3. Conlon-Bingham GM, Aldeyab M, Scott M, *et al.* Effects of antibiotic cycling policy on incidence of healthcare-associated MRSA and *Clostridioides difficile* infection in secondary healthcare settings. *Emerg Infect Dis* 2019;25:52–62.
4. Resolution WHA 68-7. Global action plan on antimicrobial resistance. In: *Sixty-eighth World Health Assembly,* Geneva, *26 May* 2015. *Annex 3.* Geneva: WHO; 2015.
5. Sharland M, Gandra S, Huttner B, *et al.* Encouraging AWaRe-ness and discouraging inappropriate antibiotic use—the new 2019 Essential Medicines List becomes a global antibiotic stewardship tool. *Lancet Infect Dis* 2019;19:1278–1280.
6. Klein EY, Milkowska-Shibata M, Tseng KK, *et al.* Assessment of WHO antibiotic consumption and access targets in 76 countries, 2000-15: an analysis of pharmaceutical sales data. Lancet Infect Dis 2020. doi: 10.1016/S1473-3099(20)30332-7.
7. Gupta K, Hooton TM, Naber KG, *et al.* International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: a 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. *Clin Infect Dis* 2011;52(5):e103–e120.
8. Metlay JP, Waterer GW, Long AC, *et al.* Diagnosis and treatment of adults with community-acquired pneumonia—an official clinical practice guideline of the American Thoracic Society and Infectious Diseases Society of America. *Am J Respir Crit Care Med* 2019;200(7):e45–e67.
9. *GLASS Guide for National Surveillance Systems for Monitoring Antimicrobial Consumption in Hospitals.* Geneva: World Health Organization; 2020.
10. Aldeyab MA, McElnay JC, Scott MG, *et al.* A modified method for measuring antibiotic use in healthcare settings: implications for antibiotic stewardship and benchmarking. *J Antimicrob Chemother* 2014;69:1132–1141.

Infection prevention versus antimicrobial stewardship: Does nasal povidone-iodine interfere with methicillin-resistant *Staphylococcus aureus* (MRSA) screening?

Cecelia Harrison MPH[1], Robie Zent BSN, RN, CCRC[2], Elyse Schneck BS (MT) ASCP[3], Cynthia E. Flynn MD[4] and Marci Drees MD, MS[2,5,6]

[1]ChristianaCare, Value Institute, Newark, Delaware, [2]Department of Medicine, ChristianaCare, Newark, Delaware, [3]Department of Microbiology, ChristianaCare, Newark, Delaware, [4]Department of Pathology and Laboratory Medicine, ChristianaCare, Newark, Delaware, [5]Department of Quality and Patient Safety and Department of Medicine, ChristianaCare, Newark Delaware and [6]Sidney Kimmel Medical College, Thomas Jefferson University, Philadelphia, Pennsylvania

To the Editor—When healthcare-associated pneumonia (HAP) is suspected, broad-spectrum antibiotics, often including vancomycin, are recommended to include coverage for methicillin-resistant *Staphylococcus aureus* (MRSA).[1] However, a primary goal of antimicrobial stewardship is to rapidly de-escalate these broad-spectrum antibiotics, based on culture results or other clinical data.[2] A causative organism can be identified in some HAP cases and the antibiotics can be appropriately tailored, but in many cases no pathogen is identified, making de-escalation more challenging. To combat this situation, intranasal MRSA screening has been suggested as a stewardship tool because the absence of MRSA in the nares has been found to have a high negative predictive value for MRSA pneumonia.[3]

Universal decolonization by applying chlorhexidine gluconate (CHG) to skin and mupirocin to the nares has been shown in large multicenter studies to reduce MRSA and other bloodstream infections.[4] Due to concerns that widespread use of mupirocin may lead to increasing resistance, many institutions have elected instead to use the antiseptic povidone-iodine (P-I) due to its antistaphylococcal properties and similar outcomes.[5–7]

Although sensitivity of culture-based MRSA screening may decline in the setting of antimicrobial or antiseptic use, PCR can also detect nonviable bacteria.[8] However, after our institution adopted universal nasal decolonization in addition to CHG bathing in our intensive care units (ICUs), staff raised concerns that MRSA nasal screening would no longer be accurate, and data were unable to be identified on this topic in the literature. The goal of this study was to determine whether nasal decolonization with P-I diminishes the utility of polymerase chain reaction (PCR)–based nasal MRSA screening.

