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Session: 267. Microbiome, Antibiotics, and Pathogenesis
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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 4×10^3 cfu in the vancomycin arm and 6.2×10^4 cfu in the NS oil arm. Mean MRSA counts were 3.3×10^5 cfu in vancomycin arm and 1.5×10^4 cfu in NS oil arm. The combination of vancomycin and NS oil had higher *Enterococcus* counts than the vancomycin alone arm (6.3×10^4 cfu vs. 4×10^3 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.

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

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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.

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

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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.

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

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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

decreasing abundance of Proteobacteria at 1 month after FMT in responders. However, those changes of microbial composition did not occur in non-responders.

Conclusion: FMT is an effective way to decolonize CPE and VRE by restoration of the gut microbiome.

Table 1. Comparisons of clinical characteristics between responders and non-responders (at 3 month).

Characteristics	Total (N=23)	Responders (N=12)	Non-responders (N=11)	p value
Age at FMT (median, years)	58.0 ± 42.5	58.0 ± 38.0	57.0 ± 68.5	0.758
Male sex (%)	13(56.5)	8(50.0)	7(63.6)	0.680
BMI (median, kg/m ²)	20.7 ± 7.2	21.4 ± 3.6	17.2 ± 8.0	0.325
Carriage MDRO				0.314
CPE	4(17.4)	3(25.0)	1(9.1)	
VRE	13(56.5)	5(41.7)	8(72.7)	
CPE/VRE	6(26.1)	4(33.3)	2(18.2)	
Duration of carriage before FMT(days)	56.0±84.0	74.0 ±157.0	55.0 ±40.0	0.281
Hospital stay of days before FMT(days)	54.5±67.0	56.0 ±163.0	56.0 ±38.0	0.902
ATB before FMT (within 1week)	14(60.9)	7(58.3)	7(63.6)	>0.999
Route of FMT				>0.999
Upper GI tract	12(52.2)	7(58.3)	5(41.7)	
Lower GI tract	11(47.8)	7(63.6)	4(36.4)	
Biology before FMT				
WBC (10 ³ /uL)	6.58±3.44	6.45 ±3.81	6.71 ±3.13	0.479
Hemoglobin (g/dL)	10.8±2.3	11.0 ±1.5	10.0±2.9	0.018
Platelet count (10 ³ /uL)	282.5±120.3	280.0 ±98.0	316.0 ±298.0	0.389
BUN (mg/dL)	12.7±7.8	13.2 ±8.9	8.0 ±10.1	0.124
Creatinine (mg/dL)	0.5±0.3	0.5 ±0.4	0.4 ±0.4	0.601
AST (IU/L)	27.5±27.0	23.0 ±16.0	30.0 ±49.0	0.139
ALT (IU/L)	20.5±24.0	20.0 ±18.0	22.5 ±26.0	0.895
Total cholesterol (mg/dL)	154.5±50.5	172.0 ±74.0	130.0 ±39.0	0.079
Triglyceride (mg/dL)	130.5±148.3	144.0 ±143.0	106.0±139.0	0.268
LDL cholesterol (mg/dL)	93.2±43.3	102.0 ±46.2	89.0 ±41.6	0.049
Albumin (mg/dL)	3.3±0.5	3.4 ±0.9	3.2 ±0.5	0.006
Fasting glucose (mg/dL)	95.0±13.3	95.0 ±13.0	95.0 ±14.0	0.901
CRP (mg/L)	6.9±22.4	3.7 ±29.6	12.3 ±20.1	0.480
Additional ATB				
ATB after FMT (within 1week)	15(65.2)	5(41.7)	10(90.9)	0.027
Hospital stay of days after FMT(days)	46.0±49.0	29.0 ±51.0	48.0 ±88.0	0.355

FMT, fecal microbiota transplantation; BMI, body mass index; MDRO, multi-drug-resistant organism; ATB, antibiotic treatment; EGD, esophagogastroduodenoscopy; CFS, colonoscopy; WBC, white blood cell; BUN, Blood urea nitrogen; AST, Aspartate transaminase; ALT, Alanine transaminase; LDL, Low density lipoprotein; CRP, C-reactive protein; S, success; F, failure; N/A, not available; C, complete; P, partial. Continuous variables are shown as medians ± IQR (3rd interquartile range-1st interquartile range) and categorical variables as numbers (percentage).

Table 2. Impact of FMT on complete and partial MDRO decolonization, with or without ATB during the first week after transplantation

Endpoint	All FMTs (N=23)		With ATB (N=19)		Without ATB (N=8)		p value
	Number	%	Number	%	Number	%	
Complete MDRO decolonization							
At 1 month	9/23	39.1	4/15	26.7	5/8	62.5	0.179
At 3 months	9/23	39.1	4/15	26.7	5/8	62.5	0.179
At 6 months	7/15	46.7	3/11	27.3	4/4	100.0	0.026
Partial MDRO decolonization							
At 1 month	10/23	43.5	4/15	26.7	6/8	75.0	0.037
At 3 months	12/23	52.2	5/15	33.3	7/8	87.5	0.027
At 6 months	9/15	60.0	5/11	45.5	4/4	100.0	0.103

FMT, fecal microbiota transplantation; MDRO, multi-drug-resistant organism; ATB, antibiotic treatment

