460. Ceftriaxone vs. Standard of Care for Definitive Treatment of Methicillin-Susceptible *Staphylococcus aureus* Infections

Jessica Snawerdt, PharmD[1]; Sarah Withers, PharmD, BCPS, MS[2] and John Schrank, MD[2]; [1]Allegheny General Hospital, Pittsburgh, Pennsylvania; [2]Prisma Health-Upstate, Greenville, South Carolina

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Background. β-Lactam antibiotics, specifically nafcillin, oxacillin, and cefazolin, have proven efficacy for methicillin-susceptible *Staphylococcus aureus* (MSSA) infections. Outpatient antimicrobial therapy (OPAT) with these agents is limited due to side effects and multiple doses required per day. Ceftriaxone, a third-generation cephalosporin, has a favorable profile for OPAT. Limited evidence supporting ceftriaxone therapy for MSSA infections prevents its widespread use.

Methods. A multi-center, retrospective cohort study comparing patients who received cefazolin or nafcillin to patients who received ceftriaxone for treatment of microbiologically proven MSSA infections was conducted from February 2016 to February 2018. The primary outcome of interest was a clinical success, defined as the absence of infection-related readmission, worsening infection, or recurrent infection within 90 days. Secondary outcomes included the rate of adverse reactions, length of stay, and impact of Infectious Diseases (ID) consult.

Results. 66 patients treated with ceftriaxone and 156 patients treated with cefazolin or nafcillin were included. Skin and soft tissue and bone and joint were the most common infections in the ceftriaxone group, whereas bacteremia was most common in the nafcillin and cefazolin group. There were significant differences in baseline age (61 years vs. 59 years; $P = 0.036$) and intravenous drug use (1 patient vs. 25 patients; $P = 0.002$) between groups. As shown in Table 1, there were significantly lower rates of clinical success with ceftriaxone compared with standard of care as a composite of all infection sites (78.8% vs. 91%; $P = 0.012$). No statistically significant differences were seen in safety outcomes or ID consultation. Length of stay was significantly longer in the nafcillin and cefazolin group (5.2 days vs. 12.8 days; $P \leq 0.0001$).

Conclusion. The results of this study indicate that patients treated with ceftriaxone for MSSA infections had significantly lower rates of clinical success compared with standard of care antibiotics. Nafcillin or cefazolin should remain as first-line agents for treatment of bone and joint infections and skin and soft-tissue infections due to MSSA.

Table 1: Primary Outcome

	Ceftriaxone (n=66)	Nafcillin/Cefazolin (n=156)	P-value
Clinical success (%)	52 (78.8)	142 (91)	0.012
Clinical success by infection site			
Bacteremia (%)	15/16 (93.8)	84/91 (92.3)	1.000
Bone and Joint (%)	14/19 (73.7)	13/14 (92.9)	0.209
Skin and soft tissue(%)	16/22 (72.7)	23/27 (85.2)	0.311
Endocarditis (%)	--	18/20 (90)	--
Other	7/9 (77.8)	4/4 (100)	0.218

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461. Management of ABSSSIs: An Assessment of Knowledge, Competence and Clinical Practices among ID Specialists

Simi Thomas. Hurst, PhD and John Maeglin, MBA; Medscape Education, Oxford, New Jersey

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Background. One of the most common bacterial infections overall and among the most common causes for ED referral and/or hospital admission, ABSSSIs continue to impart a significant public health burden. The rising tide of MDROs has limited the clinical utility of many traditional antibiotics and increasing age and comorbid conditions such as diabetes, impaired renal or hepatic function, and CVD disease further complicate patient management strategies, putting patients at increased risk for treatment failure.

Methods. A continuing medical education (CME)-certified clinical practice assessment comprising 25 multiple choice questions that measured ID specialists' knowledge, competence, confidence and current practices in the management of ABSSSIs. The survey instrument was launched on a website dedicated to continuous professional development on July 27/18. Respondent confidentiality was maintained and responses were de-identified and aggregated prior to analyses.

