Methods. A total of 7,037 non-duplicate *Eba* were collected from UTI, IAI, or LRTI in 26 sites in 6 countries in LA, as a part of the INFORM surveillance study from 2012 to 2016. Susceptibility testing was by broth microdilution using CLSI 2018 breakpoints. CAZ-AVI was tested with a fixed concentration of 4 μg/mL avibactam. Meropenem nonsusceptibility prompted β-lactamase screening by PCR and sequencing.

Results. CAZ-AVI demonstrated potent *in vitro* activity against *Eba* from UTIs, IAIs and LRTIs (99.6%, 99.8%, and 99.5% susceptible, respectively). CAZ-AVI was active against colistin-resistant and MDR *Eba* as well as meropenem-non-susceptible *Eba* not encoding metallo-β-lactamases (96.5%, 98.4% and 99.4% susceptible, respectively) (table).

	CAZ-AVI (%Susceptible, *n*)			
Phenotype	All (*n*)	UTI (*n*)	IAI (*n*)	LRTI (*n*)
Eba, All	99.6% (7,037)	99.6% (2,918)	99.8% (2,401)	99.5% (1,718)
CAZ-NS	98.7% (2,110)	98.4% (797)	99.2% (709)	98.5% (604)
MEM-NS	93.8% (372)	93.2% (147)	95.7% (116)	92.7% (109)
MEM-NS, MBL-negative	99.4% (351)	99.3% (138)	99.1% (112)	100% (101)
CST-R[a]	96.5% (144)	98.4% (63)	97.3% (37)	93.2% (44)
MDR[b]	98.4% (1,456)	98.1% (591)	98.8% (480)	98.2% (385)

Infection source: UTI, urinary tract; IAI, intra-abdominal tract; LRTI, lower respiratory tract. CAZ-AVI, ceftazidime–avibactam; CAZ, ceftazidime; MEM, meropenem; CST, colistin; MDR, multidrug-resistant; MBL, metallo-β-lactamase; NS, non-susceptible; R, resistant.

[a]Excludes Proteeae and *Serratia* spp; CST breakpoints are by EUCAST 2018.

[b]MDR, resistant to agents from ≥3 classes.

Conclusion. CAZ-AVI exhibited potent *in vitro* activity against *Eba* from UTIs, IAIs and LRTIs isolated in Latin America from 2012 to 2016 and provides a vital alternative to colistin and meropenem when MBLs are not present.

Disclosures. **M. Estabrook**, Pfizer, Inc.: Consultant, Consulting fee. IHMA, Inc.: Employee, Salary. **K. Kazmierczak**, Pfizer Inc.: Consultant, Consulting fee. IHMA, Inc.: Employee, Salary. **G. G. Stone**, Pfizer Inc.: Employee, Salary. AstraZeneca: Former Employee and Shareholder, Salary. **D. Sahm**, Pfizer Inc.: Consultant, Consulting fee. IHMA, Inc.: Employee, Salary.

2449. Validation of *In Vitro* Activity of Aminoglycosides Against Recently Isolated *Helicobacter pylori* for Commercialization of Gentamicin-Intercalated Smectite Hybrid as a New Therapeutic Agent

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Background. The eradication rate of *Helicobacter pylori* as a standard therapy based on amoxicillin and clarithromycin, exhibits a decreasing trend. Alternative approaches have been explored, but there is still controversy in the regimen change and these do not provide a satisfactory substitute to the existing standard therapy. Thus, a novel and efficient *H. pylori* eradication regimen should be developed. Smectite can serve as a drug delivery system and gentamicin-intercalated smectite hybrids (S-GEN) are expected to supersede the standard therapy for *H. pylori* eradication. In the previous study, we synthesized S-GEN complexes as a novel therapeutic agent. In a murine model, S-GEN released gentamicin to the gastric wall stably and the therapeutic effect was not inferior to the conventional standard therapy. The aim of this study was to confirm whether the minimum inhibitory concentration (MIC) of aminoglycosides applied as smectite hybrids remained low against recently isolated *H. pylori* strains.

Methods. The *H. pylori* strains were collected via endoscopic biopsy from 1,422 patients at Gangnam Severance Hospital in Seoul, Korea, between March 2015 and February 2018. Antimicrobial susceptibility tests were performed, and the MICs of eight antibiotics (amoxicillin, clarithromycin, metronidazole, tetracycline, levofloxacin, gentamicin, netilmicin, and tobramycin) were determined by using the Epsilometer test and following the European Committee on Antimicrobial Susceptibility Testing recommendations.

