinary tract infections (cUTI). To facilitate improved empiric antimicrobial targeting in cUTI, we developed a bedside instrument to predict CR. Methods: We developed a predictive model using a 60/40 split cohort approach within the Premier Research database (2009-2016) of 178 US hospitals. We included all hospitalized adult patients with a gram-negative organism in at least one urine culture, who fit our algorithm for cUTI, and were treated with an antibiotic starting on the day of the index culture and continued for <u>></u>3 days. CR was defined as any organism with an I or R in the susceptibility category to imipenem, meropenem, ertapenem, or doripenem. Results: Among 25,285 patients with cUTI, 1,357 (5.4%) were CR. The median (IQR) hospital rate of CR was 4.0% (1.6%, 6.6%). Patients with CR were more likely male (63.0% vs. 44.0%, p<0.001), black (18.1% vs. 15.0%, p=0.11), and transferred from an extended care facility (ECF) (13.2% vs. 7.6%, p<0.001) than those with carbapenem-susceptible [CS] organisms. Patients with CR also had higher comorbidity burden than CS (median [IQR] Charlson Comorbidity Index 3 [2, 4] vs. 2 [1, 3], p<0.001). Overall E. coli was the most frequent cUTI organism. Among CR pathogens P. aeruginosa predominated (54.5%), with E. coli accounting for 11.5% of all CR infections. Patients with CR were more likely than CS to have previously received antibiotics (50.3% vs. 26.1%, p<0.001), and grown a CR organism (11.8% vs. 0.9%, p<0.001). In a model assigning weighted points for: admission from ECF (1), history of weight loss (1), early mechanical ventilation (1), age<50 (2), male gender (3), catheter-associated UTI (4), prior antibiotics treatment (4) and prior CR (8), the model exhibited good discrimination (c-statistic 0.721), performing better among hospitals with low rates of CR. Conclusions: In this large US cohort of cUTI hospitalizations, CR occurred in ~5% of all cases,. A model including eight easily available factors was able to predict the risk of CR at the onset of infection with good discrimination.
Abstract Title:
Relevance of the Catheter and Bacterial Factors in Proteus Mirabilis Catheter Associated Urinary Tract Infection

Primary Author Block:
A. L. Caetano, M. J. González, V. Iribarne garay, P. Zunino, P. Scavone; Inst. de Investigaciones Biológicas Clemente Estable, Montevideo, Uruguay

Abstract Body:
Background: Catheter-associated urinary tract infection (CAUTI) is one of the most common health care-acquired infections. Proteus mirabilis is the most frequent pathogen associated with CAUTI. It produces crystalline biofilm through the bioconversion of ammonium and other salts causing the obstruction of the catheter. Different virulence factors are important for the establishment, and biofilm formation in the catheter. The presence of the catheter in the bladder increases the vulnerability to infection and can result in serious pathologies which are often difficult to treat. Methods: The aim of this work was to evaluate the association between biofilm and CAUTI. We used 6 biofilms-defective P. mirabilis strains previously generated in our laboratory. The CAUTI in mice consisted in the introduction of a 3 mm permanent segment of sterile silicone tubing. After that, a second transient catheter was introduced in order to transurethrally inoculation of 50 ul of 2 x 10^8 CFU of the different strains. The parameters evaluated were the size of the bladder, CFU in urine, classical histological analysis and immunofluorescence for bacterial localization. Results: The mutants had interrupted: ferritin, FMN-binding protein MioC, L-threonine 3-dehydrogenase, membrane transport/efflux protein, D-alanyl-D-alanine carboxypeptidase and serine tRNA genes. We have analyzed the size of the bladder and we observed a significant increase of the bladder in the case of mice with CAUTI caused with wild-type P. mirabilis strain compared to naive mice. In the case of the mutants, we did not observe significant differences compared with the wild-type strain. The ferritin, FMN-binding protein MioC and the membrane transport/efflux protein mutant strains had a significant increase of CFU during CAUTI compared with UTI. On the other hand, the D-alanyl-D-alanine carboxypeptidase and the serine t-RNA showed a significant decrease of CFU in urine in CAUTI. We observed a significant correlation between the size of the bladder and the CFU (Pearson, P=0.0014). The histological damage was higher in the case of the wild-type strain and CAUTI model. We also detected the presence of bacteria in the epithelium that was higher in CAUTI. Conclusions: The sole presence of the catheter induced damage that in some cases could contribute to the infection. We have identified two factors that are relevant for CAUTI and biofilm that are D-alanyl-D-alanine carboxypeptidase and a serine t-RNA. This result will bring new insights into CAUTI and prevention of biofilm in the catheter.
Abstract Title:
Study of Extended Spectrum B-Lactamase Producing Enterobacteriacae from Healthcare Workers from Different Hosp. in Khartoum State 2016-2017

Primary Author Block:
B. I. E. A. Elzubier, M. B. B. M. Bushra; Univ. of Med. Sci. and Technology, Khartoum, Sudan

Abstract Body:
Background: Extended Spectrum B-Lactamase Producing Enterobacteriacae (ESBL-PE) is categorized as multidrug resistant organisms and one of the most frequent nosocomial infections(1). As of to date, data on colonization and transmission patterns from Sub Sahara Africa is limited; therefore, our study aimed to estimate the prevalence of extended spectrum B-lactamase producing Enterobacteriacae faecal carriage among healthcare workers in Khartoum state. Methods: A multi-centered prospective cross sectional study was implemented in nine hospitals in Khartoum state. Faecal samples were collected from 100 healthy a-symptomatic healthcare workers and transported in carry-blair transport media to microbiology laboratory of University of Medical Science and Technology. All samples was cultured in Macconkey agar with crystal violet incubated overnight aerobically at 37°C. Then macroscopic examination of colonies applied, purification of gram’s negative bacilli performed on Macconkey agar with crystal violet for standard biochemical identification including: oxidase production test, kliglar iron agar, citrate utilization test, urease production test, indole test and motility test. standard antimicrobial susceptibility testing to third generation cephalsporins (Cefixime & Ceftazidime ), Amoxcillin, Ciprofluoxacin, Cotrimexazole and Gentamycin performed for all gram’s negative oxidase negative bacilli isolated by kirby- bauer disk diffusion method using Molar Hinton agar media. Resistant isolates to third generation cephalsporin (cefixime or ceftazidime or for both) confirmed positive as extended spectrum B-lactamase producing Enterobacteriacae by double disk diffusion method (key test) as recommended by clinical laboratory standards institute. Descriptive statistics through the statistical package for social sciences (version 23) was performed. Data were summarized including frequency tables for estimating prevalence. Results: Our results revealed that 6.0 %( n=6) of 100 healthcare workers were ESBL-PE positive. 12 %( 21/169) of the total 169 Enterobacteriacae species isolates were resistant to third generation cephalsporin with respectively 12%(21/169) and 5.6%(11/169) for Cefixime and Ceftazidime. Conclusion: The result observed that extended spectrum B-lactamase producing Enterobacteriacae colonizes healthcare workers which is a threat for both patients and healthcare givers and arise a public health concern for both patients and healthcare givers towards infection prevention and control.
Environmental Sampling Surface Area and Recovery Efficiency of Antimicrobial Resistant Bacteria: Investigating A Composite Sampling Strategy

Primary Author Block:
M. Y. Chan, L. J. Rose, J. Noble-Wang; CDC, Atlanta, GA

Abstract Body:
Environmental surface sampling and sample testing is time and resource intensive during healthcare outbreak investigations or public health intervention studies. Composite sampling, using one device for sampling multiple sites, would reduce sampling and testing time and cost. We evaluated the percent recovery (%R) of each side of a cellulose sampling sponge for five healthcare pathogens from four surface areas (areas). Determining the optimum areas for each side of this sampling tool will help standardize a composite strategy to accurately represent a larger area. Five antimicrobial resistant bacteria (Acinetobacter baumannii (AB), carbapenemase-producing Klebsiella pneumoniae (KPC), vancomycin-resistant Enterococcus faecalis (VRE), methicillin-resistant Staphylococcus aureus (MRSA), and Clostridium difficile spores (CD)) were suspended in an artificial soil and deposited as 40 µL droplets (104 CFU total) onto steel coupons of four dimensions: 50, 100, 200, and 350 in2 and allowed to dry 2 hr. Coupons were sampled in a single pass with either the face (3x3 in) or side (3x1.5 in) of a cellulose sponge. Sponges were held for one hour before homogenization in 45 mL PBS with 0.02% Tween® 80. Data was analyzed with a Welsh's t-test. Significance was set at P≤0.05. For all bacteria, the % R using the face was significantly higher than when using the side. The mean % R varied with organism and area; the % R of KPC yielded less than 5%, and %R of CD spores yielded more than 30% from all areas. The % R of KPC and CD spores was significantly higher from 50 in2 when using the face as compared to 100, 200 and 350 in2, and higher from 100 in2 when using the side, as compared to 200 and 350 in2. The % R for AB, VRE, and MRSA was similar, and therefore data was pooled for each area separately, then analyzed. For the three pooled bacteria, %R from 100 in2 was significantly higher when using both the face and the side, as compared to 200 and 350 in2. These data support a composite strategy for sampling AB, VRE, and MRSA from 100 in2 areas with both the sponge face and side, for a maximum of 400 in2 using all sides, without significant loss in % R. When sampling for CD spores or KPC, 50 in2 and 1002 are optimum with the sponge face and side, respectively, for a maximum of 300 in2. Additional work is needed to confirm the total % R for each pathogen, and to determine the limit of detection when using this composite strategy.
Abstract Title:
Unhygienic Food Handling Could Be A Source of the Spread of Intestinal Parasites & Multi-Drug Resistant Pathogenic Bacteria in Dessie Town, North Eastern Ethiopia

Primary Author Block:
B. Endallew; Addis Ababa Univ., Addis Ababa, Ethiopia

Abstract Body:
Background: Food handlers who are engaged in food preparation, transport and provision are implicated in the transmission of foodborne diseases if appropriate hygienic practices are not maintained. They could be potential sources of infections of many intestinal parasites & enteropathogenic bacteria. Hence the present study was undertaken to determine the prevalence of intestinal parasites & bacteria among food handlers of Dessie town, Ethiopia. Methods: A community based cross-sectional study was conducted from December 2013 - June 2014 to assess intestinal parasites and enteric bacterial pathogens among asymptomatic food handlers of Dessie town. Stool samples were collected from 135 food handlers. Stool microscopy and stool culture were used to determine intestinal parasites & enteric bacterial pathogens, respectively. Antimicrobial susceptibility pattern of the isolated bacteria was performed using Kirby-Bauer disc diffusion method. Results: A total of 135 food handlers were enrolled in this study. Majority of them were females 112(83%), 18-27 years old young adults 95(70.4%), grade 9-12 students 56(41.5%) & single in marital status 87(64.4%). The mean age and mean monthly income of food handlers were 25 ± 9 years and 27.5±23.2 US$, respectively. The prevalence of intestinal parasites and enteric bacterial pathogens were 10.4% and 13.3%, respectively. E.histolytica/E.dispar, 8 (5.9%) and Shigella species, 7 (5.2%) were the predominant parasitic & bacterial isolates. Six (85.7%) of the shigella isolates showed resistance to Chloramphenicol and Tetracycline while all the isolated Pseudomonas species showed resistance to all tested antimicrobials. Conclusions: It is evident that potentially contagious enteric bacterial pathogens and intestinal parasites were identified from food handlers which were presumed healthy. Hence, periodic screening of food handlers, training for food handling and hand hygiene practices, regular monitoring of the food handling practices and regular medical checkups for food handlers is highly needed.
Session Title: CIV02 - Infection Prevention and Control: Drug-Resistant Pathogens in Hospitals

Abstract Title:
Budget Impact and Cost-effectiveness of Meropenem-vaborbactam (M-V) Compared with Ceftazidime-avibactam (C-A) in US Hospitals

Primary Author Block:
K. Sulham1, W. Fan2, G. Tillotson3; 1Melinta Therapeutics, Inc., Lincolnshire, IL, 2The Med.s Company, Parisppany, NJ, 3Melinta Therapeutics, Inc., Raleigh, NC

Abstract Body:
Background: Carbapenem-resistant Enterobacteriaceae (CRE) infections continue to spread worldwide and are considered an urgent antimicrobial resistance threat. CRE infections may cost US hospitals approximately $275 million annually (nearly $30,000 per patient). Meropenem-vaborbactam (M-V) is a carbapenem/beta-lactamase inhibitor combination designed to have enhanced in vitro activity against select carbapenemase-producing Enterobacteriaceae, and is a potential new option for the treatment of severe gram-negative infections, including CRE. Here, we examine the budget impact and cost-effectiveness of M-V as compared to ceftazidime-avibactam (C-A) to aid decision making.

Methods: Two decision analytic models, a budget impact model and cost-effectiveness model, were developed from the perspective of a US hospital to examine the budget impact and cost-effectiveness of M-V for the management of hospitalized patients with suspected or confirmed CRE. Data was derived from clinical studies and published literature. Key clinical inputs included clinically-cured infection, mortality at 28 days, and incidence of renal failure. Key economic inputs included cost of drug, hospitalization length of stay (LOS) (both general ward and intensive care unit (ICU) days), treatment failure and acute renal failure; unit costs were sourced from the literature. Results: In a hospital hypothetically treating 30 patients per year, total annual costs associated with M-V were estimated to be $898,221 vs. $968,810 with C-A, for a total cost savings of $70,589 per year associated with use of M-V. M-V was dominant (more effective, less costly) compared to C-A; these results were robust to sensitivity analysis. Cost-effectiveness and budget impact differences were largely driven by improved clinical cure and mortality rates associated with M-V. While data from both TANGO I and II suggest a potential ICU LOS reduction, overall LOS in the model was conservatively assumed equal across treatment arms. Incorporating this benefit would have therefore resulted in more favorable cost-effectiveness estimates and lower total costs for M-V. Conclusions: The models’ results indicate that M-V is likely to be associated with a favorable budget impact and high cost-effectiveness for the treatment of CRE infections.
Role of Regulatory T Cells in Mother to Child Transmission of HIV

P. A. Kessler, S. P. Kaur, C. C. Ibegbu; Emory Univ. Sch. of Med., Atlanta, GA

Background: Mother-to-child transmission of HIV-1 occurs in a minority of HIV-infected mother-infant pairs, even without any interventions. The mechanisms that protect the majority of HIV-exposed infants from infection are unclear. T regulatory cells (Treg) have important immunomodulatory functions, but their role in the fetus as well as in mother-to-child transmission of HIV is under-studied.

Methods: We studied available cryopreserved peripheral blood mononuclear cells from HIV-exposed infants from the Breastfeeding, Antiretrovirals and Nutrition (BAN) Study cohort in Malawi: 64 infants were HIV-uninfected and 28 infants were HIV-infected at birth. We quantified the frequency of Treg cells (CD4+CD25+FoxP3+), and activated CD4+ and CD8+ T cells (CD38+HLADR+) by flow cytometry at birth, 6 weeks and 6, 9 and 12 months of age. Descriptive statistics were performed to describe the distributions of these lymphocyte markers according to HIV infection status; and Student’s t tests and Wilcoxon-Rank Sum tests to perform comparisons between HIV-infected and uninfected infants.

Results: T cell activation increased rapidly in the first 6 weeks of life, more pronounced on CD8+ T cells; a further increase in activation was observed at the time of weaning from breastfeeding at 6 months of age. In contrast, the frequency of Treg was stable over the first 6 weeks of life (median, 0.5%), slightly decreased between 6 weeks and 6 months (median at 6 months, 0.3%) and then slightly increased between 6 months (time of weaning) and 12 months of age (median, 0.45%). HIV-infected infants had significantly higher frequencies of activated T cells than uninfected infants (P<0.01), as expected. At the time of birth, HIV-exposed uninfected infants had higher levels of Treg, compared to infants infected in utero (P=0.03). Among infants with negative HIV tests at birth, Treg % tended to be higher in those who were HIV-infected by 6 months of life, compared with those who remained uninfected (median, 1.25% vs. 0.55%).

Conclusions: This study provides evidence that Treg may play a role in preventing mother-to-child transmission of HIV, and perhaps even delaying detection of HIV infection in the infant, likely by suppressing immune activation in the fetus and infant. Better characterization of the role of Treg in fetal and neonatal immunity may provide a valuable complementary approach to achieve eradication of mother-to-child transmission of HIV.
Abstract Title:
Altered Lipid Profiles of Mycobacterium Bovis BCG Strains Following BCG Vaccination of A Patient with Interferon-γ Receptor 1 (IfnγR1) Deficiency
Primary Author Block:
S. Shallom1, K. Arora1, H. Boshoff1, E. Sampaio1, H. Tettelin2, C. Barry1, S. Holland1, S. Rosenzweig1, A. Zelazny1; 1NIH, Bethesda, MD, 2Univ. of Maryland, Coll. of Med., Bethesda, MD
Abstract Body:
Background: Patients with primary immunodeficiencies involving the IL-12/IFNγ pathway have increased risk for mycobacterial infections. Herein we report a case of a boy with partial recessive IFNγR1 deficiency who developed disseminated BCG infection after neonatal vaccination (Bacillus Calmette-Guérin -BCG- vaccine). M. bovis BCG isolates with distinctive genotypic and phenotypic characteristics were recovered from his central nervous system and his lungs; both clinical isolates derived from the original vaccine strain. Comparative whole genome sequencing and lipid profiling were used to identify changes in lipid metabolism in the clinical isolates (BCG-lung, BCG-brain) compared to the parent strain (BCG vaccine). Methods: Vaccine and clinical strains were sequenced with the Illumina MiSeq instrument. Thin layer chromatography of strains incubated with [14C]-propionate or [14C]-acetate was used for measurement of PDIMs (phthiocerol dimycocerosates), PGLs (phenolic glycolipids), MAMEs (Mycolic acid methyl esters), FAMES (Fatty acid methyl esters) and TAG (triacylglycerol) Results: We identified single non-synonymous mutations in 3 lipid metabolism genes: Diacylglycerol O-acyltransferase, Acyl-CoA dehydrogenase and a Methyltransferase. The BCG lung had lower (~33%) amount of the keto MAME compared to the vaccine isolate, while BCG brain isolate showed an increase by ~25%. PDIM profiles showed dramatically reduced amount of the DIMB band of BCG lung and BCG brain compared to BCG vaccine. No differences were observed in the DIMA band. BCG lung had a greater amount of TAG compared to BCG vaccine. Conclusions: Our findings suggest dissimilar evolution in different host tissues of a BCG vaccine strain displaying distinct lipid profiles which could affect host cell-pathogen interactions, immunity and virulence.
Abstract Title:
Bifidobacteria-Derived Lipoproteins Inhibit Infection with Coxsackievirus B4 in Vitro