Results. To date, 2921HCPs, including 2,380 physicians have participated in the activity. Data for ID specialists who had participated as of April 17, 2019 are presented; data collection is ongoing. The majority of ID specialists (68%; $n = 268$) practiced in the inpatient setting. Despite a relatively high level of confidence in several areas (Table 1 and data not shown), the data identified several knowledge and competence gaps with regard to antimicrobial agent selection, treatment duration, and management of complicated ABSSSIs (Table 2). The most frequently cited barriers to optimal care included: (i) logistical challenges in arranging for appropriate patient follow-up (33%; $n = 122$); (ii) knowledge about appropriate duration of antibiotic therapy (19%; $n = 71$); and (iii) access to more expensive antibiotic therapies that may be more effective (19%; $n = 71$).

Conclusion. This activity identified knowledge and competency gaps in the management of patients with ABSSSIs. These findings will be used to inform the development of educational programs that may help narrow these gaps and improve patient care.

Table 1: Confidence among ID Specialists	
How confident are you in your ability to identify patients with ABSSSIs who are at high risk for treatment failure from initial antibiotic therapy? (n=268)	
1 – Not Confident	2%
2	4%
3	31%
4	42%
5 – Very Confident	22%
How confident are you in your ability to select the most appropriate antibiotic for patients with complicated ABSSSIs? (n=268)	
1 – Not Confident	< 1%
2	6 %
3	17%
4	39%
5 – Very Confident	37%

Table 2: Knowledge and Competed Gaps among ID Specialists	
Area of Assessment	% of ID specialists who did not select the most appropriate response
(n=515) When asked to identify comorbid conditions that could impact treatment response...	81% did not recognize heart failure and 71% did not recognize obesity
(n=238) When asked about guideline recommendations regarding first line treatment strategy for a 3-cm² abscess with surrounding cellulitis...	37% did not select a strategy that combined I&D with concurrent antimicrobial therapy, which recent studies suggest may be superior to I&D
(n=238) When questioned about the recommended duration of treatment for initial management of cellulitis and mild to moderate abscesses...	56% recommended 7 or more days of treatment despite IDSA guideline recommendations for initial therapy of 5 days and good stewardship principles supporting the use of the most effective antibiotic dose for the shortest effective duration
(n=221) When questioned on the appropriate management of hospitalized patient with a moderate to severe ABSSSI whose fever has resolved (normal temperature for 24h) and WBC is normalizing...	38% would have unnecessarily delayed transition to outpatient therapy with oral antibiotics, putting the patient at increased risk for hospital-acquired coinfections
(n=227) When selecting an antimicrobial agent for a patient who has undergone a successful incision and drainage of his abscess, whose fever and tachycardia resolved in the ED, is suspected of having a Gram-negative infection, and is taking an SSRI for depression...	54% did not select an agent that provides coverage for MRSA and Gram-negative species and can be used without significant drug-drug interactions with SSRIs

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462. Prospective Surveillance of Invasive Group A Streptococcal Infections in Toronto, Ontario, Canada: 1992–2017

Christopher Kandel, MD[1]; Nick Daneman, MD, MSc[1]; Walter Demczuk[2]; Wayne Gold, MD[1]; Karen Green, MSc[3]; Irene Martin, BSc[4]; Agron Plevneshi, MD[3]; Jeff Powis, MD, FRCPC, MSc[1]; Wallis Rudnick, PhD[1]; Alicia Sarabia, MD, FRCPC[5]; Benjamin Schwartz, MD[6]; Andrew Simor, MD[1]; Greg Tyrrell, PhD, FCCM, D(ABMM)[7]; Louis Valiquette, MD, MSc[8] and Allison McGeer, MD[1]; [1]University of Toronto, Toronto, ON, Canada; [2]National Microbiology Laboratory (NML), Regina, MB, Canada; [3]Sinai Health System, Toronto, ON, Canada; [4]National Microbiology Laboratory, Public Health Agency of Canada, Winnipeg, MB, Canada; [5]Trillium Health Partners, Mississauga, ON, Canada; [6]George Mason University, Fairfax, Virginia; [7]University of Alberta, Edmonton, AB, Canada; [8]Université de Sherbrooke, Sherbrooke, Quebec, Canada

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Background. *Background.* Invasive Group A streptococcal (iGAS) infections remain a substantial source of morbidity and mortality. We explore the clinical and molecular epidemiology of iGAS infections in Toronto, Ontario, Canada over a 26-year period.

