Unbiased Screening of Kawasaki Disease Sera for Viral Antigen Exposure

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**Poster Abstracts**

### 2303. Post-Exposure Prophylaxis for Animal Bites: A Low Cost Model for Enhancing Reach and Affordability of Biologicals in High Burden Countries

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**Session:** 251. Pediatric Potpourri  
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**Background.** Rabies is a preventable fatal zoonotic disease of considerably high burden in low and middle income countries of Asia and Africa. Bites from rabid animals are the cause of human rabies. WHO post-exposure prophylaxis (PEP) guidelines recommends taking both vaccine and rabies immunoglobulin for category-III bites. Strict adherence to complete recommended PEP guidelines is the single most important factor in preventing human deaths. Need to calculate the required dose/quantity of rabies immunoglobulin, a key biological, needed for adherence to WHO PEP guidelines leads to prohibitively high cost of PEP and one key reason for bite victims taking incomplete PEP. An alternate published method to inject bite sites only with rabies immunoglobulin to enhance affordability was evaluated for cost-reduction and affordability.

**Methods.** 25 bite victims requiring rabies immunoglobulin according to category-III of WHO guidelines were part of the study. All the animal bite sites were injected with adequate quantity of rabies immunoglobulin to cover only the animal bite sites completely as per published alternate method. This is in contrast to WHO PEP guidelines where calculation of immunoglobulin is done as per body weight and after injecting all the animal bite sites, the remaining quantity of immunoglobulin is injected intra-muscularly. All victims were vaccinated by intra-muscular route only. There was diversity in the profile of the 25 victims in terms of age, sex, number of wounds and body weight. Analysis was done to determine the cost reduction due to reduced quantity of immunoglobulin required in following an alternate approach to WHO PEP regimen.

**Results.** Cost of rabies immunoglobulin was reduced on an average between (50–70)% if the quantity used was enough to cover the wound sites comprehensively instead of the recommended quantity based on body weight. Follow-up was done for 9 months and none showed clinical signs and symptoms of rabies.

**Conclusion.** An evaluation to check the extent of cost reduction that could make rabies immunoglobulin, a key PEP biological, more affordable was done. The significant cost reduction could be adapted for further studies so as to bring about changes in WHO PEP guidelines which would lead to more affordability for PEP and less deaths due to rabies.

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### 2304. Validation of a Definition for K-12 Student Absenteeism Due to Influenza-like Illness (ILI) for School-based Influenza Activity Monitoring in Oregon School District, Wisconsin—ORCHARDS (Oregon Child Absenteeism and Respiratory Disease Study)

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**Background.** Syndrome-based absenteeism monitoring is proposed as an approach for early identification of influenza outbreaks in schools and surrounding communities, utilizing routinely collected attendance data. The availability of a simple, valid definition of ILI-related absence (a-ILI) is a prerequisite for monitoring.

**Methods.** We conducted a prospective study in children aged 4-19 years, between January 5, 2015 and April 11, 2017, which enrolled students with acute respiratory illness (ARI). Via home visits, the study team assessed participating students for symptoms (fever, cough, sore throat, nasal congestion, runny nose), collected nasal swabs for multiplex PCR testing, and ascertained school absence status. For analysis, ILI was defined as the presence of fever and a respiratory tract symptom (cough, sore throat, nasal congestion, or runny nose). We used multivariate binary logistic regression to assess the relationships between pathogens, absence status, and illness category.

**Results.** Of the total 661 participating students, 622 with ARI onset during school semesters remained in the analysis. Having an ILI was associated with absenteeism ($X^2=87.70; P < 0.001$), and with PCR detection of influenza A (FluA) and B (Flub), adenovirus (AD), and rhinovirus/enterovirus (R/E) (Table). While FluA, FluB, and AD were associated with positive likelihoods of a-ILI, the presence of R/E was associated with a negative likelihood of a-ILI. PCR detection of either FluA or FluB was strongly associated with a-ILI (OR=4.84; 95% CI: 2.80–8.34; P < 0.001).

**Conclusion.** A simple definition for a-ILI (absent with fever and a respiratory symptom) is strongly associated with laboratory-confirmed influenza. Accordingly, a-ILI may serve as a proxy for influenza-specific absenteeism, thus allowing school-based absenteeism monitoring for influenza outbreaks.