Primary Author Block:
K. A. El Kfoury; Lille-2 Univ., Lille, France

Abstract Body:
The aim of the present study was to investigate the potential of bifidobacteria in protecting cells from coxsackievirus B4 (CV-B4) infection. Bifidobacterial screening identified two of five strains that protected human epithelial type 2 (HEp-2) cell viability when bifidobacteria were incubated with viral particles prior to inoculation. In contrast, no effect was shown by incubating HEp-2 cells with bifidobacteria prior to CV-B4 inoculation. Cell wall lipoprotein aggregates (LpAs) secreted by the selected strains were assayed for their antiviral activity. The two LpAs exhibited antiviral activity when they were incubated with viral particles prior to inoculation of HEp-2 cells. Recombinant LpA-derived protein exhibited identical antiviral activity. To identify the peptide sequences interacting with the virus particles, LpA proteins were aligned with the peptide sequences of the north canyon rim and puff footprint onto coxsackievirus and adenovirus receptor (CAR). The in silico molecular docking study using CV-B3 as template showed lowenergy binding, indicating a stable system for the selected peptides and consequently a likely binding interaction with CV-B. Bifidobacterium longum and Bifidobacterium breve peptides homologous to the viral north rim footprint onto CAR sequence formed hydrogen bonds with several viral residues in the north rim of the canyon, which were already predicted as interacting with CAR. In conclusion, proteins from bifidobacterial LpAs can inhibit infection with CV-B4, likely through binding to the capsid amino acids that interact with CAR.
Session Number: 421  
Session Type: Poster
Session Number: 421  
Session Type: Poster
Session Title: CIV05 - Pediatric Infectious Diseases: General Pediatrics  
Session Start Date Time: 6/10/2018 12:45:00 PM  
Session End Date Time: 6/10/2018 2:45:00 PM  
Session Primary Track: Clinical Infections and Vaccines  
Abstract Control Number: 5914  
Poster Board Number: SUNDAY - 716

Abstract Title:  
Evaluation of the Karius Plasma Next-Generation Sequencing Test for Pathogen Detection in Pediatric Patients At Risk for Invasive Fungal Infection  
Primary Author Block:  
A. E. Armstrong1, J. Rossoff1, R. Aquino2, D. Hollemon2, D. K. Hong2, S. Chaudhury1, W. Muller1;  1Ann & Robert H. Lurie Children’s Hosp. of Chicago, Chicago, IL, 2Karius, Inc., Redwood City, CA  
Abstract Body:  
Background: Invasive fungal infection (IFI) is a major cause of mortality and morbidity among pediatric immunocompromised patients. Standard microbiologic culture of biopsy samples remains the diagnostic gold standard. Noninvasive biomarker testing such as Aspergillus galactomannan or β-D-glucan can provide clinically useful information, but does not give species-level identification. Next-generation sequencing (NGS) of cell-free plasma is a noninvasive approach for species-level identification of pathogens, and may guide specific treatment. Methods: Plasma from at-risk immunocompromised patients with suspected IFI was tested using NGS of extracted DNA (Karius, Redwood City, CA). After removing human reads, remaining sequences were aligned to a curated database of 1251 pathogens including 333 fungi. Organisms present above a predefined significance threshold were reported. Results: The 27 patients analyzed to date include 14 with prolonged febrile neutropenia (FN), 5 with recrudescent FN, 5 with abnormal imaging, and 3 with other findings. Four patients met established criteria for proven IFI, 2 for probable IFI, and 9 for possible IFI. NGS plasma testing identified a pathogen which was cultured from infected tissue or blood in all 4 proven cases. Among probable IFI cases, P. jirovecii was identified in a patient with pneumonia and positive β-D-glucan. Other pathogens identified with potential clinical significance included T. gondii in a patient with FN and abnormal lung imaging, and C. glabrata in a patient with FN but no other IFI criteria. Conclusion: Plasma NGS testing can detect IFI from blood. The test identified fungi from proven IFI, and detected other pathogens in both probable and possible IFI cases. NGS testing is a useful diagnostic tool in the evaluation of patients at risk for IFI.
Session Number: 421
Session Type: Poster

Session Title: CIV05 - Pediatric Infectious Diseases: General Pediatrics
Session Start Date Time: 6/10/2018 12:45:00 PM
Session End Date Time: 6/10/2018 2:45:00 PM
Session Primary Track: Clinical Infections and Vaccines
Abstract Control Number: 5019
Poster Board Number: SUNDAY - 717

Abstract Title:
Real Time Pcr Taqman Low Density Array(TLDA) Card Assay for the Detection of Vibrio Cholerae With Co Infection of Other Gut Bacterial Pathogens in Stool Specimen of Children Less Than 5 Years of Age in Karachi, Pakistan

Primary Author Block:
A. Kalam, F. Kabir, F. Aziz, I. Rizvi, S. Qureshi, N. Iqbal, F. Qamar; The Aga Khan Univ., Karachi, Pakistan

Abstract Body:
Background: Vibrio cholerae which causes watery diarrhea remains a global threat to public health and an indicator of inequity and lack of social development. Identification of Vibrio cholerae in the lab can be done by various methods with limitations, including varying sensitivities, specificities. We used a qualitative real time PCR Taqman Low Density Array (TLDA) card to simultaneously detect and identify gut viral, bacterial, and parasitic pathogens. The stool samples from Global Enteric Multicenter Study (GEMS), which was large Case Control study of moderate to severe diarrhea in children of age strata 24 to 59 months, were reanalyzed by using TLDA. Methods: This study was conducted on stool specimen from GEMS specimens. GEMS Samples from Pakistan, of n=240 cases and matched controls n=240 were processed. Nucleic Acid was extracted by using QIAamp Fast DNA stool mini kit (Qiagen, Hilden, Germany) as per manufacturer’s instruction with pretreatment step that included bead beating. Phocine herpes virus and MS2 was added as external positive control to monitor efficiency of nucleic-acid extraction and amplification (Ct value ≤ 35 considered as positive). The detection of Vibrio cholerae was carried out by using Ambion AgPath One-step RT PCR mas-ter mix in customized TaqMan Array Cards (Thermo Fisher, Carlsblad, Ca, USA) having compartmentalized probe based real time PCR assay. Results: Results showed the total positivity of Vibrio cholerae in cases 40/240 (16.6%) and in control 4/240 (1.6%). Vibrio cholerae also showed positivity in cases as co-infection with diarrheagenic E.coli (EAEC 21/240 (8.7%), ETEC 19/240 (7.9) and with EPEC 19/240(7.9%) while positivity with other gut pathogens are 23/240 (9.5%), 13/240 (5.4%) and 1/240 (0.4%) with Campylobacter, Shigella and salmonella respectively. Co-infection of Vibrio cholerae in controls with EAEC 4/240 (1.6%), ETEC 3/240 (1.2%), EPEC 3/240 (1.2%), and with campylobacter 2/240 (0.8%). There is no positive co infection of Vibrio cholerae with Shigella and salmonella in controls. Conclusions: Results of this study showed that Vibrio cholerae has high co infection with diarrheagenic E.coli and other bacterial gut pathogens in cases and comparatively low positivity in controls as co infection. Further the TLDA technique that we used has substantially increased the sensitivity and provided the higher resolution of pathogen detection.
Molecular Characterization of Enteroaggregative Escherichia coli Clin. Isolates from Children in Colombia, South America

Primary Author Block:
A. Aldrow1, J. Guerra1, A. Dharia1, A. Farfan2, O. Gomez-Duarte1; 1Univ. at Buffalo, Buffalo, NY, NY, 2Univ. de Santander, Bucaramanga, Cambodia

Abstract Body:
Enteroaggregative E. coli (EAEC) is an enteric pathogen that causes acute diarrheal disease among children and adults worldwide. An important characteristic of EAEC is its heterogeneous nature in terms of virulence gene profile. EAEC typically mediates aggregative adherence (AA) to intestinal cells, biofilm formation on intestinal mucosa and it may secrete enterotoxins. EAEC is divided into typical and atypical EAEC based on the presence or absence of the aggR gene, respectively. The objectives of this study are to identify virulence gene profiles of EAEC clinical isolates from Colombia, to evaluate the genetic relatedness among Colombian EAEC strains, and to quantify the biofilm formation phenotype among all EAEC strains. EAEC clinical isolates from children with and without diarrhea were derived from stool samples of subjects less than 5 years from Colombia (n=109), as part of previously reported IRB-approved childhood diarrhea surveillance studies. Genomic DNA from EAEC clinical isolates and E. coli controls was isolated and processed for multiplex PCR assays for identification of virulence genes. Quantitative biofilm assay was performed using microtiter plates to screen for biofilm formation (BF). Among EAEC cases, aatA, pic, sen, set1A and set1B were the most common virulence genes (71%). The pic gen was statistically associated with EAEC isolated from cases (Fisher test p-value 0.0001). Among EAEC controls, ORF3 (80%), set1A (75%), sen (73%), aggR (71%), aatA (71%) and ORF61 (71%) were the most common virulence genes. Among cases, 69% were typical EAEC and 31% were atypical EAEC. Among controls, 71% were typical EAEC and 29% were atypical EAEC. Quantitative biofilm assay showed similar results for cases and controls. Among the cases, 10% were BF high positive, 38% were BF low positive and 52% were BF negative. Among controls, 8% were BF high positive, 49% were BF low positive and 43% were BF negative. Colombian EAEC clinical isolates are a highly diverse group of strains with respect to virulence genes and BF. The only gene that was statistically associated with EAEC isolated from cases was pic, suggesting that this virulence gene may play a significant role in disease causation in pediatric populations. Further studies are necessary to better understand the role of specific genes, in addition to pic, in EAEC pathogenesis.
Abstract Title:
Clonal Expansion of the Macrolide-Resistant Sequence Type 3 Mycoplasma Pneumoniae In Korea

Primary Author Block:

Abstract Body:
Background: Mycoplasma pneumoniae is one of the major causes of community-acquired pneumonia in children and adolescents. Since the first report of a macrolide-resistant M. pneumoniae isolate from a Japanese child in 2001, several Asian countries including Korea, Japan and China have reported increased prevalence of macrolide resistance. To understand the genetic diversity of M. pneumoniae strains between outbreaks and to find a genetic background that may explain the emergence of macrolide resistance among M. pneumoniae strains, we conducted a Multilocus Sequence Typing (MLST) analysis during the five consecutive epidemics of M. pneumoniae pneumonia in Korea. Methods: M. pneumoniae was identified from children who were diagnosed with pneumonia at five tertiary hospitals in Korea from 2000 to 2016. DNA was extracted from cultivated M. pneumoniae or directly from the nasopharyngeal aspirate samples. Macrolide resistance was determined by the presence of mutations in the 23S rRNA gene through the sequencing analysis. MLST was performed on all strains and corresponding sequence type (ST) was given to each strain. Results: A total number of 146 M. pneumoniae strains were identified during the five consecutive outbreaks. Macrolide resistance rate increased from 0% (0/21) in the 2000 outbreak to 84.4% (40/45) in the 2014/2016 outbreak. Among the eight STs (ST1, ST2, ST3, ST7, ST14, ST15, ST17 and ST31) identified, ST3 (109, 74.7%) was most prevalent, followed by ST14 (22, 15.1%). Macrolide-susceptible strains consisted of eight different STs, while all of macrolide-resistant strains were ST3 (98.3%) except for one with ST14 (1.7%). The proportion of macrolide-resistant strains in ST3 remained 2.2% (1/46) till 2006/2007 outbreak and markedly increased to 82.6% (19/23) in the 2010/2012 outbreak and 95.0% (38/40) in the 2014/2016 outbreak. Conclusions: During the outbreaks of M. pneumoniae pneumonia when macrolide resistance was increasingly recognized, all of macrolide-resistant strains were ST3 except one strain. The findings demonstrated that clonal expansion of an ST3 M. pneumoniae was associated with the increase in macrolide resistance in Korea.
Abstract Title:
In-Vitro Microbiological Activity of Ceftolozane/Tazobactam, Ceftazidime/Avibactam, and Meropenem/Vaborbactam Against Ceftazidime-Nonsusceptible Enterobacteriaceae Isolates At A Child. Hosp.
Primary Author Block:
M. Bergel1, A. Evangelista1, W. Moore2, A. Chopra3, J. Cies1; 1St. Christopher’s Hosp. for Children, Philadelphia, PA, 2The Ctr. for Pediatric Pharmacotherapy, Pottstown, PA, 3NYU Langone Med. Ctr., New York, NY
Abstract Body:
Background: There are several new antimicrobial agents for use in the adult population. The clinical use of these agents in the pediatric population has been limited thus far and there is minimal data regarding the microbiological activity against pediatric isolates. The purpose of this investigation was to compare the in vitro microbiological activity of ceftolozane/ tazobactam (CT), ceftazidime/avibactam (CA), and meropenem/vaborbactam (MV) in multi-drug resistant pediatric isolates identified as ceftazidime (CAZ) non-susceptible. Methods: Clinical isolates resistant (R) to ceftazidime (CAZ) via Vitek 2 methodology were sequestered from 2016-2017. MICs for CT, CA, MV, meropenem (MEM), and ceftazidime (CAZ) were then determined by agar gradient diffusion testing. Isolates were determined as susceptible (S), intermediate (I), or R based on current CLSI and FDA breakpoints. MIC50 and MIC90 values were also calculated. Results: 30 non-duplicate clinical Enterobacteriaceae isolates were included. The % susceptible for CT, CA, MV, MEM and CAZ were 63%, 97%, 97%, 93%, and 0%, respectively. The MIC50 values (μg/mL) for CT, CA, MV, MEM and CAZ were 1.0, 0.50, 0.064, 0.064, and 24, and the MIC90 values were 16, 1.5, 0.125, 1.5, and >256. Of the 30 isolates, 2 were KPC-producers; 1 Klebsiella pneumoniae, 1 Proteus mirabilis. The Klebsiella was susceptible to CA and MV and the Proteus was resistant to all 5 agents tested. Conclusions: CA, MV, and MEM were the most active agents against the 30 CAZ nonsusceptible Enterobacteriaceae pediatric isolates with % susceptibilities of 97%, 97%, and 93%. The MIC50/ MIC90 values were 0.50/1.5 μg/mL for CA, 0.064/0.125 for MV, and 0.064/1.5 for MEM.
Session Number: 421
Session Type: Poster
Session Number: 421
Session Type: Poster
Session Title: CIV05 - Pediatric Infectious Diseases: General Pediatrics
Session Start Date Time: 6/10/2018 12:45:00 PM
Session End Date Time: 6/10/2018 2:45:00 PM
Session Primary Track: Clinical Infections and Vaccines
Abstract Control Number: 2030
Poster Board Number: SUNDAY - 721

Abstract Title:
Synergistic Effect of Antibiotics against Bacterial Pathogens Causing Diarrhea Isolated from Children Less Than 5 Years of Age

Primary Author Block:
R. Irshad; PHRC, Karachi, Pakistan

Abstract Body:
Background: Infant mortality rate in Pakistan is very high which is attributed to diarrhea. In recent years the alarming increase in antimicrobial resistance. So this research was designed to study the in vitro synergistic (combined) effect of different antibiotics against these pathogens in order to determine whether the combined antibiotic therapy may be used to treat diarrhea. Methods: Sensitivity and resistance pattern of bacterial pathogens was performed by disk diffusion method. And combined effect of existing antibiotics including Ampicillin, Cefotaxime, Cefixime, Co-trimoxazole and Ofloxacin was performed by checkerboard method. Study was approved by Ethical Review Board of National Institute of Child Health. Results: Most of the combinations showed indifferent and Antagonistic activity against bacterial pathogens causing diarrhea. But only AMP-SXT and CFM-OFX yielded synergistic activity against Vibrio and Aeromonas respectively. AMP-CFM and AMP-OFX exhibit synergistic effect against E.coli. While no combination of antibiotics proved as synergistic for Salmonella and Shigella. Conclusions: Little synergistic activity of different antibiotic combinations was observed against diarrheal isolates. And most of the combinations exhibited indifferent and antagonistic activity. Hence this can be concluded that single antibiotics are effective than combination.
Session Number: 421
Session Type: Poster
Session Number: 421
Session Type: Poster
Session Title: CIV05 - Pediatric Infectious Diseases: General Pediatrics
Session Start Date Time: 6/10/2018 12:45:00 PM
Session End Date Time: 6/10/2018 2:45:00 PM
Session Primary Track: Clinical Infections and Vaccines
Abstract Control Number: 4795
Poster Board Number: SUNDAY - 722

Abstract Title:
Improving Protection by Manipulating Bacterial Immunomodulators
Primary Author Block:
M. Cartelle Gestal, L. K. Howard, I. Hamidou Soumana, E. T. Harvill; Univ. of Georgia, Athens, GA
Abstract Body:
Background: Bordetella pertussis and other Bordetella spp. can cause whooping cough and other respiratory diseases in humans and animals. B. pertussis is reemerging, and animal disease continue to circulate despite vaccines being available. A noted failure of these is that they protect against severe symptoms, but not colonization that can allow for transmission. We have recently defined sets of gene regulated by within-host signals that we infer to be involved in manipulation of host immunity. We hypothesized that by disrupting these we are able to interfere with B. bronchiseptica manipulation of the host immune response. Methods: By generating a deletion in bsr using allelic exchange, we performed several studies using C57 mice. Vaccine experiments were performed by challenging mice with the bsr mutant and 60 days after, mice were re-challenged with 50 ul 10^5 CFU of B. bronchiseptica, B. pertussis or B. parapertussis. For the immunology experiments, mice were challenged with 50 ul 10^5 CFU of bsr mutant strain and immune cells were analyzed using flow cytometer. Results: Here we describe how this novel approach to vaccine development can generate sterilizing immunity against multiple Bordetella spp., including all three classical species, B. pertussis, B. parapertussis and B. bronchiseptica. Mice vaccinated with our novel vaccine recruit significantly higher numbers of CD4, CD8, neutrophils and B cells to the lungs, allowing for complete clearance of both the lower respiratory tract and nasal cavity. Conclusions: Our results showed that inhibiting the ability of bacteria to manipulate host immunity confers robust and long-lasting protection against further encounter with the pathogen.
Abstract Title:
Utility of Procalcitonin to Differentiate between Gram-Positive and Gram-Negative Infections in Pediatric Patients

Primary Author Block:
M. Abadeer1, W. Moore2, A. Chopra3, J. Cies1; 1St. Christopher's Hosp. for Children, Philadelphia, PA, 2The Ctr. for Pediatric Pharmacotherapy, Pottstown, PA, 3NYU Langone Med. Ctr., New York, NY