Figure 1. Decolonization delay of carbapenem-producing enterobacteriaceae(CPE) vs. vancomycin-resistant enterococci(VRE) vs. CPE/VRE

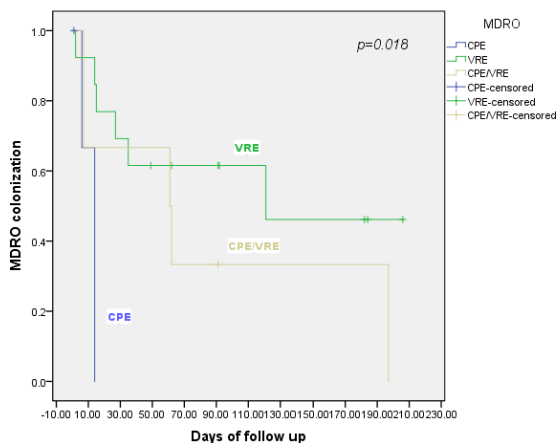


Figure 2. Changes of microbiome composition by phylum level.

Figure 2-1. Responders

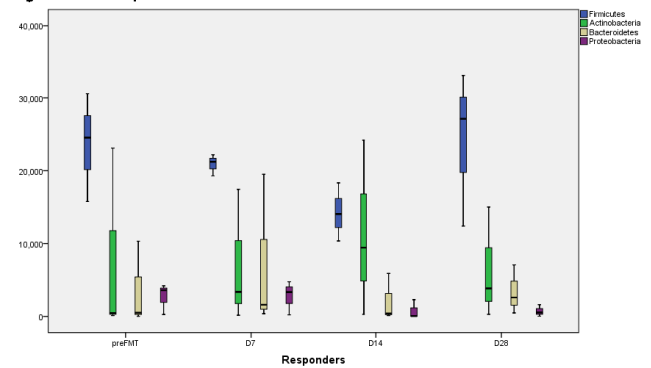
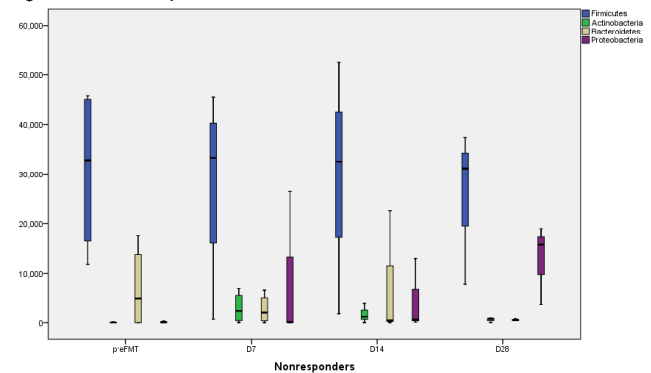


Figure 2-2. Non-responders



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2585. Changing Epidemiological Profile of Infantile Parechovirus-A3 Infection in Japan

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Background: Parechovirus-A3 (PeV-A3) causes severe disease, including sepsis and meningoencephalitis in young infants. The first case of PeV-A3 was reported in Japan in 1999 and, although epidemics have been reported every 2 to 3 years in more than 20 countries, no major epidemic has occurred in Japan since 2014.

Methods: This prospective study included febrile infants (<4 months of age) admitted at Niigata University and its affiliated hospitals, which serve about 2.5 million people, during the period from 2014 to 2018. Neonates and infants younger than 4 months presenting with fever and suspected of having viral sepsis underwent serum and/or cerebrospinal fluid (CSF) testing by real-time PCR for parechovirus-A (PeV-A) and enteroviruses (EVs), and for herpes simplex viruses, if suspected. Bacterial infection was excluded on the basis of the results of bacterial culture of blood, urine, and/or CSF. PeV-A genotype was identified by examining the viral protein 1 (VP1) sequence, and the phylogenetic tree of the VP1 sequence was constructed.

Results: Of the 277 patients evaluated, 135 (49%) were positive for PeV-A ($n = 74$, 27%) or EVs ($n = 61$, 22%). Among PeV-A patients, most had PeV-A3 ($n = 69$; 93%), followed by PeV-A4 ($n = 4$; 5%). There was a PeV-A3 epidemic in 2014 ($n = 43$); however, no cases were reported in 2015. In 2016–2018, small numbers of PeV-A3 cases were reported: 10 in 2016, 7 in 2017, and 9 in 2018. In contrast, EV cases were reported throughout this period: 8 in 2014, 22 in 2015, 10 in 2016, 5 in 2017, and 16 in 2018. When data were analyzed by season, the PeV-A3 detection rate in summer (June–August) was 93% (40/43) in 2014 and 65% (17/26) during 2016–2018, indicating an increase in the number of PeV-A3 cases in seasons other than summer. Phylogenetic analysis showed that PeV-A3 strains during 2016–2018 were part of a cluster of epidemics in 2011 and differed from those in 2014.

Conclusion: After the major PeV-A3 epidemics in 2014, we observed changes in the PeV-A3 epidemic profile, namely, a small, but constant, number of cases every year in Niigata, Japan. A future study should investigate if this trend has continued in Japan and other countries and identify the causes of this change in epidemic profile.