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1647. Real-Time Metagenomic Sequencing Reveals Discrete Transmission Clusters Within a Hospital-Associated Norovirus Outbreak

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Session: 169. Respiratory and Gastroenteritis Viruses
Friday, October 5, 2018: 2:00 PM

Background. Norovirus is the most common cause of acute gastroenteritis in the United States and a major challenge for infection control efforts. The high burden of norovirus in most communities and health care systems makes it difficult to discern viral transmission patterns using traditional epidemiological approaches alone.

Methods. We performed real-time metagenomic sequencing of norovirus isolates from an outbreak among inpatients at Seattle Children's Hospital (SCH). We also sequenced isolates from norovirus cases within the larger University of Washington (UW) Medical System that occurred during and after the outbreak.

Results. Our data showed that the month-long outbreak at SCH was actually characterized by 3 distinct concurrent transmission clusters contained within 3 different hospital units. We were able to report this information to the infection control team at SCH while the outbreak was still in progress. The virus responsible for one of these 3 clusters was genetically stable over a period of 4.5 weeks suggesting serial transmissions from a contaminated fomite, rather than patient to patient transmission. After cases meeting the epidemiological definition for hospital-acquired had ceased, we demonstrated that the virus from one of the 3 outbreak clusters continued to be transmitted to other patients within the SCH medical system. Finally, we showed that one of the patients who acquired norovirus during the outbreak developed a chronic infection with viral shedding documented up until the time of the patient's death, 8 months after the outbreak.

Conclusion. These results demonstrate the value of using metagenomics as an adjunct to traditional epidemiologic techniques in the setting of a hospital-associated norovirus outbreak. Real-time metagenomic sequencing elucidated viral transmission patterns within the outbreak while it was still in progress and follow-up sequencing revealed further infections due to an outbreak-associated viral strain even after the outbreak was thought to be over. Given this potential, metagenomic analyses represent an invaluable, largely untapped resource for improving our understanding of and reducing adverse effects from viral outbreaks.

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1648. Incidence of Norovirus and Rotavirus From Multisite Active Surveillance in Veteran's Affairs Hospitals, December 2016–February 2018: Results From the SUPERNOVA Network

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Session: 169. Respiratory and Gastroenteritis Viruses
Friday, October 5, 2018: 2:00 PM

Background. Viruses are frequently implicated in acute gastroenteritis (AGE) outbreaks, yet the endemic burden of norovirus and rotavirus disease in adult populations is not well characterized. In 2016, we implemented a multisite AGE surveillance platform capturing cases and controls in 4 VA hospitals (Atlanta, Bronx, Houston, and Los Angeles), collectively serving >320,000 patients annually.

Methods. Inpatient AGE cases and age- and time-matched controls were identified through prospective screening of admissions via standardized case definitions. Outpatient cases were passively identified using stool samples submitted for routine clinical microbiological diagnostics. Samples were tested with the FilmArray Gastrointestinal Panel, followed by genotyping of virus positives. Incidence was estimated using population denominators of unique patients served annually by site.

Results. From December 1, 2016 to February 28, 2018, 875 cases (496 inpatients, 379 outpatients), and 374 controls were enrolled. Norovirus and rotavirus prevalence was highest among outpatient AGE cases (11.6% and 2.9%, respectively) followed by inpatient cases (3.4% and 1.6%, respectively); few controls were positive (norovirus, 1.3%; rotavirus, 0%). Norovirus-associated inpatient incidence was 15.2 per 100,000 population (range by site: 10.7–19.9/100,000) and rotavirus-associated inpatient incidence was 7.5 per 100,000 population (range by site: 0–12.8/100,000). The predominant norovirus genotype was GII.P16-GII.4 Sydney (50%), and rotavirus genotype was G12P[8] (83%). Norovirus was detected every calendar month and peaked in December–January, while rotavirus peaked in April. Nine deaths were documented among AGE inpatient cases, including one norovirus-associated death.

Conclusion. Implementation of a multisite AGE surveillance platform captured a wide spectrum of illness for norovirus and rotavirus in US Veterans including outpatient visits, inpatient hospitalizations, and one norovirus-associated death. Norovirus was the leading viral pathogen and was detected year-round. Ongoing surveillance using this platform will allow for further characterization of the pathogen distribution and associated AGE disease burden in adults.

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1659. Variation in Identifying Sepsis and Organ Dysfunction Using Administrative Versus Clinical Data and Impact on Hospital Outcome Comparisons

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Session: 174. SHEA Featured Oral Abstract
Friday, October 5, 2018: 3:55 PM

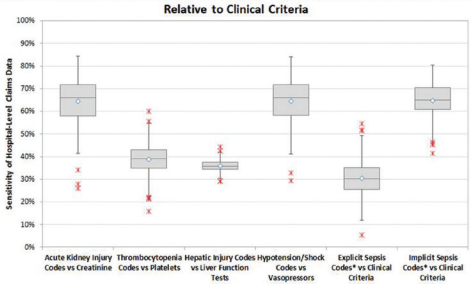
Background. Administrative claims data are commonly used for sepsis surveillance, research, and quality improvement. However, variations in diagnosis, documentation, and coding practices may confound efforts to benchmark hospital sepsis outcomes using claims data.

