Background. Avibactam (AVI) is a broad-spectrum intravenous non-β-lactam/β-lactamase inhibitor with no reported activity against metallo-β-lactamases such as New Delhi metallo-β-lactamases (NDM). Structural similarities between β-lactamases and bacterial penicillin-binding proteins (PBPs) have led investigators to explore and confirm the hypothesis that AVI may interact with PBPs of several Gram-negative and positive bacteria, in a similar manner to potent synergy has also been observed between AVI and peptide antibiotics such as polymyxin B. We hypothesized that sub-bactericidal concentrations of AVI may bind PBPs to weaken cell wall integrity and enhance lysis by the membrane attack complex of complement and by endogenous cationic antimicrobials as human cathelicidin LL-37 (hCAP18) sensitizes to endotoxin. AMPS could improve killing by neutrophils and platelets that release these effectors, thereby degrading.

Methods. Using NDM K. pneumoniae (NDM-KP) as a model, we performed LL-37 kill curves and killing assays with human serum, neutrophils and platelets in the presence or absence of AVI 4 μg/mL against NDM-KP.

Results. AVI alone lacked in vitro activity against NDM-KP. Addition of AVI to a physiological achievable concentration of LL-37 (2 mM) was bacteriical and resulted in an 8-log reduction (below detection limit) in recoverable NDM-KP CFU at 6 and 24 h; no bactericidal activity was seen in bacteria treated with LL-37 or AVI alone (P < 0.0001). AVI pretreatment dramatically sensitized NDM-KP to neutrophil and platelet killing (P < 0.0001 and P < 0.01, respectively). AVI also sensitized NDM-KP to 20% human serum, resulting in an 8-log, reduction in recoverable NDM-KP CFU within 6 h (P < 0.0001), an effect abrogated by heat treatment to inactivate complement.

Conclusion. AVI demonstrates potent synergy with peptide antibiotics and the innate immune system in vitro. Since AVI alone has scant direct antimicrobial activity and no direct inhibitory effect on metallo-β-lactamases, it is less likely to increase selective pressures toward antibiotic resistance. The use of AVI in combination with other antibiotics against drug-resistant bacterial pathogens warrants further study.

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Session: 250. Treatment of AMR Infections
Saturday, October 6, 2018: 12:30 PM

Background. Biofilms are sophisticated communities of matrix-encased and surface-associated bacteria that exhibit a distinct and specific tolerant phenotype to antibiotics, antiseptics, and with activity in a 10,000-fold. Understanding this enhanced resistance rapidly reverses when bacteria detach from the biofilm and return to a planktonic state. However, in this in vitro pharmacokinetic and pharmacodynamic (PK/PD) model we are able to expose biofilms to shear rates that are consistent with human immune and mimic antibiotic penetration and diffusion pathways from antibiotic concentration in humans.

Methods. Methicillin-susceptible ATCC 29213 and MRSA 494 strains were evaluated. Initial susceptibility tests were performed by broth microdilution method. Time kill studies were performed to identify synergy patterns for liposomal and commercial antibiotics. Biofilm eradication was investigated using antibiotics vancomycin (VAN) (commercial) vs. liposomal VAN (VAN-L) (Patent #17-1460) and also combination of VAN- cefazolin (commercial) vs. liposomal vancomycin and liposomal cefazolin (CEFZ-L) (Patent #17-1460) in biofilms for strain MRSA 494. Biofilms were generated overnight using the BioFlux Microfluidic system (Fluxion BioSciences) at constant and lapsed pictures were recorded to determine antibiotic biofilm eradication rates over 18h.

Results. MIC values demonstrated a 2-fold reduction for liposomal vancomycin (MIC of 0.25 μg/mL and azole MICs of 1 μg/mL). Since AVI alone has scant direct antimicrobial activity against MRSA 494, biofilms were generated in vitro and pictures were analyzed using Bioflux Montage software. We observed 43.6% improved eradication using VAN-L vs. commercial vancomycin. Also, combination of liposomal VAN MIC in presence of incubation and pictures were analyzed using Bioflux Montage software.

Conclusion. Our biofilm results demonstrated a 43.6% improved eradication using VAN-L vs. commercial vancomycin. Also, combination of liposomal VAN MIC in presence of incubation and pictures were analyzed using Bioflux Montage software.