Results. Finally, 140 *H. pylori* strains were analyzed in this study. The resistance rate to clarithromycin was 30.7%, although it is a major antimicrobial agent used in standard therapy. The MIC_{50} and MIC_{90} of gentamicin (MIC_{50} 0.25 mg/L, MIC_{90} 0.75 mg/L) and netilmicin (MIC_{50} 0.19 mg/L, MIC_{90} 0.75 mg/L) were lower than that of metronidazole, tetracycline and levofloxacin, which are alternative therapies for *H. pylori* eradication. In clarithromycin-resistant strains, the MIC_{50} was 0.25 mg/L and the MIC_{90} was 1 mg/L for gentamicin; for netilmicin, the values were 0.25 mg/L and 0.75 mg/L, respectively.

Conclusion. Through the use of gentamicin and netilmicin, which have low MICs for *H. pylori*, aminoglycoside-intercalated smectite hybrids are expected to emerge as a new standard therapy for *H. pylori* eradication.

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

2450. Antibiotic Treatment for Carbapenem-Resistant Enterobacteriaceae (CRE) and Outcomes in Veterans With Spinal Cord Injury/Disorder (SCI/D)

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Session: 250. Treatment of AMR Infections
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Background. A total of 282,000 people (17% veterans) in the United States have SCI/D. Infection is a significant source of morbidity and the leading cause of death in this population. Due to frequent healthcare contact and antibiotic use, SCI/D is associated with high risk of multidrug-resistant infections, including CRE. CRE are resistant to most antibiotics and associated with high mortality. The objective of this study was to describe antibiotics used for CRE infection and clinical outcomes in veterans with SCI/D.

Methods. This retrospective cohort used national VA data of veterans with SCI/D and active CRE infection (per documentation in the health record) from 2011 to 2013. CRE was defined as resistant to a carbapenem and third-generation cephalosporin. Antibiotics were described by empiric/definitive and monotherapy/combination therapy. Clinical outcomes included clinical failure/improvement, microbiological resolution, mortality and readmission in 30 days/1 year. SAS was used for analysis with significance at $P \leq 0.0125$ due to multiple comparisons.

Results. Ninety-two CRE infections (62% *K. pneumoniae*) were identified in 87 patients, most often in urine cultures (58.7%). Carbapenems (20.7%) were used most frequently for CRE treatment. Combination therapy was used more often than monotherapy (empiric 56.3%, definitive 69.0%). Definitive combinations consisted of carbapenems/polymyxins (16.7%) or carbapenems/aminoglycosides (13.3%). Clinical outcomes for definitive monotherapy vs. combination, respectively, were: clinical failure (29.6% vs. 46.7%), improvement 1–10 days (48.2% vs. 33.3%), and 11–30 days (70.4% vs. 53.3%); microbiological resolution (48.2% vs. 38.3%); mortality at 30 days (22.2% vs. 30%), 90 days (22.2% vs. 41.7%), 1 year (25.9% vs. 51.7%) and readmission at 30 days (11.1% vs. 10%) and 1 year (37% vs. 30%). No significant differences in outcomes were identified for monotherapy vs. combination therapy or susceptible vs. nonsusceptible treatment.

Conclusion. For CRE treatment in the SCI/D population, carbapenems were the most widely used drug class; combination therapy was used most frequently. No improvements in clinical outcomes were found for combination therapy as either empiric or definitive treatment or for susceptible vs. nonsusceptible treatment.

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

2451. Synergistic Activity of Ceftazidime–Avibactam in Combination With Polymyxin B Against Carbapenem-Resistant *Klebsiella pneumoniae*

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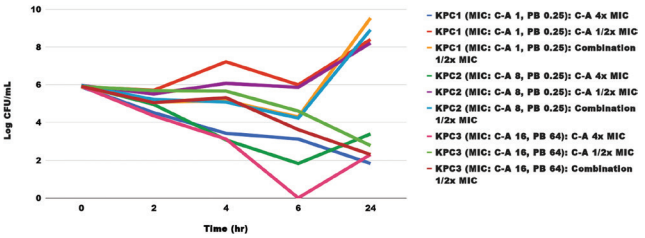
Background. Combination antimicrobial therapy is often recommended for the treatment of serious infections due to carbapenem-resistant *Klebsiella pneumoniae* (CRKP). Demonstrating synergy between ceftazidime–avibactam (C-A) and other antimicrobials *in vitro* may help elucidate the rate, magnitude, and duration of bactericidal activity and suggest combinations that may be effective in the clinical arena.

Methods. Three clinical CRKP were used for all experiments. C-A and polymyxin B (PB) MICs and time-kill analyses were performed in triplicate according to CLSI guidelines. Individual drugs were tested at ¼, ½, 1, 2, 4x MIC. A ≥3 $\log_{10}$ CFU/mL reduction compared with the starting inoculum (10^6) was considered bactericidal. Synergy was assessed by testing combinations at the highest concentration of each drug that showed no activity alone and was defined as ≥2 $\log_{10}$ CFU/mL increase in killing at 24 hours with the combination compared with most active agent alone.

