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 matrik, comprising average nucleotide identify and coverage. Bottom: Putative resistance genes identified by RGI and <u>RestInder</u> 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.



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

Margaret Omatsone, MD¹; Rafael Ponce-Terashima, MD² and Thomas Cole Baker, MD¹; ¹Medical Center of Central Georgia, Navicent Health, Macon, Georgia; ²Medical Center, Navicent Health, Macon, Georgia

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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

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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, PhD¹; Anna Seekatz, PhD²; Thelma E. Dangana, MBBS³; Teppei Shimasaki, MD, MS³; Rachel D. Yelin, MPH³; Michael Schoeny, PhD⁴; Yoona Rhee, MD, ScM³; Khaled Aboushaala, MD⁵; Lina Thabit, MBBS, MS⁴; John Murray, MS³; Jianrong Sheng, MD, PhD³; Stefanie Ollison, BS³; Pamela B. Bell, II, BA³; Louis Fogg, PhD³; Robert A. Weinstein, MD⁶; Michael Y. Lin, MD, MPH³; Vincent B. Young, MD, PhD⁷ and Mary K. Hayden, MD³; ¹University of Michigan, Ann Arbor, Michigan; ²Clemson University, Clemson, South Carolina; ³Rush University Medical Center, Chicago, Illinois; ⁴Rush University, Chicago, Illinois; ⁵Rush University Medical Center, Naperville, Illinois; ⁶Gush University 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.

In preliminary analysis, 2,480 samples were collected from 627 patients Results. 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	Acquired MDRO	OR [95% CI]	<i>p</i> -value
	(n = 494)	(n = 133)	1	
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



*133 patients acquired 170 MDROs. Abbreviations: VRE, vancomycin-resistant enterococcus; 3GCephRE, 3^{es}generation cephalosporin-resistant Enterobacteriaceae; FQRE-Enterobacteriaceae; fluoroquinolone-resistant Enterobacteriaceae; CRPA, cathapenem-resistant Pseudomonas acquipions; CRE, cathapenem-resistant Interobacteriaceae; CRBA, cathapenem-resistant Actiotabcter baumannii.





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2850. Burden of Difficult-to-Treat Antibiotic-Resistant (DTR) Gram-Negative Infections in the United States, 2012–2017

Sameer S. Kadri, MD, MS¹; James Baggs, PhD²; Sarah H. Yi, PhD, MS²; Jeffrey R. Strich, MD³; Yi Ling Lai, MPH⁴; Emily Ricotta, PhD, ScM⁴; D. Rebecca Prevots, PhD⁴; Robert L. Danner, MD¹; Hannah Wolford, MSPH²; Babatunde Olubajo, PhD, MPH²; Kelly M. Hatfield, MSPH²; Sujan Reddy, MD, MSc² and John A. Jernigan, MD, MS²; ¹National Institutes of Health Clinical Center, Bethesda, Maryland; ²Centers for Disease Control and Prevention, Atlanta, Georgia; ³National Institutes of Health, Bethesda, Maryland; ⁴National Institutes of Health, Bethesda, Maryland; ⁹National Institutes of Health, Bethesda, Maryland, Parking Maryland, P

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Background. Difficult-to-treat resistance (DTR) is a metric for clinically relevant "pan-resistance" to available high-efficacy, low-toxicity antibiotic treatment options at any given time. Previous DTR prevalence estimates in Gram-negative (GN) blood-stream isolates from 2009 to 2014 have ranged between 1 and 1.5%. We sought to estimate the national burden of DTR GN isolates and more recent trends by region, site, and species.

Methods. Clinical cultures with GN isolates were identified from inpatient encounters in hospitals reporting at least one culture with susceptibility testing for a given month to Premier Healthcare Database or Cerner Health Facts Database from 2012 to 2017. DTR was defined as intermediate susceptibility or resistance to all tested carbapenems, other β -lactams, and fluoroquinolones, but not including agents introduced 2014 onwards. For each year, a raking procedure generated weights to extrapolate the sample estimate to match American Hospital Association distributions based on US census division, hospital bed capacity, teaching status, and urban designation. A weighted means survey procedure was used to extrapolate the sample estimate to obtain national DTR burden. Trends in DTR incidence were examined by using weighted multivariable logistic regression.

Results. Extrapolating from a 373-hospital sample, the estimated 2017 US inpatient burden of DTR isolates was 3,315 (1.3%) among sterile-site and 31,509 (1.7%) among all cultures, ranging from 0.5% to 3.3% in Mountain and New England regions respectively. *P. aeruginosa* was the most common species overall (37%), while *A. baumannii* was most common among sterile sites (31%). Between 2012 and 2017, there was no annual percent change in DTR incidence for sterile sites [OR 0.99 (0.93, 1.06)] but for all cultures it decreased 4.1% annually [OR 0.95 (0.91, 0.99)], including 9% annually for *A. baumannii* [OR 0.905 (0.860, 0.953)] and *K. pneumonia* [OR 0.903 (0.824, 0.991)], respectively.

Conclusion. The US inpatient burden of GN isolates displaying DTR is relatively low, varies by region, and has remained stable or declined slightly in recent years. Periodic inclusion of emerging antibiotics in the DTR classification will allow for a dynamic index between resistance and available agents.

Figure 1. United States Inpatient Burden of Difficult-to-Treat Resistance (DTR) among Gramnegative Isolates in [A] all clinical cultures and [B] sterile-site clinical cultures in 2017.

The estimated 2017 U.S. burden of DTR Gram-negative isolates among [A] sterile-site clinical cultures (i.e. 3,315 or 1.3%) and [B] overall clinical cultures (i.e. 31,509 or 1.7%) is shown distributed across 9 US Census divisions. The %DTR represents the percentage of gram-negative isolates that display difficult-to-treat resistance (DTR).

Data Source: 373 hospitals reporting to the Premier Healthcare Database or Cerner Health Facts Database in 2017 extrapolated to match American Hospital Association Annual Survey Distributions.

Subfigure A

Estimated Percent of Difficult to Treat (DTR) by Region, Sterile Specimens



Subfigure B:

Estimated Percent of Difficult to Treat (DTR) by Region, All Specimen Sources

