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Session: P-39. HAI: Gram-negatives (MDR-GNR)

Background. *Enterobacter cloacae* is a Gram-negative rod with chromosomally-induced Amp-C β-lactamase with multidrug-resistant potential. Joint Trauma System guidelines for treating combat wounds include prophylaxis with cefazolin and ertapenem, potent inducers of Amp-C. We evaluated clinical characteristics, antibiotic utilization, and outcomes associated with battlefield-related *E. cloacae* infections.

Methods. All initial solitary (those with single isolates) and serial *E. cloacae* isolates (≥24 hours from initial isolate from any site) were collected from the Trauma Infectious Disease Outcomes Study (6/2009-12/2014). Inclusion required *E. cloacae* isolation from a clinical infection. Amp-C-inducing β-lactams were classified based on induction potential and lability to the Amp-C β-lactamase as Amp-C induction levels.

Results. Of 653 *E. cloacae* isolates, 253 met inclusion criteria – 64 patients had only initial isolates, 54 patients had serial isolates. Patients were largely male (99%), median age 23 years (IQR 21-27), with injury severity score of 34 (IQR 24-45). Initial isolates were wound (70%), respiratory (22%), blood (7%), urine (1%), and other (1%). Patients commonly had blast injuries (89%), required ICU admission (95%), and had a median hospital stay of 57 days (IQR 39-82). Patients with serial isolates showed a trend towards earlier clinical infection (5 vs 8 days, P = 0.07). They were also less likely to receive carbapenems prior to *E. cloacae* isolation compared to those with only initial isolates (4% vs 38%) and more likely to receive 1st generation cephalosporins (79% vs 58%, P = 0.01). The serial isolate group received more days of 1st generation cephalosporins (median 6 days vs 2.5 days, P = 0.01). Cumulative antimicrobial therapy trended towards significance and was greater with the serial isolates (median 100 days vs 74 days, P = 0.08). There was no difference in number of surgical interventions between those with and without serial isolates (P = 0.54). Overall, 6 patients died.

Conclusion. *E. cloacae* infections after battlefield trauma were frequently encountered and associated with exposure to 1st generation cephalosporins. Serial infections did not correlate to worse patient outcomes but displayed a trend towards an overall greater duration of antibiotic use.

Disclosures. **William N. Bennett, V, MD**, **Abbvie** (Shareholder)**Amgen** (Shareholder)**Nabriva** (Shareholder)

789. Susceptibility of Phenotypic Subsets of *Pseudomonas aeruginosa* Isolates to Cefiderocol and Comparator Agents from SIDERO-WT 2014-2019

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Session: P-39. HAI: Gram-negatives (MDR-GNR)

Background. Multidrug-resistant (MDR) phenotypes are frequently observed among *P. aeruginosa* (PsA) isolated from hospitalized patients. This study describes the *in vitro* activities of cefiderocol (CFDC) and comparator agents against various non-susceptible (NS) phenotypic subsets of MDR PsA isolates from the SIDERO-WT multi-national surveillance program.

Methods. Clinical PsA isolates were collected from North America (NA) and Europe in 2014-2019 and tested for susceptibility at a central laboratory. MICs (μg/ml) were determined for CFDC, ceftazidime-avibactam (CZA), ceftolozane-tazobactam (C/T), colistin, cefepime, meropenem (MEM), and ciprofloxacin by broth microdilution according to CLSI guidelines. Aztreonam-avibactam (avibactam fixed concentration of 4 μg/ml) and imipenem/relebactam (I/R) were only tested during SIDERO-WT Year 5 (i.e. 2019). Susceptibility was interpreted according to current FDA and 2021 CLSI breakpoints.

