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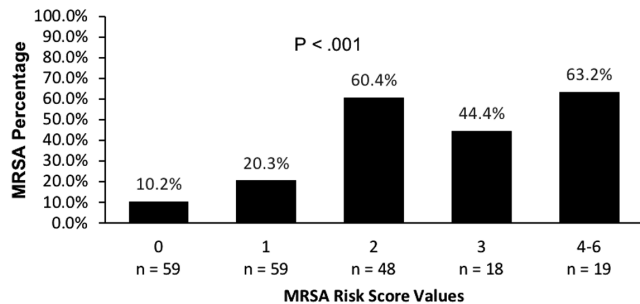
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Background. Anti-MRSA antibiotic under- and overprescribing for ABSSSI is common. To address this, we previously developed an MRSA risk assessment tool using prior literature and patient data from a single health system in Detroit, Michigan, USA. The objective of this study was to validate this risk assessment tool internationally.

Methods. Multicenter, international, prospective cohort study. Inclusion: age \geq 18 y; purulent ABSSSI from July 2016 to March 2018. Exclusion: no culture; osteo-articular infection; bite wounds; odontogenic infections. Patient MRSA risk scores were computed using the following criteria (point value): previous MRSA infection/colonization (2); previous hospitalization (1); previous antibiotics (1); chronic kidney disease (1); intravenous drug use (1); HIV/AIDS (1); diabetes with obesity (1). The likelihood ratio of each patient's score was used to convert local surveillance MRSA percentage (prior probability) into an individual patient estimated MRSA probability (posterior probability). The predictive performance of local surveillance MRSA percentage, MRSA risk score, and estimated MRSA probability were quantified using the area under the Receiver Operating Characteristic curve (aROC) and compared using the Hanley and McNeil method.

Results. 203 patients from 7 international sites included. The most common infection types were wound (28.6%), abscess (25.1%), and cellulitis with an abscess (20.7%). MRSA was observed in 33% of patients and ranged from 10% in Beijing, CN to 58.8% in Mexico City, MX. MRSA was significantly more prevalent among patients with higher MRSA risk scores (Figure 1). The MRSA risk score aROC (95% CI) [0.748 (0.678–0.819)] was significantly greater than local surveillance MRSA percentage [0.646 (0.569–0.722)] ($P = 0.016$). The estimated MRSA probability aROC [0.781 (0.716–0.845)] was significantly greater than local surveillance MRSA percentage ($P < 0.001$) but not the MRSA risk score ($P = 0.192$).

Figure 1. MRSA Percentage by MRSA Risk Score Result



Conclusion. The MRSA risk score and estimated MRSA probability were significantly more predictive of MRSA ABSSSI compared with local MRSA surveillance percentage. Further study, including potential impact of this MRSA risk assessment tool on prescribing patterns are required before widespread application.

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290. Safety and Effectiveness of Oral Sodium Fusidate (Fusidic Acid) as Chronic Antibiotic Suppressive Therapy in Patients With Staphylococcal Bone or Joint Infections

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Background. Fusidic acid (FA) is an anti-staphylococcal agent used to treat chronic bone and joint infections (BJI) due to the availability of an oral formulation

and its MRSA activity. Though used widely throughout the world for decades, FA is not approved in the USA.

Methods. To evaluate the safety and effectiveness of FA as chronic suppressive therapy in patients with staphylococcal BJI, we enrolled 30 patients in a prospective, single-arm, multi-center study in the USA. Eligible patients had refractory infections that could not be managed surgically and/or had not responded to previous antibiotic treatment. In Part A of the study, all patients received 6 months of oral FA treatment. In the first 1–2 weeks, patients could receive a companion antibiotic. Clinical success was based on lack of need for surgery or additional antibiotics. After all patients completed Part A of the study, an interim analysis was performed. In Part B of the study (ongoing), patients who completed Part A and require continued suppressive therapy may continue to receive FA for a total of 24 months.

