2575. Dramatic Time-Dependent Changes of Bacterial and Fungal Taxonomic Signatures in 4 Body Regions of ICU Patients

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Background: It has been hypothesized that intensive care unit (ICU)-related complications like nosocomial pneumonia or gastrointestinal dysfunction are associated with disturbances of normal host microorganisms. However, these alterations are largely unknown in ICU patients. The bacterio- and mycobiota in 4 body regions in 14 ICU patients was investigated after admission until death or discharge to other wards.

Methods: Medical ICU patients were sampled with pharyngeal swabs, endotracheal aspirates, gastric secretions and stools or rectal swabs (in constipated patients). V1-V2 (16S rRNA gene) and eukaryoitic ITS sequencing was performed as previously described as well as denoizing, transformation into amplicon sequence variants and analysis using qiime2 and LEfSe (LDA Score > 3.0, P-value < 0.05). For sequence classification databases SILVA 132 (16S) and UNITE version 7.2 (ITS) were used.

Results: Samples were obtained at multiple time points from day 1 up to day 47 with a median of 11 samples per patient (range 2 to 17). In 11 patients all intended body regions were sampled (stool was missing in two patients and gastric secretion in two patients). The length of ICU stay and number of antibiotics administered during ICU stay was associated with loss of diversity in all investigated body sites. Taxonomic profiling showed a significant reduction of physiological members from the oral and fecal microbial community (e.g., *Clostridiales*, *Bacteroidales*, *Faecalibacterium* spp. etc.) after 2 weeks at the ICU. In contrast, *Enterococcus* spp. and *Staphylococcus* spp. were enriched in the gastric and fecal microbiota. *Candida* spp. dominated fungal communities of all body sites investigated. *Staphylococcus aureus* was associated with ITS positive, *Candida* spp. dominated samples throughout all body sites, while *Pseudomonas aeruginosa* was associated with ITS-negative samples.

Conclusion: The length of the ICU stay and the number of different antibiotics administered during the stay at the ICU are associated with severe intestinal dysbiosis, determined by loss of physiological microbes, decreased bacterial richness and domination of low-diversity fecal microbiota. Early colonization of *Candida* spp. might favor a co-existance of a *Staphylococcus* spp.-dominated microbiota in the ICU.

Disclosures. All authors: No reported disclosures.

2576. The Microbiome of Recurrent Bacterial Vaginosis Compared with Asymptomatic Controls

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Background: Bacterial vaginosis (BV) affects nearly 1 in 3 women in the United States and is poorly understood. The study of the vaginal microbiome, using 16S rRNA-gene amplicon sequencing, has increased our knowledge of BV. We aimed to characterize the vaginal microbiome of women with recurrent BV firstly in comparison to controls, and secondly in comparison to a sub-population of our asymptomatic controls, positive for *Gardnerella vaginalis* via a vaginal pathogens DNA direct probe test (DNA probe).

Methods: Women aged 18–40 years, with recurrent BV, and asymptomatic controls were prospectively enrolled. Vaginal samples were collected from each participant. DNA was extracted, amplified using primers targeting the V3-V4 variable region of the 16S rRNA-gene, and then sequenced and processed through a hybrid Qiime MICCA bioinformatics pipeline. We also tested for G. vaginalis using the DNA probe.

Results: Seventeen recurrent BV patients and 46 controls were enrolled. B diversity (*P* = 0.045), but not alpha diversity (*P* = 0.076) differed between groups. The genera *Gardnerella* and *Prevotella* were relatively more abundant, while Lactobacillus was relatively less abundant in recurrent BV vs. control groups. Of the patients for whom results of the DNA probe for *Gardnerella vaginalis* were available, 11 (69%) recurrent BV patients and 14 (35%) controls were positive. Control patients, negative by the DNA probe test, showed decreased alpha diversity (*P* = 0.0001) and significantly different β diversity (*P* = 0.001) compared with recurrent BV patients. Neither alpha (*P* = 0.31) nor β (*P* = 0.096) diversity differed between recurrent BV patients and controls that were *G. vaginalis* positive.

