Figure 2: Number of major phyla present between patient groups. Patients who acquired an MDRO had fewer major phyla present. Major phyla include Firmicutes, Proteobacteria, Bacteroidetes, Actinobacteria, Verrucomicrobia, Fusobacteria, Synergistetes, and unclassified bacteria.

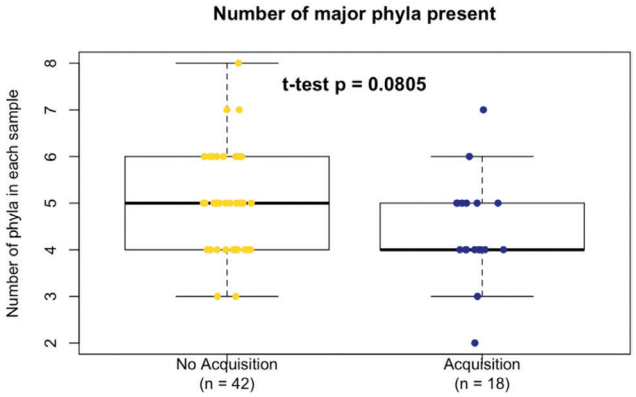
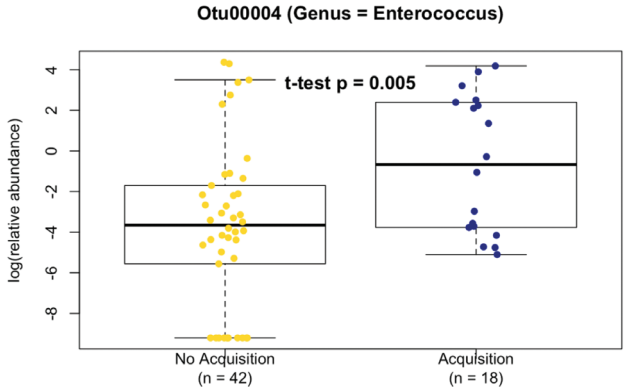


Figure 3: Log-transformed relative abundance of operational taxonomic unit 00004 (OTU00004) at baseline between patient groups. OUT00004 is the fourth most abundant OTU across samples and associated with the *Enterococcus* genus.



Disclosures. **All Authors:** No reported Disclosures.

2847. Comparative Genomics and Clonal Tracking of Multi-drug-Resistant Uropathogens Implicates the Fecal Microbiome as a Potential Reservoir for Recurrent Urinary Tract Infections

Robert Thanert, PhD[1]; Kimberly Reske, MPH[2]; Tiffany Hink, BS; MT, ASCP[3]; Meghan Wallace, BS[3]; Bin Wang, MS[1]; Drew Schwartz, MD, PhD[1]; Carey-Ann Burnham, PhD[4]; Sondra Seiler, BA[1]; Candice Cass, Associate in Arts[3]; Erik R. Dubberke, MD, MSPH[2]; Gautam Dantas, PhD[3] and Jennie H. Kwon, DO, MSCI[5]; [1]Washington University, St. Louis, Missouri; [2]Washington University in St. Louis, St. Louis, Missouri; [3]Washington University School of Medicine, St. Louis, Missouri; [4]Washington University in St. Louis School of Medicine, St. Louis, Missouri; [5]Washington University - School of Medicine, St. Louis, Missouri

Session: 295. Microbiome Science

Saturday, October 5, 2019: 2:45 PM

Background. Multi-drug-resistant organisms (MDRO) have complicated the treatment of urinary tract infections (UTIs), especially in patients with recurrent UTIs (rUTI). The objective of this pilot prospective cohort study is to determine the role of the fecal microbiome in rUTIs.

Methods. Stool and urine specimens were prospectively collected from patients with MDRO UTIs at 6 time points during and after the UTI, and with any rUTI. Specimens underwent semi-quantitative culture on differential and selective media for MDROs, and isolates underwent phenotypic susceptibility testing and whole-genome sequencing. Comparative genomics and clonal tracking were used to detect clonal uropathogen strains in the urinary and gastrointestinal tracts. Resistance genes, resistance-plasmids, and virulence genes of MDROs were characterized *in silico*.