Results. Most patients (83%) had orthopedic hardware infections. Therapy was considered successful at the 6-month visit in 18 patients (60%). Microbiological persistence was observed in eight patients, with three cases of decreasing FA susceptibility (including one case of resistance). Among 29 patients who experienced a treatment-emergent adverse event (TEAE), the most frequently reported events were: urinary tract infection ($n = 9$), peripheral edema/swelling ($n = 8$), nausea/dyspepsia ($n = 7$). Seven patients experienced TEAEs related to study drug; mild gastrointestinal disorders were most common. Two treatment-related events (unrelated to therapeutic failure) led to discontinuation of study drug

Conclusion. Patients with refractory BJI have few treatment options. In our study, 60% of infections were effectively suppressed for 6 months with FA treatment. The frequency of TEAEs was high, though not unexpected in this population with many chronic diseases. FA was well-tolerated with few patients experiencing treatment-related AEs leading to study drug discontinuation. FA administered chronically as monotherapy may lead to decreasing susceptibility and treatment failure in some patients; thus, combination therapy is warranted for this indication.

Disclosures. A. Sheets, Melinta Therapeutics: Employee, Salary. D. Graham, Cempra: Grant Investigator, Research grant. R. Darouiche, Cempra: Grant Investigator, Grant recipient. A. Strayer, Melinta Therapeutics, Inc.: Employee and Shareholder, Salary.

291. Effect of Previous Antibiotic Exposure on the Yield of Bone Biopsy Culture in Patients With Osteomyelitis

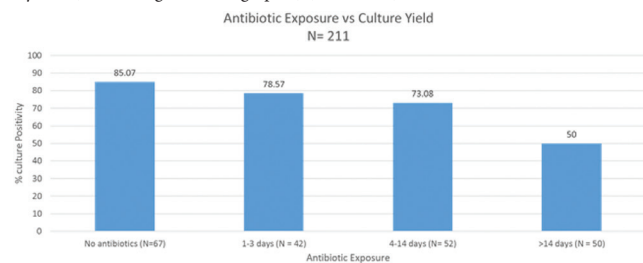
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Background. Bone biopsy and culture are gold standards for the diagnosis of osteomyelitis and are key factors in defining the etiology and treatment of osteomyelitis. There is concern that recent antibiotic exposure will decrease the sensitivity of microbiologic cultures.

Methods. A retrospective analysis was performed of patients who underwent bone biopsy for evaluation of osteomyelitis at the University of Nebraska Medical Center from 2014 to 2017. Microbiological culture data were compared with the number of days of antibiotic treatment the patient received prior to biopsy. Days of antibiotic use was divided into quartiles and the Cochran-Armitage test was used to test whether antibiotic exposure was associated with culture yield. Fisher's exact test and the Mann-Whitney test were used to compare anatomic location, diagnostic method, tobacco use, median WBC, ESR, CRP with culture positivity. Multivariable logistic regression was used to determine independent predictors of culture positivity.

Results. A total of 211 patients were studied. Descriptive statistics: 63% male, 85% Caucasian, median age: 55 years, duration of osteomyelitis prior to biopsy: median 39 days (mean 139 days). Location of osteomyelitis: lower extremity 48%, sacral/pelvic 19%, skull/facial 12%, spine 11%, upper extremity/chest 9%. Within 2 weeks prior to biopsy, the median value of the maximum WBC count, ESR, and CRP was 10.5, 66, and 5.7, respectively. A significant negative linear trend between culture positivity and days of antibiotic exposure ($P < 0.0001$) was observed (Figure 1). The rate of culture positivity was 85.07% for patients diagnosed with osteomyelitis who did not receive antibiotics and dropped to 78.57%, 73.08%, and 50% for patients who received 1–3 days, 4–14 days, and >14 days of antibiotics, respectively. Other independent predictors of culture positivity included elevated CRP ($P = 0.0017$) and clinical diagnosis of osteomyelitis (vs. histologic or radiographic) ($P = 0.0042$).



Conclusion. There is a clear negative linear correlation between pre-bone biopsy antibiotic exposure and culture positivity in patients diagnosed with osteomyelitis. In addition, elevated CRP and method of osteomyelitis diagnosis independently correlate with culture positivity.