Methods. The Toronto Invasive Bacterial Diseases Network has performed population-based surveillance for iGAS infections in metropolitan Toronto and Peel regions since 1992. Participating microbiology laboratories report and submit sterile site specimens for central processing. M typing was performed on iGAS isolates until September 2006; thereafter *emm* typing was performed. Clinical information was collected by chart review using standardized collection forms.

Results. Over the 26-year period there were 2819 iGAS infections, representing an average incidence of 2.85 per 100,000 residents with a nadir of 1.65 in 1993 and a peak of 4.52 in 2014. Nosocomial infections occurred in 8.9% (251/2,819). There was substantial variation in annual incidence rates over the study period with increases from 1992 until 2002 and then 2004 until 2014 (analysis for trend, $P < 0.001$). Skin and soft-tissue infections were the most common clinical presentation, accounting for 33.2% (936/2,819), followed by bacteremia without a focus in 15.4% (435/2,819). Necrotizing fasciitis was observed in 7.4% (208/2,819) and criteria for toxic shock

syndrome were met in 17.6% (497/2,819). Overall case fatality within 30 days of hospitalization was 15.3% (95% confidence interval 14.0 to 16.6) and did not change over time. M serotype distribution varied yearly with the most common type being M1 at 22.2% (626/2,189) followed by M12 at 8.2% (230/2,189), then M89 at 5.8% (163/2,189). Antibiotic susceptibility was available from 1998 onwards with overall clindamycin susceptibility at 92.3% (1,957/2,121) and erythromycin susceptibility at 87.9% (1864/2,121).

Conclusion. The incidence of iGAS in Toronto, Ontario has varied over time, with no recent increase apparent. Similar to worldwide observations, M1 serotype was the most commonly isolated; most common serotypes demonstrated cyclical variation. Case fatality rates have remained relatively constant making the development of a vaccine imperative.
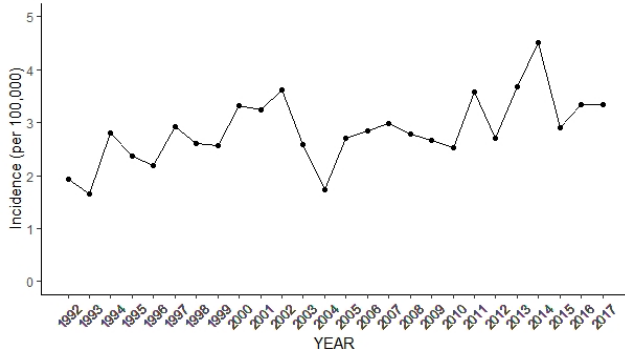
463. Evaluation of Trimethoprim-Sulfamethoxazole Utilization for Skin and Soft-Tissue Infections During Emergency Department Visits at Two Community Teaching Hospitals

Esther King, PharmD[1]; Dimple Patel, PharmD, BCPS AQ-ID[2];
Robert Roland, DO[1]; Jason Kessler, MD[2]; Amar Saini, PharmD, MHS[1] and
Nimit Jindal, PharmD Candidate[3]; [1]Overlook Medical Center, Summit, New Jersey; [2]Morristown Medical Center, Morristown, New Jersey; [3]The Ernest Mario School of Pharmacy, Somerset, New Jersey

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Background. Increasing trimethoprim/sulfamethoxazole (TMP/SMX) resistance has been noted among inpatient and outpatient isolates of methicillin-resistant *S. aureus* (MRSA) at two community teaching hospitals in Northern New Jersey. The purpose of the study is to evaluate the indications for TMP/SMX prescriptions for adult Emergency Department (ED) discharges. In addition, since IDSA guidelines for the management of skin and soft-tissue infections (SSTIs) do not recommend the use of anti-MRSA antibiotics for non-purulent SSTIs, we chose to determine guideline concordance of antibiotic selection for non-purulent SSTIs.