Results. A total of 110 isolates (95 *Escherichia coli*, 2 *Klebsiella pneumoniae*, 13 *Proteus mirabilis*) were cultured from the urine and stool of 15 patients (7 non-rUTI, 8 rUTI). Clonal uropathogens were isolated between the urinary tract and their intestinal reservoir (Figure 1). Integration of clonality information with semiquantitative culturing implicated three potential routes for recurrence of UTIs: (i) bladder colonization following an intestinal bloom of uropathogens, (ii) reinfection from an external source, and (III) bacterial persistence within the urinary tract (Figures 2 and 3). Antibiotic susceptibility testing and genomic profiling indicated that antibiotic-resistant uropathogen populations colonizing the urinary tract and intestinal reservoir at symptomatic and asymptomatic timepoints have similar resistance profiles that are largely determined via a pool of shared resistance plasmids (Figure 3).

Conclusion. This study provides the first time-resolved analysis of uropathogen persistence following UTIs, showing that clonal antibiotic-resistant uropathogens can be detected in both the urine and stool at varying time points post-initial infection. The study implicates 3 potential routes of rUTI, including uropathogen persistence within the gut microbiota, reinfection from an external source, and persistent bacteriuria. Study findings could be utilized to inform future diagnostics and therapies for treatment of rUTIs.

Figure 1. Clonal diversity of the uropathogen population varies between individual patients. **a**, UTI-associated E. coli belong to the major phylogroups D and B2. **b**, Heatmap of pairwise single nucleotide polymorphism distances in the core genome between all E. coli isolates.

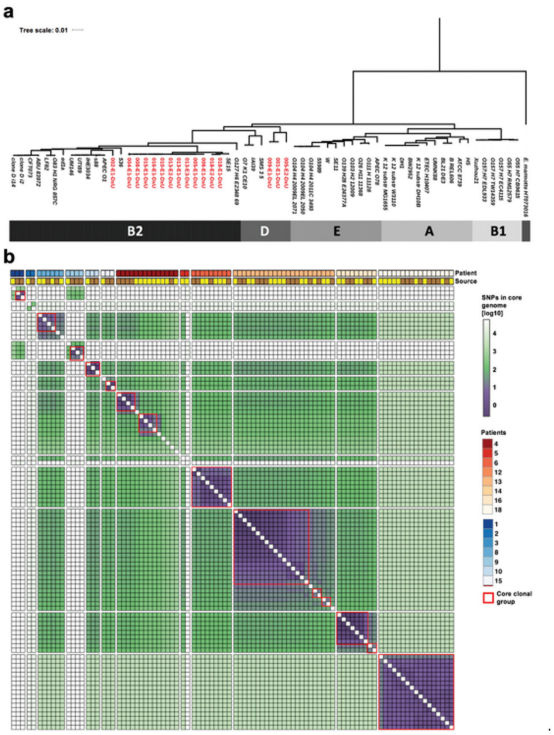


Figure 2. Recurrent urinary tract infections are associated with differences in stool and urine uropathogen density.

Legend: Non-rUTI patients are shown on the top panel, patients with rUTIs are shown on the bottom panel. Subsequent episodes for rUTI patients are depicted from bottom to top in the bottom panel. Bubble size corresponds to enumeration of colony forming units grown on species specific selective agar plates. Bubble border color indicates the within-patient core clonal groups for the corresponding isolate cultured from each sample. Missing culture data is indicated by grey fields. A red line indicates the timeframe in which a rUTI patient experienced a recurrence.