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292. Ceftolozane/Tazobactam for Treatment of Osteomyelitis due to Multi-Drug-Resistant *Pseudomonas aeruginosa*

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Background. Ceftolozane/tazobactam (C/T) has potent activity against *Pseudomonas aeruginosa* (PA). Clinical data describing the use of C/T for PA osteomyelitis are limited. Our purpose is to describe clinical and microbiologic outcomes of adult patients treated with C/T for multidrug-resistant (MDR-PA) osteomyelitis.

Methods. This was a retrospective study of hospitalized patients who received C/T ≥ 48 hours for MDR-PA osteomyelitis between June 2015 and July 2017. MDR-PA was defined as resistance to ≥ 1 antibiotic from ≥ 3 antibiotic classes. Osteomyelitis was diagnosed by imaging, presence of systemic inflammatory signs and symptoms, elevated C-reactive protein, and positive culture for MDR-PA. Combination antibiotic therapy was defined as systemic antibiotics susceptible to MDR-PA for ≥ 48 hours with C/T. Clinical cure was defined as complete or partial resolution of signs and symptoms of infection without need for escalation of antimicrobials during inpatient and outpatient therapy. Microbiological success is defined as eradication of MDR-PA in follow-up bone cultures. Descriptive statistics were used and presented at percent or median [Interquartile range].

Results. Eighteen patients met inclusion and four patients were lost to follow-up. Demographics were male (81.2%), age 58.5 [53.5–68.5] years, 61.1% admitted to ICU, Charlson Comorbidity Index 5.5 [4–8] and APACHE II score 13.5 [11–21]. Site of osteomyelitis was pelvic in 55.6%, sacral in 22.2% and other sites in 22.2%. Surgical debridement occurred in 22.2%, and osteomyelitis was polymicrobial in 77.8%. Duration of hospitalization was 23.5 [12–37] days and all cause in-patient mortality was 16.7%. The median mean inhibitory concentration of C/T was 2 [2–4] $\mu\text{g/mL}$. Median total duration of C/T was 42 [27–42] days. Combination antibiotics were used in 27.8% (16.7% polymyxins, 11.1% aminoglycosides, 5.6% ciprofloxacin) and 2 patients on polymyxins developed renal insufficiency. No patient developed hypersensitivity, neurologic events or *C. difficile* infections. Overall, clinical cure was 64.3% and 4 patients had repeat cultures with 75% achieving a microbiologic cure.

Conclusion. These preliminary data suggest C/T maybe an option for treating patients with MDR-PA osteomyelitis, but more data are needed.

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293. Concurrent Atlantoaxial Septic Arthritis and Septic Thrombosis of the Ophthalmic Vein due to *Staphylococcus aureus*: A Case Report and Review of the Literature

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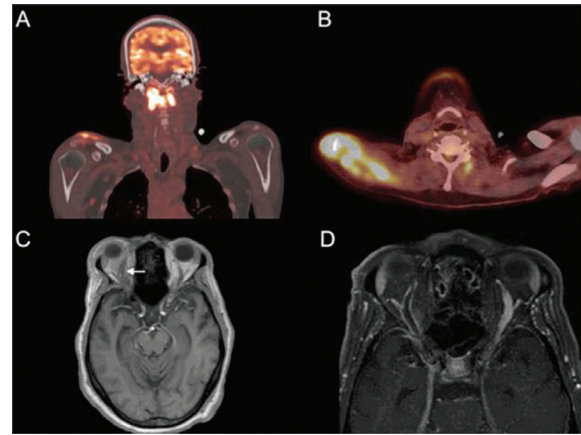
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Background. Atlantoaxial joint septic arthritis and superior ophthalmic vein thrombosis (SOVT) are uncommon sequelae of infections. Here, we describe a patient who presented concurrently with two uncommon manifestations of a common pathogen, methicillin-susceptible *Staphylococcus aureus* (MSSA), and review the associated literature. A 68-year-old man presented to the hospital with a 4-day history of worsening neck pain, right shoulder pain, and one episode of diplopia. He reported left wrist pain and swelling 3 weeks prior to presentation. A whole body ¹⁸F-positron emission tomography scan detected abnormal hypermetabolic activity in the atlantoaxial joint and in the right shoulder (Figure 1A and B). Magnetic resonance imaging revealed the presence of right SOVT (Figure 1C and D). Blood cultures grew MSSA. He underwent debridement of his right shoulder and was started on intravenous cefazolin. Conservative management of his atlantoaxial septic arthritis was unsuccessful and several weeks into his antibiotic course, he developed right-arm weakness for which he underwent C4 fusion to address atlanto-axial instability.