Abstract Body:
Background: Gram-positive (GP) and gram-negative (GN) bacteria activate different Toll-like receptors signaling pathways resulting in production of different proinflammatory cytokines that stimulate procalcitonin (PCT) release. Adult data suggests median PCT values are higher in GN bloodstream infections (BSI) compared to GP BSI yet there is limited data on whether PCT can differentiate between GP and GN BSI in pediatric patients. The aim of this study was to evaluate whether PCT can discriminate infections caused by GP and GN organisms. Methods: This was a single-center, retrospective medical record review. All patients with documented blood stream infection (BSI) with a single organism and/or meningitis (MEN) from January 2013 to December 2017 were eligible for inclusion. Patients with a documented BSI or MEN and a PCT level were included. During this time period, there was no standard protocol for obtaining PCT levels and patients with polymicrobial infections were excluded. All analyses were performed using IBM SPSS Version 24 (SPSS Inc., Chicago, IL). Results: 44 patients, 27 males and 17 females, with BSI and/or meningitis were included. The median age in the GN group was 9.5 months (IQR 3 months-3.75 years) compared with 9 months (IQR 2 months-4 years) in the GP group, p = 0.85. The median weight was 9.75 kg (IQR 4.7-15.3 kg) in the GN group compared with 7.8 kg (IQR 3.7-16 kg) in the GP group, p = 0.42. The median PRISM score was 14.5 (IQR 9-20.75) in the GN group compared with 15 (IQR 9.5-27.7) in the GP group, p = 0.43. The median PCT in the GN group was 8.11 ng/mL (IQR 1.62-23.95) vs 8.32 ng/mL (IQR 1.26-22.44) in the GP group, p = 0.6 Conclusions: This preliminary pediatric data suggests in the setting of BSI and/or meningitis, the elevation in PCT is similar whether the causative organisms is a GP or GN organism.
Abstract Title:
Diagnosis of Neonatal Septicemia; Thinking Beyond Blood Culture
Primary Author Block:
A. Gopang; Pakistan Hlth. Res. Council, Karachi, Pakistan
Abstract Body:
Background: Neonatal sepsis (NS) is a major cause of neonatal admissions to hospital and mortality. This study was conducted to evaluate different methods for rapid and reliable diagnosis of NS with an aim to rationalize the use of antibiotics and stay in Neonatal Intensive Care Unit. Objectives: To compare the different available methods for rapid and reliable diagnosis of neonatal sepsis. Study Design, Settings and Duration: This comparative study was conducted in Emergency Department of National Institute of Child Health (NIC) Karachi for the period of six months. Subjects and Methods: Neonates who were brought to the emergency department of National Institute of Child Health with suspicion of NS were clinically examined. Those, supposed to be septic were included as study population and informed written consent was taken from their parents. After this, 3 ml blood was drawn for complete blood count (CBC), blood culture, C-reactive protein (CRP), polymerase chain reaction (PCR) and neutrophilic ratio. PCR and CRP results were compared with blood culture for specificity, sensitivity, positive and negative predictive values. Results: Out of 129 neonates, 23 (17.82%) were positive for bacterial DNA by PCR method while 42 (32.55%) were positive for infection when tested for C reactive protein marker of the blood. Whereas, only 15 (11.62%) were positive by blood culture. Sensitivity and specificity of PCR were 60% and 88% while positive and negative predictive values were 39% and 94% respectively. Sensitivity and specificity of C reactive protein were 60% and 71% while positive and negative predictive values were 21% and 93% respectively. Conclusion: Our study revealed high specificity and positive predictive values of PCR suggesting that PCR is more reliable, rapid and specific adjunct of blood culture for diagnosis of NS. Key words: Neonatal sepsis, blood culture, PCR, CRP.
Detection of Group B Streptococcus (Gbs) Infection of Twin Neonates from Breastmilk Using Indirect and Direct Molecular Methods

Background: Group B Streptococcus (GBS) infections are the leading cause of neonatal meningitis and sepsis generally emerging during the first week of life. GBS colonization of the mother is surveyed during pregnancy although non-detection of GBS does not preclude the possibility of infection. Here, we present the case of twins diagnosed with GBS infection at age 1-month and the subsequent source investigation.

Materials and Methods: Pediatric blood cultures were drawn following clinical sepsis suspicion and identification confirmed by MALDI-ToF and PCR. Antepartum and peripartum surveillance swabs were enriched in LIM-broth and the Cepheid Xpert GBS LB PCR assay used to detect the 3' DNA region adjacent to the cfb gene of S. agalactiae. Cepheid PCR of breastmilk was done using direct and indirect (enriched) samples. Known concentrations of GBS was added to PCR-negative breastmilk to access the limit of detection and quantify samples. Results: Indirect antenatal PCR failed to detect GBS upon labor presentation. Twins were born at 30 weeks gestation by C-section and received rule-out sepsis evaluation and 48h of antibiotic prophylaxis. At age 35 days, male twin was symptomatic for sepsis and blood cultures grew GBS. Female twin became symptomatic five days later prompting additional PCR surveillance of the mother’s groin, axilla, breast, and perirectal areas but no GBS was detected. The mother’s breastmilk was GBS positive despite no clinical evidence of mastitis at day 35 post-partum. Indirect and direct PCR of stored breastmilk collected from 18-40 days post-partum detected GBS at day 35 and 40 with no samples provided in between. Quantitation was 8,000 and 10,000 CFU/mL, respectively, with development of mastitis on day 36. GBS was detected in breast milk pump attachments and collection bottles. Limit of detection (LoD) of the assay was 10-fold higher than (10^3 CFU/mL) than that of LIM-broth and assay internal controls remained valid. Conclusion: GBS surveillance is an exhaustive predictor of infection risk. Despite the inability to detect GBS colonization of the mother using traditional sampling and enriched PCR, GBS was detected in breastmilk and is the likely source of neonate infection. Breastmilk GBS detection using direct and indirect PCR methods were concordant, although direct methods had a higher LoD suggesting breastmilk may have slight assay interference but does not invalidate PCR utility. Furthermore, this case demonstrated the potential for direct screening of perinatal GBS screening prior to the clinical onset of mastitis.
Abstract Title: Chronic Otitis Media with Effusion: Microbiome Analysis by qPCR and 16s rRNA Deep Sequencing

Primary Author Block:
V. Cantarelli1, C. Dias1, M. R. Pereira2, D. Pereira2, M. P. Mott1, S. Nakamura3, D. Motooka3, T. Iida3; 1Federal Univ. of Hlth.Sci. of Porto Alegre, Porto Alegre, Brazil, 2Hosp. Moinhos de Vento, Porto Alegre, Brazil, 3Res. Inst. for Microbial Diseases, Osaka Univ., Suita, Japan

Abstract Body:
Background: Acute otitis media is a common condition of childhood. Treatment include antibiotics and, in case of chronic otitis media with effusion (COME), surgical treatment may be necessary. Bacterial pathogens frequently associated with these conditions are Streptococcus pneumoniae (Sp), Haemophilus influenzae (Hi), and Moraxella catarrhalis (Mc). 16S rRNA deep sequencing has been used to determine the microbiome of different tracts; however, its role in COME has not been widely investigated. Methods: Middle ear fluid (MEF) samples were collected from 75 children less than 5 years-old with COME during 2016-2017, with indication for surgical treatment. Fluids were collected during myringotomy to place the ventilation tube. Samples were submitted to nucleic acid extraction for qPCR and 16S rRNA deep sequencing. qPCR was used for specific detection of classic pathogens (Sp, Hi, and Mc) and 16S rRNA deep sequencing was used to assess the microbiome of MEF. Results: qPCR revealed the presence of bacterial pathogen in 67/75 (89.3%) patients. Hi was the most prevalent bacteria found in 59 (78.7%) patients, followed by Sp in 20 (26.7%). Co-infection by Hi and Sp was found in 16 (21.3%). Mc was found in 10 (13.3%), but in 8 patients it was found concomitant with Hi. Sequencing results confirmed the presence of bacterial DNA in all samples, with >98% concordance with qPCR. Sequencing analysis of MEF revealed the presence of at least 16 genera with >0.1% mean relative abundance. Conventional pathogens represented <25% of bacterial DNA found in our samples. The most relative abundant genera were Corynebacterium (31%), Haemophilus (17%) Alloiococcus (15%), Propionibacterium (10%), Staphylococcus (9%) and Streptococcus (6%). Other Gram-negative bacilli comprised 5%. Miscellaneous other bacteria, including anaerobes represented <1%. Conclusions: Although qPCR targeting conventional pathogens associated with COME was positive in 89.3% of patients, sequencing revealed other potential players. In contrast with other studies, our data showed that conventional pathogens represented <25% of bacterial DNA, with >75% of detected DNA belonging to other bacterial genera, especially Corynebacterium, Propionibacterium, Alloiococcus and staphylococci. Results suggest that COME may be the product of the interaction of the host response with a complex bacterial community. Understanding the mutual interaction of this bacterial community may be relevant to better understand the management of children with these conditions.
Abstract:
Pre-Admission Antibiotic Therapy and its Effect on Outcome in Cases of Mastoiditis: Implication for Antibiotic Stewardship

M. Patel, N. Skalidi, S. King, K. Tzifa; Birmingham Women's and Children's NHS Fndn. Trust, Birmingham, United Kingdom

Background: Mastoiditis is a complication of acute otitis media with potential for intracranial involvement and increased morbidity. There is concern that restricting antibiotic use for otitis media, as a result of improved antibiotic stewardship in primary care may lead to more complications of mastoiditis. The aim of this study is to investigate the effect of preadmission antibiotic therapy on prognosis in paediatric patients with acute mastoiditis and the differences in morbidity in patients less than two years old.

Methods: Records from the Birmingham Children’s Hospital admissions database, from 2012-2016 inclusive, with diagnosis of acute mastoiditis were retrieved and reviewed retrospectively. The data were analysed for duration of symptoms, preadmission antibiotic therapy, delay in antibiotic administration, laboratory results, management of complications and duration of hospitalisation.

Results: 77 patients were included. 32 patients (41.5%) had received antibiotic treatment before admission while 45 patients (58.5%) had not. The mean duration of symptoms prior to the admission was 4.1 days (SD=4.8) in the untreated group and 6.3 days (SD=4.7) in the group who received antibiotics. Preadmission antibiotic therapy did not significantly influence clinical outcomes (need for surgery or neurological complications) (p=0.915) or length of hospitalization (p=0.336) between the two groups. Similarly, preadmission antibiotics did not influence the clinical outcome in patients less than two years old (p=0.928). No significant difference was found in regards to complication rates in the age group of 0-23 months and 2-16 years (p= 0.657). Interestingly, patients who had a delayed prescription of antibiotics (after 4 days of symptoms) or did not receive a second line antibiotic due to treatment failure, were associated with complications (p=0.021) with a higher significance in the over two years old age group (p=0.003). High CRP values were observed in patients who had preadmission antibiotics but they were not predictive of a worse clinical outcome (p=0.665). Conclusions: Preadmission antibiotic therapy does not influence the clinical outcome in children with acute mastoiditis, including children <2 years of age. High CRP values do not predict a worse outcome. In those who received preadmission antibiotics, delay resulted in worse outcome. This patient group requires further investigation.
Abstract Title:
The Dark Side of Meningitis: All that We Do Not Know from 13 Years of Surveillance in Bangladesh

Primary Author Block:

Abstract Body:
Background: Meningitis is a major cause of illness and death, specifically in resource-poor countries. However, limited data on aetiology and lack of credible burden estimates of meningitis from South Asia hinder effective treatment and prevention strategies. We initiated a surveillance in 2004 in Bangladesh to monitor epidemiology of meningitis in <5 children. Methods: Between 2004 - 2016, we prospectively enrolled and collected cerebrospinal fluid (CSF) samples from suspected meningitis patients under the age of 5 years, based on WHO definitions, in three pediatric hospitals. Total number of leukocytes/mm3 (TLC) were determined for all samples; culture, latex agglutination test (LAT) and qPCR with primers to detect Neisseria meningitidis, Streptococcus pneumoniae, Haemophilus influenzae and Group B Streptococcus were performed on all samples with >9 TLC. Outcome of these cases were noted. Results: In the 13 years, 23,140 CSF samples were collected from suspect meningitis patients, of which 8,125 samples had >9 TLC. A bacterial etiology could only be detected in 1,585 (20%) cases; 337 of 4,306 (8%) samples with TLC 10-99, 383 of 2,008 (19%) samples with TLC 100-499, and 865 of 1,811 (48%) samples with TLC ≥500 could be attributed to an etiology. Overall, no bacterial etiology could be detected in 6,540 of 8,125 (80%) cases with TLC of >9 and most notably, in 946 of 1,811 (52%) of samples with >499 TLC. Within etiology-positive cases (n=1,585), 59% were discharged and 5% died and similarly, within etiology-negative cases (n=6,540), 62% were discharged and 6% died. Conclusions: This study presents the largest and longest surveillance study of meningitis in Bangladesh. While aetiology-positive samples have always been the prime focus, and disease estimates are often based on them, it is important to acknowledge the burden of meningitis whose causative agents are unknown. Despite the use of different diagnostics, including qPCR, we were not able to attribute aetiology to a large number of cases, including those with ≥500 TLC, which are highly probable cases of bacterial meningitis. It is imperative to develop methods to decipher the causative agents of these aetiology-negative cases; whether the pathogens are common suspects or not, the data generated will guide evidence-based intervention strategies to fight meningitis.
Abstract:
Early Diagnosis of Measles for Better Management and Control of Infection

Primary Author Block:
G. Fatima1, S. Kainat2, S. Kazmi3; 1Civil Hosp., Karachi, Pakistan, 2Civil Hospatal, Karachi, Pakistan, 3Dadabhoy Inst. of Higher Ed., Karachi, Pakistan

Abstract Body:
Background: Measles is a highly contagious vaccine preventable viral disease which affects the respiratory system of children under 14 years of age. The disease and is endemic due to improper vaccination and poor living conditions in many countries of the world including Pakistan. Vaccination provides lifelong immunity to the children. This study was designed to know the best laboratory diagnostic test for early diagnosis of measles virus infection to facilitate better management of disease and prevention of its complications like SSPE. Methods: A total of 106 blood samples and nasal secretions were collected in viral transport medium (VTM) and kept at -80°C till tested. from clinically diagnosed cases of measles with history of high grade fever and typical symptoms of measles (running nose, conjunctivitis and rashes), between the age of 2-12 years, visiting Pediatric units of Civil Hospital, Karachi. Measles virus specific IgM antibodies in blood samples by ELISA and measles virus RNA in nasal secretions by real time PCR, and genotyping of virus was also carried out at NIH - Islamabad. Demographic data including age, gender, socioeconomic status, especially vaccination against measles and duration of fever were recorded. Results: Out of 106 blood samples of patients, 48 (45.3%) children exhibited measles specific IgM antibodies. Among measles positive children, 18 children had received measles vaccination. Measles virus RNA was detected in all 106 samples of nasal secretions. Genotype analysis indicated Measles virus genotype B2 as the most prominent causative strain. Among the vaccinated group of 18 children, only 6 (33.3%) were positive for measles IgM, while among the unvaccinated group 42 (47.7%) tested positive for measles specific IgM, All measles specific IgM positive children (N=48) had history of fever for three days and more while others had fever of less than three days. Females (52%) were affected slightly more than males (48%). Conclusions: Anti-Measles IgM test can be used for early diagnosis of measles after three days of onset of fever for better management. A negative test does not exclude measles. Measles virus RNA can be detected in nasal secretion irrespective of duration of fever. Measles infection in vaccinated children reflects on the efficacy of vaccines in Pakistan. The poor quality of routine vaccination program plus lack of proper surveillance system are some of the factors responsible for rise in measles cases in Pakistan.
Abstract Title:
Association of Intestinal Helminthic Infection, Atopy & Allergic Disorder among Primary Sch. Children

Primary Author Block:
D. D. Abera, A. Tsegaye; Addis Ababa Univ., Addis Ababa, Ethiopia

Abstract Body:
Background: Intestinal helminthic infections have been suggested to play protective role from allergic sensitization & atopic diseases. There is a concern that deworming could increase the prevalence of atopic disease in endemic populations. However, there is inconsistent & little information about the relationship between helminthic infection and allergic disease in the case of deworming set up in Ethiopia

Methods: A cross sectional study was conducted among 526 school children aged 5 to 14 years from three selected government primary schools in Sululta woreda. Information on socio-demographic characteristic, associated risk factors & allergic symptoms were obtained using questionnaire, moreover allergen skin tests to Dermatophagoides pteronyssinus & Blatella germanica (cockroach) were performed to assess atopy status. From all children, fresh stool samples were collected & processed by direct wet mount, Kato-Katz technique & formol-ether concentration technique

Results: Of the total 526 school children 58.2% (306) were females. Overall 24% (n=126/526) had questionnaire based allergic symptoms while 5.1 % (n=27/526) had skin prick test reactivity, 16.9% of them (n=89/526) had intestinal helminthic infection. All helminthic infections were with low intensity level. There was no association between helminthic infection & allergic symptoms (OR=1.30, 95% CI=0.778-2.171, P=0.317). Ascaris lumbricoides infection was positively associated with skin test reactivity (AOR=4.307, 95%CI=1.143-16.222, P=0.031). Atopy was significantly associated with increased allergy symptoms (AOR=2.787, 95%CI=1.253-6.197, P=0.012). Short term deworming had no effect on atopy but has a protective effect on allergic symptom

Conclusions: Low intensity & low prevalence of helminthic infection in our findings may have contributed to the non-significant association of allergy & helminthes infection; however, Ascaris lumbricoides was positively associated with atopy. Further longitudinal study is recommended to examine the mechanism of Ascaris lumbricoides infection for the development of atopy.
Abstract Title:
Cluster of Lymphadenitis Due to Nontuberculous Mycobacterium in Children and Adolescents 8-15 Years of Age

Primary Author Block:
H. Lee1, K. Yun2, K. Park1, J. Park1, H. Kim1, J. Paik1, W-J. Jeong1, Y. Jung1;  1Seoul Natl. Univ. Bundang Hosp., Seongnam, Korea, Republic of, 2Seoul Natl. Univ. Children's Hosp., Seoul, Korea, Republic of

Abstract Body:
Background: Nontuberculous mycobacterial (NTM) lymphadenitis is a widely under-recognized entity, and data on the true burden in children are unavailable. However the overall prevalence seems to be increasing, possibly related with increase in diagnosis. We report an interesting cluster of NTM lymphadenitis among nine children during a six-month period. Methods: This study includes children diagnosed with NTM lymphadenitis from November 2016 to April 2017 in South Korea. Electronic medical records were searched for clinical and laboratory manifestations, and pathology slides were reviewed for lymph node biopsy specimens. AFB culture was done and detection and sequencing for genes rpoB and hsp65 were done using PCR amplification. Results: During the six-month period, nine children presented as NTM lymphadenitis. All subjects were 8-15 years of age, previously healthy, male subjects and had unilateral, nontender, cervicofacial lymphadenitis for more than 3 weeks with no response to empirical antibiotics. None of the subjects complained of systemic symptoms including fever, myalgia, fatigue and weight loss. Three children had 2 lesions, and lesions were located in submandibular (N=7), preauricular (N=3) and submental (N=1) area and violaceous skin color change was seen in five subjects. Lymph node biopsy, showed chronic granulomatous inflammation (N=8) with caseous necrosis (N=3), focal necrosis (N=3) and one had inadequate specimen. Interferron gamma assay was negative in all subjects. Tb PCR was negative for all subjects, rpoB and hsp65 PCR was positive for 2 subjects and 1 subject showed growth on AFB culture with M. haemophilum. According to survey on history of exposure, although there was various common exposure sources between subjects, all reported to attend the same sports complex. Surgical excision was done in 4, medication in 3 subjects, and 2 were on medical observation. Conclusions: NTM lymphadenitis is rare, but increasing in detection. NTM lymphadenitis may occur in children and adolescents, the diagnosis requires a high index of suspicion and microbial identification is difficult. Further studies on the epidemiological and clinical features are needed.
Abstract Title:
Saffold Virus: A Lesser-Known Emerging Human Cardiovirus in Acute Flaccid Paralysis, India