Methods. We evaluated the sensitivity of claims data for sepsis and organ dysfunction relative to clinical data from the electronic health records of 193 US hospitals. Sepsis was defined clinically using markers of presumed infection (blood cultures and antibiotic administrations) and concurrent organ dysfunction. Organ dysfunction was measured using laboratory data (acute kidney injury, thrombocytopenia, hepatic injury), vasopressor administrations (shock), or mechanical ventilation (respiratory failure). Correlations between hospitals' sepsis incidence and mortality rates by claims (using "explicit" ICD-9-CM codes for severe sepsis or septic shock) versus clinical data were measured by the Pearson correlation coefficient (r) and relative hospital rankings using either data source were compared. All estimates were reliability-adjusted to account for random variation using hierarchical logistic regression modeling.

Results. The study cohort included 4.3 million adult hospitalizations in 2013 or 2014. The sensitivity of hospitals' claims data for sepsis and organ dysfunction was low and variable: median sensitivity 30% (range 5–54%) for sepsis, 66% (range 26–84%) for acute kidney injury, 39% (range 16–60%) for thrombocytopenia, 36% (range 29–44%) for hepatic injury, and 66% (range 29–84%) for shock (Figure 1). There was only moderate correlation between claims and clinical data for hospitals' sepsis incidence ($r = 0.64$) and mortality rates ($r = 0.61$), and relative hospital rankings for sepsis mortality differed substantially using either method (Figure 2). Of 48 (46%) hospitals, 22 ranked in the lowest sepsis mortality quartile by claims shifted to higher mortality quartiles using clinical data.

Conclusion. Variation in the completeness and accuracy of claims data for identifying sepsis and organ dysfunction limits their use for comparing hospital sepsis rates and outcomes. Sepsis surveillance using objective clinical data may facilitate more meaningful hospital comparisons.

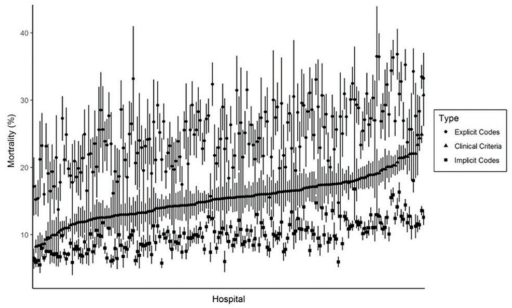
Figure 1. Variation in the Sensitivity of Hospitals' Organ Dysfunction and Sepsis Codes Relative to Clinical Criteria



*Explicit Sepsis Codes = Severe Sepsis (995.92) or Septic Shock (785.52) *(Primary Analysis)*
*Implicit Sepsis Codes = Infection AND Organ Dysfunction Codes *(Secondary Analysis)*

Boxes indicate the median hospital sensitivity (middle line), 25th quartile (lower box line), and 75th quartile (upper box line). Diamonds indicate the mean hospital sensitivity. Outliers are indicated by X (near outliers) and O (far outliers), as defined by values more than 1.5 times the interquartile range from the interior quartile boxes.

Figure 2. Hospital sepsis mortality rates ranked by clinical criteria and compared to claims data



Hospitals are ranked from left to right according to mortality rates for sepsis as defined by clinical criteria. For each hospital, the corresponding sepsis mortality by explicit sepsis codes (severe sepsis or septic shock – primary analysis) and implicit sepsis codes (infection + organ dysfunction codes – secondary analysis) is displayed. All mortality rates are reliability-adjusted.

Disclosures. **All authors:** No reported disclosures.

1663. Marked Improvement in Pandemic H1N1 Component Shedding and Immunogenicity in 2017–2018 Russian-Backbone Live Attenuated Influenza Vaccine (LAIV) in Gambian Children