Methods. We reviewed previous reports describing atlantoaxial septic arthritis ($n = 6$) and septic ophthalmic vein thrombosis ($n = 6$).

Results. Previous reports of atlantoaxial septic arthritis detailed clinical presentations of subacute to acute onset of neck pain with fever, five of which were due to *S. aureus*. Four of the cases required a surgical intervention involving the cervical spine. Previous reports of SOVT describe patients ipsilateral proptosis, ptosis and chemosis. In all six cases, the SOVT developed in concurrence with a head and neck infections. Three cases required surgery or an interventional procedure for source control. Two cases recovered completely and three cases improved but with diplopia or permanent loss of vision in the affected eye.

Conclusion. Even with early recognition and prompt initiation of antibiotic therapy, our patient still suffered from long-term sequelae atlantoaxial septic arthritis and SOVT, a testament to the potential for MSSA to cause severe infections.



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294. Spondylodiscitis After Spine Surgery: Microbiology, Clinical Findings, Outcome and Comparison With Spontaneous Spondylodiscitis

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Background. Although postoperative spondylodiscitis has become a major problem, consensus on empirical antibiotics therapy is still controversial. To find out appropriate management of postoperative spondylodiscitis, this study investigated the microbiology, clinical characteristics, and outcome of postoperative pyogenic spondylodiscitis (P-PS) and compared with spontaneous pyogenic spondylodiscitis (S-PS).

Methods. This retrospective cohort study evaluated patients with microbiologically proven spondylodiscitis from three university-affiliated hospitals in South Korea between January 2005 and December 2015, with a follow-up of at least 12 months after completion of antibiotics or until the patient was transferred. Patients with prosthesis at the time of diagnosis of spondylodiscitis or who had a spine operation within 1 year of the diagnosis of spondylodiscitis were defined as having postoperative spondylodiscitis. The spine operations included discectomy, laminectomy, arthrodesis, and instrumentation for stabilization of the spine.

Results. The study evaluated 104 patients with P-PS and 441 patients with S-PS. In P-PS, the most common isolate was *S. aureus* (34%), followed by coagulase-negative staphylococci (31%), and the proportion of methicillin-resistant strains was 75%. In S-PS, the most common isolates were *S. aureus* (47%) and streptococci (21%). Of the staphylococci, 39% were methicillin resistant in S-PS. The proportion of patients with Gram-negative bacilli was 14% in P-PS and 20% in S-PS. Pre-existing or synchronous nonspinal infection (13% vs. 33%, $P < 0.001$) was observed more frequently in S-PS. Although the duration of antibiotic use was similar in both groups, surgical procedures were done more frequently in P-PS. The mortality rate was similar in both groups. However, the treatment failure and relapse rates at 12 months were higher in the P-PS group (23% vs. 13%, $P = 0.009$; 14% vs. 7%, $P = 0.028$, respectively). Methicillin-resistant *S. aureus* was associated with treatment failure or relapse.

Conclusion. Gram-positive organisms, mainly methicillin-resistant staphylococci, should be considered when prescribing empirical antibiotics in P-PS. Although surgical drainage was applied more often in P-PS than in S-PS, the treatment failure and relapse rates at the 12-month follow-up were higher in P-PS.

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295. Outcomes of Orthopedic Hardware-Related Osteomyelitis Treated Via a County Hospital Outpatient Parenteral Antimicrobial Therapy (OPAT) Program

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Background. Orthopedic hardware-related osteomyelitis (OHRO) is associated with high morbidity and cost from prolonged courses of antibiotics and additional surgery. There is limited published data describing OPAT for the treatment of OHRO.