Primary Author Block:
H. Maan, T. Dhole, J. Singh; Sanjay Gandhi Post-Graduate Inst. of Med. Sci., Lucknow, India

Abstract Body:
Though the wild polioviruses have been eradicated from India, the cases of nonpolio acute flaccid paralysis (NP-AFP) of undefined etiology continues to occur in the region. Saffold viruses (SAFV), a recently discovered member of the Cardiovirus genus belonging to family Picornaviridae had been shown to cause infection of the central nervous system. No studies from India so far have recognized the detection and identification of SAFV. First, sequence independent single primer amplification (SISPA) method was performed on culture supernatants of one stool sample NP-AFP inoculated in green monkey kidney cells and that had produced uncharacterized cytopathic effects. Random PCR amplification products produced as a result of SISPA were subsequently cloned and sequenced, on subsequent sequence analysis revealed 78-85% identity to SAFV encoded proteins. The SAFV presence in NP-AFP sample explored by SISPA technique given us the opportunity to prospectively detect and characterize SAFV in NP-AFP cases of unknown etiology for SAFV. Thus, a total of 1116 stool samples collected from AFP cases in Uttar Pradesh, India, between May 2015 and June 2017, tested negative for virus isolation by WHO algorithm, were subjected to SAFV screening targeting the 5′ untranslated region (UTR). The viral genotypes were also established by VP1-gene amplification and sequencing. 108 (9.6%) samples tested positive for SAFV detection by 5′UTR assay. The SAFV positive samples for further characterization based on VP1 gene and sequencing revealed identification of 70 SAFV strains in NP-AFP children belonging to seven different genotypes as SAFV-1 (n=6;8.5%), SAFV-2 (n=6;8.5%), SAFV-3 (n=10;14.2%), SAFV-4 (n=23;32.8%), SAFV-5(n=3;4.3%), SAFV-6 (n=7;10%) and SAFV-7 (n=15;21.4%). Co-infection in SAFV positive samples with other viruses such as parechovirus, enterovirus and cosavirus were observed for eight AFP cases. The SAFV infection appeared higher (67.1%) in younger children than 6 years of age, showed the seasonality distribution with the highest rate of isolation between late summer and early fall of winter. The SAFV positive AFP cases were from the different districts of Uttar Pradesh such as: Badaun, Barabanki, Hardoi, Azamgarh, Raibareli, Rampur, Sitapur, Lucknow and Kheri region of the state. This study documents the first report of SAFV detection from India and provides the prevalence of saffold virus with the emergence of SAFV-4 and SAFV-7 as the most common type of SAFV in India.
Abstract Title:
Outstanding Abstract Award: Early Bayesian Dose Adjustment of Vancomycin in Children : A Randomized Controlled Trial

Primary Author Block:

Abstract Body:
Background: Methicillin-resistant staphylococcal infections are still a global burden. Area under the curve (AUC) of the serum concentrations versus time over 24 hours to minimum inhibitory concentration (MIC) ratio is the pharmacokinetic (PK) parameter that best predicts vancomycin efficacy. An AUC0-24/MIC ≥ 400 is the admitted target for vancomycin therapeutic drug monitoring (TDM). Its therapeutic range is narrow and difficult to achieve because of a wide interindividual variability, especially in children. The aim of this study was to assess if an early Bayesian dose adjustment of vancomycin would increase the rate of target attainment, in the first 24 hours of treatment.

Methods: We conducted an open-label single-center prospective randomized controlled trial in two parallel groups : the routine care were compared with an early vancomycin TDM (3 hours after treatment initiation) followed by an early Bayesian dose adjustment. The Bayesian estimation was made using a previously published population PK model that included age, body weight and serum creatinine as covariates. The primary study endpoint was the proportion of patients of each group achieving the therapeutic range of vancomycin at the 24th hour of treatment, defined by a ratio of AUC0-24/MIC ≥ 400 and ≤ 800 h. Results: Among the 99 patients aged 3 months to 17 years randomized in intensive care unit, gastroenterology and immunohematology units, 82 had analyzable data. All of them received a continuous infusion of vancomycin. The proportion of patients who achieved the pharmacological target of vancomycin within the first 24 hours was 85% in the Bayesian group versus 57% in the control group (p=0.007). In the Bayesian group, vancomycin dose was increased in 79% of patients, decreased in 8% of patients and was not modified in 5 patients (13%). There was no statistically significant difference between the two groups regarding iatrogenic events. Conclusions: This study is the first to prospectively assess the contribution of early Bayesian dose adjustment of vancomycin. It increased the proportion of children achieving vancomycin pharmacological target at the 24th hour of treatment.
Abstract Title:
Prediction of Cd8+ T Cell Epitopes of Pedv Spike Protein Using Immuno-Informatic Approach

Primary Author Block:
K. Polyiam1, M. Ruengjitchatchawalya2, T. Laomettachit2, K. Poomputsa1, P. Mekvichitsaeng3, Y. Roshorm1; 1Biotechnology, Bangkok, Thailand, 2Bioinformatics and Systems Biology, Bangkok, Thailand, 3Pilot plant Dev. and Training Inst., Bangkok, Thailand

Abstract Body:
Porcine Epidermic Diarrhea (PED), which is caused by Porcine Epidemic Diarrhea Virus (PEDV), is a huge trouble and causing economic loss in swine industry worldwide. Genome of PEDV is positive-sense, single stranded RNA that exhibits highly genetic variation; thus, a universal vaccine is needed to protect pigs from global strains of PEDV. We aim to generate a universal PEDV vaccine by combining multiple epitopes derived from different strains of PEDV into one antigen. In this study, we identified CD8+ T cell epitopes of Spike (S) protein derived from various PEDV strains using immuno-informatic tools. Amino acid sequences of PEDV S protein were retrieved from NCBI and 924 accession numbers were obtained. Using SeaView program, sequences of S protein were grouped into 14 groups based on sequence similarity. Consensus sequence of each group was generated using Unipro UGENE program and then used for CD8+ T cell epitope prediction. NetMHC version 4.0 and NetCTLpan version 1.1 were used to predict CD8+ T cell epitopes that can bind to swine leukocyte antigen class I alleles (SLA-I). Using NetMHC, putative epitopes were selected based on percentile ranking score and MHC-I binding affinity and 25 predicted epitopes were obtained. When predicted by NetCTLpan, 19 predicted epitopes were obtained by selecting based on MHC prediction, TAP prediction and cleavage prediction scores. Epitopes obtained from in silico prediction will be put together as a string of epitopes and potency to stimulate CD8+ T cell response of each epitope will be further studied.
Abstract Title: Outstanding Abstract Award: Pilvax - A Novel Peptide Delivery Platform for the Dev. of Mucosal Vaccine

Primary Author Block:
C. J. Tsai, J. M. Loh, T. K. Proft; The Univ. of Auckland, Auckland, New Zealand, Auckland, New Zealand

Abstract Body:
Background: Vaccines remain the most cost-effective and feasible means of infectious disease control in the community. Vaccine development has evolved from killed or live attenuated microorganisms to well-defined synthetic vaccines based on individual proteins or peptides. However, peptide antigens are usually poorly immunogenic and sensitive to proteolytic degradation, and thus require conjugation to carrier proteins, and administration with potentially toxic adjuvants. Lactic acid bacteria have become promising vehicle for delivering active molecules to mucosal sites. We propose that the group A streptococcus (GAS) pilus structure expressed on the surface of the non-pathogenic surrogate Lactococcus lactis can be an ideal carrier for antigenic peptides. Pili (sing. Pilus) are hair-like protrusions from the cell surface. GAS pilus usually consists of 3 structural proteins that are highly immunogenic.

Methods: We identified several regions within the backbone pilin(Spy0128) of a serotype M1 strain that can be replaced with the model peptide OVA324-339. The modified pilus structure was expressed on the surface of L. lactis. Pili assembly and display were analysed by western blot and quantified by flow cytometry using specific anti-M1_Spy0128 antibodies. Mice were immunised intranasally with the resulting L. lactis live vaccines, and serum, saliva and bronchoalveolar lavage fluid samples were obtained and analysed for Spy0128 and Ova-specific antibodies. Results: Insertion of the Ova324-339 peptide into the βE-βF, the β3-β4 or β9-β10 loop regions of Spy0218 resulted in assembled pili. Intranasal immunisation of mice with the resulting recombinant L. lactis strain produced strong Ova-specific antibody responses in serum and bronchoalveolar fluid. We have further shown that it is possible to insert more than one peptide into the same integration site, and peptide epitopes can be incorporated into structurally similar but antigenically different pilus structure, expanding the versatility of the PilVax platform. Conclusions: The PilVax technology provides a novel system for developing peptide vaccines for mucosal delivery. Other benefits of PilVax include low production costs, as no chemical peptide coupling is required and the modified bacteria can easily be shipped in lyophylised form. Furthermore, no potentially toxic adjuvants are required and the vaccine can be delivered needle-free to a mucosal site. These advantages are highly desired in developing countries, where efficacious vaccines are most needed.
Determinants of Transplacental IgG Transfer in HIV-Infected Pregnant Women

Primary Author Block:

Abstract Body:
Factors that modulate the transplacental transfer of maternal IgG are not fully defined. In HIV-infected women, the transplacental transfer is impaired, offering a unique setting to define clinical, placental, and antibody determinants of IgG transfer. We measured HIV and standard vaccine antigen-specific IgG serum concentrations in 167 HIV-infected women and their infants in US and Malawi cohorts by a binding antibody multiplex assay. The measured IgG antibodies were: HIV Env antigens, tetanus toxoid, pertussis toxin, influenza, rubella virus capsid, hep B surface antigen, RSV surface antigen, and diphtheria toxin. Transplacental IgG transfer efficiency was calculated as the infant cord blood IgG concentration over maternal serum IgG concentration X 100. Maternal total serum IgG levels were measured by ELISA. The Fc region glycan profile of IgG antibodies was measured by capillary electrophoresis. RNAseq was performed on placental biopsy samples. From 167 HIV-infected women, 3 patterns of maternal transplacental IgG transfer phenotypes were observed: efficient, variable, and poor IgG transfer. 11 pairs had efficient IgG transfer against most tested antigens, whereas in 82 pairs the IgG transfer was variable from one antigen to another. Finally, 74 pairs had poor IgG transfer across most tested antigens. Maternal plasma viral loads and total serum IgG levels were statistically significantly higher in U.S. HIV-infected women with poor transplacental IgG transfer (p < 0.02, p < 0.0001, respectively). Maternal gp120 and V3-specific IgG serum magnitude responses negatively correlated with transplacental IgG transfer of gp120 and V3-specific IgG, but this was not observed for other antigen-specific IgG. Poorly transferred gp120-specific IgG had higher frequencies of Fc region fucosylation (p <0.0001) compared to efficiently transferred pertussis and tetanus toxoid-specific IgG. Interestingly, placental Fc receptor expression levels were variably expressed in women with variable transplacental IgG transfer. Fc receptor neonatal (FcRn) expression ranged from 1.01-7.1 reads per kilobase million expression levels in HIV-infected women with variable transplacental IgG transfer compared to 2.3-6.5 in women with poor transfer. In HIV-infected women, the transplacental IgG transfer efficiency can have efficient, variable, and poor phenotype. IgG characteristics such as serum magnitude, Fc region glycan profiles, and placental Fc receptor expression levels are all important for transplacental IgG transfer efficiency.
Development of Single Dose Vaccines for Emerging Infectious Diseases, Preclinical Data for Novel Ebola, Lassa Fever and Zika Vaccines

Primary Author Block:
F. Guirakhoo, N. McCurley, R. Basu; GeoVax, Inc., Smyrna, GA

Abstract Body:
Background: GeoVax MVA platform technology is built on a 4th generation MVA vector system that is improved for high expression and stable transgenes during manufacture. It has the advantages of being a live replication-competent vector in avian cells for manufacturing, yet replication-deficient in mammalian cells for vaccination, thus inherently safe. Importantly, MVA vaccines elicit protective T cell as well as antibody responses in animals and humans. The MVA platform can be combined with the potent immunogenicity of Virus Like Particles (VLPs) (e.g. MVA-VLP-HIV, -Ebola, -Marburg, -Sudan, and -Lassa fever) or be used to express proteins in their native conformations (e.g. MVA-NS1-ZIKA) enabling vaccines that induce full protection after a single dose. In this work, we present preclinical data for vaccines against Ebola, Lassa fever and Zika and show that a single dose intramuscular (IM) inoculation can protect immunocompetent animals against a lethal challenge. Methods: MVA-VLP vaccines were constructed for Ebola (using VP40 and GP), Lassa fever (Z and GPC) and Zika (NS1, eliminates the risk of Antibody Dependent Enhancement, ADE, of infection associated with other vaccines based on the envelope antigens). Vaccine viruses were characterized in vitro for genetic stability, VLP formation (Electron microscopy), sequencing and WB. Inoculations were done in rodent species (mouse, guinea pigs and hamsters) as well as non-human primates. Immunogenicity (ab response) and T cell responses were determined to assess functionality and correlation of protections. Results: Zika: A single immunization of MVA-NS1 Zika by the IM route provided 100% protection against a lethal challenge dose of a neurovirulent ZIKV delivered directly into the brain. All control animals lost weight and died within 1 week. Efficacy of MVA-VLP Ebola vaccine candidate was determined in Guinea pigs, hamsters and rhesus monkey lethal challenge models (BSL4). A single dose of MVA-VLP-LASV protected mice against a lethal challenge delivered directly into the brain. Discussion: Three different vaccines provided full protection after a single dose against 3 different family of viruses using lethal challenge models. These data demonstrate a broad utility of the platform for vaccine against infectious diseases especially suited to combat epidemic in resource constrained countries.
Abstract Title:
Using Human Monoclonal Antibodies to Better Understand Influenza Virus Evolution
Primary Author Block:
S. Diaz¹, S. Zost², S. Hensley²; ¹Univ. of Puerto Rico, Mayaguez, Mayaguez, PR, ²Univ. of Pennsylvania, Philadelphia, PA
Abstract Body:
Influenza A viruses (IAVs) have constituted a threat to public health for centuries. Two subtypes of IAVs, H1N1 and H3N2, circulate in humans and cause annual epidemics with high morbidity and mortality. The hemagglutinin (HA) glycoprotein of IAVs is the major target of neutralizing antibodies (Abs), which are thought to mediate protective immunity following infection or vaccination. However, in a process called antigenic drift, IAVs rapidly accumulate HA mutations that allow the virus to escape Ab-mediated neutralization. This evasion of pre-existing immunity is the reason that IAV vaccines must be updated on a near-annual basis, and occasionally vaccine strains can be mismatched with circulating strains. This was the case during the 2014-15 influenza season, when a new clade 3C.2a H3N2 strain with a novel glycosylation site emerged. Previous work by our lab has shown that this glycosylation dramatically reduces the ability of Abs in human sera to bind and neutralize the H3N2 viruses. It is unclear, however, whether Abs from some individuals were able to cross-react with this glycosylated strain, and if so, where these more cross-reactive Abs bind. In this work, we address this question by examining a panel of monoclonal Abs (mAbs) elicited by an H3N2 vaccine from 2010 via ELISA. Although many Abs failed to recognize the glycosylated H3, some bind this antigenically distinct strain, suggesting that they are broadly reactive. Understanding how these broadly-reactive mAbs are elicited and recalled is essential to improve vaccine efficacy.
Intranasal Dosing of Rabbits: Dose Volume and Handling of Dosed Animals

S. Rose, T. Plachta, J. Justen, K. Nelson; MPI Res., Mattawan, MI

Delivery of vaccine therapy is traditionally done via injection. However, vaccine delivery at the site of mucosal infection is potentially more directly efficacious, enhancing the local immune response. One such site is the upper respiratory mucosa, spurring investigation of targeted intranasal vaccine delivery. Proper consideration of animal models for mucosal delivery of potential therapeutics is a critical component of the preclinical evaluation of mucosal immunization. Here we address the evaluation and dosing of the rabbit for upper respiratory mucosal immunization. While often used for vaccine safety studies, rabbit models do not have large nasal cavities and thus dose volume may be a significant factor. Given these issues, an investigation of the appropriate volume for nasal dosing in this less traditional model species was conducted. Rabbits were intranasally dosed with dyed saline, using a range of restraint methods and a maximal dose level was identified. A subset of dosed animals was necropsied and lungs evaluated for macroscopic and microscopic evidence of dye or respiratory lesions. While dye was noted in the upper respiratory tract and the lungs of multiple animals, with increasing incidence at high dose volumes, there was no microscopic evidence of dye or of lung or tracheal lesions. This evidence suggests that high dose volumes of intranasally dosed material will potentially be aspirated by dosed rabbits. However, aspiration of the relatively small amounts of fluid, in the absence of a specific irritant or inflammatory component to the test material, does not seem to cause microscopically visible lesions in the lower respiratory tract.
Comparable Serologic Responses to Two Different Combinations of Inactivated Hav Vaccines in Hiv-Positive Patients During the Acute Hepatitis A Outbreak

K-Y. Lin1, S-M. Hsieh2, W-H. Sheng2, Y-C. Lo3, Y-C. Chuang2, A. Cheng2, S-C. Pan2, G-J. Chen2, H-Y. Sun2, C-C. Hung2, S-C. Chang2; 1Natl. Taiwan Univ. Hosp. Jin-Shan Branch, New Taipei City, Taiwan, 2Natl. Taiwan Univ. Hosp., Taipei, Taiwan, 3Ctr.s for Disease Control, Taipei, Taiwan

Background: Hepatitis A virus (HAV) vaccination has been recommended for at-risk HIV-positive individuals. However, the reemerging hepatitis A outbreaks worldwide have constrained vaccine supply. The limited supply of vaccines raises concerns about interchangeability of different HAV vaccines, but the serologic responses to different 2-dose combinations of inactivated HAV vaccines have rarely been evaluated. Methods: In response to an outbreak of acute hepatitis A, HIV-positive individuals testing negative for HAV IgG between 1 June 2015 and 30 September 2016 were advised to receive 2 doses of HAV vaccine combinations with of HAVRIX® or VAQTA® at 6 months apart. The primary outcome was serologic response in intention-to-treat (ITT) with last-observation-carried-forward (LOCF) analysis at weeks 28-36. Results: In this prospective observational study, 946 HAV-seronegative, HIV-positive individuals for who completed 2-dose HAV vaccination were included: 395 received HAVRIX® as the first dose followed by VAQTA® (HAVRIX®-VAQTA®) and 551 received 2 doses of VAQTA® (VAQTA®-VAQTA®). In ITT with LOCF analysis, the seroconversion rate at weeks 28-36 was 82.3% for the HAVRIX®-VAQTA® group and 80.9% for the VAQTA®-VAQTA® group (difference, 1.3%; 95% CI, -6.3% to 3.7%). Before administration of the second dose, the serologic responses increased over time and were better enhanced by VAQTA® compared with HAVRIX® (53.0% versus 32.4%, P <0.05). The factors associated with seroconversion at weeks 28-36 were a younger age (per 1-year decrease, AOR, 1.06; 95% CI, 1.02-1.11), and a higher CD4 count (per 10-cell/mm3 increase, AOR, 1.04; 95% CI, 1.02-1.05) and undetectable plasma HIV RNA load at vaccination (AOR, 2.92; 95% CI, 1.38-6.18). Conclusions: While administration of the first dose with VAQTA® elicited faster and better serologic responses overtime than with HAVRIX®, serologic responses to vaccine combinations of HAVRIX®-VAQTA® versus VAQTA®-VAQTA® were similar during the outbreak of acute hepatitis A.
Session Title: CIV06 - Vaccines and Immunization Science: Viruses and Pertussis

Abstract Title: Serum Cross-Reactivity Following Oral Immunization of A Norovirus Vaccine in Ferrets and Humans

Background: Noroviruses (NoV) are the leading cause of epidemic acute gastroenteritis and foodborne diarrheal disease in humans, particularly in confined environments such as schools, cruise ships, and hospitals. There are no approved vaccines against NoV. One primary obstacle to successful NoV vaccination is the great degree of antigenic diversity among strains due to rapid viral evolution.

