2570. A Randomized Controlled Trial of *Lactobacillus rhamnosus* GG on Multidrug-Resistant Organism (MDRO) Colonization

Adriana M. Rauseo, MD[1]; Tiffany Hink, BS, MT, ASCP[2];
Kimberly Reske, MPH[1]; Sondra Seiler, BA[1]; Kerry Bommarito, PhD[1];
Victoria J. Fraser, MD[1]; Carey-Ann D. Burnham, PhD[1];
Erik R. Dubberke, MD, MSPH[1]; [1]Washington University at St. Louis, St. Louis, Missouri; [2]Washington University School of Medicine, St. Louis, Missouri

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

Background. MDRO present a greater threat to public health than ever before, and antimicrobial options are decreasing. Altered colonic microbiota following antimicrobial exposure allows for subsequent colonization by MDRO. Ingestion of prophylactic *Lactobacillus rhamnosus* GG (LGG) could be an approach to prevent the spread of, and subsequent infection due to MDRO, by promoting a healthy bacterial milieu within the colon.

Methods. This is a prospective, double-blinded, randomized clinical trial in which a total of 87 subjects on broad-spectrum antibiotics were randomized to receive LGG twice daily (n = 43) vs placebo (n = 44). Stool or rectal swab specimens were collected for culture at enrollment, every 3 days during admission, and at discharge. Selective media were used to detect the following MDRO: *Clostridioides difficile* (CD), vancomycin-resistant *Enterococcus* (VRE), and antibiotic-resistant Gram-negatives (GN). The primary outcome was MDRO acquisition. Secondary outcomes included analysis for loss of any MDRO if colonized at enrollment, and acquisition or loss of individual MDRO.

Results. Subjects in both groups had similar prevalence of colonization with any MDRO at study enrollment (LGG 40% vs. placebo 39%), with similar colonization prevalence for individual MDRO (Figure 1). There was no difference in any MDRO acquisition (LGG 27%, placebo 33%, OR 1.36, 95% CI 0.42–4.41) or any individual MDRO acquisition (Figure 2). There was also no difference in loss of any MDRO (LGG 18%, placebo 24%, OR 1.44, 95% CI 0.27–7.68) or any individual MDRO (Figure 2).

Conclusion. LGG administration did not prevent acquisition of MDRO or accelerate loss of MDRO colonization.

Figure 1. Prevalence of MDRO colonization at study enrollment and post-enrollment

Variable	LGG N=43 N (%)	Placebo N=44 N (%)	OR (95% CI)	p
Any MDRO at study enrollment	17 (40)	17 (39)	0.96 (0.41 – 2.28)	0.93
ESBL Enterobacteriaceae	4 (9)	2 (5)	0.46 (0.08 – 2.68)	0.43
Ciprofloxacin resistant Enterobacteriaceae	3 (7)	0 (0)	Undef	0.12
Other MDRO Enterobacteriaceae	4 (9)	5 (11)	1.25 (0.31 – 5.01)	1.00
Any MDRO Enterobacteriaceae	9 (21)	7 (16)	0.72 (0.24 – 2.13)	0.55
MDR Pseudomonas	1 (2)	1 (2)	0.98 (0.06 – 16.13)	1.00
VRE	7 (16)	9 (21)	1.32 (0.44 – 3.94)	0.62
CD	12 (28)	6 (14)	0.41 (0.14 – 1.21)	0.10
Any MDRO post-enrollment	21 (49)	22 (50)	1.05 (0.45 – 2.43)	0.91
ESBL Enterobacteriaceae	4 (9)	4 (9)	0.98 (0.23 – 4.18)	1.00
Ciprofloxacin resistant Enterobacteriaceae	6 (14)	1 (2)	0.14 (0.02 – 1.25)	0.06
Other MDRO Enterobacteriaceae	3 (7)	3 (7)	0.98 (0.19 – 5.12)	1.00
Any MDRO Enterobacteriaceae	10 (23)	7 (16)	0.62 (0.21 – 1.83)	0.39
MDR Pseudomonas	1 (2)	1 (2)	0.98 (0.06 – 16.13)	1.00
VRE	10 (23)	14 (32)	1.54 (0.60 – 3.98)	0.37
CD	11 (26)	6 (14)	0.50 (0.15 – 1.38)	0.16

MDRO indicates multidrug resistant organism; ESBL, extended spectrum beta-lactamase; VRE, vancomycin resistant *Enterococcus*; CD, *Clostridioides difficile*