Results. The different phenotypic subsets and susceptibility of tested compounds are shown in the table. Among 7700 PsA isolates, 47.7% and 23% were from respiratory and gastrointestinal sources of infection. CFDC inhibited 97.5% and 99.9% of all PsA at its FDA-S and CLSI-S MIC breakpoint of ≤1 and ≤4, respectively. CFDC had the lowest MIC_{90} of all tested agents and >99% S at an MIC ≤4 for all phenotypic subsets. At a MIC ≤1, CFDC displayed high susceptibility rates against all subsets including ≥88% S against CZA-NS, C/T-NS, I/R-NS, and MEM+I/R-NS isolates. Against MDR subsets, comparator agents consistently demonstrated lower activity than CFDC; 88% of MEM+C/T-NS and MEM+CZA-NS isolates had a CFDC MIC≤1 while 15.6% and 20.3% were S to I/R, respectively. 86% of MEM+CZA+C/T-NS and 80.4% CZA+C/T+I/R-NS isolates were S to CFDC. CFDC inhibited 98.1% and 99.4% of PsA isolates from NA (n = 3548) at a MIC of ≤1 and ≤4, respectively. In NA isolates that were MEM+C/T-NS; 85.7% of PsA isolates had a MIC ≤1 to CFDC and 33.3% and 28.6% were S to CZA and I/R, respectively.

	Cefiderocol			Ceftazidime-avibactam	Ceftolozane-tazobactam	Imipenem-Relebactam	
	n	MIC ≤1 μg/ml	MIC ≤4 μg/ml	% Susceptible	% Susceptible	n	% Susceptible
All	7700	97.50	99.95	93.81	93.99	711	90.99
MEM - NS	1759	94.20	99.83	74.99	76.07	143	61.22
CZA - NS	477	88.10	100	0	24.32	22	25.58
C/T - NS	463	88.10	99.78	22.03	0	16	19.51
I/R - NS	134	89.60	99.25	52.24	50.75	41	0
C/T + I/R - NS	66	84.80	100	22.73	0	10	0
CZA + C/T - NS	361	86.10	100	0	0	9	13.56
CZA + I/R - NS	64	84.40	100	0	20.31	14	0
CZA + C/T + I/R - NS	51	80.40	100	0	0	8	0
MEM + CZA - NS	440	88	100	0	21.82	18	20.25
MEM + C/T - NS	421	87.90	100	18.29	0	14	15.58
MEM + I/R - NS	133	89.50	99.25	52.63	51.13	41	0
MEM + CZA + C/T - NS	344	86	100	0	0	9	10.71
MEM + CZA + I/R - NS	63	84.10	100	0	20.63	63	0
MEM + C/T + I/R - NS	65	84.60	100	23.08	0	65	0

MEM: Meropenem; NS: Non-susceptible; CZA: Ceftazidime/avibactam; C/T: Ceftolozane/tazobactam; I/R: Imipenem/relebactam

Conclusion. CFDC demonstrated potent *in vitro* activity against a variety of phenotypic subsets of MDR *P. aeruginosa* isolates as compared to agents that are commonly used to treat MDR PsA infections including strains NS to other agents. These data support the use of CFDC as an important treatment option for MDR PsA.

Disclosures. **Sean Nguyen, PharmD**, **Shionogi Inc** (Employee) **David Fam, PharmD**, **Shionogi** (Employee) **Daniel F. Sahm, PhD**, **IHMA** (Employee)**Pfizer, Inc.** (Independent Contractor) **Meredith Hackel, PhD MPH**, **IHMA** (Employee)**Pfizer, Inc.** (Independent Contractor) **Roger Echols, MD**, **Shionogi** (Consultant) **Yoshinori Yamano, PhD**, **Shionogi** (Employee)

790. Evaluation of an Enhanced CPE Screening Program in an Acute Care Hospital in South Korea

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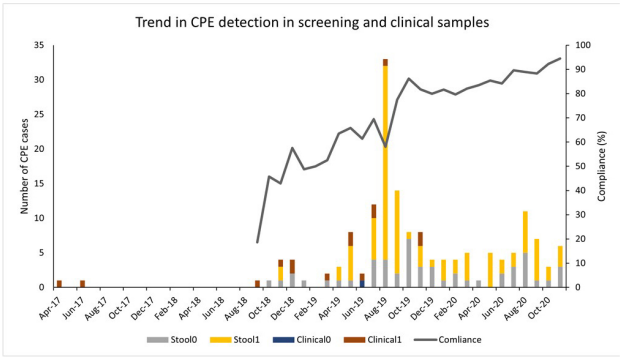
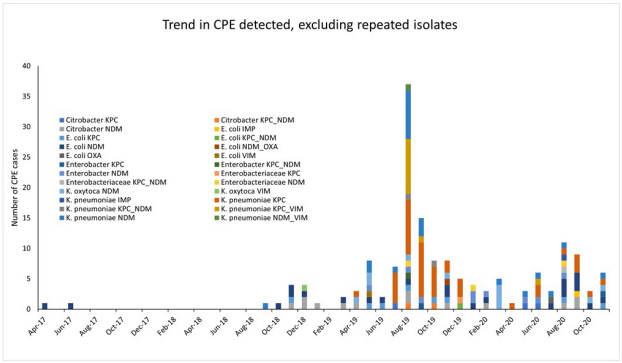
Session: P-39. HAI: Gram-negatives (MDR-GNR)