Methods: A clinical trial using an oral recombinant adenovirus-based vaccine expressing norovirus VP1 from strain GI.1 (Norwalk) was performed in 2017 (NCT03125473). Serum from immunized subjects was run in IgA and IgG ELISAs using plates coated with VLPs from genotypes GI.1, GI.3, or GI.4. Similarly, ferrets were immunized with an oral adenovirus-based vaccine expressing norovirus VP1 from genotype GII.4, strain Sydney 2012. VLPs from strains 2002, 1995 from genotype GII.4 and GII.17 were tested in IgG and IgA ELISAs. Results: Significant cross-reactivity to GI.3 and GI.4 VLPs was observed in human serum samples vaccinated with GI.1, with negligible cross-reactivity to GI.4. Remarkably, in ferrets vaccinated with GII.4, strain Sydney 2012, overall IgG titers in serum 56 days after vaccination increased 7-fold to homologous GII.4 Sydney VLPs, 3 and 2-fold to the 1995 and 2002 strain-VLPs, respectively, and 6-fold to GII.17 VLPs. For serum IgA, overall titers increased 3-fold against the homologous Sydney 2012 VLPs; 1.3-fold against 2002 VLPs and 4-fold against 1995 VLPs. Importantly, the titers against genotype GII.17 increased almost 8-fold. Conclusions: Although vaccination with the Norwalk strain did not result in significant cross-reactivity against the GII.4 genotype, a higher degree of heterologous cross-reactivity for animals vaccinated against the GII.4 genotype was observed. This is important clinically since strains of the GII.4 genotype are responsible for pandemic waves. These results suggest that oral delivery of a norovirus antigen has the potential to elicit an immune response that can recognize heterologous challenge strains. Importantly, this may help reduce the need for periodic antigen modification in a potential NoV vaccine.
Abstract Title:
DNA Vaccine Encoding Hantavirus Gc and Lamp Induced Long-Term Immune Protection

Primary Author Block:
K. Yang, D. Jiang, G. Zhang, Y. Li, G. Xuan, Q. Meng, N. Liu, A. Ping, M. Fang, J. Zhang; the Fourth Military Med. Univ., Xi'an, China

Abstract Body:
Background: Hantavirus is a single-stranded RNA virus from Bunyaviridae, infection of which result in hemorrhagic fever with renal syndrome (HFRS) characterized by fever, hemorrhage and impairment of renal function. Hantaviral diseases with high case fatality rate threaten human health and safety due to the absence of broadly effective antiviral treatments or vaccines. pVAX-LAMP/Gn, a DNA vaccine encoding Hantavirus structural antigen Gn fused with lysosome-associated membrane protein (LAMP), was previously proved to efficiently establish long-term immune protection in mice. In present study, pVAX-LAMP/Gc was developed as a novel candidate, showing promising efficacy. Methods: Two eukaryotic vectors were constructed as experimental groups named pVAX-Gc and pVAX-LAMP/Gc. pVAX and pVAX-LAMP were set as control groups, inactived vaccine as positive control. After sequencing and target proteins expression being successfully identified, high purified endotoxin-free plasmids were extracted. Female adult BALB/c mice were divided into 5 groups and immunized with the recombinant plasmids, respectively. BALB/c mice were immuned every three weeks for three times. The booster immunization was applied after half a year for long-term immunity analysis. Blood was taken from caudal vein two weeks after every immunization. The humoral responses elicited by Hantavirus Gc were measured by specific antibody and neutralizing antibody valence. The cellular responses were measured by ELISpot assay. To measure the protective efficacy, virus challenging in vivo were conducted by viral load detection after prophylactic immunization. Results: Indirect ELISA results showed that the specific antibody titer of pVAX-LAMP/Gc group was higher than pVAX-Gc and inactivated vaccine group (p<0.05). After three times immunization, average antibody titer of pVAX-LAMP/Gc can reach to 1:2560. The result of ELISpot suggested the IFN-γ secretion frequency of pVAX-LAMP/Gc group increased by two or three times, whereas pVAX-Gc and inactivated vaccine had no significance. Conclusions: LAMP trafficking strategy greatly enhanced specific immune responses to Hantavirus envelope glycoprotein Gc. It helped to elicit strong humoral and cellular response but did no harm to organs and tissues. Further investigations are warranted in the future to explore the promising strategy on other immunogenic Hantaviral antigens.
Abstract Title:
Development of A Novel Yeast Derived Dengue Oral Subunit Vaccine

Primary Author Block:
J. Bal1, N. N. Luong2, J. Chun1, K-K. So3, Y-H. Ko3, J. Park3, Y-S. Jang3, D-H. Kim3; 1Inst. for Molecular Biology and Genetics, Jeonju, Korea, Republic of, 2Dept. of Biology, Hue Univ., Hue, Viet Nam, 3Inst. for Molecular Biology and Genetics, Dept. of Bioactive Material Sci., Jeonju, Korea, Republic of

Abstract Body:
The number of cases of dengue, a severe tropical neglected disease is constantly rising due to scarcity of effective treatment and licensed vaccines. Comprising of four genetically distinct serotypes, dengue virus causes serious life-threatening infections. A vaccine conferring simultaneous and durable immunity to all four DENV serotypes is the need of the hour. Oral administration represents an improvement in antigen delivery technology. This study was thus aimed at developing and exploring the efficacies of Escherichia coli heat-labile toxin B-subunit (LTB) fused dengue virus synthetic envelop domain III expressed whole Saccharomyces cerevisiae cells (WC) as well as cell free extracts (CFE) as possible oral vaccines in female Balb/c mice. Mice were orally administered per dose with 1.6 g fresh weight of recombinant WC and CFE extracted from equivalent amounts in two week intervals for four weeks followed by monitoring changes in systemic, mucosal and cellular immune responses through ELISA and FACS analysis. CFE stimulated a comparatively higher dengue-specific IgG and IgA than WC. Antigen-specific B-cell responses in isolated lymphoid cells from the spleen and Peyer's patches further showed higher immune response in CFE than WC. Furthermore, both CFE and WC stimulation rendered elevated cell mediated immunity as evidenced from raised cytokine levels such as that of interferon γ (IFN-γ) and IL-17 in the isolated splenocytes. Sera from CFE vaccinated mice successfully neutralized all four DENV serotypes and demonstrated markedly higher neutralizing titers compared to those from WC-fed mice. These results indicate a significant potential of CFE preparations from yeast cells expressing this dengue fusion protein to emerge as a safe, potent and inexpensive subunit dengue vaccine candidate.
Human Papillomavirus Sero-Prevalence and Sexual Attitudes Amongst A Cohort of Hiv Positive Women in the Gambia

Primary Author Block:
H. Bah Camara1, M. Anyanwu2, G. Mattiuzzo3, L. Gillard4, E. Wright5, P. Kimmitt1; 1Univ. of Westminster, London, United Kingdom, 2Edward Francis Teaching Hosp, Banjul, Gambia, 3Natl. Inst. of Biol. Standard and Control, Hertfordshire, United Kingdom, 4Viapath, Bedford Hosp., Bedfordshire, United Kingdom, 5Univ. of Sussex, Brighton, United Kingdom

Abstract Body:
Human papilloma virus (HPV) is known to be associated with cervical cancer (CC) and its precursors, squamous intraepithelial lesions (SIL). Studies have shown that CC are higher amongst human immunodeficiency virus (HIV) infected women and is often more aggressive and difficult to treat in this group. The extent of this correlation is such that the CDC and WHO have included CC to the case definition of acquired immunodeficiency syndrome (AIDS). In the Gambia, the national HIV sero-prevalence is 1.9%. However, HPV sero-prevalence amongst HIV positive women is unknown. The aim of the study was to determine HPV sero-prevalence, sero-conversion and persistence infection in a cohort of HIV positive women and to evaluate their attitudes towards safer sexual behaviours. HIV positive women (N = 28, Age 20-49 yrs) with a CD4+ ≥500/mm3 participating in a bigger HPV prevalence study were recruited into a cohort and followed up for 18 months. Serum, Pap smear and epidemiological data on sexual behaviour were collected at baseline and at 9 months interval. Serum samples were screened in triplicate against HPV 16, 18, 35, 51, 52 and 58 using pseudo-typed virus neutralisation assay. Cytology was carried out by two different cytologists and results confirmed by a pathologist. HPV sero-prevalence was found to be 53.6% (15/28) at baseline. Of the 15 participants tested positive, 8 were positive with a single serotype with HPV 51 accounting for 20.0% (3/15), 13.3% (2/15) HPV 52, and 16, 18 and 58 each at 6.7% (1/15). Seven (7) women were sero positive with multiple HPV serotypes with HPV52 being prevalent. Baseline cytology results showed 4 women with severe HSIL, positive for HPV 16 (2), HPV 51(2 with 1 with suspicion of CC invasion) and 3 participants with low grade cervical lesions. Follow up results showed: 1 CC with HPV 51, 1 HSIL with persistence HPV 51, 2 HSIL with HPV 16 and 1 HSIL with persistent positivity with HPV 51/ 52. 2 participants sero-converted at 9 months and 6 remaining sero-negative participants were found still sero-negative at the 18 months follow up visit. Persistent and new infection at18 months were observed more with HPV serotype 52. Epidemiological baseline data on sexual behaviours showed participants do not use condom during sexual intercourse. Subsequent data on sexual behaviours during follow up showed no change in attitude towards safer sex. This data shows that other oncogenic HPV types order than HPV 16 may also be responsible for HSIL/CC and there is the need to strengthen the education on safer sex practices in the prevention of HIV and HPV in the Gambia.
Session Title: CIV06 - Vaccines and Immunization Science: Viruses and Pertussis
Session Start Date Time: 6/10/2018 12:45:00 PM
Session End Date Time: 6/10/2018 2:45:00 PM
Session Primary Track: Clinical Infections and Vaccines
Abstract Control Number: 4340
Poster Board Number: SUNDAY - 747

Abstract Title:
Validation of Inactivated Ibdv Vaccine Prepared from Locally Isolated Variant Strain in Egypt
Primary Author Block:
S. Elmahdy1, N. Adel2; 1Central Lab. for Evaluation of Vet. Biologics- Ministry of Agriculture (CLEVB) laboratory, Cairo, Egypt, 2Vet. Serum and Vaccine Res. Inst. (VSVRI), Cairo, Egypt

Abstract Body:
Background: This study was carried out to validate inactivated infectious bursal disease virus (IBDV) vaccine which prepared from local isolate (Giza-2014) with Montanide ISA70VG as oil adjuvant. Validation of this vaccine requires the evaluation of its safety and efficacy. Methods: Validation was determined in two SPF chicken groups. Safety was applied in 1st group of 50 "3 weeks old" SPF chickens; (25 birds vaccinated with double dose and the rest kept as control). The efficacy evaluated in 2nd group of 50 "100 day old" SPF layer birds by given one dose of vaccine. The antibody response is measured from 3to 6 weeks after vaccination by SNT. Egg collected at 5to7weeks post vaccination for hatching. 30 progeny chickens are challenged at 21 day of age via eye drop with 103.5 EID50 / Dose of virulent strain. Protection percent was assessed by histopathological examination for bursa of fabricious at 3-4 days after challenge. Results: It revealed that; IBD vaccine under test was safe and effective with protection percentage 93 % and SNT antibody titers were ranged between( 7.5 -7.9). Bursa of fabricious of unvaccinated parents was affected. Conclusions: It was concluded that inactivated vaccine prepared from local isolated IBDV strain was valid and effective for use to control gumboro disease in Egypt.
Abstract Title:
Genetic Variability among the Circulating Avian Influenza Virus Serotype H9n2 and its Relationship with the Vaccine Failure in Commercial Poultry

Primary Author Block:
N. Siddique; Natl. Agricultural Res. Ctr., Islamabad, Pakistan

Abstract Body:
Background: Pakistan has experienced multiple incursions of avian influenza virus serotypes H7N3, H5N1 and H9N2 in commercial poultry since 1995. Although, no case of High Path (HP) AI has been reported from Pakistan since July 2008. Low Path serotype H9N2 appears to have become endemic and despite use of vaccines from multiple sources, numerous new outbreaks every year result in mortality among young chicks and significant decline in egg production in laying flocks. The study reported here reflects comparative evaluation of H9N2 isolates recovered during 1999-2017 from vaccinated or non-vaccinated chickens, backyard poultry and wild birds. Methods: The clinical specimens (Tissues & swabs) were subjected to virologic evaluation through embryonated SPF chicken egg inoculation. Subtype identification was determined by HA, HI techniques along with RT-PCR and QRT-PCR procedures. Antigenic cartography study of selected LP H9N2 viruses was performed to find out the immunogenic and antigenic potential. The purified PCR products were directly used for cycle sequencing and sequenced in a genetic analyzer. Phylogenetic analysis was conducted using MEGA -4. The gene sequences were submitted to GenBank Results: Phylogenetically the circulating LP H9N2 subtype revealed close relationship to the Iranian, Middle Eastern and Indian H9N2 lineages. The sequence analysis revealed noticeable genetic diversity including gene reassortment and attainment of large number of point mutations, specifically in HA and NA genes which may be affecting the compatibility of these viruses during cartographic analysis. Some of H9N2 isolates, having higher rate of point mutations, showed least compatibility during cartography assay and were symptomatically found to be associated with high mortality in the affected flocks. Sequence analysis also revealed two types of LP cleavage site motifs (RSSR & KSSR) at HA1 of these isolates, unique deletion of 6 amino acids at 225-230 positions, presence of α-2,6 linked sialic acid by retaining leucine instead of glutamine at 226 position, addition and deletion of glycosylation sites, antiviral drug sensitivities and unique PL motif (ESEI) at the C-terminal of NS1 gene of some isolates. Conclusions: It was observed that H9N2 isolates recovered from wild birds and vaccinated poultry during 2009-2017 showed highest rate of point mutation in surface glycoproteins. Although, the effects of these unique point mutations were not reported earlier, the possibility of their involvement in failure of H9 vaccine in use cannot be ignored.
Abstract Title:
Immunogenicity and Efficacy of A Thermostable Live-Attenuated Influenza Vaccine in Ferrets

Primary Author Block:

Abstract Body:
Background: Human seasonal influenza epidemics occur yearly, with an estimated 25-50 million infections occurring in the United States alone. Annual vaccination is the most effective strategy for the prevention and control of seasonal influenza. Seasonal influenza vaccination strategies include live-attenuated and inactivated influenza vaccines (LAIV and IIV, respectively), having trivalent and quadrivalent vaccine formulations. While LAIV may have some benefits over IIV, thermostability is a concern and potency of these vaccines can be negatively affected if not maintained at adequately cold temperatures. Methods: Here, we thermostabilized LAIV (tLAIV), created with the A/Leningrad/134/17/1957 master donor virus, at ambient temperatures using Preservation by Vaporization (PBV, Patent No. US 9,469,835). Subsequently, a ball mill was used to micronize the dry formulation for respiratory powder delivery, the infectivity of the tLAIV over one year was determined, immunogenicity assessed, and the efficacy of the dry powder vaccine in ferrets was examined. Results: Infectivity studies demonstrated essentially no loss in titer of tLAIV lots stored at room temperature over one year. Moreover, there were only modest decreases in titer of tLAIV lots stored at 37°C. Immunogenicity of tLAIV was assessed in ferrets vaccinated intranasally with the dry powder vaccine and compared to liquid LAIV stored at -80°C. Replicating LAIV was detected in nasal washes of tLAIV vaccinated ferrets and vaccination elicited robust mucosal antibodies, and serum hemagglutination-inhibition titers comparable to standard liquid LAIV, indicative of protection. Ferrets vaccinated with tLAIV were protected when challenged with an antigenically matched strain, A/TX/50/2012 (H3N2). Conclusions: These results support the use of PBV stabilization for LAIV to reduce cold-chain requirements and improve stability of LAIV, as well as dry powder intranasal delivery of tLAIV as an effective immunization strategy eliciting protective influenza-specific immune responses.
Abstract Title:
2016-2017 DoD Influenza Surveillance: H3N2 Predominance and Appearance of Influenza B Amino Acid Deletions

Primary Author Block:

