

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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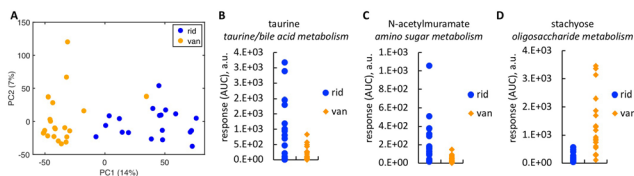
**Session:** 267. Microbiome, Antibiotics, and Pathogenesis  
**Saturday, October 5, 2019: 12:15 PM**

**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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**Session:** 267. Microbiome, Antibiotics, and Pathogenesis  
**Saturday, October 5, 2019: 12:15 PM**

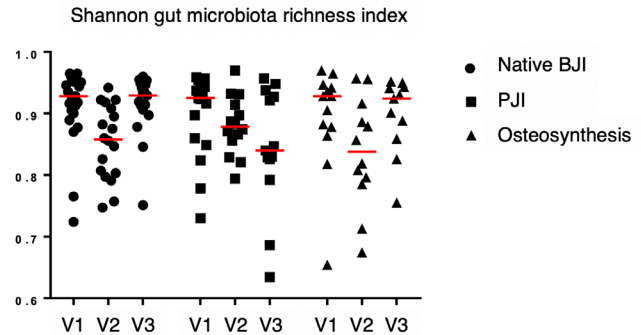
**Background:** There is growing interest about the deleterious impact of antibiotics on loss of gut symbiosis, called dysbiosis. As patients with BJI require antibiotics usually during 6 to 12 weeks, it is of interest to determine whether dysbiosis is frequent in this population, and if it could potentially 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 Simpson 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.



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

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

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**Session:** 267. Microbiome, Antibiotics, and Pathogenesis  
**Saturday, October 5, 2019: 12:15 PM**

**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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**Session:** 267. Microbiome, Antibiotics, and Pathogenesis  
**Saturday, October 5, 2019: 12:15 PM**

**Background:** Antimicrobials disrupt the gut microbiota by reducing gut microbiome diversity and quantity. *Galleria mellonella* provides an invertebrate model that is inexpensive, easy to maintain, and does not require specialized equipment. This study investigated the feasibility of using *G. mellonella* as an *in vivo* model to evaluate the effect of different antimicrobials on gut microbiota.

**Methods:** To determine baseline gut microbiota composition, the gut contents of *G. mellonella* were extracted and genomic DNA underwent shotgun meta-genomic sequencing. To determine the effect of infection and antibiotic use, 30 larvae were injected (left proleg) with  $\sim 1 \times 10^5$  colony-forming unit (cfu) of methicillin-resistant *Staphylococcus aureus* (MRSA) and were randomized 1:1:1 to treatment with vancomycin (20 mg/kg) or a natural antimicrobial (*Nigella sativa* seed oil, 70 mg/kg; NS oil), or a combination. The larvae were kept at 37°C post-infection and monitored daily for 72 hours for activity, extent of cocoon formation/growth, melanization, and survival. Two larvae from each group were randomly selected and homogenized with PBS as controls. After 24 hours of incubation, gut contents were extracted and plated for MRSA and *Enterococcus* cfu counts.

**Results:** Metagenomics analysis showed the gut microbiota composition of *G. mellonella* larvae was dominated by a subset of closely-related *Enterococcus* species. After 24 hours of exposure, mean *Enterococcus* counts were  $4 \times 10^3$  cfu in the vancomycin arm and  $6.2 \times 10^4$  cfu in the NS oil arm. Mean MRSA counts were  $3.3 \times 10^5$  cfu in vancomycin arm and  $1.5 \times 10^4$  cfu in NS oil arm. The combination of vancomycin and NS oil had higher *Enterococcus* counts than the vancomycin alone arm ( $6.3 \times 10^4$  cfu vs.  $4 \times 10^3$  cfu, respectively), suggesting that NS oil may have a role in protecting the gut microbiota.

**Conclusion:** This study provides preliminary evidence to support the potential use of *G. mellonella* to assess the *in vivo* effect of a natural and synthetic antimicrobial on the gut microbiota.

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

#### 2582. The Association Between Dietary Fiber and Diet and Gut Colonization with *Clostridium difficile*

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**Session:** 267. Microbiome, Antibiotics, and Pathogenesis  
**Saturday, October 5, 2019: 12:15 PM**

**Background:** There is little research on the relationship between diet and *Clostridium difficile* infection. Animal studies have shown potential benefits of dietary fiber in modulating *C. difficile* infection.

**Methods:** In 2016–2017, we carried out a microbiota study among adults in the Survey of the Health of Wisconsin, a population-based health survey collecting data on a wide range of health determinants and outcomes. We administered the Dietary History Questionnaire and asked about risk factors for *C. difficile* and collected fecal samples for 16S rRNA sequencing of gut microbiota and cultured for *C. difficile*. Dietary components were standardized to 1,000 kcal energy intake. Logistic regression was used to examine diet factors associated with *C. difficile* colonization. The quasi-conditional association test (QCAT) was performed to identify taxa that were significantly associated with fiber intake.