Methods

We conducted a prospective cohort proof-of-concept study at our 1,200-bed community-based academic healthcare system from February to July 2019, with an enrollment goal of 20 participants for a convenience sample. Participants were eligible if they were aged ≥18 years, had been admitted to a medical ICU or stepdown unit, and had undergone baseline MRSA nasal screening by PCR (GeneXpert, Cepheid, Sunnyvale, CA) as ordered by their provider that was positive for MRSA. We excluded patients whose expected ICU or stepdown unit length of stay was <48 hours, those whose initial MRSA screen was performed after ≥2 doses of nasal P-I, and those who did not have nasal P-I decolonization performed for any reason (eg, allergy, patient refusal). Participants could only be enrolled once in the study. Verbal informed consent was obtained from each participant.

Intranasal P-I (Aplicare, 7.5%) was applied twice daily for 5 days or until ICU discharge, according to the protocol. Due to availability, Medline P-I (10%) was used from June 2019 until the end of the study. All positive PCR results underwent confirmatory testing via nonquantitative culture using MRSA-specific media (CHROMagar). All baseline PCR-positive results were

Author for correspondence: Cecelia Harrison, E-mail: Cecelia.K.Harrison@Christianacare.org

PREVIOUS PRESENTATION: These data were presented at IDWeek 2020 on October 22–26, 2020, during a virtual poster session.

Cite this article: Harrison C, *et al.* (2022). Infection prevention versus antimicrobial stewardship: Does nasal povidone-iodine interfere with methicillin-resistant *Staphylococcus aureus* (MRSA) screening?. *Infection Control & Hospital Epidemiology*, 43: 945–947, https://doi.org/10.1017/ice.2021.152

Table 1. Demographics and Clinical Characteristics

Characteristic	All Patients (N=20)
Age, mean (SD)	72.4 (10.8)
Sex, female, no. (%)	13 (65)
Race, no. (%)	
White	16 (80)
Black	4 (20)
Hispanic (%)	2 (10)
Location admitted from, no. (%)	
Home	12 (60)
Long-term care facility	7 (35)
Other residential facility	1 (5)
Prior history of MRSA, no. (%)	8 (40)
Active infection suspected, no. (%)	14 (70)
Admitting diagnoses, no. (%)[a]	
Respiratory	12 (60)
HAP	3 (12)
Other pneumonia	8 (32)
COPD/COPD exacerbation	3 (12)
Respiratory failure	2 (8)
Nonrespiratory infections	4 (16)
MRSA bacteremia	1 (4)
Sepsis	1 (4)
Osteomyelitis	1 (4)
Urinary tract infection	1 (4)
Non-infectious[b]	4 (16)

Note. COPD, chronic obstructive pulmonary disease; HAP, healthcare-associated pneumonia; MRSA, methicillin-resistant *Staphylococcus aureus*; SD, standard deviation.
[a]Patients may have had >1 admitting diagnosis.
[b]Included anticholinergic syndrome (n=1), alcohol-related diagnoses (n=2), acute kidney injury (n=1), and shock esophagitis (n=1).

confirmed via culture. Follow-up MRSA PCR tests were obtained after 4–6 days, immediately prior to intranasal P-I application, or at least 8 hours after the most recent application. All follow-up samples also underwent confirmatory culture. We used descriptive statistics to define patient demographics and calculated sensitivity of MRSA PCR, using culture as the comparative standard for our study. We conducted all analyses in SAS version 9.4 software (SAS Institute, Cary, NC). This study was approved by the ChristianaCare Institutional Review Board.