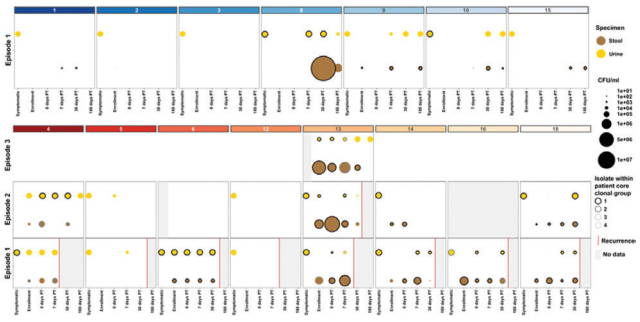
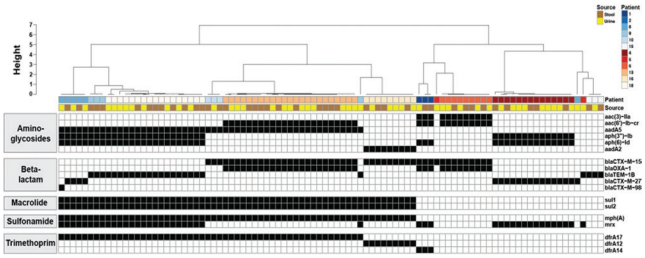


Figure 3. Antimicrobial resistant *E. coli* colonizing the intestinal and urinary tract share a pool of resistance plasmids.

Legend: Top: Hierarchical clustering of the putative resistance plasmids for of all isolates based on the Hadamard matrix, comprising average nucleotide identify and coverage. Bottom: Putative resistance genes identified by RGI and Resfinder on all putative resistance plasmids are depicted. Resistance genes are grouped by antibiotic class on the y-axis. Black squares indicate the presence of a specific resistance gene in the resistance plasmid pool of an isolate.



Disclosures. Carey-Ann Burnham, PhD, BioFire: Research Grant; bioMerieux: Research Grant; Cepheid: Research Grant; Luminex: Research Grant.

2848. Spatial Distribution of Community-Acquired Extended-Spectrum β-Lactamase-Producing Enterobacteriaceae Infections and its Association with Sewer Overflows in Middle Georgia

Margaret Omatsone, MD[1]; Rafael Ponce-Terashima, MD[2] and Thomas Cole Baker, MD[1]; [1]Medical Center of Central Georgia, Navicent Health, Macon, Georgia; [2]Medical Center, Navicent Health, Macon, Georgia

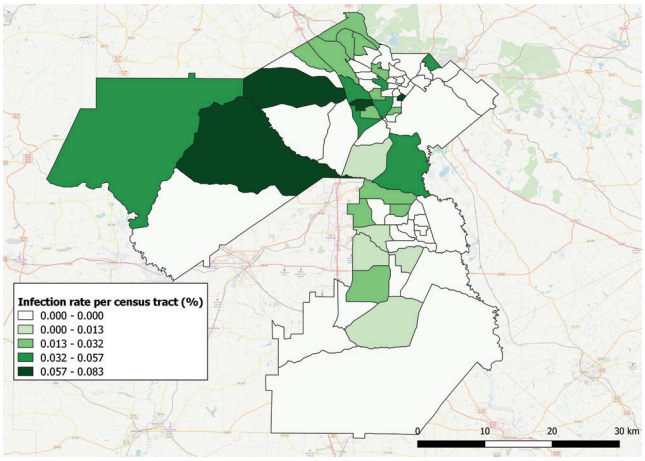
Session: 296. New Insights into MDRO Gram-Negatives
Saturday, October 5, 2019: 1:45 PM

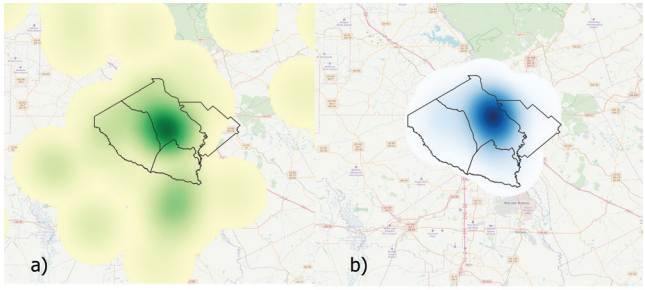
Background. Extended-spectrum β-lactamase-producing Enterobacteriaceae (ESBL-PE) were described first in relation to hospital-acquired infections. However, infections by these organisms acquired in the community have become a public health problem. There are no well-known risk factors for acquisition of these bacteria in the community. Surface waters and sanitation conditions may serve as reservoir and transmission.