Methods. TMP/SMX susceptibility data for *S. aureus* from 2014 to 2018 at two community teaching hospitals were compiled. A retrospective chart review was then conducted of all adult patients who were discharged from the ED with an antibiotic prescription from January to March 2019. Antibiotic indications were extracted based on ED diagnosis and review of the medical record. In patients treated for non-purulent cellulitis, antibiotic prescription information and antibiotic allergies were collected and assessed for guideline concordance. Guideline-concordance for non-purulent cellulitis was defined as treatment with B-lactams or clindamycin.

Results. TMP/SMX susceptibility against *S. aureus* is displayed in Figure 1. Of 338 patients discharged with a prescription for TMP/SMX, 60% were treated for SSTIs, 30% were treated for urinary tract infections, and 10% were treated for other indications. Among 203 patients treated with a TMP/SMX-containing regimen for SSTIs, 76% had purulent or wound-related infection. Of 137 patients treated for non-purulent cellulitis, 68% of antibiotic regimens were guideline-concordant. In addition, 19% of antibiotic regimens for non-purulent cellulitis contained TMP/SMX.

Conclusion. A substantial reduction in TMP/SMX susceptibility among MRSA, but not MSSA, isolates has been observed. Opportunities to improve utilization of TMP/SMX for SSTIs exist at our institutions. Additional studies are warranted to determine the factors associated with increasing TMP/SMX resistance in MRSA.
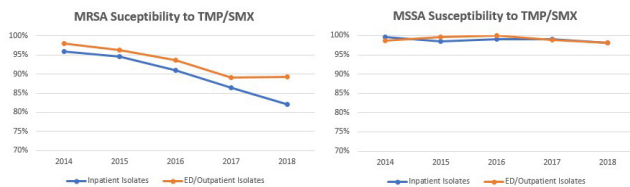
464. Fecal *Staphylococcus aureus* in the Neonatal Intensive Care Unit

Mike Carl, MD[1]; Olivia Milburn[1]; Emma Uible[2] and David Haslam, MD[1]; [1]Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio; [2]Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio

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Background. *Staphylococcus aureus* colonization in infants in the neonatal intensive care unit (NICU) often leads to repeated infections and severe disease. Methicillin-resistant *S. aureus* (MRSA) and methicillin-sensitive *S. aureus* (MSSA) infections are major causes of NICU outbreaks. Current national practice in NICUs utilizes nare swab surveillance for *S. aureus*. We hypothesize that infants colonized in the stool with *S. aureus* may go unrecognized particularly when nare swab negative, allowing for a transmission reservoir. While it is unclear why some *S. aureus* nare carriers are also stool colonized, isolates tend to have clonality. A true prevalence of *S. aureus* fecal carriage is not well understood and variable.

Methods. Available stool samples were prospectively collected from 42 of 55 infants admitted in a level IV NICU on a single day, per Cincinnati Children's institutional review board approval. Nare swab results were obtained from electronic medical records. DNA was isolated from stool and shotgun metagenomic sequencing was performed via Hiseq Illuminex 2500. The presence of *S. aureus* and MRSA were defined as having >100 sequencing reads and a mecA DNA read fraction ratio >40 per stool sample, respectively.