Results

Of the 25 patients initially enrolled, 20 completed the study. Reasons for dropping out included refusal of P-I (n = 2) and inability to collect a follow-up MRSA screen (n = 5). Of these 20 patients, the median age was 72 years and most were female. Most (70%) were admitted with active infection suspected, and 40% had a known MRSA history. Most (60%) were admitted with suspected respiratory infections (Table 1). Patients underwent a mean of 8.1 nasal P-I applications (range, 4–13) prior to follow-up testing, with no significant difference in the number of doses between MRSA-positive and MRSA-negative results at follow-up (8.3 and 7.4, respectively). At follow-up, 16 (80%) of 20 remained MRSA positive via both PCR and culture. Of the 4 patients with negative follow-up results, 1 was negative by both PCR and culture, and 3 were PCR positive and culture negative. All 4 had received ≥1 doses of vancomycin, and 1 patient had received ≥1 doses of linezolid. The sensitivity of follow-up MRSA PCR testing was 100%.

Discussion

In this study, PCR remained highly sensitive for nasal MRSA colonization even after multiple applications of P-I; therefore, prior receipt of nasal P-I should not deter MRSA screening for stewardship or other purposes. The limitations of this study included the small sample size, loss to follow-up due, change of P-I formulations during the study, inconsistent number of P-I doses prior to final MRSA screening, and lack of quantitative MRSA cultures to determine the dose response to P-I application. However, the fact that most patients remained culture positive after 4–13 applications raises concerns that P-I may be less effective than mupirocin for clearing nasal colonization or that off-the-shelf P-I is less effective than specific nasal formulations.[9]

We could not identify any direct comparisons of P-I and mupirocin for decolonization of human nares, although P-I has been shown to successfully decolonize the nares in the immediate treatment period.[10] Notably, 80% of our study participants remained positive; thus, larger studies using quantitative cultures to further investigate the effectiveness of both nasal P-I and mupirocin are needed. But as even culture-negative samples remained PCR positive, stewardship teams should feel comfortable de-escalating anti-MRSA antibiotics based on a negative MRSA screen, even in the setting of nasal P-I use.

Acknowledgments. The authors thank the physician and nursing leadership of the ChristianaCare Medical ICU, Wilmington ICU and Transitional Medical Unit, as well as all the staff nurses, who assisted us in the planning and execution of this project.

Financial support. No financial support was provided relevant to this article.

Conflicts of interest. All authors report no conflicts of interest relevant to this article.

References

1. Kalil AC, Metersky ML, Klompas M, *et al.* Management of adults with hospital-acquired and ventilator-associated pneumonia: 2016 clinical practice guidelines by the Infectious Diseases Society of America and the American Thoracic Society. *Clin Infect Dis* 2016;63(5):e61–e111.
2. Redfield RR, Khabbaz R. Core elements of hospital antibiotic stewardship programs. Centers for Disease Control and Prevention website. https://www.cdc.gov/antibiotic-use/core-elements/hospital.html. Published 2014. Accessed November 30, 2020.
3. Parente DM, Cunha CB, Mylonakis E, Timbrook TT. The clinical utility of methicillin-resistant staphylococcus aureus (MRSA) nasal screening to rule out MRSA pneumonia: a diagnostic meta-analysis with antimicrobial stewardship implications. *Clin Infect Dis* 2018;67:1–7.
4. Lee BY, Bartsch SM, Wong KF, *et al.* Beyond the intensive care unit (ICU): countywide impact of universal ICU *Staphylococcus aureus* decolonization. *Am J Epidemiol* 2016;183:480–489.
5. Hill RLR, Casewell MW. The in-vitro activity of povidone-iodine cream against *Staphylococcus aureus* and its bioavailability in nasal secretions. *J Hosp Infect* 2000;45:198–205.
6. Reimer K, Wichelhaus TA, Schäfer V, *et al.* Antimicrobial effectiveness of povidone-iodine and consequences for new application areas. *Dermatology* 2002;204 suppl 1:114–120.

