

613. Transmission of Influenza Virus in Mother and Infant Transmission Events in Nepal

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Session: 63. Maternal-Child Infections

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Background. Influenza immunization of pregnant women provides protection of the infant against influenza disease. A potential mechanism of protection is prevention of maternal illness that may result in secondary transmission to infants. We aim to characterize influenza transmission in mother-infant pairs.

Methods. Pregnant mothers were enrolled in a randomized controlled trial of influenza immunization in rural Nepal from April 2011 to April 2013. Mothers and infants were surveyed weekly until 180 days post-partum for respiratory illness and mid-nasal swabs were collected at time of illness and tested for influenza virus by reverse-transcriptase polymerase chain reaction (RT-PCR). We defined a transmission episode as a mother-infant pair with an influenza-positive illness within 14 days of each other. Influenza viruses were strain-typed by RT-PCR and/or mass spectrometry.

Results. Seventeen mother-infant transmission episodes occurred with maternal illness preceding infant illness in 12 (70.6%). Of transmission pairs, 12 (70.6%) were influenza B, three (17.6%) H3N2 influenza A, one (5.9%) H1N1 influenza A, and one (5.9%) unspecified influenza A. Five (29.4%) mothers received the influenza vaccine. Successful strain-typing with RT-PCR/mass spectrometry of 11 pairs revealed that 10 (90.9%) were synonymous strains. Figure 1 shows the start of respiratory symptoms and virus type associated with influenza illness in the 17 mother-infant pairs.

Conclusion. Mothers are an important source of infant influenza infection. Transmission was confirmed with nearly all paired transmissions demonstrating a similar strain. The majority of transmission events occurred in nonvaccinated mother-infant pairs.

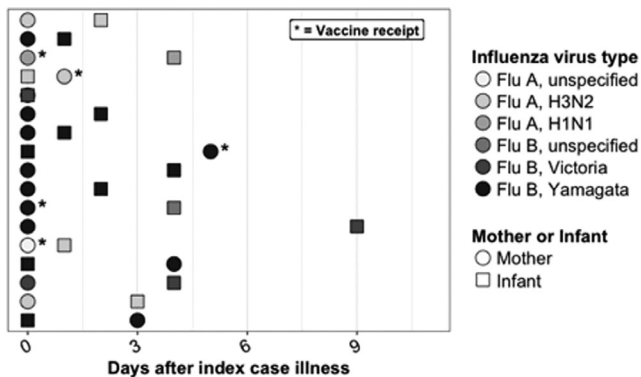


Figure 1: Influenza transmission events in mother-infant pairs. Symbols represent first day of respiratory symptoms associated with influenza-positive illness.

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614. Modeling Changes in Gastrointestinal and Respiratory Tract Bacterial Community Diversity Attributable to Common Antibiotic Exposures During Long-Term Acute Care

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Background. Reduced gastrointestinal tract bacterial community diversity has been associated with increased risk for healthcare-associated infections, including *Clostridium difficile* infection. We sought to develop a model for concomitant change in bacterial community

diversity at gastrointestinal and respiratory tract sites, drawing upon a recently completed cohort study of 92 subjects recruited from a long-term acute care hospital (LTACH) for dense longitudinal oral, endotracheal aspirate (ET), and stool specimen collection.

Methods. We evaluated the first 30 subjects enrolled from the LTACH cohort, for whom complete antibiotic administration data and 16S rRNA gene (V1-V2 amplicon) sequencing data were available. Sequencing was performed via the Illumina HiSeq platform; operational taxonomic units (OTUs) were formed and taxonomy assigned (GreenGenes 13.8) via the QIIME 1.9.1 pipeline. Generalized linear mixed effects models were fit using R (3.5.0), Stan (2.1.7), via the "rstan" and "rethinking" packages.

Results. We evaluated 472 subject-days of study enrollment across the 30 subjects (median 15 days/subject). ET specimens were available for all subject-days; oral and stool for 357 and 177 subject-days, respectively. We modeled daily change in Shannon diversity across oral, ET, and stool specimens, parameterized with daily exposure to cefepime, piperacillin-tazobactam, meropenem, IV vancomycin, and oral vancomycin. All parameters fit with Rhat value lower than 1.1. Absent antibiotic exposure on the previous day, the daily change in Shannon diversity at all sites was near zero. The largest observed effect was oral vancomycin on stool (daily delta Shannon: -0.6, 95% CI: -1.38 to 0.09). All estimated effects for intravenous antibiotics on the stool, and for all antibiotics at other sites were smaller.

Conclusion. Small daily changes in bacterial community diversity were attributable to individual antibiotics, but all 95% certainty intervals crossed zero in this pilot study. Further work will focus on modeling specific taxonomic changes attributable to individual antibiotics and antibiotic interactions.

Disclosures. All authors: No reported disclosures.

615. Can We Restore the Lung Microbiome with Fecal Microbiota Transplant (FMT)?

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Background. Unabated use of antibiotics for human diseases, in livestock and aquaculture has resulted in natural selection of multi-drug-resistant organisms (MDROs). The emergence of pan-resistant strains of *Pseudomonas* spp. pose a major threat to patients appropriately exposed to antibiotics (e.g., cystic fibrosis, lung transplant recipients). This organism evades antibiotics by a combination of efflux pumps, harboring multiple-resistant genes and acquiring low permeability of the outer membrane. Altering the gut microbiome could potentially modify the lung microbiome of patients colonized or infected with MDROs.

Methods. A 17-year-old patient with CF developed recurrent exacerbations with an extreme drug-resistant *Pseudomonas aeruginosa*; due to the lack of effective antibiotics to treat her while awaiting a decision to proceed with lung transplantation, sputum cultures were collected as part of clinical care. We modeled patient-derived isolate of predominantly MDR *Pseudomonas* in C57Bl6/j mice, where we engrafted the isolate into humanized murine lungs and studied host cytokine responses and microbial composition of the gut and lungs to the engraftment.

Results. Our data shows that there is a dominant IL6- and IL17-mediated immune response to the engraftment, accompanied by measurable changes to the lung and gut microbiota. We also show that some of these changes can be reversed by fecal microbial transplant (FMT) of 'normal' microbiota into the gut and lungs.

Conclusion. This murine model results suggest a potential role and effectiveness of gut FMT as a therapeutic measure for MDR bacterial infection in the lungs. Further studies are required to assess response in humans.

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616. Vancomycin Is Frequently Administered to Hematopoietic Cell Transplant Recipients Without a Provider Documented Indication and Correlates with Microbiome Disruption and Adverse Events

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Background. The gut microbiome of hematopoietic cell transplant (HCT) recipients correlates with the risk of acute graft- vs.-host disease (aGVHD). IV vancomycin is the most commonly used nonprophylactic antibiotic in HCT recipients at our center. We evaluated indications for vancomycin use and impact of vancomycin exposure on the microbiome.

Methods. Antibiotic exposures and provider-documented indications for vancomycin use were assessed through chart review. We assessed adherence to guideline-based recommendations for vancomycin use for courses during neutropenic fever. Weekly stool samples collected from HCT patients before and up to 100 days post-transplant in a previously described cohort had bacterial composition determined from 16S rRNA amplicons analyzed with a phylogeny classifier and was correlated with vancomycin exposure using mixed effects modeling to correct for overlapping and repeated antibiotic exposures.