Abstract Body:
Background: The DoD Global Respiratory Pathogen Surveillance Program conducts testing on respiratory specimens collected from a world-wide network of sentinel sites using viral culture, molecular PCR based assays, and sequencing to detect and characterize influenza viruses. USAFSAM influenza sequence data contribute to the selection of influenza vaccine strains. Methods: Around 6,000 respiratory specimens were analyzed at USAFSAM from October 2016 to September 2017 for the presence of influenza using the CDC RT-PCR assays, and roughly 2,300 of these specimens were positive for influenza A or B. The hemagglutinin (HA) gene from 964 of these were sequenced at USAFSAM using Sanger sequencing. An additional 178 HA sequences from partner DoD laboratories at AFRIMS, NAMRU-2, NHRC, and WRAIR were analyzed and reported alongside USAFSAM data. DNASTAR and BioEdit software were used to assemble the raw data, build phylogenetic trees, and perform cluster analysis. Results: A total of 1,142 influenza HA sequences were analyzed for the 2016-2017 season, including 875 influenza A (824 H3N2, 50 H1N1pdm09, and one H3N2v) and 267 influenza B (121 Victoria clade V1A, 146 Yamagata clade Y3). A representative selection of 2016-2017 HA sequences were used to create phylogenetic trees that demonstrate the diversity of circulating strains and the genetic relatedness to vaccine strains. For influenza A(H3N2) specimens, 31.4% were clade 3C.2a, 59.3% were subclade 3C.2a1, and 9.2% were clade 3C.3a. For influenza A(H1N1)pdm09 specimens, 8% were clade 6B and 92% were subclade 6B.1. One influenza H3N2 variant (H3N2v) from Texas was identified as swine origin. In the influenza B Victoria lineage, 32.2% had a double amino acid deletion at residues 162-163. One of the influenza B Yamagata specimens was found to have a single amino acid deletion at residue 527. Conclusions: For the 2016-2017 season, influenza A(H3N2) was the dominant subtype with the majority in subclade 3C.2a1, and remained the dominant subtype going into the 2017-2018 season with evidence of a shift towards clade 3C.2a. Most A(H1N1)pdm09 strains were in clade 6B.1, which contains the 2017-2018 A(H1N1)pdm09 vaccine strain, A/Michigan/45/2015-like virus. The emergence of influenza B strains with amino acid deletions may indicate an adaptive change among influenza B viruses, and requires continued surveillance. This DoD surveillance program contributed HA sequence data to the CDC and to the Vaccines and Related Biological Products Advisory Committee (VRBPAC) 2017-2018 influenza vaccine strain selection.
Abstract:
Qualification of the Vesicular Stomatitis Virus Strain Indiana Nucleocapsid Protein Rt-qPCR Assay for Evaluation of An Ebola Virus Vaccine Candidate
Primary Author Block:
C. O'Connor1, Y. Choi1, R. Krile2, C. Badorrek1, C. Sabourin1, J. Rogers1; 1Battelle, West Jefferson, OH, 2MCS-JVAP, Fort Detrick, MD
Abstract Body:
The Zaire Ebola virus (ZEBOV) recombinant vaccine candidate uses Vesicular Stomatitis Virus (VSV) strain Indiana as the vector for the ZEBOV glycoprotein (GP). A real-time reverse transcription quantitative polymerase chain reaction (RT-qPCR) assay was developed to detect the rVSV-ΔZEBOV-GP by targeting a portion of the VSV nucleocapsid protein (NP) gene and quantitating it with a qualified synthetic RNA reference standard (RS) dilution series. Under efforts funded by the US Department of Defense (DoD) Joint Program Executive Office Chemical-Biological Defense Medical Countermeasure Systems’ Joint Vaccine Acquisition Program (MCS-JVAP), this VSV NP RT-qPCR assay was qualified in non-human primate (NHP) and mouse urine and whole blood matrices according to the Food and Drug Administration (FDA) Guidance for Industry. Qualification included calculation of dilutional linearity of the test material, repeatability, and intermediate precision. The assay was also evaluated for robustness, specificity, sample stability and PCR-inhibition due to intrinsic factors. The rVSV-ZEBOV-GP test article was diluted over a range of concentrations and spiked into naïve NHP and mouse urine and whole blood (i.e., samples not spiked with test article). A set of samples that represented this range and also included naïve samples was processed to extract RNA and perform RT-qPCR by three technicians each on three separate days. The data was plotted as input concentration rVSV-ΔZEBOV-GP (plaque forming units/mL) against output RT-qPCR result (copies/mL). Dilution points which provided linearity (slope of 0.80 - 1.20) were included in the calculation of total variance per matrix. The geometric mean at the lowest useable concentration represented the limit of quantitation (LOQ) for that given matrix. The LOQ for NHP whole blood and urine was 7.81E+03 copies/mL and 1.80E+03 copies/mL, respectively. The LOQ for mouse whole blood and urine was 1.12E+03 copies/mL and 8.24E+02 copies/mL, respectively. The VSV NP RT-qPCR assay was defined as a reliable one to be used for quantitation of rVSV-ΔZEBOV-GP in subsequent regulated studies, supporting efforts to obtain licensure of this novel Ebola virus vaccine candidate.
Abstract Title:
Development of A Technique for Intranasal Delivery of An Influenza Virus Vaccine Candidate
Primary Author Block:
J. Justen1, S. Rose1, H. Wenzel2, G. Sweet1, K. Nelson1; 1MPI Res., Mattawan, MI, 2PATH, Washington, DC
Abstract Body:
Several influenza vaccines are available to prevent seasonal and pandemic influenza, and they include both inactivated vaccines delivered via intramuscular injection and live attenuated influenza vaccines (LAIV) delivered intranasally. Mucosal delivery of LAIV is unique in that a protective local immune response is developed. Proper consideration of animal models for potential prophylactic intervention is a critical component of the preclinical evaluation of mucosal immunization. Ferrets, while not commonly used for toxicology studies, support influenza virus infection, replication, and transmission similar to humans, and thus the intranasal model of vaccination is particularly appropriate to model safety of a LAIV candidate. Ferrets do not have extensive nasal cavities and dose volume may be a limiting factor. Given these issues, an investigation of the planned volume for nasal administration was conducted prior to conducting a multi-dose toxicology study of a LAIV. Ferrets were anesthetized and dyed saline was instilled intranasally. Ferrets were then necropsied to identify extension of dye into the sinus cavities. This pilot study demonstrated 0.5 mL of vaccine could be successfully administered to ferrets and delivered to the appropriate mucosal surfaces. In the toxicology study of the LAIV, serological analysis of treated animals showed seroconversion, demonstrating successful immunization by the developed technique and relevance of this model for intranasal vaccination with a live attenuated influenza virus. Further, microscopic evaluation of multiple nasal sections and the lower respiratory tract did not reveal any treatment related lesions in either the vehicle control or LAIV treated animals.
Abstract Title:
Velogenic Viscerotropic Newcastle Disease Virus Infection Suppresses Antibody Response to Infectious Bursal Disease Vaccination in Chickens

Primary Author Block:
D. C. Eze1, E. C. Okwor1, P. C. Eze1, A. O. Igwe2, I. Onyema1, J. O. A. Okoye1; 1Univ. of Nigeria, Nsukka, Nigeria, Nsukka, Nigeria, 2Michael Okpara Univ. of Agriculture, Umudike, Abia State, Umudike, Nigeria

Abstract Body:
The velogenic viscerotropic Newcastle disease (vvND) virus (vvNDV) infection in chickens is associated with high mortalities, severe atrophy, necrosis and depletion of the lymphocytes in lymphoid organs. However, there is limited information on the ability of these lesions to cause immunosuppression in surviving chickens. Three hundred and thirty cockerels at two weeks of age were divided into three groups: Vaccinated and challenged (VC) group containing 90 chickens, Unvaccinated challenged (UC) 150 chickens and Unvaccinated unchallenged (UU) 90 chickens. Chickens in VC group only were vaccinated with La Sota vaccine at 2 weeks of age. At four weeks of age, chickens in VC and UC were inoculated with vvNDV. On days 14, 28 and 42 post challenge (PC) some chickens in the three groups were removed and vaccinated against infectious bursal disease (IBD). Antibody response was assayed. The UC group had severe clinical signs with 90% total mortality. VC chickens had lesions in the lymphoid organs which were severe like those of UC. The antibody titres against IBD were significantly higher (P<0.05) in the UU than VC and UC on days 14, 28 and 42PC vaccinations. These observations show that vvNDV infection can cause immunosuppression in both vaccinated and unvaccinated chickens. This will be a big problem for poultry producers in vvND is enzootic countries.
Abstract Title:
Outer Membrane Vesicle (OMV) Typing of 4cmenb Vaccine; A Scalable and Portable Genomic Nomenclature

Primary Author Block:
C. Rodrigues1, H. Chan1, K. Jolley1, O. Harrison1, C. Vipond2, M. Maiden1; 1Univ. of Oxford, Oxford, United Kingdom, 2Natl. Inst. for Biological Standards and Control, Hertfordshire, United Kingdom

Abstract Body:
Introduction: Outer membrane vesicle (OMV) vaccines have been used against serogroup B meningococcal epidemics caused by a single genotype and porin A (PorA) type. OMV vaccines demonstrated some heterologous activity in children and adults, but very little activity in infants. In the UK, 4CMenB vaccine Bexsero®, containing OMV vaccine from the New Zealand epidemic, MeNZB™, has been introduced into the infant immunisation schedule. Enhanced surveillance methods do not measure the effect of OMV proteins other than PorA. Therefore, we developed a typing scheme to catalogue the diversity and distribution of OMVs proteins in UK invasive meningococcal disease (IMD) cases. Methods: The 24 most abundant outer membrane proteins were determined using mass spectrometry and published literature (1). Respective genes were identified in reference genome NZ05/33 and described using NEISp nomenclature. Deduced peptide sequence variants were assigned arbitrary integers, for each of the 24 loci. Each unique combination of the 24 peptide loci was assigned a “Bexsero® OMV type” (BOMV, BOMV-1 refers to NZ05/33). BOMV types were clustered into groups matching 20/24 loci using eBURSTv3. This was used to analyse 3506 UK IMD isolates from 2010/11 to 2016/17. All data and typing schemes are publicly-available on PubMLST.org/Neisseria. Results: There was variation in diversity of BOMV proteins; FbpA (NEISp0578) had least variants (n=40) and TbpA (NEISp1690) had most variants (n=955). There were 2772/3506 isolates that matched 1-5 components of MeNZB™ including: FbpA (NEISp0578), NspA (NEISp0612), putative periplasmic protein (NEISp1063), protein of unknown function (NEISp1066), and macrophage infectivity potentiator (NEISp1487). BOMV types were available for 71.1% of isolates, and were highly associated with clonal complex (cc), and the recombinant Bexsero® antigens (Cramer’s V >0.96). BOMV clustering identified ccs associated with specific serogroup, i.e. W:cc11 (cluster 1149) and C:cc11 (cluster 1158). Discussion: This is the first study to comprehensively catalogue the diversity of OMV proteins used in vaccines against IMD. The association between other antigenic variants and cc suggest that discrete bacterial populations emerge and propagate and studies investigating this will inform future vaccine formulations. This rapid, scalable and portable method will facilitate further study into the role of synergistic, minor antigens or reactogenic proteins in the OMV, to optimise future vaccine developments.
Activation of Amino Acid Deprivation Sensor Gcn2 Programs Protective Immunity against Dengue Virus

Primary Author Block:
S. Afroz, N. Khan; Univ. of Hyderabad, Hyderabad, India

Abstract Body:
Background: Recent findings have unearthed a link between host antiviral defences and amino acid response pathway (AAR) that can be crucial in the creation of vaccines against challenging viruses. Activation of AA deprivation sensor GCN2 has been shown to enhance antigen-specific T cell responses to YF17-D vaccine. Further, antiviral activity of GCN2 against few RNA viruses is well documented. Herein we have evaluated the implications of GCN2 activation in modulating immune responses to DENV envelope domain III (DENrEDIII) protein, the most potent vaccine candidate against DENV, in in-vivo mice model, focusing towards the enrichment of antigen-specific B cell memory responses to provide long lasting-protective immunity against Dengue virus infection. Methods: 6 to 8 weeks old male Balb/c mice (n=10 per group) were intraperitoneally injected with or without Halofuginone, a pharmacological activator of GCN2 at a dose of 0.1mg/kg body weight for 4 days followed by subcutaneous injection of 20 µg of DENrEDIII protein. The booster was given with the identical dose of antigen at day 14 of primary injection. The mice were sacrificed at day 28 post-primary injection for further analysis of immune responses in spleen, blood, and lymphnode. The immunized mice were bled through the tail vein at 14th and 28th day for serum extraction to detect virus neutralizing antibody titers. Results: Our results showed that there was a profound enhancement in the DENrEDIII specific serum IgG levels with high virus neutralization titers upon activation of the GCN2 pathway. Further, qRT-PCR analysis showed the upregulation of gene signatures in draining lymphnodes which are involved in antigen-specific memory B cell formation and regulate the proliferation and differentiation of germinal centre B cells upon GCN2 activation. Antigen-specific T cell responses were also elevated upon activation of GCN2 pathway as evident from the increased production of DENrEDIII -specific IFN-γ and IL-2 producing CD4+ and CD8+T cells. Conclusions: Our findings highlight the adjuvanting functions of GCN2 mediated AAR activation in augmenting the magnitude and quality of antigen-specific memory CD4+ and CD8+ T cells as well as programming antigen-specific B-cell responses to germinal centre pathway favoring the production of long-lived antibodies against DENV. This study would certainly generate new outlooks towards the immunoprophylaxis of DENV infection and other infectious diseases.
Abstract Title:
2009 Pandemic H1N1 Virus-Like Particle Vaccine Induces Superior Protection Over Split Influenza Virus Vaccine

Primary Author Block:
F. Quan; Kyung Hee Univ. Sch. of Med., Seoul, Korea, Republic of

Abstract Body:
Background: Influenza virus-like particle (VLPs) vaccines are a promising alternative to conventional egg-based vaccines. Methods: In this study, we investigated and compared the protective efficacy of the 2009 pandemic H1N1 VLP vaccine containing hemagglutinin (HA) and matrix protein (M1) with commercial monovalent H1N1 pandemic split vaccine. Mice were intramuscularly immunized and after 4 months mice were challenge infected with homologous virus (A/California/04/2009, H1N1) or heterosubtypic virus (A/Philippines/82, H3N2). Results: Mice immunized with 2009 pandemic H1N1 VLPs showed higher levels of antibodies IgG and IgG2a against 2009 H1N1 viruses. Mice that were immunized with 2009 pandemic H1N1 VLPs showed a higher protective efficacy in lowering lung viral loads against homologous virus or heterosubtypic virus than split influenza virus vaccine. Mice immunized with VLPs showed little or no proinflammatory lung cytokines IL-6 when it was challenged with homologous 2009 pandemic H1N1 viruses. Antibody-secreting cells were detected in the spleen of immunized mice. Conclusion: Taken together, these results indicate that nonreplicating influenza VLPs represent a better protective efficacy than commercial human vaccine and VLPs are promising vaccine candidates for the development of a safe and effective vaccines.
Abstract Title:
Developing A Novel Broadly Protective Bordetella Vaccine Based on Type Iii Secretion Sys. Proteins

Primary Author Block:
J. P. Stewart, S. B. Tallapaka, F. J. Martinez-Becerra, Q. Zheng, W. D. Picking, W. L. Picking; Univ. of Kansas, Lawrence, KS

Abstract Body:
There has been a significant reemergence of whooping cough (pertussis) in recent years. While there is an acellular pertussis (aP) vaccine available against the bacterial pathogen Bordetella pertussis, studies have shown that the aP vaccine fails to provide long lasting protection and those who receive it when young can become asymptomatic carriers later in life. The goal of this project is to develop a vaccine that can induce long lasting immunological memory against B. pertussis based on its type III secretion system. The T3SS is found in many gram-negative bacteria and is used to inject effector proteins into host cells. B. pertussis uses its T3SS to aid in colonization of and persistence in the human upper respiratory tract. Because the proteins that make up the Bordetella T3SS are highly conserved within the genus, a vaccine based on T3SS components should be protective against B. pertussis, B. bronchiseptica, and B. parapertussis. To produce a T3SS-based vaccine, we genetically fused two proteins: the T3SS needle tip-associated protein, Bsp22, and one of two translocator proteins, BopB, to produce a recombinant protein 22BF. Mice were vaccinated with 22BF and an adjuvant (double mutant heat-labile toxin or dmLT) on days 0, 14, and 28. On day 56, mice were challenged intranasally with a sublethal dose of B. bronchiseptica. Mice were necropsied and lungs were collected to determine the bacterial burden within the lungs after 3 and 7 days post-infection. Immune organs were then harvested to measure antibody secreting cells. Mice vaccinated with 22BF had greatly reduced weight loss and decreased lung colonization. The vaccinated with 22BF also had higher serum IgG titers against BopB and Bsp22 than did mice vaccinated with either protein (BopB or Bsp22) alone. Vaccination with 22BF also led to higher numbers of antibody secreting cells than did either protein alone. These findings demonstrate proof of concept in a small animal model that the T3SS-based subunit vaccine 22BF can provide protection against Bordetella infection. Future studies will target the use of 22BF in stimulating sterilizing immune against B. pertussis.
Abstract Title:
Development of Mucosal Vaccines to Protect against Pertussis

Primary Author Block:
D. T. Boehm1, J. M. Hall1, T. Y. Wong1, C. B. Blackwood1, E. S. Kilic1, M. P. Gutierrez2, W. Witt1, S. Bradford1, M. E. Varney1, M. Barbier1, F. H. Damron1; 1West Virginia Univ., Morgantown, WV, 2Univ. Natl. de La Plata, La Plata, Argentina

Abstract Body:
The number of pertussis cases in the United States is on the rise, and has recently been classified as the most poorly controlled bacterial vaccine preventable disease in the US. Multiple studies suggest that the protection provided by the acellular pertussis vaccines (aP) wanes quickly. The baboon model of pertussis has shown that aPs do not protect against asymptomatic carriage or transmission. The reemergence of pertussis and inadequate vaccine efficacy creates the need for the development of an improved aP vaccine. In this study, we used the murine immunization and challenge model to systematically evaluate a mucosal pertussis vaccine composed of the DTaP supplemented with a Th1/Th17 adjuvant (IN-caP). Curdlan is a Th1/Th17 skewing adjuvant and may also function to retain the DTaP antigens in the upper airway. The overall immune response was quantified at one and three days post-challenge by measuring: bacterial burden in the airway, immune cell populations in the lung, blood, and nasal cavity lavage, antibody and cytokine production. Mice immunized with IN-caP showed significant decreases in bacterial burden in the respiratory tract compared to naïve mice. IgG antibodies against pertussis toxin were found in both the IP-aP and IN-caP immunized groups. IN-caP immunization significantly reduced pro-inflammatory cytokine levels following challenge compared to whole-cell vaccinated mice, again to levels seen following aP immunization. Likewise, we observed decreased leukocyte levels in the blood and respiratory tract compared to mock-vaccinated and whole-cell immunized and challenged mice. Together these data indicate that IN-caP immunized mice are clearing the challenge infection. Interestingly, we observed increased antigen specific production of IL-17 by splenocytes from IN-caP immunized mice. These findings establish that mucosal aPs can protect against Bp challenge and offer similar protection to IP-aP immunized mice. We aim to translate these pre-clinical efficacy trials into other models and seek to develop a booster intranasal pertussis vaccine.
Bordetella pertussis Vaccine Composition Regulates Hematopoietic Stem and Progenitor Cell Frequency During Vaccination and Subsequent Infection

Abstract Body:

Whooping cough (pertussis) is a re-emerging infectious disease in worldwide. Current acellular vaccines (ACVs) against B. pertussis are hypothesized to wane in efficacy each year after immunization. We hypothesized that whole cell vaccines (WCVs), unlike waning ACVs, induce hematopoietic stem and progenitor cell (HSPC) expansion and differentiation processes that are necessary for life-long protection. While HSPC innate immune signaling and expansion play critical roles in directing immune responses to infection, little is known about their roles in vaccine efficacy. To test our hypothesis, we assessed bone marrow HSPC frequency, peripheral blood composition, and immune cell proportions in the spleen and thymus upon vaccination as well subsequent infection. We found that upon vaccination, the bone marrow Lineage-Sca1+cKit+ (LSK) cell population undergoes progressive expansion in WCV mice when compared to ACV and PBS-injected control mice. Additionally, peripheral white blood cells and spleen size increase in WCV mice, suggesting that bone marrow cells mobilize to the blood and spleen, where extramedullary hematopoiesis is known to occur. Upon infection, myeloid cells have been demonstrated to leave the spleen, enter infected tissues, and produce cytokines that favor the generation of Th1 cells. Occurring more rapidly in WCV mice, LSK cell frequency increases and spleen size decreases upon B. pertussis challenge in both WCV and PBS-injected mice when compared to ACV mice. WCV mice exhibit increased peripheral blood monocytes, neutrophils, and lymphocytes when compared to other groups. RNA sequencing of HSPCs at the time of vaccination and infection suggest a role for interferon signaling in inducing these processes. Taken together, our data suggest that HSPC expansion, differentiation, and mobilization upon WCV immunization may prime the host to better respond to pathogen, and that formulating next generation ACVs with adjuvants that stimulate HSPC expansion, such as TLR4 agonists, may enhance vaccine efficacy.
Abstract Title:
Cross-Validation of A Standardized Pertussis Multiplex Serological Assay to Quantify Antibodies in Human Dried Blood Spot and Plasma