Methods. We conducted a retrospective study over 12 months of patients who had positive cultures with ESBL-PE in our laboratory. We excluded patients with hospitalization in the previous 3 months, those in skilled nursing facilities, and those whose culture was taken 3 or more days after hospitalization. Geographic Information System analysis was performed based on patient's residence, population, and sewer overflow public data.

Results. Among 485 patients with cultures positive for ESBL-PE in 2018, 64 were included in the study. Mean age was 54, and 68.7% were females. Organisms isolated were *E. coli* (78.2%) and *K. pneumoniae* ESBL (21.8%). These were isolated from urine 47 (73.4%), blood 5 (7.8%), abscess 6 (9.3%), ulcers 5 (7.8%), and sputum 1 (1.5%). Antibiotic exposure in the preceding 3 months was noted in 12 patients (18.7%). Spatial distribution of patients in the community was not random based on nearest neighbor analysis (Z score = −2.6). Kernel density estimation showed clustering of cases. Infection rates were calculated per census tracts. There was poor correlation between infection rate and mean family income (R2 = 0.18, $P = 0.017$). Analysis of Kernel density estimations showed that sewer overflow distribution explained over 50% of the variance of distribution of cases with ESBL-PE (R2 = 0.51, $P < 0.001$).

Conclusion. Patients presenting with infections due to ESBL-PE acquired in the community did not have a random spatial distribution. Other factors besides prior antibiotic use and financial status should be investigated. Proximity to sanitary sewer overflows may be a contributing factor. Location of residence within a community may aid in identifying patients at risk for acquisition of ESBL-PE.





a) Heatmap of community-acquired ESBL-PE infections by patient's residence.
b) Heatmap of sewer overflow events in Macon-Bibb county, Georgia

Disclosures. **All Authors:** No reported Disclosures.

2849. Gut Microbiota Differences at the Time of Medical Intensive Care Unit (MICU) Admission Are Associated with Acquisition of Multi-drug-Resistant Organisms (MDROs) Among Patients Not Already Colonized with an MDRO

Christine Bassis, PhD[1]; Anna Seekatz, PhD[2]; Thelma E. Dangana, MBBS[3]; Teppei Shimasaki, MD, MS[3]; Rachel D. Yelin, MPH[3]; Michael Schoeny, PhD[4]; Yoona Rhee, MD, ScM[3]; Michelle Ariston, BS[3]; Karen Lolans, BS[3]; Enrique Cornejo Cisneros, MD, MS[3]; Khaled Aboushaala, MD[5]; Lina Thabit, MBBS, MS[4]; John Murray, MS[3]; Jianrong Sheng, MD, PhD[3]; Stefanie Ollison, BS[3]; Pamela B. Bell, II, BA[3]; Louis Fogg, PhD[3]; Robert A. Weinstein, MD[6]; Michael Y. Lin, MD, MPH[3]; Vincent B. Young, MD, PhD[7] and Mary K. Hayden, MD[3]; [1]University of Michigan, Ann Arbor, Michigan; [2]Clemson University, Clemson, South Carolina; [3]Rush University Medical Center, Chicago, Illinois; [4]Rush University, Chicago, Illinois; [5]Rush University Medical Center, Naperville, Illinois; [6]Rush University Medical Center; Cook County Hospital, Chicago, Illinois; [7]University of Michigan Medical School, Ann Arbor, Michigan

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Background. Among hospitalized patients, underlying variation in gut microbiota may confer differential risk for gut MDRO acquisition.