Conclusion: The microbiome of recurrent BV patients is distinct from that of asymptomatic controls; recurrent BV patients exhibit different β diversity, less *Lactobacillus* and more *Gardnerella* and *Prevotella*. Asymptomatic *Gardnerella vaginalis*-colonized controls demonstrate similar microbiome profiles to those of recurrent BV patients. These findings suggest that individual factors may influence whether or

not a patient with a BV microbiomic profile experiences symptoms. Further investigation into these mechanisms could yield insights into the treatment of recurrent BV.

Recurrent Bacterial Vaginosis Patients Cluster Separately from Control Patients
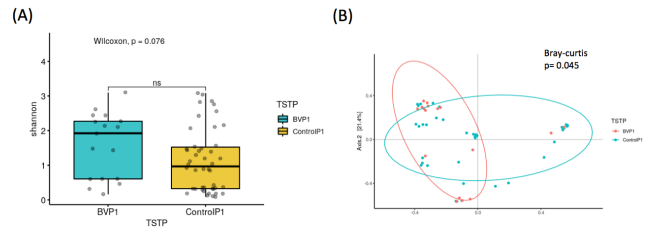
(A) Alpha diversity is not significantly different between recurrent BV and control groups (p = 0.076). (B) Beta diversity significantly differs between recurrent bacterial vaginosis and control groups (p=0.045).

Control Patients Colonized with *Gardnerella Vaginalis* Have Similar Microbiomic Profiles (alpha and beta diversity) to Recurrent Bacterial Vaginosis Patients
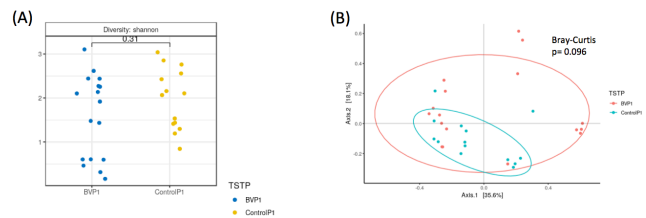
Neither (A) Alpha diversity (p=0.31) nor (B) Beta diversity differ significantly between recurrent BV patients and control patients colonized with *Gardnerella vaginalis* (p = 0.096).

Disclosures. All authors: No reported disclosures.

2577. Periodontal Disease and the Oral Microbiome in Alcohol-Dependent Individuals

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Background: Periodontal disease results from a polymicrobial infection composed of pathogenic bacteria that colonize the oral cavity, resulting in loss of periodontal attachment and alveolar bone. Periodontitis can increase the risk or exacerbate other comorbidities. Alcohol use increases the risk of periodontitis, but there is little knowledge about periodontitis among people who misuse alcohol.

Methods: As part of a larger oral and gut microbiome study, this analysis examines the oral microbiome in the occurrence and severity of periodontitis among alcohol-dependent (AD) subjects undergoing a 28-day inpatient alcohol treatment program. Tongue brushings were collected from 22 subjects within the first week of admission, and 16S rDNA sequencing was performed. All subjects had a dental examination during their inpatient stay. This analysis divided periodontal disease status into three major groups–no disease, mild or moderate disease, and severe disease. One-way ANOVA was used to compare microbial genera across the 3 groups.

Results: Nineteen (86%) of the subjects had periodontitis: 16 had mild or moderate disease, and 3 had severe disease. Statistically different microbial genera in at least one of the three groups (P ≤ 0.05 corresponding to FDR ≤ 0.25) that had a relative abundance of at least 0.5% include: *Bifidobacterium, Lactobacillus, Parvimonas, Peptostreptococcus, Porphyromonas,* and *Treponema*. Surprisingly, the subjects with no periodontitis had increased abundances of genera that are often pathogens, *Porphyromonas* and *Peptostreptococcus*. Subjects with severe periodontitis had increased abundances of known pathogens *Treponema* and *Parvimonas*, as well as *Lactobacillus*, which has been associated with dental caries.