Primary Author Block:
G. Rajam, E. Kim, S. Park, S. Paulos, D. Patel, A. Jeyachandran, E. Wong, J. Schiffer; CDC, Atlanta, GA

Abstract Body:
Background: CDC has developed and validated a microsphere based multiplex antibody capture assay (MMACA) for the simultaneous quantification of Bordetella pertussis (Bp) antigen specific immunoglobulin G (IgG) in human serum. Considering the logistical limitations in studies involving neonates and infants, dried blood spot (DBS) and plasma are increasingly being used as clinical specimens for serological testing. DBS offers an alternative to serum for rapid and efficient sample collection with fewer on-site equipment requirements and considerably lower storage and transport costs. The purpose of this cross-validation study is to demonstrate the comparability of MMACA to quantify Bp antigen specific IgG in these clinical specimens. Methods: For MMACA, microspheres (Luminex) with distinct fluorescence spectrum were conjugated to five Bp antigens: Pertussis toxin (Pt), Pertactin (Prn), Filamentous Hemaglutinin (Fha), Fimbriae (Fim2/3), and adenylate cyclase toxin (Act) and used to capture Bp antigen specific antibodies in a single serological reaction (5-plex). A panel of 20 paired human DBS/serum samples and 15 paired human plasma/serum samples were tested for Bp antigen specific IgG in two separate experiments. Precision, accuracy and concordance correlation coefficient (CCC) for each Bp antigen was calculated using SAS. Results: The Deming regression of the median anti-Bp antigen specific antibody concentration values in DBS and serum produced a precision of 0.992 - 0.995, an accuracy of 0.995 - 0.998 and a CCC of 0.989 - 0.991 for Bp antigens. Similarly, The Deming regression values in plasma and serum produced a precision of 0.979 - 0.991, an accuracy of 0.992 - 0.999 and a CCC of 0.979 - 0.995 for five different Bp antigens. A CCC ≥ 0.95 is considered to indicate near perfect equivalence. Conclusions: MMACA was successfully cross-validated to quantify anti-Bp antibodies in human DBS and plasma.
Abstract Title:
Developing Better Vaccines: How Differences in P. Aeruginosa and B. Pertussis Pathogenesis Impact Host Immune Response

Primary Author Block:

Abstract Body:
In the context of cystic fibrosis (CF), respiratory pathogens are of utmost importance. Pseudomonas aeruginosa is one of the main etiological agents of pneumonia in CF patients and a major cause of morbidity and mortality. More recently, Bordetella species have been isolated from the lungs of CF children and shown to be associated with worsening of the symptoms and decreased lung function. Because pathogens of this nature are the primary cause of mortality in CF patients, understanding underlying mechanisms through which they cause infection is crucial to developing novel treatments. Antibiotics are currently the first line of treatment against respiratory pathogens in CF patients. Current increases in the incidence of antibiotic resistance enhance the need to develop preventative, rather than reflexive, treatments for such pathogens. Vaccination is a tried and true method for preventing bacterial infection, and for both Bordetella pertussis and P. aeruginosa, vaccination using heat-killed bacteria is an effective way to prevent subsequent infection. While both pathogens cause respiratory infections, their pathogeneses are distinctive, as is the host immune response. Thus, we hypothesized that effective vaccines against these pathogens would interact with the immune system and have different effects to be protective in each infection model. Using a murine model of whole cell vaccination and then infection, we compared the immune response to each pathogen through determination of bacterial burdens, organ weights, and through utilization of flow cytometry analysis of spleen, lung, and thymus. We first observed that in the case of P. aeruginosa, there is an increase in lung weight after infection in a naïve animal, which is not seen in the case of B. pertussis. Conversely, white blood cell populations, particularly neutrophils, are increased in B. pertussis, but not P. aeruginosa, infected naïve animals. After vaccination with heat-killed B. pertussis, this change in total white blood cell count is mediated. Additionally, we see that there are opposing cellular responses to whole-cell vaccination. P. aeruginosa vaccination increases neutrophils after infection whereas whole-cell vaccination using B. pertussis results in a mediation of the increase seen in naïve infection. These changes, in addition to changes in myeloid and lymphocyte cell populations, as determined by flow cytometry analysis, may prove important in designing future vaccination strategies that more precisely target these pathogens to prevent initial infection.
Abstract Title:
Modeling Correlates of Protection for Pre-Clinical Pertussis Vaccine Development

Primary Author Block:
C. G. Cooper, F. H. Damron; WVU, Morgantown, WV

Abstract Body:
Pertussis is a highly contagious bacterial upper respiratory disease caused by Bordetella pertussis that primarily presents as paroxysms of coughing with inspiratory whoop and post-tussive vomiting that gradually decrease over 8 weeks. Incidence rates dropped significantly with introduction of whole-cell pertussis vaccine in the 1940s. A less reactogenic acellular vaccine was developed in the 1980-90s that did not contain endotoxin. The Center for Disease Control has documented increasing incidence of pertussis in children in the US with peaks every 3-5 years and despite high vaccine coverage. Current evidence suggests that acellular pertussis vaccines wane in efficacy and do not block transmission or fully protect against asymptomatic infection. There is a need to develop a vaccine combining the efficacy of whole cell vaccine with the safety profile of acellular vaccines. It is clear that whole cell induces immunity via Th1/17 responses but the acellular vaccine induces a Th2 response due to the alum adjuvant. Studies have shown it is possible to skew the Th2 immunity back to a Th1/17 profile in pre-clinical models such as mice. In order to systematically develop a new vaccine, we created a logical and predictive model to direct our studies. Mice were immunized and boosted with decreasing doses of whole cell or acellular vaccine. Immunized and non-immunized control mice were challenged with B. pertussis. Approximately 30 correlates of protection were measured for each mouse including spleen and lung weight, CFUs of B. pertussis in trachea, lung and nasal washes, cytokine production, and WBC recruitment. These datasets were used to establish the baseline Th2 or Th1/17 vaccine profiles. We then compared these model profiles to an experimental acellular vaccine containing the RTX antigen, a toxoid for of the adenylate cyclase toxin. These data were compared into our in silico models to characterize the overall immune responses. The R2, or coefficient of determination, was used to infer the goodness of the fit. Our data suggested that inclusion of RTX slightly skewed the helper cell responses towards a Th1 response which validated our approach. We next modeled intranasal immunization of an experimental acellular pertussis vaccine and we observed that changing the route of administration, altered the immune response more closely resembling whole cell immunization. Our studies allow us to further evaluate improving vaccines in a more predictive manner which we will help use to predict outcomes before empirical determination of experimental vaccines.
Session Number: 460  
Session Type: Poster Talk  
Session Title: HIV Infection  
Session Start Date Time: 6/10/2018 1:45:00 PM  
Session End Date Time: 6/10/2018 2:35:00 PM  
Session Primary Track: Clinical Infections and Vaccines  
Abstract Control Number: 9357  
Poster Board Number:  

Abstract Title:  
Moderator  
Primary Author Block:  
Estee Torok; Univ. of Cambridge, Cambridge, United Kingdom  

Abstract Body:
Abstract Title:
Risk of Developing Liver Disease in Hev-Hiv-Seropositive Individuals in Nepal

Primary Author Block:
B. P. Gupta1, K. D. Manandhar1, R. Kurmi2; 1Tribhuvan Univ., Kathmandu, Nepal, 2Bhawani Hosp., Birgunj, Nepal

Abstract Body:
Background: Hepatitis E virus (HEV) infection is endemic in certain areas of the world such as Nepal. In this setting, HEV infection in immunocompromised patients could contribute to liver disease as the virus could induce a differential liver-specific immune response. In this regard, some studies in Spain have shown an association between HEV seroprevalence and cirrhosis among HIV-infected patients. In this study we aimed to address if HIV-infected individuals co-infected with HEV have differential degrees of liver fibrosis in an endemic area for the virus. Methods: We prospectively evaluated 200 HIV-infected individuals on antiretroviral therapy, in a clinic in rural Nepal between 2016 and 2017. Serum samples were collected and clinical information obtained concomitantly. Samples were analyzed for multiple components of a variety of liver fibrosis scores (AST, ALT, platelets, albumin, cytokeratin-18), as well as CD4 counts. HEV IgG was measured by ELISA using a Wantai kit. Statistical analyses were performed using Wilcoxon score methods. Results: The median age of patients was 31 years (IQR 14-40) and 61% were males. Forty-three percent of patients (N:87) were positive for HEV-IgG. The average CD4 count was 551/mm3 in those HEV-positive and 674/mm3 in those HEV-negative (p=0.3). We found no association between consumption of boiled or filtered water, food predilection or presence of gastrointestinal symptoms and HEV seroprevalence. We found a significant association between HEV-seropositivity and elevated Fib4 and NAFLD fibrosis scores: median Fib4 score 1.31 vs 0.87 for HEV-positive and -negative respectively (p=0.001) and median NAFLD fibrosis score of -1.88 vs -2.43 for HEV-positive and -negative respectively (p=0.01). APRI scores were similar among both groups (0.31 vs 0.32 respectively). Interestingly, in a subset of 80 patients, we found no correlation among CK-18 levels and HEV seropositivity. However there was no association between CK-18 and BMI, CD4 counts or the presence of diabetes. Conclusions: We found higher Fib4 and NAFLD fibrosis scores among HIV/HEV positive individuals, suggesting an increased liver fibrosis profile among this group. Further studies using other fibrosis markers such as liver biopsy or liver stiffness measurements should be performed.
Altered Antibody Responses in Persons Infected with HIV-1 During Prep

I. K. Parker1, G. Khalil1, M. Martin1, W. Leelawiwat2, S. Vanichseni3, K. Choopanya3, W. Switzer1, J. McNicholl1, A. Hickey1, K. Curtis1; 1CDC, Atlanta, GA, 2Thailand Ministry of Publ. Hlth.-US CDC Collaboration, Nonthaburi, Thailand, 3Bangkok Tenofovir Study Group, Bangkok, Thailand

Background: Pre-exposure prophylaxis (PrEP) is an effective HIV prevention tool, though its efficacy is dependent upon adherence. The Bangkok Tenofovir Study (BTS), which evaluated the efficacy of oral tenofovir (TDF) among persons who inject drugs (PWID), demonstrated a 49% reduction in the risk of HIV-1 acquisition in study participants who received PrEP as compared to a placebo. In such studies, it is important to characterize the impact of PrEP on HIV antibody responses in persons who become infected during treatment in order to understand the potential impact on timely diagnosis and treatment. Methods: Longitudinal HIV-1-specific antibody responses were evaluated in 42 participants (placebo=28; PrEP=14) who acquired HIV during the BTS. HIV-1 antibody levels and avidity to three envelope proteins (gp41, gp160, and gp120) were measured in the plasma using a customized Bio-Plex (Bio-Rad) assay. A Kaplan Meier analysis was performed for each biomarker to compare the proportion of study subjects who exceeded an assay threshold between treatment groups. Mixed models were used to identify longitudinal differences in antibody levels and avidity between groups. Results: Overall, among PWID longitudinal antibody levels and avidity were notably lower in the PrEP breakthrough group compared to the placebo group. Kaplan Meier analyses demonstrated a significant difference between treatment groups for all Bio-Plex biomarkers (p<0.05). Longitudinal gp120 antibody levels within the PrEP breakthrough group were significantly decreased compared to the placebo group (mixed model; p<0.05). Conclusion: We document an impact on envelope antibody maturation in PWID study subjects who became infected while receiving PrEP, which has significant implications for HIV diagnosis as PrEP use expands. Delayed maturation of the antibody response to HIV may increase the window of detection for antibody-based tests and impact the estimation of population-based incidence.

<a href="http://files.abstractsonline.com/CTRL/6f/7/3ce/7ef/e61/471/faf/f4e/123/c30/86e/9d/g7485_1.png" target='_blank' address=no><img src="http://files.abstractsonline.com/CTRL/6f/7/3ce/7ef/e61/471/faf/f4e/123/c30/86e/9d/g7485_1.png" alt="" border="0" width="600" height="341" /></a>
Abstract Title:
Frequency of Broadly Neutralizing Antibodies in Hiv-1 Chronically Infected Individuals in Ugandan Clades A and D

Primary Author Block:
C. Kintu; Makerere Univ. Kampala, Kampala, Uganda

Abstract Body:
Aim: The study was aimed at assessing frequencies of neutralizing antibodies in individuals affected with the commonest HIV-1 clades A and D in Uganda. Methods: This was a cross-sectional study of 83 HIV-1 chronically infected Anti-Retroviral Therapy (ART) naïve adults who were enrolled from Medical Research Council (MRC) cohort and The AIDS Support Organization (TASO) Clinic in Entebbe. Samples of Plasma were tested for the neutralization activity against a panel of 3 clade A and D viruses using the Neutralization Assays. Neutralization assays were performed using Env pseudovirus viruses in the TZM-bl cell-based assay. Neutralization values were obtained as the plasma dilutions at which virus entry was inhibited by 50% compared to that in the absence of plasma (IC50). A plasma sample was scored as displaying neutralizing activity against a particular virus if at least 50% inhibition of infection was recorded at the lowest plasma dilution tested (1: 20) in at least two independent neutralization assays. Results: Clade A viruses are better neutralized compared to clade D viruses. Individuals whose titers were above 1080 (labeled red required further sample dilution. 51.81% of the participants had their antibody neutralization titers above 40. There was a significant difference between the proportion of clade A viruses neutralized and those of clade D as obtained statistically using the Mann-Whitney test with a p-value < 0.0001. The neutralization titers obtained for the individual clade A viruses Q23.17, Q769.d22 and Q842.d12 were much higher than those for clade D viruses QA013.H1, Q857.B3 and QD435.5B. Conclusion: Generally, the frequency of neutralizing antibodies was found to be much higher in Clade A compared to Clade D. This implies that in case of a vaccine design, emphasis should be put on Clade D subtype since it’s harder to neutralize naturally. List of figures<br />

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Q23.17</th>
<th>Q769.d22</th>
<th>Q842.d12</th>
<th>QA013.H1</th>
<th>Q857.B3</th>
<th>QD435.5B</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of Viruses neutralised</td>
<td>286.29</td>
<td>40</td>
<td>181.38</td>
<td>181.38</td>
<td>286.29</td>
<td>181.38</td>
</tr>
<tr>
<td>ID</td>
<td>Value 1</td>
<td>Value 2</td>
<td>Value 3</td>
<td>Value 4</td>
<td>Value 5</td>
<td>Value 6</td>
</tr>
<tr>
<td>-----</td>
<td>---------</td>
<td>---------</td>
<td>---------</td>
<td>---------</td>
<td>---------</td>
<td>---------</td>
</tr>
<tr>
<td>1</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>2</td>
<td>40</td>
<td>484</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>3</td>
<td>159</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>4</td>
<td>55.11</td>
<td>40</td>
<td>40</td>
<td>77</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>5</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>6</td>
<td>57</td>
<td>76</td>
<td>80</td>
<td>40</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>7</td>
<td>541</td>
<td>40</td>
<td>141</td>
<td>40</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>8</td>
<td>1080</td>
<td>45</td>
<td>71</td>
<td>40</td>
<td>193</td>
<td>40</td>
</tr>
<tr>
<td>9</td>
<td>1080</td>
<td>635</td>
<td>340</td>
<td>40</td>
<td>61</td>
<td>178</td>
</tr>
<tr>
<td>10</td>
<td>116</td>
<td>106</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>11</td>
<td>1080</td>
<td>40</td>
<td>82</td>
<td>40</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>12</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>Row</td>
<td>Column 1</td>
<td>Column 2</td>
<td>Column 3</td>
<td>Column 4</td>
<td>Column 5</td>
<td>Column 6</td>
</tr>
<tr>
<td>-----</td>
<td>----------</td>
<td>----------</td>
<td>----------</td>
<td>----------</td>
<td>----------</td>
<td>----------</td>
</tr>
<tr>
<td>1</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>2</td>
<td>50.0</td>
<td>50.0</td>
<td>50.0</td>
<td>50.0</td>
<td>50.0</td>
<td>50.0</td>
</tr>
<tr>
<td>3</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>4</td>
<td>1339</td>
<td>1339</td>
<td>1339</td>
<td>1339</td>
<td>1339</td>
<td>1339</td>
</tr>
<tr>
<td>5</td>
<td>1080</td>
<td>1080</td>
<td>1080</td>
<td>1080</td>
<td>1080</td>
<td>1080</td>
</tr>
<tr>
<td>6</td>
<td>79</td>
<td>79</td>
<td>79</td>
<td>79</td>
<td>79</td>
<td>79</td>
</tr>
<tr>
<td>7</td>
<td>55</td>
<td>55</td>
<td>55</td>
<td>55</td>
<td>55</td>
<td>55</td>
</tr>
<tr>
<td>8</td>
<td>33.3</td>
<td>33.3</td>
<td>33.3</td>
<td>33.3</td>
<td>33.3</td>
<td>33.3</td>
</tr>
<tr>
<td>9</td>
<td>180.91</td>
<td>180.91</td>
<td>180.91</td>
<td>180.91</td>
<td>180.91</td>
<td>180.91</td>
</tr>
<tr>
<td>10</td>
<td>102</td>
<td>102</td>
<td>102</td>
<td>102</td>
<td>102</td>
<td>102</td>
</tr>
<tr>
<td>Titer Value</td>
<td>% of Virus Neutralized</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-------------</td>
<td>------------------------</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 40.000</td>
<td>40.001 - 99.99</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>100 - 999.999</td>
<td>999.99 - 1000000</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 100000</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 1: Neutralization titres for six virus Panel

Figure 2: (a) Average neutralization titres per clade, (b) Proportion of viruses neutralized per Clade

Figure 3: Total Percentage of individuals that neutralized
Session Number: 465
Session Type: Rapid Fire
Session Title: Global Health and Epidemiology
Session Start Date Time: 6/10/2018 3:00:00 PM
Session End Date Time: 6/10/2018 3:45:00 PM
Session Primary Track: Clinical Infections and Vaccines
Abstract Control Number: 9362
Poster Board Number:

Abstract Title:
Moderator
Primary Author Block:
A. Krishna Rao;

Abstract Body:
Abstract Title:
Detection and Molecular Characterization of Polio Virus Isolates Obtained from Apparently Healthy Children and Sewage in Maiduguri, North Eastern Nigeria

Primary Author Block:
F. Tahir; Abubakar Tafawa Balewa Univ., Bauchi - Nigeria, Bauchi, Nigeria