Results. MICs: C-A 1, 8, 16 mg/L; PB 0.25, 0.25, 64 mg/L. C-A alone was bactericidal against all strains at 4× MIC (mean 24 hours bacterial reduction of 3.42 $\log_{10}$ CFU/mL). PB at 4× MIC was bactericidal for all strains at 6 hours (mean bacterial reduction of 3.58 $\log_{10}$ CFU/mL) but regrowth to control levels was seen at 24 hours. C-A alone at ½× MIC and combinations at ½× MIC for strains KPC1 and KPC2 yielded minimal killing followed by regrowth (mean 24 hours total bacterial count of 8.77 $\log_{10}$ CFU/mL). In contrast, bactericidal activity was observed at 24h with C-A alone at ½× MIC and in combination at ½× MIC (3.14 and 3.62 $\log_{10}$ CFU/mL reduction, respectively) for strain KPC3. Synergy was not observed for any isolate at the concentrations tested.

Conclusion. C-A demonstrated concentration-dependent bactericidal activity against all CRKP whereas PB showed initial bactericidality followed by regrowth and development of resistance. The combination of C-A and PB was not synergistic against C-A and PB susceptible or resistant CRKP isolates. Our data do not support the use of ceftazidime–avibactam in combination with polymyxin B for CRKP.

Figure 1. Time-kill Analyses of C-A Alone and in Combination With PB.



Disclosures. **E. Wenzler**, Melinta Therapeutics: Speaker's Bureau, Speaker honorarium.

2452. Treatment and Outcomes of Daptomycin-Nonsusceptible Methicillin-Resistant *Staphylococcus aureus* Bloodstream Infections

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Background. Daptomycin (dap) is approved as an alternative to vancomycin (van) for therapy of methicillin-resistant *Staphylococcus aureus* (MRSA) bloodstream infection (BSI). Cases of therapy failure associated with the emergence of daptomycin-nonsusceptible (DNS) MRSA strains have been documented. Information on the treatment and outcome of DNS MRSA BSI is scarce. This study describes the treatment and outcome of patients with DNS MRSA BSI at our healthcare center.

Methods. This is a retrospective review of patients with DNS (E-test MIC >1.0 µg/mL) MRSA BSI at a tertiary healthcare center in Detroit, Michigan between September 24, 2005 and March 31, 2018. The variables collected were: BSI source, inpatient and discharge antibiotic therapy, BSI duration, in-hospital and 90-day mortality, and 90-day MRSA BSI recurrence. Inpatient therapy was defined as the treatment used for the most consecutive days from index DNS MRSA blood culture during hospitalization. Discharge therapy is the treatment used post-discharge or on the expiration date. Antibiotics used for ≤2 days were excluded.

Results. A total of 32 nonduplicate patients with DNS MRSA BSI were identified. One patient with an inaccessible chart was excluded. The source of BSI was endovascular in 9 (29%) patients, secondary BSI in 14 (45%), central-line associated in 3 (10%), and unknown in 5 (16%). A total of 24 different antibiotic regimens were used to treat DNS MRSA BSI. Van monotherapy was the most commonly used regimen for inpatient and discharge therapy, followed by dap + ceftaroline (cef). Table 1 is a summary of the results.

Table 1: Treatment and Outcomes of Patients with DNS MRSA BSI

Inpatient Therapy	Discharge Therapy (*n*)	In-Hospital Mortality, *n*(%)	90-Day Mortality, *n*(%)	Mean BSI Duration (days)	90-Day BSI Recurrence, *n*(%)
van (10)	van (8) cef (1) dap + cef (1)	3(30)	4(40)	2.9	3(30)*
dap + cef (5)	cef + dap (3) cef + van (1) van (1)	0(0)	0(0)*	4.4	1(20)**
lin ± gen ± rif (5)	lin (3) van + sxt (1) quin/dal (1)	1(20)	3(60)	6.8	1(20)
other (11)		4(36)	4(36)	3.5	2(22)*
Totals		6(26)	11(35)	4.4	7(23)

gen = gentamycin; rif = rifampin; lin = linezolid; sxt = TMP-SMX; quin/dal = quinupristin/dalfopristin.

*1 pt with unknown status.

** 3 patients with unknown status.

Conclusion. A variety of therapeutic regimens was used to treat DNS MRSA BSI in our cohort. However, van monotherapy was the most common inpatient and discharge regimen.