Results. Of the 42 stool samples sequenced, 33 were *S. aureus* (15 MSSA, 18 MRSA) positive. All infants with nare positive MSSA (*n* = 9) were colonized in the stool with a 93% and 100% sensitivity and specificity, respectively. While infants with nare positive MRSA (*n* = 10) were stool colonized with 100% and 83% sensitivity and specificity, respectively. Three nare positive infants with MRSA had S.a. in the stool but lacked the presence of mecA. When comparing clinical nare swabs to stool metagenomic surveillance, sensitivities were 60% for MSSA and 56% for MRSA.

Conclusion. Infant colonization of *S. aureus* in the NICU remains a major problem despite current national surveillance and isolation practices. We found that nare swab surveillance for *S. aureus* in infants significantly underestimated colonization rates when compared with shotgun metagenomics of stool. These results suggest that nare swabs alone may not have adequate sensitivity and the implementation of stool surveillance should be considered to augment current practices. Future study is necessary to understand how the *S. aureus* stool reservoir contributes to transmission

465. Comparative Efficacy of Double vs. Single Antibiotic Regimens for the Empiric Treatment of MRSA-Induced Acute Bacterial Skin and Skin Structure Infection

Abdullah A. Alhifany, PharmD[1];
Nisrin Bifari, Bachelor's degree in doctor of pharmacy [2]; Yasser Alatawi, PhD[3];
Saad Ullah Malik, MD[4] and Thamer Almangour, BScPhm, PharmD, BCPS, BCIDP[5]; [1]Umm Al-Qura University, Makkah, Saudi Arabia; [2]Alhada armed force hospital, Makkah, Saudi Arabia; [3]Umm Al Qura University, Makkah, Saudi Arabia; [4]University of Arizona, Tucson, Arizona; [5]King Saud University, Riyadh, Ar Riyad, Saudi Arabia

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Background. The initial management of Acute bacterial skin and skin structure infection (ABSSSI) is burdensome. It requires empirical antibiotic therapy that covers both gram-positive and gram-negative bacteria. Vancomycin plus aztreonam are the most commonly used antibiotic combination, nonetheless, they have many limitations which limits their use. Hence, many new single agents with MRSA and gram-negative coverage, oral options, and/or good safety profile have been developed to be a potential alternative such as: ceftaroline, ceftobiprole, tigecycline and the recent FDA approved antibiotic (delafloxacin). In the absence of head-to-head trials comparing these agents, we decided to conduct a network meta-analysis for these therapeutic regimens.

Methods. A Bayesian network meta-analysis of randomized clinical trials identified in PubMed/Medline and Embase databases was conducted. We performed both fixed and random effect models for clinical cure as the primary outcome of interest. Additionally, rankograms were generated using the surface under the cumulative ranking curve (SUCRA) to obtain the treatment ranking probabilities in relation to their relative effect.

Results. We identified 10 eligible studies involving 4,914 patients. The indirect comparison demonstrated that delafloxacin showed no difference in terms of clinical cure compared with ceftaroline (OR, 0.82, 95% Cr.I 0.39–1.8), ceftobiprole (OR, 0.79, 95% Cr.I 0.32–1.9), SOC (OR, 1.2, 95% Cr.I 0.62–2.4) and tigecycline (OR, 1.0, 95% Cr.I 0.45–2.2) in the fixed effect analysis, nor in the random-effect analysis (OR, 0.8, 95% Cr.I 0.26–2.2; OR, 0.78, 95% Cr.I 0.2–3.0; OR, 1.2, 95% Cr.I 0.51–3.1; and OR, 0.96, 95% Cr.I 0.30–3.0), respectively. Furthermore, the ranking probabilities in the fixed-effect and random-effect analysis showed that ceftaroline was ranked the first in terms of clinical cure (SUCRA, 40.02%) followed by ceftobiprole (SUCRA, 22.80%), delafloxacin (SUCRA, 16.60%), SOC (SUCRA, 13.80%), and then tigecycline (SUCRA, 6.70%).

Conclusion. Ceftaroline, ceftbiprole, delafoxacin, SOC and tigecycline are similarly effective. However, delafloxacin provides better convenience. Further comparative studies regarding their safety are needed.