Figure 2. Primary and secondary outcomes

Variable	LGG N=43 N (%)	Placebo N=44 N (%)	OR (95% CI)	p
MDRO acquisition[a] (n=53 with no MDRO at enrollment)	7/26 (27)	9/27 (33)	1.36 (0.42 – 4.41)	0.61
ESBL (n=81)	0/39 (0)	2/42 (5)	Undef	0.49
Ciprofloxacin resistant Enterobacteriaceae (n=84)	3/40 (8)	1/44 (2)	0.29 (0.03 – 2.88)	0.34
Other MDRO Enterobacteriaceae (n=78)	1/39 (3)	2/39 (5)	2.05 (0.18 – 23.63)	1.00
Any MDRO Enterobacteriaceae (n=71)	3/34 (3)	3/37 (8)	0.91 (0.17 – 4.86)	1.00
MDR Pseudomonas (n=85)	0/42	0/43		
VRE (n=71)	5/36 (14)	6/35 (17)	1.28 (0.35 – 4.66)	0.75
CD (n=69)	2/31 (7)	2/38 (5)	0.81 (0.11 – 6.07)	1.00
MDRO loss[b] (n=34 with MDRO colonization at enrollment)	3/17 (18)	4/17 (24)	1.44 (0.27 – 7.68)	1.00
ESBL (n=6)	0/4	0/2		
Ciprofloxacin resistant Enterobacteriaceae (n=3)	0/3	0/0		
Other MDRO Enterobacteriaceae (n=9)	2/4 (50)	4/5 (80)	4.00 (0.21 – 75.66)	0.52
Any MDRO Enterobacteriaceae (n=16)	2/9 (22)	3/7 (43)	2.63 (0.30 – 23.00)	0.60
MDR Pseudomonas (n=2)	0/1	0/1		
VRE (n=16)	2/7 (29)	1/9 (11)	0.31 (0.02 – 4.41)	0.55
CD (n=18)	3/12 (25)	2/6 (33)	1.50 (0.18 – 12.78)	1.00
New MDRO acquisition[c] (n=87)	8 (19)	12 (27)	1.64 (0.60 – 4.53)	0.34
No MDRO ever (n=87)	19 (44)	18 (41)	0.87 (0.37 – 2.05)	0.76
Persistent Colonization with MDRO (had MDRO at enrollment and >=1 time post-enroll) (n=87)	14 (33)	13 (30)	0.87 (0.35 – 2.16)	0.76

MDRO indicates multidrug resistant organism; ESBL, extended spectrum beta-lactamase; VRE, vancomycin resistant *Enterococcus*; CD, *Clostridioides difficile*
[a]Not colonized with any MDRO at enrollment but colonized at >=1 time point post-enrollment
[b]Colonized with any MDRO at enrollment but not post-enrollment
[c]Acquisition of any new MDRO, regardless of whether the patient was not colonized at enrollment or was colonized with a MDRO but acquired a different MDRO

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

2571. Norovirus Infection and Gut Microbiota in Transplant Recipients

Pearlie P. Chong, MD, MSCR; Pearlie P. Chong, MD, MSCR;
Sarah K. Hussain, MSc; Nicole Poulides, MA; Laura Coughlin, MA;
Andrew Y. Koh, MD; UT Southwestern Medical Center, Dallas, Texas

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

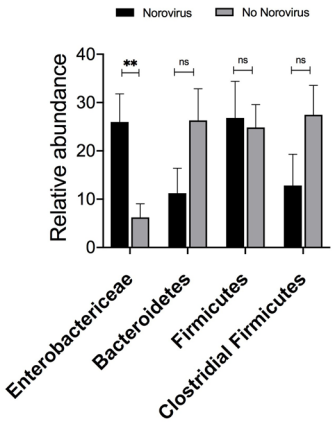
Background. *In vitro* studies have shown that enteric viruses require the gut microbiota (specific members of the Enterobacteriaceae family) for efficient infection of the gastrointestinal tract. Human norovirus (NV) infection in transplant recipients may be chronic and severe. The role of gut microbiota has not been defined in this setting. We hypothesized that gut microbiota diversity and composition are different in norovirus-infected transplant patients.

Methods. We performed a single-center, pilot, prospective cohort study of adult solid-organ transplant and hematopoietic stem cell transplant recipients with diarrhea. Serial fecal samples were collected and processed for gDNA. Norovirus levels were quantified by PCR and gut microbiota profiling determined by 16S rRNA gene sequencing.