Conclusion: We observed that periodontitis accompanies chronic AD, given that 86% of our subjects had the disease. While some microbiome differences for individuals with and without periodontitis were not consistent with the existing literature, this

may have many explanations. Future studies should consider how chronic AD could change the microbial ecology of the mouth and lead to further infection as well as utilizing multiple oral sites and a larger sample size to better understand the relationship between AD and periodontal disease.

Intramural funds from NIH

Disclosures. All authors: No reported disclosures.

2578. Narrow-Spectrum Antibiotic Treatment of Clostridium difficile Infection Improves Preservation of Intestinal Metabolic Profile

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Background: Commensal gut bacteria are thought to protect against *C. difficile* infection (CDI) by producing metabolites that inhibit *C. difficile* germination and growth. Alternatively, the protective effect could reflect nutrient competition or other mechanisms of chemical communication that also involve the host. CDI treatment using a broad-spectrum antibiotic such as vancomycin (VAN) dramatically depletes commensal bacteria. This dysbiosis can persist for several weeks after end-of-therapy (EOT), and is associated with increased recurrence risk. In this study, we investigate the hypothesis that treating CDI with a more selective antibiotic reduces collateral damage to the intestinal microbiota, preserving or restoring a CDI-inhibitory metabolic profile.

Methods: Stool samples were collected from CDI patients treated with either a narrow- (RDZ) or broad-spectrum antibiotic (VAN) at days 1, 10 (EOT), 25, and 40. Global metabolite profiles were measured by untargeted LC-MS.

Results: Untargeted metabolite analysis showed broad differences in the metabolic activity of intestinal microbiota of RDZ- and VAN-treated subjects (Figure 1). At EOT, 28% of LC-MS features detected in both RDZ and VAN samples were differentially present (FDR corrected *P*-value <0.05). Over 80% of the differentially present features were elevated in the RDZ group, indicating diminished capacity of microbiota from VAN subjects to generate diverse metabolic products. Pathway analysis found significant differences in purine, taurine, tyrosine, and bile acid metabolites. The VAN group showed a 5-fold decrease in free taurine, a major conjugation substrate of primary bile acids released by bacterial bile salt hydrolases. VAN treatment also decreased fermentation products of aromatic amino acids and amino sugars derived from mucin degradation. Oligosaccharides were the major metabolite class elevated in VAN subjects.

Conclusion: Our data suggest that RDZ treatment correlates with enhanced preservation of bacteria-derived ligands regulating intestinal immune function and substrates of bacterial metabolism. These metabolic profile differences between a narrow- and broad-spectrum antibiotic may contribute to their varying efficacy in preventing CDI recurrence.
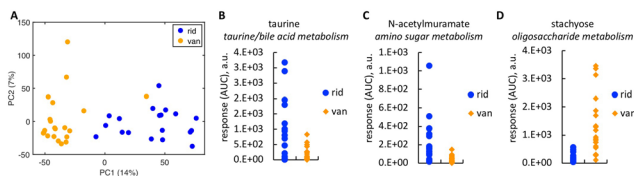
Disclosures. All authors: No reported disclosures.

2579. Impact on the Gut Microbiota of the Prolonged Antimicrobial Therapy in Patients with Bone and Joint Infection (BJI): Results From the OSIRIS Prospective Study in France

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Background: There is growing interest about the deleterious impact of antibiotics on loss of gut symbiosis, called dysbiosis. As patients with BJI require antibiotics usually during 6 to 12 weeks, it is of interest to determine whether dysbiosis is frequent in this population, and if it could potentially reversible or not.

Methods: Multicentric prospective cohort study in France (EudraCT 2016-003247-10) including patients with 3 categories of BJI: native, osteosynthesis-related and prosthetic joint infection (PJI). At the time of suspicion (V1), at the end of therapy (V2) and then 2 weeks after stopping therapy (V3), blood and fecal samples were collected. Extracted DNA from stool was sequenced using shotgun metagenomic sequencing based on illumina library and Iseq instrumentation. Data run through a dedicated

pipeline in order to produce microbiome indexes such as Sympson or Shannon diversities indexes. Gut microbiome and inflammation markers were analyzed including fecal neopterin, a maker of gut inflammation.