Abstract Body:
Expanded Programme on Immunization (EPI) is one of the strategic approach of controlling childhood diseases including poliomyelitis. This study was carried out to isolate and characterize polio virus from apparently healthy children and sewage in an effort to complement the Acute Flaccid Paralysis (AFP) surveillance for wild poliovirus in Maiduguri metropolis. Stool and sewage samples were collected and screened for the presence of the virus according to procedures described by WHO Polio Laboratory Manual (2004). Out of 400 stool samples of apparently healthy children assessed, (2.8%) were found to be positive of which 4 (1.9%) were male and 7 (3.8%) were females. Accordingly 263(66%) had vaccination history while 143(36%) had no vaccination against any serotype. None Polio Enterovirus (NPENT) was found to be 34(8.5%) and only 1(0.25%) was wild polio virus (Type 1). The VP1 sequence of the wild isolate NIE-BOS-JRE-16-44C2 was PV1 WEAFB1 orphan virus in cluster N7B, matching the known NIE-BOS-DAM-13-005 and NIE-BOS-BAM-11-012 at 95.8% nt. Out of the 36 litres of Sewage samples from 12 different location, 10(27.8%) were positive for serotype P2 and P3 with P2 having the least 4(40%) and P3 6(60%). Only NPENT was obtained from the sewage samples, distributed as follows; Dalori camp1 and teachers village each with 2(6.7%) followed by Dalori camp2, Gubio camp, Muna custom, Muna Haruna and Farm centre camp each with 1(3.3%). The findings clearly indicates a prevailing immunity gap among children in the IDP camps despite the campaigns using bivalent Oral Polio Vaccine (bOPV), “Sabin -like” strains isolated from some of the settlements establish a good vaccine response and shedding of the virus by the children. Key Words: Poliovirus, Molecular Characterization, Apparently Healthy Children, Sewage, Maiduguri, Nigeria *Correspondent Author
Abstract Title:
Efficacy of Topical Treatments for Cutaneous Leishmaniasis: A Systematic Review and Network Meta-Analysis

Primary Author Block:
T. Thy1, A. Zayan2, M. Kamel3, A. Ahmed4, T-H. Hoang1, M. Othman4, K. Luu1, S. Nguyen5, A. Haleem6, H. Nasser7, R. Yaf8, O. Mattar9, K. Hirayama10, N. Huy10; 1Univ. of Med. and Pharmacy at Ho Chi Minh City, Ho Chi Minh, Viet Nam, 2Menoufia Univ., Menoufia, Egypt, 3Minia Univ., Minia, Egypt, 4Al-Azhar Univ., Cairo, Egypt, 5Univ. of Sci. and Technology of Hanoi, Ha Noi, Viet Nam, 6Ain Shams Univ., Cairo, Egypt, 7 Cairo Univ., Cairo, Egypt, 8Damascus Univ., Damascus, Syrian Arab Republic, 9Kasr Al Ainy Sch. of Med., Cairo, Egypt, 10Nagasaki Univ., Nagasaki, Japan

Abstract Body:
Background: Leishmaniasis is a parasitic disease that is considered to be one of the most neglected tropical diseases presented in more than 90 countries all over the world, especially in poor population. Among all leishmaniasis forms, cutaneous leishmaniasis (CL) is considered the most frequent and dangerous form. It causes lesions on different locations and leads to scars or even severe incapacity. Glucantime has been a standard treatment; however, because of various side effects and inconvenience of applying systemic treatments, topical alternatives have been recommended. There is still no conclusion of the most effective topical treatment for CL, therefore, this systematic review and network meta-analysis was conducted to evaluate the efficacy of all the available topical treatments of CL.

Methods: Searches of nine electronic databases and a manual search were performed to find out clinical trials reporting tropical treatments of CL. Screening and data extraction were completed by three independent reviewers. Risk of bias was assessed using the Cochrane Collaboration’s tool. Complete healing cases were evaluated at three, six, twelve weeks and endpoint. Data were analyzed using network meta-analysis (NMA). Results: We included 41 clinical trials. Among that, 38 articles reported complete healing cases per patients. NMA showed that trichloroacetic acid plus glucantime was the most effective option for treating CL followed by topical herbal extract Z-HE. Compared with a standard treatment of CL, glucantime, a combination of glucantime and a topical treatment such as gel extract of Cassia, imiquimod, yarrow, terbinafine or honey showed more advantages, respectively. Trichloroacetic acid and liposomal amphotericin B were other recommended single topical treatments because of better efficacy than the systemic arm. All topical treatments except ketoconazole and shiunko were indicated to have more efficacy than placebo. Efficacy of some topical arms was reported in three studies using complete healing rate of lesions. Miconazole was better than clotrimazole while Thio-Ben was as effective as systemic glucantime. Results evaluated in different time points brought the same conclusion. Conclusions: Adding topical drugs to systemic treatment brings much more effects and among arms, trichloroacetic acid showed the most significant difference. Monotherapy of topical
treatments such as Z-HE, trichloroacetic acid, liposomal amphotericin B or Thio-Ben is also a good selection.
Abstract Title:
Outcomes of Current Treatments for Middle East Respiratory Syndrome: A Systematic Review and Meta-Analysis

Primary Author Block:
T. Thy1, M. Morra2, T. Le1, M. Kamel3, A. Ghazy4, A. Altibi5, D. Lu6, V. Nguyen1, M. Mostafa7, S. Ahmed8, S. Elabd9, S. Fathima10, V. Tran11, A. Omrani12, Z. Memish13, K. Hirayama14, N. Huy14; 1Univ. of Med. and Pharmacy at Ho Chi Minh City, Ho Chi Minh, Viet Nam, 2Alazhar Univ., Cairo, Egypt, 3Minia Univ., Minia, Egypt, 4Shebin El-Kom Teaching Hosp., Menofeya, Egypt, 5Univ. of Jordan, Amman, Jordan, 6Pham Ngoc Thach Univ. of Med., Ho Chi Minh, Viet Nam, 7Tanta Univ., Tanta, Egypt, 8Cairo Univ., Giza, Egypt, 9Benha Univ., Benha, Egypt, 10Deccan Coll. of Med. Sci., Univ. of Hlth.and Sci., Hyderabad, India, 11Univ. of California, Los Angeles, CA, 12King Faisal Specialist Hosp. and Res. Ctr., Riyadh, Saudi Arabia, 13Ministry of Hlth., Riyadh,, Riyadh, Saudi Arabia, 14Inst. of Tropical Med. (NEKKEN), Leading Graduate Sch. Program, and Graduate Sch. of BioMed. Sci., Nagasaki Univ., Nagasaki, Japan

Abstract Body:
Background: Middle East Respiratory Syndrome (MERS), which is a respiratory disease caused by Middle East Respiratory Syndrome Coronavirus (MERS-CoV). Infected patients suffered from various clinical appearances from asymptomatic to serious acute respiratory distress or death. Currently, there is still no standard cure for MERS and also no vaccine against MERS-CoV. Furthermore, the risk of the outbreak has increased. Therefore, a systematic review and meta-analysis were conducted to evaluate all available treatments for MERS. Methods: A systematic search on ten databases and manual search were handled to retrieve any study giving information of treatments for MERS. Screening and extraction were done by three reviewers. Quality was assessed using CARE statement for case reports and nine metrics tool for nonrandomized studies. Mortality rates were meta-analyzed using STATA software. The classification and regression tree model (CART) was performed to evaluate independent variables that predict fatality results. The mean survival days was calculated for two data sets of Kaplan-Meier survival curves including from hospital admission and from the onset of symptoms to death. Results: Ten case reports, two case series, and four observational studies were included. Among that, the combination of IFN and ribavirin was the most frequent treatment used; however, the mortality rate which was as high as 71% in IFN-treatment group did not change in the only supportive-treatment group. Comparison between three types of IFN brought no statistically significant difference in the fatality. The rate of fatality increased in patients who were older or suffered from the chronic renal disease, hypertension or diabetes mellitus or antiviral admission delay. There was the insignificant difference in mortality rate regarding gender, ribavirin, corticosteroid, oseltamivir, IFN beta 1a, IFN alpha 2b, IFN alpha 2a, congestive heart failure or other comorbidities. CART showed that chronic renal diseases as the best model to predict mortality. Mean of survival days from admission was not significantly different
between groups in contrast of significant difference in mean of survival days from onset of illness. Conclusions: The intervention of antiviral treatment such as the combination of IFN and ribavirin did not bring more effects on mortality rate than supportive-only arms; however, mean of survival days from onset of symptoms in IFN group was longer than supportive-only one. Comorbidities or postponement of antiviral treatment is related to worse outcomes.
Abstract Title:
Increasing Ex-Vivo Tolerance of Gambian Plasmodium Falciparum Isolates to Amodiaquine and Lumefantrine, Partners of Artemisinin-Based Combination Therapies

Primary Author Block:
H. Mbye; Univ. of Ghana, Accra, Ghana

Abstract Body:
In vitro drug susceptibility studies complement efficacy trials by assessing the effect of individual components of artemisinin-based combination therapies (ACTs) on parasite survival (Witkowski et al., 2013). These can enable early detection of changes in parasite susceptibility to ACT components before the onset of clinical failure. This is particularly crucial given the need for early warning for resistance or tolerance to ACTs in Africa, as artemisinin-resistant Plasmodium falciparum spreads across South East Asia (World Health Organisation, 2016). The high prevalence of malaria in Africa sees an ever-increasing amount of antimalarial pressure on parasite populations as national malaria control programme scale up efforts to eliminate the disease (World Health Organisation, 2016). In this study, 262 Plasmodium falciparum isolates, collected over 3 transmission seasons as part of therapeutic efficacy studies from the West of The Gambia (2013-2015), were analysed by in vitro methods; 50% inhibitory concentration (IC50) for partner drugs and, ring-stage survival assay (RSA); to determine ex vivo susceptibility to artemisinin-derivatives. Plasmodium falciparum isolates showed increasing tolerance to quinolines (Lumefantrine and Amodiaquine) but remained susceptible to artemisinin derivatives; Artemether and Dihydroartemisinin. However, the RSA results showed growth in 26% (13/50) of isolates from 2015, after exposure to 700nM of Dihydroartemisinin. Increased ring survival positively correlated with IC50 for Sulphadoxine and artemisinin-derivatives but negatively with Lumefantrine and Quinine. Increased Lumefantrine tolerance could be due to selection from Artemether-Lumefantrine; the first-line ACT in The Gambia. With the use of SP for chemoprevention, correlation between Sulphadoxine and increased ring survival against Dihydroartemisinin, calls for continuous and rigorous surveillance to sustain the useful lifespan of currently employed ACTs in Africa.
Malaria Co-Infections: A Diagnostic Challenge in Malaria Endemic Regions of Sub-Saharan Africa

Background: In sub-Saharan regions with holoendemic malaria transmission clinicians primarily focus on malaria diagnostics. Hence, febrile patients with malaria co-infections might receive treatment for non-causative parasitaemia, while the co-infecting agent remains overlooked. This study aims to determine the burden of malaria co-infections among hospitalised children with severe febrile illness and their association with parasite densities.

Methods: Between November 2013 and April 2015 all children (age ≥30 days and ≤15 years) with a temperature ≥ 38.0°C, admitted to the Agogo Presbyterian Hospital in central Ghana were included in the study. Malaria parasitaemia was determined and blood, stool, urine, respiratory and cerebrospinal fluid specimens were screened for parasitic, bacterial and viral pathogens. Associations of Plasmodium densities with other pathogens were calculated. Non-febrile, healthy controls were recruited to analyse associations of febrile disease and parasitaemia.

Results: From November 2013 to April 2015 1238 children were enrolled out of 4169 admissions. A clinical/microbiological diagnosis could be made in 1109 (90%) patients, with Plasmodium parasitaemia (n=728 [59%]) being predominant. This was followed by lower respiratory tract infections (n=411 [34%]; most frequent Streptococcus pneumoniae, n=192 [46%]), urinary tract infections (n=218 [18%]; Escherichia coli, n=21 [10%]), gastrointestinal infections (n=210 [17%]; rotavirus, n=32 [33%]) and invasive bloodstream infections (n= 62 [5%]; Salmonella spp., n=47 [75%]). Out of 537 healthy children, 83 (15%) revealed malaria parasites, of which 90% had a parasite count below 12,000/µl. In Plasmodium infected children the frequency of lower respiratory tract-, gastrointestinal- and bloodstream infections increased with decreasing parasite densities.

Conclusions: With half of all malaria patients revealing an alternative cause for the fever episode and 15% of healthy children being parasitaemic, malaria co-infections play a substantial role in the paediatric population of malaria endemic countries. In a hospital setting, the likelihood of comorbidity with a nonmalarial disease is reversely correlated with increasing blood levels of malaria parasites. Hence, parasite densities provide important information as an indicator for the probability of coinfections, in particular to guide antimicrobial medication.
Abstract Title:
Outstanding Abstract Award: Insecticide Resistance is Not Associated with Malaria Prevalence in Anopheles Gambiae S.l. (Diptera: Culicidae) Mosquitoes in Guinea

Primary Author Block:
E. Collins1, N. M. Vaseli1, M. Sylla2, A. H. Beavogui2, J. Orsborne1, S. Irish3, T. Walker1, L. A. Messenger3; 1London Sch. of Hygiene and Tropical Med., London, United Kingdom, 2Ctr. Natl. de Formation et de Recherche en Santé Rurale de Maferinyah, Maferinyah, Guinea, 3CDC, Atlanta, GA

Abstract Body:
Background: The threat of insecticide resistance across sub-Saharan Africa is anticipated to have severe implications for the continued effectiveness of our repertoire of malaria vector control interventions. However, evidence linking the operational failure of control strategies to the presence of local, resistant mosquito populations is lacking. Methods: In an area of high malaria transmission in Forecariah Prefecture, Guinea, we investigated the impact of insecticide resistance intensity on malaria infection prevalence of Anopheles gambiae s.l. Intensity of resistance to carbamates and pyrethroids was assessed using CDC bottle bioassays and underlying resistance mechanisms investigated using piperonyl butoxide (PBO) based CDC synergist assays. A subset of specimens underwent ovarian dissection to determine parity (a proxy for age) and molecular assays were performed to detect Plasmodium falciparum infection and insecticide resistance genes (Ace-1, kdr and N1575Y). Results: In Forecariah Prefecture, pyrethroid resistance was intense as evidenced by mosquito populations which were not only resistant to ten times the insecticide concentration required to kill susceptible individuals, but were also capable of surviving these doses for up to two hours. Insecticide resistance was not associated with decreased capacity to transmit malaria, with no significant differences observed between P. falciparum oocyst or sporozoite rates among susceptible and resistant vectors (χ²=0.89; p=0.345 and χ²=2.10; p=0.148, respectively). Resistant mosquitoes had significantly lower parity rates, i.e. were younger, than susceptible individuals. However, the small proportion of intensely resistant vectors were more likely to be parous (χ²=4.13; p=0.042 and χ²=4.39; p=0.036, for survivors exposed to five and ten times the diagnostic dose of insecticides respectively). Conclusions: Restoration of mosquito susceptibility to pyrethroids following pre-exposure to PBO and the non-association between N1575Y frequency and vector mortality rate indicate that over-expression of P450 monooxygenases is the predominant mechanism driving pyrethroid resistance. Our findings contrast with a number of laboratory studies reporting reduced fitness in insecticide-resistant vectors and highlight the need for additional studies across a range of areas of differing resistance and malaria transmission intensities.
Abstract Title:
Cholera in Haiti: Seven Years Later

Primary Author Block:

Abstract Body:
Introduction: In January 2010, a massive earthquake devastated Haiti. This was followed in October 2010 by a massive cholera outbreak. Since then, and over the past 7 years, thousands of cholera cases and deaths have been documented throughout Haiti. After much controversy, scientific investigations traced the source of the cholera outbreak to a Nepalese United Nation Peacekeeping camp in Haiti. Cholera had not occurred in Haiti before 2010. This report describes recent progress in cholera control efforts in Haiti.

Methods: Cases were defined as any case of acute, profuse, watery diarrhea, with or without vomiting occurring in a department of Haiti affected by cholera. Data was obtained from the National Cholera Surveillance System which includes public and private-public institutions.

Results: Table 1: The national number of Cholera cases in Haiti reported by the National Cholera Surveillance System per year.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>National number of Cholera cases</td>
<td>185,210</td>
<td>351,839</td>
<td>101,354</td>
<td>58,917</td>
<td>29,078</td>
<td>46,038</td>
<td>41,905</td>
<td>13,680</td>
<td>828,021</td>
</tr>
</tbody>
</table>

The cholera incidence rate was 18 per 1000 (18/1000) residents in 2010, with a peak in 2011 at 34/1000 residents, and a drop in the rate to 1/1000 residents in 2017. Cholera deaths were highest in year 2010 at 2.2/100 cases, and lowest in year 2017 at 1/100 cases. Three of the 10 departments of Haiti, including Artibonite, Centre, and Ouest, together have reported more than 67% of the cholera cases per year, except in year 2016 (61.19%). Cholera control interventions have included efforts from national and international partners in combating the outbreak, including implementing alert/response system, campaigns to promote sanitation and hygiene, and oral
cholera vaccine campaigns. Conclusion: Considerable progress has been made to control the outbreak of cholera in Haiti, despite significant challenges related to funding, water and sanitation infrastructure, and widespread poverty. These efforts can serve as a model for the control of cholera in other resource-limited countries. Eradication of cholera from Haiti remains a difficult-to-reach goal.
Abstract Title:
Exploratory, Phase II Controlled Trial of Shiunko Ointment Local Application Twice A Day for 4 Weeks in Ethiopian Patients with Localized Cutaneous Leishmaniasis

Primary Author Block:
O. Ahmed; Armauer Hansen Res. Inst., Addis Ababa, Ethiopia

Abstract Body:
Cutaneous leishmaniasis (CL) is a major tropical skin disease which represents a worldwide public health and social problem in many developing countries including Ethiopia. Study in Peru have showed 46 out of 53 (86.8%) patients had complete cure after local administration of Shiunko for 4 weeks, with complete absence of parasites in lesion biopsy at the end of treatment. The aim of the present study was therefore to evaluate the clinical efficacy and safety of Shiunko ointment when applied on the lesion twice a day for 4 weeks in Ethiopian patients with LCL. Patients were randomized to receive treatment with Shiunko ointment or placebo (n = 20, each), applied on the lesion twice a day for 4 weeks. Clinico-parasitological assessments were performed before treatment, weekly for 4 weeks, and then 4, 8, and 12 weeks after the end of treatment A marked reduction in lesion size was observed on week 16 of treatment in the Shiunko compared with placebo group (69% and 22% reduction, resp.). The overall rate of lesion reduction during the four weeks of treatment was significantly faster in the Shiunko group. Shiunko provided significant effect on wound closure in patients with ulcerated lesion.

The clinical efficacy and tolerability of Shiunko were comparable to placebo with regard to its clinicoparasitological response (cure rate and parasitological clearance). Results of this preliminary study may suggest that Shiunko could be useful as adjuvant or as complementary treatment, not as alternatives to current treatment. Its attractive action includes fast lesion healing with a significantly smaller lesion at week 16 of treatment compared with placebo. In addition, its action was promoted in ulcerative lesions.