Background. Carbapenemase-producing Enterobacteriaceae (CPE) poses a great challenge in infection control in healthcare settings. A screening and contact precautions are recommended to prevent the spread of CPE among patients. However, screening strategies differ among countries and healthcare facilities.

Methods. In September 2018, we launched a CPE screening program at a 660-bed hospital in South Korea, which targeted previously colonized patients, patients with history of admission < 1 month or transferred patients or ICU-admitted patients. Once patients were identified to have CPE, they were isolated in a single room. After a CPE outbreak in July-Aug 2019, the enhanced screening program was implemented, which included patients with additional risk factors (exposure to hospitals in the past 6 months, receipt of hemodialysis or invasive procedures or rehabilitation) combined with weekly screening in ICU-admitted patients. Screening methods changed from two consecutive rectal screening swabs with chromogenic agar to initial screening with Xpert-Carba-R PCR, followed by one or two consecutive tests with chromogenic agar. We compared the CPE incidence in screening and clinical cultures before and after the enhanced screening program introduction (Sep 2018-Nov 2020).

Results. A total of 14,318 (2,178 vs. 12,140) were screened among 49,980 admitted patients and screening compliance increased from 18.6% to 94.5%. The number of CPE detection increased from 44 to 154 cases and the proportion of CPE-positive screening per 1000 admissions increased 0.6 to 2.2. However, the number of clinical CPE cultures decreased from 11 to 3 (Figure). Among screened patients, time-to-positivity was markedly reduced by 1.9 days (2.96 vs. 1.02 days) during the post-period. Additional 70 patients were detected: 36 due to serial screening in the ICUs and 34 due to enhanced on-admission screening. Factors significantly associated with positive screening were previous exposure to hospital (OR 3.5; 95% CI 1.7-7.1) and receipt of hemodialysis (OR 4.3; 95%CI 1.9-9.2). CPE isolates and carbapenemase genes were diverse (Figure). Trends in CPE detection in screening and clinical samples (upper), and bacterial species with detected carbapenemase genes (lower).





Conclusion. The study results showed that the enhanced screening program enabled us to identify the previously undetected CPE colonized patients and to decrease clinical CPE cultures.

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

792. Outbreak of Multidrug-resistant *Pseudomonas aeruginosa* in a Tertiary Healthcare System in Detroit

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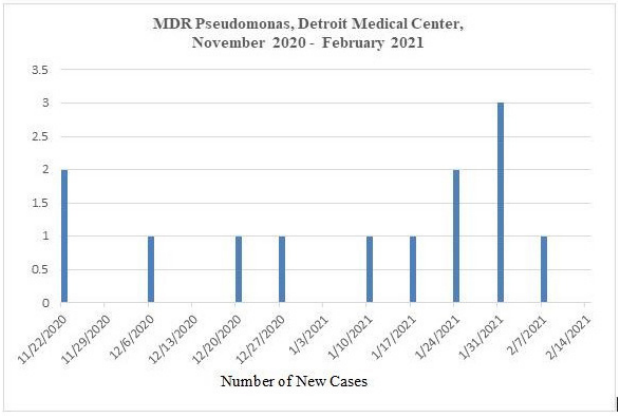
Session: P-39. HAI: Gram-negatives (MDR-GNR)

Background. *Pseudomonas aeruginosa* is one of the most common causes of healthcare-associated infections in critically ill patients and those with suboptimal immunity. However, the development of multidrug resistant *Pseudomonas aeruginosa* (MDR Pa) creates an even great disease burden and threat to both the hospital and local community health. The purpose of this study is to illustrate a descriptive analysis of a cluster of MDR *Pseudomonas,* during a local surge of SARS-CoV-2 (COVID 19) pandemic. The goal is to shed more light on the troublesome parallel during outbreaks, such as COVID-19 and consequential secondary outcomes.