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### 2305. Unbiased Screening of Kawasaki Disease Sera for Viral Antigen Exposure

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**Background.** Kawasaki Disease (KD) is a serious inflammatory childhood illness. KD is associated with a high prevalence of antecedent infections, including infections with viruses and bacteria. These viruses and bacteria are thought to be involved in the disease etiology. We hypothesized that KD sera samples contain viral antigens that are specific to these infections. We aimed to develop an unbiased screening method for viral antigens in KD sera.

**Methods.** We screened sera, from 217 KD patients and 46 healthy controls, with a multiplex microarray, which simultaneously measured 175 viral antigens. The multiplex microarray was designed to be unbiased, meaning any new antivirus could be incorporated without further design. We performed control experiments to determine any false-positive reactions and to optimize the microarray.

**Results.** The microarray results confirmed our hypothesis that KD sera contain viral antigens specific to infections that are aetiologically linked to KD. The microarray showed that KD sera contained viral antigens that correlated with the patient’s previous medical history.

**Conclusion.** The microarray results have important implications for the understanding of KD pathogenesis, and could lead to new therapeutic targets.

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Background. Kawasaki disease (KD) is a medium-vessel vasculitis with a prediction for coronary arteries and is of unknown etiology. KD is responsible for the majority of acquired pediatric cardiovascular disease in the industrialized world, and is associated with development of coronary artery aneurysms in approximately 25% of untreated patients. Epidemiologic, pathologic, and clinical characteristics of KD display notable overlap with common pediatric viral illnesses, leading some to hypothesize that a viral infection is the inciting agent for KD.

Methods. We investigated viral exposure history in KD patients by utilizing a recently developed technique to profile sera against the known human virome in an unbiased manner. We screened sera from KD patients admitted during active phases of illness from 35 patients meeting clinical diagnostic criteria for KD, preferentially selecting patients with coronary involvement and/or late presentation. Control samples included healthy children and patients with known viral infections. Using phage immunoneutralization sequencing (PINS) technology, we sequenced the phage display library expressing epitopes that cover the complete reference protein sequences of the known 206 viruses with human tropism.

Results. The mean patient age was 4.6 years (range 0.4–16.9) and mean day of illness at acute sample collection was 14.5 days (range 5 to 32). A majority of patients demonstrated coronary artery changes during the course of their illness (22/35, 62%). Sera from patients with KD demonstrated patterns of viral infection to common pediatric viruses with similar signal intensity and distribution to healthy control children.

Conclusion. Although sera obtained early in the disease course could have missed a titer rise, we conclude that patients with KD do not exhibit unique serologic evidence of infection to known viruses or a viral exposure history that differs from age-similar healthy children.

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2306. Familial and Environmental Impact on Colonization with Antibiotic-resistant Organisms in the Neonatal Intensive Care Unit

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Colonization with antibiotic-resistant organisms (AROs), including methicillin-resistant S. aureus (MRSA), places neonatal intensive care unit (NICU) patients at increased risk for infection. Infants are routinely screened for MRSA colonization, but reservoirs for ARO acquisition in the NICU are poorly understood. Identifying infants with known MRSA nasal colonization and a control group of infants with negative MRSA screening swabs, and their parents, were enrolled in a prospective cohort study. Weekly swabs were obtained to identify AROs from 4 infant body sites, 3 parental body sites, and 5 high-touch environmental surfaces in the NICU to determine the most effective surveillance strategies used to identify AROs.

Results. Samples were collected 1–14 times (median 7) from 11 MRSA-colonized infants, 7 control infants, 17 mothers, and 9 fathers. Of MRSA-colonized infants, 9 (82%) were colonized with MRSA in the nares, 6 (55%) in the umbilicus, 8 (73%) in the inguinal folds, and 6 (55%) in the rectum over the study period. Six (55%) MRSA-colonized infants had persistent colonization (i.e., 3 consecutive positive samples) despite receiving decolonization measures. One (14%) control infant was colonized with MRSA during longitudinal sampling. Sixteen (89%) infants were colonized with MRSA at least once. Sampled Gram-negative rods (GNRs) were isolated from 14% of infants, 22% were sensitive to gentamicin, 80% to cefazidime, 33% to cefepime, 2% to meropenem, and 56% to ceftolozane/tazobactam.

Conclusion. Extranasal body sites, parents, and environmental surfaces serve as potential reservoirs of ARO acquisition and transmission in NICU infants.