**Results:** In our general population sample of adults [(N = 238; 58% female; mean (range) age = 54 (18–94)], the prevalence of gut colonization with *C. difficile* was 9.2% (18 toxigenic/3 non-toxicogenic). After adjusting for age, sex, and antibiotic use, *C. difficile* colonization was associated with usual daily fiber consumption over the last year. ORs (95% CI) in the highest vs. lowest quartile were 0.18 (0.03, 0.89) for total fiber, 0.09 (0.01, 0.77) for soluble fiber, and 0.10 (0.1, 0.80) for insoluble fiber. Lower odds of *C. difficile* colonization were associated with greater consumption of dark green vegetables and less consumption of solid fats, total saturated fats, and added sugar, but not significantly. Omega 3 fatty acids and fruit consumption were either non-monotonically or not associated with *C. difficile* colonization. Higher levels of total dietary fiber intake were also associated with increased colonization by bacteria within the order Clostridiales, the families Coriobacteriaceae, Lactobacillaceae, and Veillonellaceae, and the genera *Bifidobacterium*, and *Lactobacillus*.

**Conclusion:** Higher average daily dietary fiber (total, soluble, and insoluble) appears to be associated with lower odds of gut colonization with *C. difficile*. Future research should examine the impact of dietary interventions on *C. difficile* colonization and infection.

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

#### 2583. Short-term Impact of Antimicrobial Exposure on Fecal Carriage of Resistant Microorganisms

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**Session:** 267. Microbiome, Antibiotics, and Pathogenesis  
**Saturday, October 5, 2019: 12:15 PM**

**Background:** The relationship between antimicrobial use and subsequent resistance is complicated; this study assesses the short-term impact of antimicrobial use on fecal carriage of resistant microorganisms. This is a sub-study of an ongoing trial comparing 7 vs. 14 days of antimicrobial treatment for male urinary tract infection. This analysis quantifies the effect of 1–2 weeks of systemic antimicrobial use on the fecal flora within 1 week of completing therapy.

**Methods:** The parent study has enrolled 216 subjects, with 178 enrolled in the optional resistance sub-study. Subjects received either ciprofloxacin or trimethoprim/sulfamethoxazole (SXT), randomized to 7 vs. 14 days therapy. Subjects provided 2 stool specimens, 1 during treatment and 1 a week after completing study medication. Samples were plated on media for Gram-positive and negative growth, including T-7 plates with ciprofloxacin and SXT added to select for resistant organisms. Resistance to 22 antimicrobials was assessed, with resistance reported by: number of isolates with any antimicrobial resistance, total number of resistant drugs/isolate, and number of isolates with multi-drug resistance (resistance to 3 or more different antimicrobial classes).

**Results:** Overall, 143 (80%) subjects provided 2 stool samples, with 104 (73%) having growth from at least 1 of the samples. Fifty-one of 143 (36%) had microbial growth from both samples. From these 51 paired samples, there were 255 total strains isolated (117 from the first sample, 138 from the second), with some yielding multiple organisms (range, 1–5). From sample 1, 110/117 (94%) isolates had any antimicrobial resistance, vs. 131/138 (95%) from sample 2 (P = .79). Mean number of resistant drugs/isolate was 7.4 in sample 1 and 5.8 in sample 2 (P = .009). Multi-drug resistance was seen in 102/117 (87%) isolates from sample 1 vs. 85/138 (62%) isolates in sample 2 (P < .001).

**Conclusion:** The fecal flora of patients on antimicrobial therapy for UTI has a significant increase in resistant microorganisms compared with samples obtained shortly after antimicrobial completion. This may reflect repopulation of the fecal flora with less-resistant strains after the selection pressure of therapy has been removed. After unblinding, we will assess if differences in resistance are affected by therapy duration.

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

#### 2584. Effects of Fecal Microbiota Transplantation for Decolonizing Multidrug-Resistant Organism

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**Session:** 267. Microbiome, Antibiotics, and Pathogenesis  
**Saturday, October 5, 2019: 12:15 PM**

**Background:** Increasing prevalence of multidrug-resistant microorganisms (MDRO) results in poor clinical outcomes, longer hospitalizations and higher health-care costs. It is likely that MDRO colonization can lead infections to vulnerable patients. Currently, however, MDRO decolonization strategies are lacking. The purpose of this study was to prove the efficacy of FMT on decolonization of carbapenemase-producing Enterobacteriaceae (CPE) and vancomycin-resistant enterococci (VRE) carriers.

**Methods:** This study was a prospective, open-label, uncontrolled, single-center pilot study of FMT for digestive tract colonized CPE, VRE, or CPE/VRE patients between March 2018 and February 2019. Fecal solution obtained from healthy unrelated donors was infused to recipient's gut. Fecal samples of recipients were collected before and after FMT until 1 year. We compared characteristics of subjects succeed in decolonization during study period (responders) with subjects who failed to decolonize MDRO by FMT (non-responders). Furthermore, microbiome analyses were performed to investigate the influence of microbial characteristics of recipients on the outcome of FMT.

**Results:** Decolonization was achieved in 12/23 (52.2%) during study period. Hemoglobin (11.0 vs. 10.0, P = 0.018), low-density lipoprotein cholesterol (102.0 vs. 89.0, P = 0.049), and albumin (3.4 vs. 3.2, P = 0.006) levels were higher in responders. Antibiotic treatment (ATB) within 1 week after FMT were less common in responders (41.7% vs. 90.9%, P = 0.027). Patients with no ATB approached frequent decolonization at 1 (75.0% vs. 26.7%; P = 0.037) and 3 months (87.5% vs. 33.3%; P = 0.027). The rates of decolonization were significantly different between CPE, VRE and CPE/VRE colonizer (75.0% vs. 38.5% vs. 66.7%; P = 0.018). Gut microbiome of responders showed a higher richness and diversity than non-responders before (294 vs. 274 by Ace; 2.6 vs. 1.8 by Shannon) and after (345 vs. 260 by Ace; 2.9 vs. 2.1 by Shannon) FMT. The microbiota composition analysis revealed increasing abundance of Bacteroidetes and