Methods. Rectal swab samples were collected from patients ≤2 days of MICU admission and then daily in the 27-bed MICU of an acute care hospital in Chicago, IL over 1 year. Patients were screened for MDRO colonization by selective culture (see Figure 1 for MDRO types); those with ≥2 swabs and MICU stays ≥3 days were studied. Bacterial 16S rRNA gene amplicon sequences were used for microbiota analysis. Medical records were reviewed.

Results. In preliminary analysis, 2,480 samples were collected from 627 patients who acquired 170 MDROs (Figure 1). Debilitation, co-morbidities, and certain medical devices were associated with MDRO acquisition, though admission MDRO status was not (table). While no interactions were detected between admission MDRO status and clinical predictors of MDRO acquisition, there were significant differences in gut microbiota composition at the time of MICU admission between patients colonized with an MDRO on admission and those not colonized ($P < 0.001$, using analysis of molecular variance (AMOVA) on distances). Therefore, we stratified our analysis by admission MDRO colonization status. For patients MDRO-colonized at admission, there were no significant differences in microbiota of patients who later did or did not acquire a new MDRO (AMOVA P-value = 0.32). For patients not MDRO-colonized on admission, there was a significant difference in microbiota of patients who later acquired an MDRO and those who did not (AMOVA P-value: 0.026). Differentially abundant operational taxonomic units (OTUs, based on 3% sequence difference) included OTUs classified as Anaerococcus and as other Clostridiales (higher in patients who remained uncolonized) and as Enterococcus (higher in patients who acquired an MDRO) (Figure 2). Diversity was also higher in patients who remained uncolonized (Wilcoxon test P-value: 0.035) (Figure 3).

Conclusion. Among patients not already colonized with an MDRO on admission, we identified gut microbiota differences associated with MDRO acquisition that could help explain patient-level variation in MDRO colonization resistance.

Table 1. Univariate Associations of Clinical Factors with MDRO Acquisition (*N* = 627 patients)

	Did Not Acquire MDRO (*n* = 494)	Acquired MDRO (*n* = 133)	OR [95% CI]	*p*-value
Age in years, mean ± SD	62 ± 17	61 ± 17	1.00 [0.99, 1.01]	0.62
Female, *n* (%)	267 (54)	68 (51)	1.12 [0.77, 1.65]	0.55
Race, *n* (%)				0.27
African American	214 (43)	68 (51)	1.37 [0.90, 2.09]	0.14
Asian/Other/Unknown	81 (16)	19 (14)	1.01 [0.56, 1.84]	0.96
Caucasian	199 (40)	46 (35)	*Referent*	
Functional status before admission, *n* (%)				**<0.001**
Completely dependent with ADLs	**130 (29)**	**59 (50)**	**2.76 [1.75, 4.36]**	**<0.001**
Required some assistance with ADLs	87 (19)	21 (18)	1.47 [0.82, 2.63]	0.20
Completely independent for ADLs	237 (52)	39 (33)	*Referent*	
Charlson Comorbidity Index, median ± IQR	**4 ± 5**	**6 ± 6**	**1.07 [1.01, 1.12]**	**0.019**
Medical Devices on Admission, *n* (%)				
Central venous catheter	**147 (30)**	**56 (42)**	**1.70 [1.14, 2.52]**	**0.0083**
Gastrostomy tube	**47 (10)**	**21 (16)**	**1.78 [1.02, 3.11]**	**0.039**
Urinary bladder catheter	94 (19)	33 (25)	1.40 [0.89, 2.20]	0.1473
Tracheostomy	29 (6)	14 (11)	1.87 [0.96, 3.65]	0.063
Antibiotic receipt after MICU admission and before first rectal swab collection, *n* (%)	**341 (69)**	**104 (78)**	**1.61 [1.02, 2.53]**	**0.039**
Total length of MICU stay in days, median ± IQR	**4 ± 3**	**7 ± 10**	**1.15 [1.11, 1.20]**	**<0.001**
Admission rectal swab sample MDRO-positive, *n* (%)	279 (56)	66 (50)	0.76 [0.52, 1.11]	0.16