Session: 250. Treatment of AMR Infections
Saturday, October 6, 2018: 12:30 PM

Background. Urinary tract infection (UTI) is one of the most common infectious diseases and in 2007 accounted for 10.5 million primary care visits in the US. Advancing age and comorbidities, such as chronic kidney disease (CKD) and diabetes, affect antimicrobial prescribing habits. Sulfamethoxazole/trimethoprim (SMX-TMP), nitrofurantoin, and fosfomycin are first-line recommendations for uncomplicated cystitis. In an aging male population with potential allergies or contraindications to the above, fosfomycin is a potential option for treatment.

Methods. A retrospective chart review of fosfomycin prescribing habits at a large VA medical academic center. Patients were selected based on fosfomycin prescription in both inpatient and outpatient settings from January 1, 2004 to December 5, 2017.

Results. Inclusion excluded indication, organism(s), susceptibility, duration of treatment (CKD), and clinical success. Treatment success was defined as no representation with UTI symptoms for 30 days.

Conclusion. Fosfomycin is an antibiotic recommended for simple cystitis due to its safety profile, less collateral damage (gut flora disturbance), and low resistance as currently known. This review displays the largest ESBL cohort identified in the literature and uniquely used in a predominant male population. These findings suggest that ESBL producing bacteria can be treated successfully with fosfomycin in a male population as well as uncomplicated cystitis. However, caution should be used with cathereterized patients as treatment was less effective regardless of isolated bacteria.

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2394. Different Clostridium difficile Ribootypes Among Patients With Colonization, Initial Clinical Disease, and Recurrent Clinical Disease

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Session: 250. Treatment of AMR Infections
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Background. C. difficile is the most common cause of hospital infections with a spectrum of presentation from asymptomatic carrier to severe recurrent diarrhea. Certain C. difficile ribotypes are associated with severe disease, but there are little data on ribotypes in asymptomatic carriers or severe recurrent disease. The aim of this study was to compare virulence potential of C. difficile ribotypes with clinical disease severity.

Methods. This retrospective study included patients aged ≥18 years at NorthShore University HealthSystem (NUSHS) from February 1, 2015 to May 30, 2017. Three groups of patients with positive PCR test for C. difficile toxin gene were selected: (1) Asymptomatic patients positive for rectal carriage; (2) symptomatic outpatients with a single positive test (CDI); and (3) patients with recurrent CDI who underwent FMT. Clinical data were extracted from the Enterprise Database Warehouse. Isolates underwent fluorescent PCR ribotyping and were assigned to clades. Ribotypes with "high" (e.g., 027 and 078) and “low” (e.g., 106) virulence potential were defined as such. Virulence potential of cryptic ribotypes were considered "unknown." We used X’ and independent samples median tests to compare categorical and continuous variables, respectively.

Results. 129 C. difficile isolates (asymptomatic, N = 66; CDI, N = 33; FMT, N = 30) were ribotyped with 60 types identified. Median age was higher in asymptomatic patients [80.5 (IQR 70.8–90) years] compared with both CDI and FMT [69 (58–81) and 69 (51–83.5) years, respectively, P = 0.004]. Low virulence ribotypes were identified more frequently in asymptomatic patients than with those CDI or FMT (22/66 vs. 8/33 vs. 1/30, respectively, P = 0.006). High virulence ribotypes were found in all groups, with highest frequency in the FMT group (23/30) vs. asymptomatic (25/67) or CDI (13/33), P = 0.001.

Conclusion. Patients with severe or recurrent CDI had ribotypes associated with high virulence potential. In addition, asymptomatic carriers were more likely to have ribotypes of C. difficile historically associated with a low virulence potential. Molecular C. difficile typing may have a role in evaluating asymptomatic C. difficile colonisation vs. clinical disease.

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2395. Mechanism-Based-Susceptibility Testing (MBST) Using Disc Diffusion Assays (DDA) to Guide Treatment of Multidrug- and Extensively Drug-Resistant Pseudomonas aeruginosa (MDR-XDR Pa) In a Cystic Fibrosis (CF) Lung Transplant Recipient: Are We Ready for Combination Therapy vs. MDR XDR Pa?

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2396. Fosfomycin Resistance Among Carbapenem-Resistant Enterobacteriaceae Clinical Isolates in Connecticut, 2017

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