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2307. Surveillance for Antimicrobial-resistant Organisms in Infants Transferred to the Neonatal Intensive Care Unit: Trends in Colonization and Practices

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Background. Infections with antibiotic-resistant organisms (AROs), i.e., methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant enterococci (VRE), and multi-drug-resistant Gram-negative rods (MDR-GNR) among infants hospitalized in the Neonatal Intensive Care Unit (NICU) are associated with mortality and serious morbidities. Implementing appropriate infection control policies may help prevent transmission of AROs. However, the most effective strategies for surveillance of AROs in the NICU are unclear. Prior data collected from infants transferred from outside hospitals to 2 NICUs affiliated with New York-Presbyterian (NYP) Hospital detected low rates of ARO colonization in the first week of life. Thus, in 2013 the strategy of performing surveillance on infants transferred to NYP NICUs was changed to performing targeted surveillance on infants transferred >7 days of life (DOL). The purpose of this study was to assess this change in surveillance strategy and monitor ARO colonization trends in the NICU.

Methods. Data from all infants transported to the NICUs at NYP from 2007 to 2016 were used. Risk factors for colonization with AROs including demographics and admitting diagnoses were explored using a multivariable binomial mixed model clustered by transferring hospital and controlled for NYP NICU. Trends in ARO colonization for infants transferred >7 days of life over time were assessed. A Fisher’s exact test was used to determine if MRSA risk factors were associated with the change in surveillance policy.

Results. From 2007 to 2016, 2925 infants were transferred to the NYP NICUs, 1101 at Site 1 and 1824 at Site 2; 2571 (88%) had surveillance for at least 1 ARO. There were 226 positive surveillance cultures in 204 infants (8%); 94 (3.7%) for MRSA, 78 (3%) for VRE and 54 (2%) for MDR-GNR. In the final models, transfer DOL remained a highly significant (OR per day = 1.018, CI1.014, 1.022, P < 0.001) predictor of colonization with any ARO. There was no significant increase in the incidence of transferred infants colonized with AROs over time in either NICU; this remained true in infants that were <7 days of life at Site 1.

Conclusion. These data continue to support the rationale for our change in surveillance policy. Further studies should evaluate the effect of this strategy on ARO transmission in the general NICU population.

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2308. Clinic Characteristics Are Not Associated with the Risk of Healthcare-associated Influenza-like Illness (HA-ILI) Among Young Children in Pediatric Primary Care Settings

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Background. The majority of pediatric healthcare encounters for influenza-like illness (ILI) take place in ambulatory settings where there may be multiple opportunities for respiratory virus transmission. Recent evidence shows that a poor clinic visit increases the risk of ILI among young children. We hypothesized that clinic factors would be associated with the risk of HA-ILI among children <6 years old by a primary care encounter.

Methods. We conducted a prospective cohort study of a sample of 1308 children presenting to any of the 31 primary care clinics in a large pediatric healthcare network for a non-ILI clinic visit during three consecutive respiratory seasons (2012/13 – 2014/15). HA-ILI cases were defined as any ILI encounter within 8 days after a non-ILI visit. Clinic factors (waiting room patient density or number of ILI encounters at the clinic) and patient factors (age ≤2 years and >2 years) were combined to create a 5 category composite variable. Logistic regression models after applying sampling weights evaluated associations between HA-ILI risk and patient age, daycare attendance, gender, influenza vaccine receipt and waiting room patient density.

Results. Our cohort included 367 HA-ILI cases and 941 non-cases. The majority (48.6%) were ≤2 years and did not attend school, 52.8% were male, and 18.9% received flu vaccine. Mean clinic patient density was 44.2 patients/1000 square feet. In multi-variable models, only the young age/daycare attendance composite variable was significantly associated with increased HA-ILI risk (OR 2.06, 95% CI 1.48,2.88). No clinic characteristics were associated with HA-ILI risk and risk did not vary by site.

Conclusion. In our cohort of young children, HA-ILI was not associated with the measured clinic characteristics that we hypothesized may increase respiratory virus transmission risk. Instead HA-ILI risk was highest in young daycare attendees who may be more likely to engage in behaviors that increase respiratory virus exposure risk or seek out healthcare services when sick. This suggests that HA-ILI may be more strongly influenced using other behavioral factors rather than clinic factors.

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