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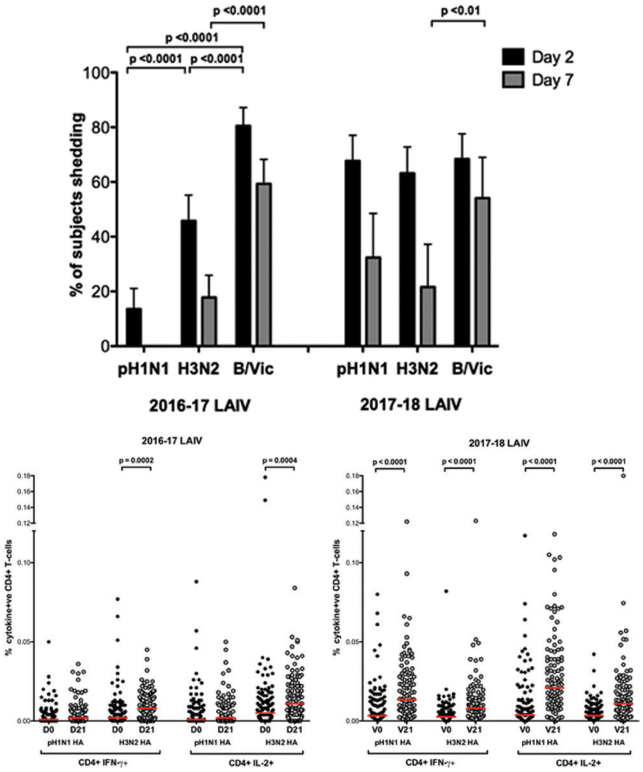
Session: 178. PIDS Featured Oral Abstract
Friday, October 5, 2018: 3:30 PM

Background. Recent observational studies in the United States have reported reduced effectiveness of the Ann Arbor-backbone live attenuated influenza vaccine (LAIV), coinciding with emergence of 2009 pandemic H1N1 (pH1N1). A recent RCT in Senegal of the Russian-backbone LAIV also showed no efficacy, with pH1N1 the predominant vaccine-matched strain circulating during the study. The reasons for this reduced effectiveness and efficacy are unclear but may involve pre-existing immunity or pH1N1 virus-specific factors. We explore these underlying reasons through an LAIV immunogenicity study in Gambian children across 2 influenza seasons.

Methods. Gambian children aged 24–59 months (n = 118) were given 2016–17 northern hemisphere Russian-backbone trivalent LAIV. Vaccine shedding, haemagglutinin inhibition (HAI) titre, influenza-specific T-cell responses, and mucosal IgA were measured using RT-PCR, HAI assay, flow cytometry, and ELISA, respectively. The following year, a further 127 children were given 2017–2018 formulation LAIV, where the pH1N1 strain was updated.

Results. In 2016–2017, significantly less pH1N1 shedding (13.6% children) was seen compared with H3N2 (45.8%) and B/Victoria (80.5%). Similarly, poor pH1N1-specific HAI (5.1% seroconversion), mucosal IgA (18.6% responders) and T-cell responses (<10% responses to pH1N1 HA) were seen, whereas significantly greater responses in ≥1 immune compartments were seen to H3N2 and B/Victoria. pH1N1 shedding was not related to pre-existing immunity in 2016–2017. Vaccination with 2017–2018 LAIV showed improvement in pH1N1 shedding with no significant difference between strains: 67.7%, 63.2%, and 68.4% children shedding pH1N1, H3N2, and B/Victoria at day 2 post-LAIV (see Figure 1). This was matched by enhanced pH1N1 HA-specific T-cell responses, with 47.1% children showing a $CD4^+IFNg^+$ and 54.4% a $CD4^+IL2^+$ response (see Figure 2). HAI and mucosal IgA data for 2017–2018 are currently being generated and will be presented, as well as key interactions between the parameters measured.

Conclusion. Our data suggest that poor pH1N1 A/California strain replication *in vivo* may explain recent suboptimal LAIV performance and suggest that an improvement can be expected with new pH1N1 strains included in current LAIV formulations.



Disclosures. **All authors:** No reported disclosures.

1715. A Randomized, Double-Blind, Placebo-Controlled Multicenter Phase 2 Trial to Examine the Effects of DAS181 in Immunocompromised (IC) Patients With Parainfluenza Virus (PIV) Lower Respiratory Tract Infection (LRTI) on Supplemental Oxygen (SO)

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Session: 199. Clinical Trials that May Change Your Practice
Saturday, October 6, 2018: 8:45 AM

Background. PIV infections are an important cause of morbidity and mortality in IC patients. DAS181, a sialidase fusion protein, has demonstrated activity in preclinical and clinical studies.

Methods. Adult IC patients diagnosed with PIV LRTI on chest imaging and required SO ≥ 2 L/minute were randomized 2:1 (stratified by mechanical ventilation [MV] at baseline) to nebulized DAS181 (4.5 mg in 3.5 mL/day) or matching placebo for up to 10 days. The primary endpoint was the proportion of patients reaching clinical stability survival (CSS, defined as alive, resolution of SO requirement, and normalization of vital signs) by Day 45.

Results. From 2014 to 2016, 110 patients were randomized and received study drug (74 DAS181 and 36 placebo). Median age was 57 years (range, 18–85). The majority were hematopoietic cell transplant (HCT) recipients (74), followed by hematological malignancy/solid tumor patients on chemotherapy (29), and lung transplant recipients (7). Day 45 CSS was achieved by 39.2% of DAS181-treated patients