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

2453. Repeated Exposures to Minocycline/Rifampin and + Chlorhexidine Combination Used to Coat Catheters Fails to Induce Antimicrobial Resistance

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Background. Central venous catheters (CVC) impregnated with minocycline and rifampin (M/R) are recommended for use in high-risk patients to reduce catheter related bloodstream infections (CRBSI). We developed a second generation antimicrobial CVC with addition of chlorhexidine (CHD) for extended spectrum activity against virulent Gram-positive and Gram-negative bacteria as well as yeast. In this study we examined the potential for induced resistance with repeated exposure to M/R+CHD.

Methods. Potential to induce resistance was evaluated by exposing a broad-spectrum of CRBSI pathogens to serial passages of sub-inhibitory concentrations of M/R+CHD and retesting MICs following each passage. Susceptibility to individual agents in the combination were assessed, to identify organisms that were originally resistant to the individual agents in the combination. A total of 24 Gram-positive, Gram-negative, and yeast pathogens were evaluated for baseline MICs following standard CLSI procedures. Subsequently, organisms that were exposed to one half the MIC were cultured and MICs retested. This process was carried out for a total of 21 passages to assess trends in MICs and potential for induction of resistance. Any organism with ≥4 fold increase in MIC were then passed in broth alone to assess phenotypic adaptation.

Results. Synergy in the triple combination of M/R + CHD was detected for several resistant organisms that had low susceptibilities to the individual components but were highly susceptible to the combination. After a series of 21 passages, the organisms maintained the same MIC values as baseline with no clinically significant increases. One strain of Enterobacter showed a 4-fold MIC increase; however, the MIC returned to baseline after culturing in broth alone.

Conclusion. Repeated exposure of M/R + CHD failed to show induced antimicrobial resistance among a large number of pathogens with both low and high susceptibilities. Furthermore, any increase in MIC returned to baseline with the removal of the stressor (M/R + CHD), indicating that the increase in MIC was a phenotypic adaptation rather than induced resistance. Surveillance studies assessing development of resistance will need to be conducted in a clinical setting.

Disclosures. **I. Raad**, The University of Texas MD Anderson Cancer Center: Shareholder, Licensing agreement or royalty. The University of Texas MD Anderson Cancer Center: Shareholder, Dr. Raad is a co-inventor of the Nitroglycerin-Citrate-Ethanol catheter lock solution technology which is owned by the University of Texas MD Anderson Cancer Center (UTMDACC) and has been licensed to Novel Anti-Infective Technologies LLC, in which UTMDACC and Licensing agreement or royalty.

2454. Pertussis Vaccine Effectiveness and Waning Immunity in Alberta, Canada: 2004–2015

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Session: 251. Adolescent Vaccines
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Background. Despite childhood vaccination coverage rates exceeding 75%, pertussis is still frequently reported in Canada. In Alberta, pertussis incidence ranged from 1.8 to 20.5 cases per 100,000 persons for 2004–2015. Most cases occurred in those aged < 15 years. We investigated pertussis vaccine effectiveness (VE) using a test-negative designed (TND) study.

Methods. All individuals who had undergone a real-time PCR laboratory test for *Bordetella pertussis* between January 1, 2004 and August 31, 2015, in the province of Alberta, Canada were included. Vaccination history was obtained from Alberta's immunization repository. Vaccination status was classified as complete, incomplete, or not vaccinated, based on the province's vaccination schedule. Multivariable logistic regression models were used to estimate adjusted odds ratios (aOR) and 95% confidence intervals (95% CI) for pertussis infection by time since last vaccination, comparing those with complete or incomplete vaccination to those not vaccinated. We adjusted for age, sex, income, urban/rural status, and the presence of a co-morbid condition. Vaccine effectiveness (VE) was calculated as [(1-aOR)*100].

Results. Of 28,154 individuals tested, 2,297 (12.3%) tested positive for *B. pertussis*. Among those with complete vs. no vaccination, VE was 88% (95% CI 85–91%) at 1 year, 83% (95% CI 79–86%) at 1 to 3 years, 70% (95% CI 63–76%) at 4 to 6 years, 28% (95% CI 12–42%) at 7 to 9 years, and -4% (95% CI -53 to 29%) at 10 or more years since a last dose of a pertussis vaccine (Figure 1). VE was similar but attenuated in the incompletely vaccinated group, with a comparable waning of immunity.

Conclusion. Pertussis VE was high in the first year after vaccination, then declined noticeably after 5 years. Our results suggest there is a large number of adolescents and adults susceptible to pertussis. Regular boosters throughout childhood, adolescence, and during pregnancy are critical to protect those at greatest risk of infection and complications. Further validation of the strengths and weaknesses of the TND for assessing pertussis VE is needed.