Results. Twenty-five transplant recipients were included: 9 with NV infection and 16 without. Age (61 ± SEM 2.3 years vs. 54 ± 3.5 years; P = 0.172), duration of diarrhea prior to diagnosis (105 ± 43 days vs. 20 ± 7 days; P = 0.146), prior cumulative antibiotic use (42 ± 12 days vs. 46 ± 17 days; P = 0.646), anti-anaerobic antibiotic use (7 ± 3 days vs. 11 ± 6 days; P = 0.643) and length of hospitalization (12 ± 6 days vs. 12 ± 3 days; P = 0.624) were not different between transplant recipients with and without NV infection. Interestingly, the relative abundance of Enterobactericeae was significantly higher in NV-infected transplant recipients compared with those without NV infection (26 ± 5.8% vs. 6.2 ± 2.8%; P = 0.017, Mann–Whitney) (Figure 1). In contrast, the abundance of the Phyla Bacteroidetes (11.2 ± 5.2% vs. 26.3 ± 6.5%; P = 0.191), and Firmicutes (26.8 ± 7.6% vs. 24.9 ± 4.7%; P = 0.803), were not significantly different between those who were NV and not NV-infected. Of note, the diversity metrics of Shannon (3.5 ± 0.4 vs. 3.8 ± 0.3; P = 0.637) and inverse Simpson indices (1.3 ± 0.1 vs. 1.1±0.1; P = 0.419) were not significantly different between the two groups.

Conclusion. Norovirus-infected transplant recipients had a significantly higher relative abundance of Enterobactericeae in their gut microbiota compared with transplant recipients without norovirus infection. Future studies are needed to explore if this association is mechanistically important for norovirus infection.

Figure 1



Solid organ transplant recipients who are norovirus-infected have increased Enterobactericeae abundance in the gut compared to counterparts without norovirus infection

Gut microbiota abundance as determined by 16S rRNA sequencing of fecal specimens collected from solid organ transplant recipients (n = 9 norovirus-infected, n = 16 no norovirus infection). All data shown are means ± SEM. Statistical analysis by Mann-Whitney test. **, p<0.01; ns, not significant.

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

2572. The Impact of Antibiotics on the Composition of the Vaginal Microbiota

Sima L. Sharara, MD[1]; Khalil Ghanem, MD, PhD[1];
Rebecca Brotman, PhD, MPH[2]; Courtney Robinson, MS[2]; Jacques Ravel, PhD[2];
Susan Tuddenham, MD, MPH[1]; [1]Johns Hopkins University School of Medicine, Baltimore, Maryland; [2]University of Maryland Institute for Genome Sciences, Baltimore, Maryland

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

Background. The impact of antibiotics on the composition of the vaginal microbiota (VMB) is poorly defined. We analyzed the VMB of women before and after the use of antibiotics.

Methods. We used samples from a cohort of reproductive-aged women who submitted vaginal swabs and clinical data over a 2-year period. 16S rRNA gene sequencing was conducted, and VMB was categorized into 7 community state types (CSTs): four dominated by *Lactobacillus* spp. and three low in *Lactobacillus*, dominated by *Streptococcus* spp. (CST VI), *Bifidobacterium* spp. (CST VII), or comprising a variety of anaerobes (CST IV). CSTs were further categorized as *Lactobacillus*-dominated (LD) or non-*Lactobacillus*-dominated (NLD). We compared paired vaginal samples collected within 48 hours prior to and 48 hours after completion of antibiotics in 40 women (N = 10 systemic metronidazole, N = 6 vaginal metronidazole, N = 5 trimethoprim-sulfamethoxazole, N = 9 amoxicillin, N = 5 azithromycin, N = 5 other), to time-matched samples in 56 controls. Exact logistic regression was used to evaluate the impact of antibiotics on LD status controlling for baseline CST, race, menses, and hormonal contraceptive use.

Results. Women who received antibiotics were 25 times more likely to be in an LD state after antibiotics compared with those who did not receive antibiotics (p = 0.0017). NLD to LD transitions occurred almost exclusively in patients receiving metronidazole. Of 13 women who began in NLD (N = 12 in CST IV) and then received metronidazole, 84.6% (N = 11) transitioned to LD (CST III, *L. iners*-dominated). Of 7 women who started in an NLD state and received non-nitroimidazole antibiotics, only two (receiving clindamycin or amoxicillin) transitioned to an LD state. None of the 20 women who

began in a LD state transitioned to a non-LD state after antibiotics. 12 controls were in an NLD state at baseline, of these 11 remained NLD at the second time point. 44 controls started in an LD state and all remained in LD at the second time point.