Methods. From November 2020 through February 2021, 16 patients exposed to the intensive care units of a tertiary healthcare system were infected or colonized with a multidrug-resistant strain of P. aeruginosa (Figure 1). Outbreak investigation was conducted via retrospective chart review of the first eight cases and prospective analysis of the latter eight cases. The isolates collected prospectively were analyzed for taxonomic identification, antimicrobial resistance profile, and phylogenetic analysis. Clinical characteristics of all patients were collected, and epidemiological investigation was carried out. MDR is defined as resistance to at least four classes of antibiotics: third-generation cephalosporins, fluoroquinolones, aminoglycosides, and carbapenems.

Figure 1. Epidemiological Curve of Cases of Multidrug-resistant Pseudomonas aeruginosa in the Detroit Medical Center from November 2020-February 2021



Results. Of the 16 cases of MDR Pa infections, seven died within five months (Table 1). Antimicrobial resistance gene profiling detected blaOXA and blaPAO beta-lactamase genes in all the samples. One sample contained an additional blaVIM resistance gene, although this patient was colonized and not actively infected. The analysis suggests existence of two clusters demonstrating relatedness and possible horizontal transmission. Timing of this cluster of cases coincides with surge of COVID-19 cases. This highlights the importance of infection control measures and antimicrobial stewardship.

Table 1. Characteristics of patients infected with multidrug-resistant Pseudomonas aeruginosa (MDR-Pa) at Detroit Medical Center, November 2020 to February 2021

Patient	Age	Gender	Charlson Comorbidity Index	Time to isolation of MDR Pseudomonas aeruginosa	Outcome
1	41	Male	0	<48 hours from admission	Expired
2	63	Female	5	>48 hours from admission	Hospice
3	23	Male	4	>48 hours from admission	Admitted
4	55	Male	7	>48 hours from admission	Expired
5	48	Female	4	>48 hours from admission	Expired
6	35	Female	5	>48 hours from admission	Discharged
7	43	Male	9	<48 hours from admission	Discharged
8	71	Female	7	<48 hours from admission	Discharged
9	67	Female	0	<48 hours from admission	Expired
10	74	Female	4	>48 hours from admission	Discharged
11	78	Male	6	>48 hours from admission	Expired
12	58	Male	6	>48 hours from admission	Expired
13	42	Male	0	>48 hours from admission	Expired
14	84	Female	5	<48 hours from admission	Discharged
15	25	Female	4	>48 hours from admission	Discharged
16	59	Female	7	>48 hours from admission	Discharged

Conclusion. Since early 2017 studies show there is a growing prevalence worldwide in transferable resistance, particularly for β-lactamases and carbapenemases, MDR Pseudomonas. This study emphasizes an irony paralleled during a pandemic, the needed efforts to prevent unintentional lapses in patient safety.

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

793. Rifabutin Use in Staphylococcal Prosthetic Material Infections: A Case Series

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Session: P-40. HAI: Gram-positives (MRSA, MSSA, VRE)

Background. Bacterial biofilm formation is of clinical concern among patients with staphylococcal infections involving prosthetic material. While rifampin has in-vitro, animal and clinical data to support its adjunctive role in these types of infections, its potent induction of multiple cytochrome P450 enzymes and P-glycoprotein transport system proteins can pose significant drug-drug interactions. Rifabutin has comparable in-vitro anti-staphylococcal activity but less drug-drug interaction potential than rifampin. However, minimal clinical data exists to support rifabutin use as adjunctive treatment of prosthetic infections.

Methods. This case series describes 7 patients who received adjunctive rifabutin for staphylococcal prosthetic material infections between February 2018 and January 2021 at Massachusetts General Hospital. The primary outcome of infection recurrence was defined as need for surgical intervention for suspected or proven recurrence infection within 6 months after starting rifabutin therapy. Incidence of adverse effects was the main secondary outcome.