clavulanic acid (CL) abolished the InE in vitro. The aim of this study was to evaluate the effectiveness of the combination in vivo at clinically achievable concentrations of both CFZ and CL.

Methods. S. aureus TX0117, a type A Bla+ clinical isolate from a patient who failed CFZ therapy and TX0117-cured (TX0117c), a derivative of TX0117 which lacks β-lactamase, were used in a rat model of endocarditis. One animal per treatment strain, in addition to historical controls (n = 22), was sacrificed at the start of therapy to assess colony forming units (CFU) per gram of vegetation at T = 0. CFZ 50 mg/kg alone (n = 1) or CFZ 50 mg/kg plus CL 4 mg/kg (n = 7) was given IM every 8 hours for 72 hours. Doses were calculated to mimic routine standard concentrations of given IM (CFZ and/or PO or CL) in humans. Rats were sacrificed 16 hours after the last antibiotic dose. Aortic valves were aseptically excised, weighed, homogenized in 1 ml of saline and the entire volume was plated in serial 10-fold dilutions on mannitol salt and/or brain-heart infusion (BHI) plates. Representative recovered colonies were tested for β-lactam activity using nitrocefin. CFU comparisons between groups were done by the Mann-Whitney, Wilcoxon unpaired test with significance at p < 0.05.

Results. At baseline, there was no significant difference between the CFU of controls infected with both strains. At the start of therapy, TX0117 alone had a reduction of 2 ± 0.6 CFU/g, while the CFZ plus CL arm had a 7.1 ± 0.5 CFU/g reduction, a statistically significant difference between the two arms (P = 0.0002). CFZ treatment of the TX0117c strain lacking βlactase activity was similar to CFZ+CL (6.5 ± 0.6 log CFU/g, CFZ reduction, P = 0.0001).

Conclusion. Against Bla+ TX0117, the addition of CL, at a dose mimicking human PO kinetics, restored the efficacy of CFZ and overcame the InE. This provides a proof-of-concept for the use of oral CL with CFZ when there is a concern for the InE.

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139. Epidemiology of Inappropriate Empiric Antibiotic Therapy for Bacteremia Based on Discordant In vitro Susceptibilities: Risk Factors and Taxon-level Variation in Burden and Outcome in 156 US hospitals, 2000–2014

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Session: 42. The Cutting Edge in Antimicrobial Resistance Emergence Therapy Thursday, October 5, 2017: 10:30 AM

Background. Discordance between in vitro susceptibility and empiric antibiotic therapy is inextricably linked to antibiotic resistance and decreased survival in bloodstream infections (BSI). However, its prevalence, patient- and hospital-level risk factors, and impact on outcome in a large cohort and across different pathogens remain unclear.

Methods. We examined in vitro susceptibility interpretations for bacterial BSI and corresponding antibiotic therapy among inpatient encounters across 156 hospitals from 2000 to 2014 in the Center Healthfacts database. Discordance was defined as nonsusceptibility to initial therapy administered from 2 days before pathogen isolation to 1 day before final susceptibility reporting. Discordance prevalence was compared across taxa; risk factors and its association with in-hospital mortality were evaluated by logistic regression. Adjusted odds ratios (aOR) were estimated for patient-, hospital- and facility-level factors.

Results. Of 33,161 unique encounters with BSls, 4,219 (13%) at 123 hospitals met criteria for discordant antibiotic therapy, ranging from 3% for pneumococci to 55% for E. faecium. Discordance was higher in recent years (2010–2014 vs. 2005–2009) and was associated with older age, lower baseline SOFA score, acute renal failure (aOR = 1.8 [95% CI 1.4–2.3]), and failure of initial therapy (aOR = 1.7 [1.1–2.5]). Among Gram-positive taxa, the risk of mortality from discordant therapy was significantly higher for S. aureus (aOR = 1.3 [1.1–1.6]) but unchanged for streptococcal or enterococcal BSls.

Conclusion. The prevalence of discordant antibiotic therapy displayed extensive taxon-level variability and was associated with patient and institutional factors. Discordance detrimentally impacted survival in Gram-negative and S. aureus BSls. Understanding reasons behind observed differences in discordance risk and their impact on outcomes could inform stewardship efforts and guidelines for empiric therapy in sepsis.
140. Evolution of Antibiotic Tolerance During Oxacillin, Daptomycin and Dalbavancin Therapy Result in Breakthrough *Staphylococcus aureus* Bacteremias

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**Session:** 42. The Cutting Edge in Antimicrobial Resistance Emergence Therapy

**Thursday, October 5, 2017: 10:30 AM**

**Background.** Clinicians can employ suppressive antimicrobial therapy in patients with persistent or relapsing bacteremia. However, bacteria with favorable susceptibility profiles may exhibit antimicrobial tolerance wherein bacteria cannot proliferate yet can survive in high concentrations of antibiotics. The antimicrobial tolerance phenotype can thwart efforts to prevent bacteremia recurrence with prolonged exposure to antimicrobials and may contribute to breakthrough bacteremias while the patient is receiving active therapy. Here we present a patient case consisting of multiple episodes of breakthrough *Staphylococcus aureus* bacteremia over several years in the setting of appropriately dosed antimicrobial suppressive therapy and describe organism mutations that developed during therapy.

**Methods.** Six clinical bloodstream isolates were recovered from the patient during distinct episodes of MSSA bacteremia over a 5-year period. The identified source for each bacteremia was a central line infection (CLABSI). Isolates recovered were susceptible to the individual therapies received, which included oxacillin, daptomycin, and dalbavancin. Bacterial whole genome sequence data were collected using Illumina technology.

**Results.** The first two isolates (USA600) and the last four isolates (USA800) represent distinct populations and suggest that a distinct MSSA strain displaced the previous population between bacteremia episodes 2 and 3. Of note, all of these strains were able to survive and establish breakthrough bacteremias despite favorable susceptibility profiles to the agents used as suppressive therapy. Although the MICs remain low and in the susceptible range, these isolates progressively developed significant antimicrobial tolerance phenotypes, which coincided with mutations in *wupK* (yscO), *htrA2*, *fnW*, *ehb* and *iars* that may be advantageous to survival under antibiotic pressure.

**Conclusion.** These genetic, phenotypic and patient case data identify important changes that can occur in bacterial populations over time that are distinct from antibiotic susceptibility. These findings point to factors that may result in breakthrough bacteremia, limiting the clinical utility of antimicrobial suppressive therapy.

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879. Medical Students Have Limited Awareness, Knowledge, Beliefs, and Experiences of Pre-exposure Prophylaxis (PrEP) for HIV Prevention

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**Session:** 93. Preventing and Identifying New HIV Infections

**Thursday, October 5, 2017: 2:00 PM**

**Background.** While studies of healthcare professionals have shown increasing awareness, knowledge, positive beliefs, and prescribing practices of emtricitabine/tenofovir pre-exposure prophylaxis (PrEP) for HIV prevention, PrEP is still underutilized in clinical practice. PrEP knowledge is associated with increased prescription so early education of healthcare professionals is recommended, but the extent of PrEP education in medical school is unknown. In this analysis, we describe medical students' awareness, knowledge, beliefs, and experiences regarding PrEP.

**Methods.** Medical students at 18 US allopathic medical schools completed a survey on knowledge, beliefs, and experiences of PrEP in May–June 2016. Knowledge was