Conclusion. In the short term, metronidazole results in a transition of the VMB from a NLD to a *L. iners*-dominated state. There was little impact of non-nitroimidazole antibiotics on the VMB. Studies assessing longer-term impact of antibiotics on the composition of the VMB are needed.

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

2573. Impact of Anaerobic Antibacterial Spectrum on Cystic Fibrosis Lung Microbiome Diversity and Pulmonary Function

Michael Jason. Bozzella, DO, MS[1]; Hollis Chaney, MD[1]; Iman Sami, MD[1]; Geovanny Perez, MD[1]; Anastassios Koumbourlis, MD, MPH[1]; James Bost, PhD[1]; Robert Freishtat, MD, MPH[1]; Keith Crandall, PhD[2]; Andrea Hahn, MD, MS[1]; [1]Children's National Health System, Washington, DC; [2]George Washington University, Washington, DC

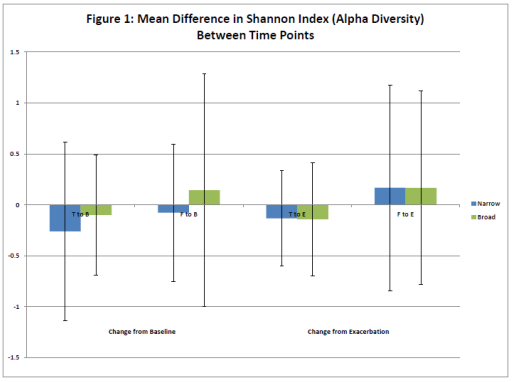
Session: 267. Microbiome, Antibiotics, and Pathogenesis
Saturday, October 5, 2019: 12:15 PM

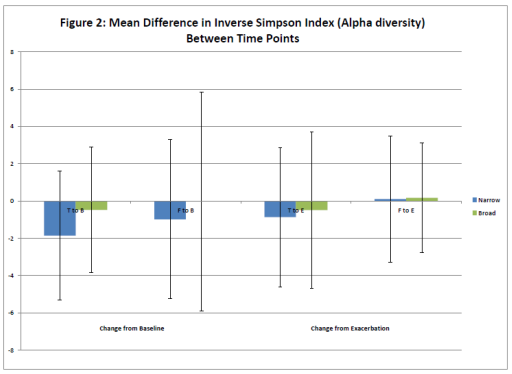
Background. Next-generation sequencing has shown the cystic fibrosis (CF) lung microbiome to be a complex polymicrobial community. Anaerobic bacteria decrease in relative abundance with older age and disease progression, and may impact host inflammatory state. Persons with CF suffer from recurrent pulmonary exacerbations (PEs) that are treated with broad-spectrum antibiotics. Our objectives were to examine the effect of broad-spectrum (BS) vs narrow-spectrum (NS) anaerobic antibacterial treatment on bacterial diversity, and on pulmonary function recovery.

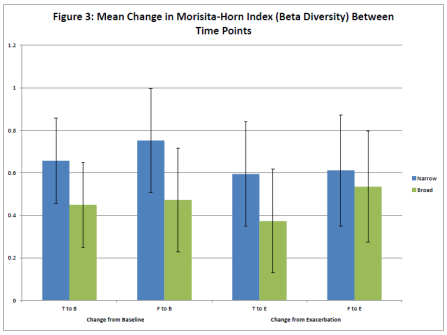
Methods. Pulmonary function tests (PFTs) and respiratory samples were collected as part of a prospective 18 month longitudinal study in CF patients at 4 time points, baseline (B), pulmonary exacerbation (E), end of exacerbation treatment (T), and follow-up (F). Treatment antibiotics were classified as broad or narrow based on anaerobic activity. 16S rRNA sequencing generated operational taxonomic units for analysis. Alpha diversity (relative abundance) was calculated via Shannon Index and Inverse Simpson formulas and β diversity (similarity in community composition) by Morisita-Horn (MH). Differences in diversity indices and PFTs were compared with regard to BS vs NS anaerobic activity, and statistical significance determined by GLS regression.

