8. The Association of Molecular Characteristics, Vancomycin MIC and Clinical Outcomes in Methicillin-susceptible Staphylococcus aureus Osteoarticular Infections in Children
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Background. Methicillin-resistant Staphylococcus aureus, particularly those belonging to the USA300 pulsectyle and bearing Panton–Valentine leucocidin (pvl) have been well described to cause severe osteoarticular infection (OAI). Vancomycin minimum inhibitory concentration (MIC) ≥ 1.5 µg/ml has been demonstrated to contribute to disease severity in MRSA bacteremia. Little data exist to describe the spectrum of outcomes in MSSA OAI in terms of molecular characteristics and vancomycin MIC.

Methods. OAI isolates were identified from 2011 to 2016 and subjected to vancomycin E-tests. MSSA isolates underwent PFGE, PCR for pvl, and a stepwise assay to determine accessory gene regulator (agr) group. A review of the medical record was performed. Orthopedic complications included chronic osteomyelitis, pathologic fracture, and growth arrest.

Results. During the study period, 167 cases of S. aureus OAI were identified; 115 were MSSA (68.9%). 29.1 and 26.1% of MSSA isolates were USA300 and agr-positive, respectively. USA300 isolates were more likely to be pvl-positive (66.7 vs. 13.6%, P < 0.001) and agr1 (80% vs. 57.5%, P = 0.01). The presence of pvl was associated with agr1 (P = 0.03), larger abscesses (6 vs. 2 cm, P = 0.04), ECU admission (16.7 vs. 3.5%, P = 0.03) and a longer length of stay (11 vs. 6 days, P = 0.05). agr III and IV were associated with a higher rate of orthopedic complications (36.4 vs. 13.9%, P = 0.03 and surgical procedures (90.1 vs. 64.5%, P = 0.02) than other agr groups. An increase in the proportion of MSSA isolates with a vancomycin MIC ≥ 1.5 µg/ml occurred in the study period (P = 0.007). In MSSA, vancomycin MIC ≥ 2 µg/ml was associated with agr III (P = 0.07) and higher rates of orthopedic complications (P = 0.08) and venous thrombosis (P = 0.06). Figure 2.

Conclusion. MSSA accounts for 70% of S. aureus isolates causing OAI at TCH. While pvl-positive strains are associated with worse short-term outcomes, agr III and IV are associated with long-term morbidity. Vancomycin E-test MICs appear to be increasing among MSSA; vancomycin MIC ≥ 2 µg/ml are associated with agr III and adverse clinical outcomes suggesting that this may be a surrogate for disease severity. Further work is needed to understand the contribution of these factors to invasive MSSA disease.

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83. Impact of Vancomycin Serum Trough Concentrations and Vancomycin AUC/MIC on Vancomycin Response, In Hospital Outcomes and Acute Kidney Injury in Pediatric Staphylococcus aureus Pneumonia
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Background. Vancomycin AUC/MIC > 400 was initially shown to be beneficial in adults with staphylococcal pneumonia. Current practice guidelines recommend targeting serum vancomycin trough concentrations (VTC) of 15–20 µg/ml in adults with severe MRSA infection to approximate these AUC/MIC goals. Small studies have shown no benefit to VTC > 15 µg/ml in children with osteomyelitis or bacteremia. We describe the impact of VTC and AUC/MIC on outcomes of pediatric S. aureus pneumonia.

Methods. Cases of S. aureus pneumonia from January 1, 2011 to December 31, 2016 were reviewed. Patients treated with vancomycin <48 hours were excluded. Susceptible (SV) vancomycin response (SVR) was considered any combination of duration of fever, bacteremia or ICU stay > 75%-tile, need for re-operation, or mortality. The highest VTC and AUC obtained in the first 96 hours of therapy was used in analyses. Vancomycin MIC was determined with the E-test. Acute kidney injury (AKI) was defined as a doubling of the baseline serum creatinine.

Results. Thirty-six patients were identified meeting inclusion criteria with a median age of 0.7 years. 75% of isolates were MRSA and 70.4% were USA300. 80.6% of patients were admitted to the ICU and 52.8% were intubated. No benefit was observed in terms of duration of fever, bacteremia, ICU stay, ventilator or hospital days or rates of SVR between patients with VTC > or <15 µg/ml. There were substantial increases in rates of AKI with higher VTC (66.7 vs. 24.2%, P < 0.001). Among 23 patients for whom AUC/MIC determinations were possible, none achieved an AUC/MIC > 400; the median AUC/MIC = 42 (IQR: 32–51). Eighty-eight% of isolates had an MIC ≥ 1.5 µg/ml. There was no correlation between values of AUC/MIC and length of ICU or hospital stay or SVR (AUROC 0.45).

Conclusion. While the sample size is limiting, VTC >15 µg/ml did not provide clinical benefit to children with S. aureus pneumonia compared with lower VTC levels; while at the same time predisposing to nephrotoxicity. AUC/MIC > 400 is rarely achieved in children with S. aureus pneumonia and may not be a realistic goal in this infection given the rarity with which this occurs, the frequency of high MICs and the very young age of the typical patient. Large multicenter studies are required to understand optimal vancomycin dosing and monitoring in children with invasive MRSA infections.

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84. Comparative Effectiveness of β-lactams Vs Azithromycin for Treatment of Outpatient Pediatric Community-acquired Pneumonia
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Background. Guidelines recommend amoxicillin as first-line therapy for mild, community-acquired pneumonia (CAP) in healthy, immunized children because of its effectiveness against S. pneumoniae. However, macrolides, which have inferior anti-pneumococcal activity, are the most commonly prescribed class of antibiotics for outpatient CAP. We aimed to determine the comparative effectiveness of β-lactam vs. macrolide antibiotics for the treatment of CAP.

Methods. We conducted a retrospective cohort study in 31 pediatric primary care practices. Patients 3 months to 18 years of age with CAP diagnosed between January 1, 2009 and December 31, 2013 were identified by ICD-9-CM codes. Clinical data were abstracted electronically: Treatment failure was defined as change in antibiotic by the pediatrician, emergency department (ED) visit, or hospitalization for pneumonia in the 2 weeks following diagnosis. Multivariable logistic regression models including children prescribed monotherapy of amoxicillin, broad-spectrum β-lactam antibo

Disclosures. Of 10,470 children who received antibiotics for pneumonia, 4252 (40.6%) received amoxicillin, 4459 (42.6%) received macrolides, and 1759 (16.8%) received broad-spectrum β-lactams. The groups differed by age category, proportion of insurance type, insurance document date, ordering of a chest X-ray, and prior antibiotic exposure. Treatment failure occurred in 633 children (6.1%); 418 required a change in antibiotic by the pediatrician, 169 required an ED visit, and 47 required hospitalization. In the adjusted model, macrolide prescribing was associated with a decreased odds of treatment failure in children <5 years old (aOR = 0.52, 95% CI 0.34, 0.78) and in children ≥5 years old (aOR = 0.32, 95% CI 0.25, 0.41). In practices with the lowest macrolide use, this relationship persisted (OR 0.46; 95% CI 0.23, 0.92).