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.

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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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Session: 64. Microbiome and Beyond

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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 “stan” 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 ET, and stool, and specimens, parameterized with daily exposure to cephalosporins, macrolactam-tazobactam, 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 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.

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

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Session: 64. Microbiome and Beyond

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Background. Unwanted 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 antibiotic 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 microbiota composition of the gut and lungs to the engrafment.

Results. Our data shows that there is a dominant IL6- and IL17-mediated immune response to the engulfment, accomplished by measurable changes to the lung and gut microbiota. We also showed 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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Session: 64. Microbiome and Beyond

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Background. The gut microbiome of hematopoietic cell transplant (HCT) recipients correlates with the risk of acute graft-versus-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.
Results. Thirty seven of 70 (53%) of patients received vancomycin over 61 courses with a mean duration of 8 days; 14 (23%) of these courses were with neutropenic fever. No indication was documented by the provider for 21 (34%) vancomycin courses (Figure 1). Almost half of all courses given for neutropenic fever did not meet guideline indications (Figure 2). Adverse effects occurred in 19 (31%) of vancomycin courses, including 17 (94.7%) associated with acute kidney injury.

Vancomycin was associated with reduced relative abundance of organisms correlated with reduced risk of subsequent severe acute graft vs. host disease and Clostridium scindens, an organism protective against C. difficile infection (CDI) (Figure 3, in bold).

Conclusion. Indications for vancomycin were poorly documented and infrequently guideline based. Adverse events occurred in 1 in 3 courses of vancomycin. Vancomycin correlated with microbiome changes which have been associated with increased risk for aGVHD and CDI.

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617. Characterization and Development of the Infant Gut Virome: A STORK Study
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Background. There is little known about the dynamics of the infant virome and how it relates to healthy growth and development. This study will establish the baseline gut virome and observe dynamic changes in a cohort of infants from birth to 3 years old. We hypothesize that changes in the gut virome will impact growth and immune development.

Methods. One hundred and twenty-eight infants were enrolled in the Stanford's Outcome Research in Kids (STORK) cohort prior to 36 weeks gestation. Stool samples were collected at an average of 90, 134, 162 days old/infant. Baseline data were collected at birth (height, weight, length, Apgar's score, antibiotic use) and health surveys were collected weekly. Stool samples (n = 477) were extracted using the EZ1 Viral Kit (Qiagen). Libraries were prepared using the Nextera XT Kit (Illumina) and sequenced on an Illumina HiSeq 2500 on rapid mode (150/150 bp paired-end sequencing). Datasets were analyzed using SURPI; a bioinformatic pipeline for pathogen detection.

Results. A subset of the infants were tested (n = 27), 54% of which were male. The infants were 62% white, Hispanic, 26% white, non-Hispanic, 8% Asian, and 4% other. Seventy-five stool samples—sequenced at an average depth of 22 million reads—were analyzed from the 27 infants. Vertebrate viruses (42.8%) and phages (45.2%) represented the majority of the viral reads, while the other reads were invertebrate, plants or protozoa (12%). Virome abundance, richness, and diversity were 5.5e+04 species reads per million, 55.5 on the Choao Richness scale, and 1.45 on the Shannon Diversity Index respectively, with values increasing as the infants aged. The phage families most commonly identified were Myoviridae, Podoviridae, and Siphoviridae. There were seven different human viral families observed: Adenoviridae, Astroviridae, Caliciviridae, Paroviridae, Picornaviridae, Reoviridae, and Anelloviridae. Five infants were documented to have cold symptoms within 7 days of sampling, they were found to have matravirus C (1), maamastrovirus 1 (1), bocavirus (3). Three infants were documented to have caliciviruses (2) and adenovirus (1); however, no symptoms were reported.

Conclusion. This study will comprehensively characterize the development of the human virome and monitor its effect on growth and immune development.

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618. Do Clinical Factors Affect Microbial Engraftment After Fecal Microbiota Transplantation in Recurrent Clostridium difficile Infection? 
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Background. Fecal microbiota transplantation (FMT) is an effective treatment for recurrent Clostridium difficile infection (rCDI). Few studies have evaluated clinical factors associated with microbial engraftment. We describe microbial changes post-FMT and clinical factors impacting engraftment.

Methods. Patients undergoing FMT for rCDI via colonoscopy were enrolled. Clinical data and stool were collected pre- and 8 weeks post-FMT. Microbial profiles were assessed by 16S rRNA sequencing. Difference in microbial alpha and beta diversity between groups was determined. Significance testing was assessed using Mann–Whitney U tests. The Jenkins and PERMANOVA tests (JSD) between donor and their recipient post-FMT was used as a measure of engraftment.

Results. A subset of 12 patients received an FMT from 12 unique donors. The efficacy rate was 92%. Mean recipient age was 60 years (range: 33–87) with more females (7/12).

Recipient pre-FMT alpha diversity was significantly lower than the JSD of the recipients' pre-FMT series (P = 0.04, Figure 1a). This difference dissipated post-FMT (P = 0.67). On beta-diversity analysis, the recipients' pre-FMT samples clustered separately from their post-FMT samples (P = 0.01, Figure 1b), with the post-FMT samples shifting closer to the JSD and donor samples. Proteobacteria was dominant in patients' pre-FMT samples and were substantially reduced post-FMT, combined with an expansion in Bacteroidetes (Figure 2).

On linear regression analysis, clinical factors (age, sex, previous recurrent CDI episodes, inflammatory bowel disease, proton pump inhibitor, immunosuppression, previous anti-CDI antibiotic courses, probiotics) were not significantly associated with engraftment outcomes.

Conclusion. There is a significant and durable shift in recipients' microbial profile to resemble their donor post-FMT. Recipients' pre-FMT clinical factors did not significantly affect microbial engraftment. Future metagenomic studies may help elucidate whether clinical factors impact engraftment.

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Figure 1: (A) Alpha diversity. (B) Bray–Curtis principle component plot.