Results: Concerning the 62 patients included (mean age, 60 years; mean duration of antibiotics, 66 days), 27 had native, 14 had osteosynthesis and 21 had PJI. The most frequently prescribed drug was a fluoroquinolone, followed by a third-generation cephalosporin and vancomycin. Stools from 42 of them were analyzed as per protocol. Overall, the mean Shannon richness index decreased from 0.904 at V1 to 0.845 at V2; the Bray-Curtis index underlined the difference in microbiome reconstitution at V3 in comparison with V1. We report significant microbiome loss of diversity at V2, that was reversible at V3 in patients with native BJI and osteosynthesis-related BJI, but not in patients with PJI (figure). Fecal neopterin increased between V1 and V2 (mean 221.6 and 698.1 pmol/g of feces, respectively) and then decreased at V3 (422.5 pmol/g), and could be a potential surrogate marker of gut dysbiosis. Of note, patients with abnormal CRP at the end of antibiotics had high neopterin values, that raises the hypothesis that abnormal CRP at the end of antibiotics could be in relation with gut dysbiosis rather than uncured BJI.

Conclusion: The impact of antibiotics on the gut microbiota of patients with BJI seems to be significant, especially in patients with PJI who could be candidate for fecal microbiota transplantation.

Shannon gut microbiota richness index
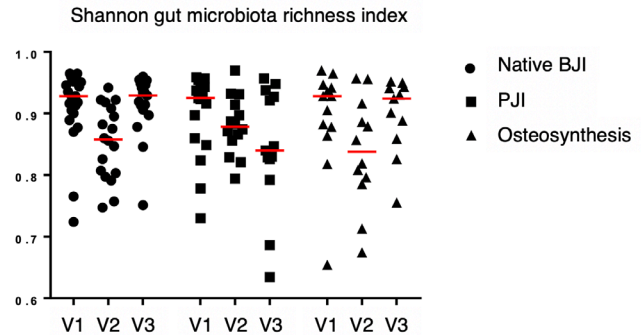
Disclosures. All authors: No reported disclosures.

2580. Serial Microbiome Analysis in a Patient with Multiple Failed Fecal Microbiome Transplantations

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Background: Fecal microbiota transplantation (FMT) is recommended to treat refractory or recurrent cases of *Clostridioides difficile* infection (CDI) through restoration of a healthy intestinal microbiome. The procedure has reported success rates of 90% or higher for CDI, but several risk factors for FMT failure have been identified. Here we present a case of a patient failing four FMT procedures over a 2-year period, with accompanying microbiome and metagenomic analyses.

Methods: Seven serial *C. difficile*-positive stool samples were collected as part of an ongoing surveillance system in Texas. Samples, including the index case, represented independent CDI episodes interspersed between four separate FMT procedures between 2016 and 2018. PCR ribotype (RT) testing, 16S rRNA gene sequencing, MIC testing, multidrug-resistant organism (MDRO) screening, and shotgun metagenome sequencing were conducted for each of the samples.

Results: The patient was a 42-year-old female with various comorbidities, including systemic lupus erythematosus. She received continuous non-CDI antibiotic courses throughout her CDI therapy for a variety of infections. The vancomycin MICs in infecting *C. difficile* strains increased with cumulative vancomycin exposure. Multidrug-resistant organisms were detected in stool, including *Enterococcus* spp., MRSA, and *Candida glabrata*. The first five of the seven strains were RT 078–126, one was mixed RT 002 and RT 054, and one was RT 002. The analysis of 16S rRNA gene sequences demonstrated that microbial diversity was never restored after FMT procedures. A strong correlation between microbial and functional gene compositions suggests that fecal samples share many microbial species with associated functional genes.

Conclusion: A number of systems biology changes were observed in a patient with persistent CDI despite multiple FMTs. The lack of FMT engraftment was most likely due to continuous broad-spectrum antibiotic exposure in an immunocompromised patient.

Disclosures. All authors: No reported disclosures.

2581. An Invertebrate Model to Study Gut Microbiome Dysbiosis

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