Conclusion. Previous same class antibiotic exposure remains a major predictive factor for macrolide resistance. History of treatment failure is a predictive factor for macrolide and fluoroquinolone failure. HIV infection and immune compromise are risk factors for IPD infection with penicillin resistant pneumococci. Hospital acquisition of infection is no longer a risk factor for fluoroquinolone resistance.

Disclosures. All authors: No reported disclosures.

2402. Daptomycin Pulmonary Eosinophilia: Review of Cases and New Hyperacute Syndromic Presentation
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Session: 250. Treatment of AMR Infections Saturday, October 6, 2018: 12:30 PM

Background. Daptomycin pulmonary eosinophilia (DPE) has been described as a rare event. Since the Food and Drug Administration (FDA) first described the syndrome in 2014, there has been a significant increase in the number of cases being reported worldwide.

Methods. Retrospective review from local VA pharmacy and OPAT database of adverse drug events (ADE) with daptomycin from 2010 to April 2018. Data evaluated include, age, gender, weight, body mass index (BMI), daptomycin dosing, indication for use, duration of therapy, time to symptom onset, Creatinine clearance, white cell count (WCC), Neutrophil count (WCC), Sepsis criteria (Seps), admission to intensive care unit (ICU), and clinical outcomes or interventions.

Results. There were 363 unique initiations of Daptomycin in the time period. There were 17 DPE (5%) and 3 CPK (0.6%) events in this time period. The medians for all DPE sites were: Age 68 years (range 55–93), BMI 29 m2/kg (range 21–49.5), daptomycin dose 500 mg (>7 mg/kg), baseline CrCl 35.5 mL/minute, eosinophilia at onset of DPE 9% (8–44%), and duration of therapy to onset was 21 days (1–33). All recovered on removal of daptomycin, but 5 patients required adjunctive corticosteroid therapy. Four patients had a severe and novel acute respiratory event within 48 hours of a new initiation of daptomycin therapy. All 4 patients had prior exposure to daptomycin in the last 12 months. They presented with hypoxic respiratory failure, abnormal chest x-rays and/or CT chest scans, with preceding systemic fevers and fatigue after the first dose. All had low grade Seps (3–5%) on prior use, and all recovered rapidly with discontinuation of daptomycin.

Conclusion. DPE may be underreported and is associated with doses of 500 mg or >7 mg/kg, with CrCl <35 mL/minute and older age. Of concern are the new cases of hyperacute DPE within 48 hours of re-exposure to daptomycin that we have seen, who had prior low grade eosinophilia. Close monitoring of these factors may be warranted in risk individuals.

Disclosures. All authors: No reported disclosures.

2403. Comparison of Daptomycin Combination Therapy With Ceftaroline Or Oxacillin Against Methicillin-Resistant Staphylococcus aureus (MRSA) Isolates Causing Persistent Bacteremia
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Session: 250. Treatment of AMR Infections Saturday, October 6, 2018: 12:30 PM

Background. Increasing evidence suggests that daptomycin (DAP) demonstrates in vitro synergy in combination with other anti-staphylococcal agents, including ceftaroline (CFT) and oxacillin (OXA), against MRSA. Nevertheless, optimal combinations remain undefined. Here, our objective was to compare DAP in combination with CFT or OXA against MRSA bloodstream isolates collected from patients with persistent bacteremia despite >7 days of prior monotherapy.

Methods. Minimum inhibitory concentrations (MICs) for DAP, CFT, and OXA were determined in duplicate by reference broth microdilution methods. We used time-kill analyses (TKA) to test free peak concentrations (IC90) of DAP (8 µg/mL), CFT (16 µg/mL), and OXA (4 µg/mL) alone and in combination against 1 × 108 CFU/mL to simulate high-inocula infections. Bactericidal and synergistic activity were defined as a ≥3-log decrease in CFU/mL and >2-log decrease in CFU/mL in combination compared with the most active single agent, respectively, at 24 hours.

Results. A representative isolate was selected from 12 patients with persistent MRSA bacteremia. Median (range) MICs were 0.5 (0.5–1), 0.5 (0.5–1), and 64 (64–2128) µg/mL for DAP, CFT, and OXA, respectively. DAP was determined in duplicate by reference broth microdilution methods. We used time-kill analyses (TKA) to test free peak concentrations (IC90) of DAP (8 µg/mL), CFT (16 µg/mL), and OXA (4 µg/mL) alone and in combination against 1 × 108 CFU/mL to simulate high-inocula infections. Bactericidal and synergistic activity were defined as a ≥3-log decrease in CFU/mL and >2-log decrease in CFU/mL in combination compared with the most active single agent, respectively, at 24 hours.

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CFU/mL) against 60% and 20% of isolates exposed to DAP+CPT or DAP+OXA, respectively.

**Conclusion.** Among persistent MRSA bloodstream isolates, combinations of DAP + CPT or OXA demonstrates synergy and statistically greater killing effects in vitro at Cmax concentrations than DAP alone. Log kills were greatest with DAP+CPT, which merits further validation in pre-clinical models.

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**Synergistic Effect of Sitafloxacin and Colistin Against MDR-AB Isolates (n = 264) Using the Checkerboard Assay**

| Antimicrobial Agents | Synergy (FICI ≤ 0.5) | Partial Synergy (FICI 0.5–<1) | Additive (FICI = 1) | Indifference (FICI 1–<4) | Antagonism (FICI ≥4) |
|----------------------|----------------------|-------------------------------|--------------------|-------------------------|----------------------|
| Sitafloxacin and colistin | 9(3.4) | 99(37.5) | 75(28.4) | 81(30.7) | 0(0) |

**Figure 1:** MIC reduction of colistin in combination with sitafloxacin against MDR-AB (n = 264).

**Figure 2:** Time–kill curves for sitafloxacin and colistin alone against two isolates of MDR-AB.