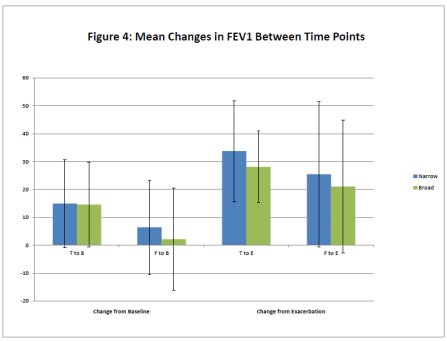
Results. Changes in alpha diversity for BS vs NS were not significantly different ($P > 0.05$) (Figures 1 and 2). Community composition measured by MH was consistently more similar for NS than BS (T-B: 0.66 vs. 0.45, $P = 0.04$; F-B: 0.75 vs. 0.47, $P < 0.01$) (Figure 3). Recovery of forced expiratory volume in 1 second (FEV1) from E to F was significantly higher in the NS group (25.4 vs. 21.0, $P < 0.01$) (Figure 4).

Conclusion. While antibiotic spectrum did not influence bacterial abundance, BS therapy led to higher changes in community composition from B and E onset following antibiotic administration compared with NS therapy. The differences in β diversity suggest BS therapy can have a lasting impact on community composition. As those receiving NS therapy had similar or better recovery of pulmonary function than those with BS, there is no indication that NS therapy leads to worse clinical outcomes. A limitation may be that children receiving BS therapy tended to have more severe disease.









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

2574. Temporal Changes in the Vaginal Microbiome During Treatment for Bacterial Vaginosis: Is *Lactobacillus Iners* an Important Player?

Elizabeth O. Shay, BA[1]; Oluwatosin Goje, MD[2]; Roshan Padmanabhan, PhD[3]; Charis Eng, MD, PhD[2]; [1]Cleveland Clinic Lerner College of Medicine, Cleveland, Ohio; [2]Cleveland Clinic Foundation, Cleveland, Ohio; [3]Lerner Research Institute, Cleveland, Ohio

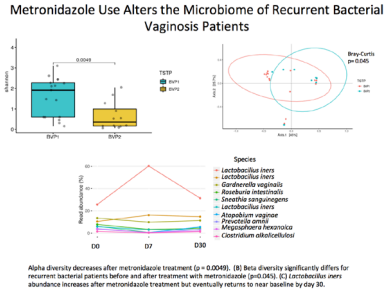
Session: 267. Microbiome, Antibiotics, and Pathogenesis
Saturday, October 5, 2019: 12:15 PM

Background. Bacterial vaginosis (BV) is the most common vaginal condition affecting women of reproductive age and yet it remains poorly understood. Recurrent BV causes significant emotional and psychological distress and can prove difficult to resolve with currently available treatments. We aimed to investigate the microbiome of recurrent BV patients at various time points in relation to oral Metronidazole treatment.

Methods. Women aged 18–40 years, with recurrent BV, were prospectively enrolled. Vaginal samples (lavage) were collected at baseline (D0), at 7–10 days (D7) and 30–40 days (D30) after initiation of oral metronidazole treatment (500 mg BID, 7 days). DNA was extracted, amplified using primers targeting the V3-V4 region of the 16 srRNA, and then sequenced and processed through a hybrid Qiime MICCA bioinformatics pipeline.

Results. Seventeen recurrent BV patients were enrolled. Alpha diversity decreased ($P = 0.0049$) after the first week of treatment with oral metronidazole, but increased ($P = 0.0062$) to near baseline by D30. *Lactobacillus iners*, was the dominant *Lactobacillus*, with transient increase in this species corresponding with metronidazole treatment. There was also a decrease in *Gardnerella vaginalis* that re-normalized to baseline at 30 days. Of the 10 recurrent BV patients with data for all three time points, 4 relapsed by D30. B diversity differed significantly between patients that relapsed and those that did not (p = 0.044). Alpha diversity did not differ between the groups (p = 0.07).

Conclusion. The dominant Lactobacillus pretreatment in this cohort was L.iners. Oral metronidazole was associated with a decrease in alpha diversity, decrease in *G. vaginalis* and increase in *L. iners*. Although *L. iners* increased after metronidazole treatment, this increase was not sustained by D30. Treatment with metronidazole, only temporarily altered the microbiome. Further studies are needed to clarify the role of *L. iners* in recurrent BV.



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