https://doi.org/10.1017/ice.2021.152 Published online by Cambridge University Press

7. Block C, Robenshtok E, Simhon A, Shapiro M. Evaluation of chlorhexidine and povidone iodine activity against methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococcus faecalis* using a surface test. *J Hosp Infect* 2000;46:147–152.
8. Shenoy ES, Noubary F, Kim JY, *et al.* Concordance of PCR and culture from nasal swabs for detection of methicillin-resistant *Staphylococcus aureus* in a setting of concurrent antistaphylococcal antibiotics. *J Clin Microbiol* 2014;52:1235–1237.
9. Rezapoor M, Nicholson T, Tabatabaee RM, Chen AF, Maltenfort MG, Parvizi J. Povidone-iodine–based solutions for decolonization of nasal *Staphylococcus aureus*: a randomized, prospective, placebo-controlled study. *J Arthroplasty* 2017;32:2815–2819.
10. Anderson MJ, David ML, Scholz M, *et al.* Efficacy of skin and nasal povidone-iodine preparation against mupirocin-resistant methicillin-resistant *Staphylococcus aureus* and *S. aureus* within the anterior nares. *Antimicrob Agents Chemother* 2015;59:2765–2773.

Whole-genome sequence analyses by a new easy-to-use software solution support the suspicion of a neonatal ward outbreak of methicillin-resistant *Staphylococcus aureus* (MRSA) and transmission between hospitals

Marie Louise Slott Jensen[1,2,3], Ming Chen[3,4], Mette Detlefsen[2], Janne Kudsk Klitgaard[2,6], Thomas Emil Andersen[1,2] and Michael Kemp[3,5,7]

[1]Department of Clinical Research, University of Southern Denmark, Odense, Denmark, [2]Department of Clinical Microbiology, Odense University Hospital, Odense, Denmark, [3]Center for Bacterial Genomics in Southern Denmark, University of Southern Denmark, Odense, Denmark, [4]Department of Clinical Microbiology, Hospital Southern Jutland, Soenderborg, Denmark, [5]Department of Regional Health Research, University of Southern Denmark, Odense, Denmark, [6]Department Biochemistry and Molecular Biology, Research unit of Molecular Microbiology, University of Southern Denmark, Odense, Denmark and [7]Department of Clinical Microbiology, Zealand University Hospital, Slagelse, Denmark

To the Editor–Methicillin-resistant *Staphylococcus aureus* (MRSA) occasionally causes outbreaks in hospitals, often in departments where newborns receive treatment.[1,2] Hospital-acquired infections by MRSA may have a lethal outcome[3] and expenses for infection control measures for containing hospital outbreaks may become very high.[4] Surveillance of MRSA is essential for early detection and interruption of transmission. Whole-genome sequencing (WGS) is successfully used for comparing isolates of MRSA.[1,2,5] Multilocus sequence typing (MLST) is a traditional high-resolution typing method based on allele sequences. MLST sequence types (STs) can be extracted from WGS data. An even higher resolution is obtained when the number of alleles analyzed is increased as in the WGS-based method core genome MLST.[6] Both methods have shown their value in several studies of MRSA.[2,4,7] 1928 Diagnostics is a WGS-based online solution that requires no bioinformatic experience from the user. The system allows comparison and characterization of several bacteria, including *S. aureus* (9). Raw sequence data are uploaded to the 1928 Diagnostics server (https://www.1928diagnostics.com). A built-in quality check ensures that sequences of poor quality (low sequencing coverage) are not processed. For *S. aureus*, results include individual MLST ST, antibiotic resistance mechanisms (resistance genes and mutations associated with resistance), and virulence gene profiles. A core genome sequence-based cluster tree shows the relatedness of isolates. Published experience on the use of 1928 Diagnostics for hospital surveillance is limited. We tested 1928 Diagnostics in a retrospective analysis of a neonatal ward outbreak of MRSA ST22 after transfer of a patient from another hospital.

The index patient was a newborn transferred to hospital A from the neighboring hospital B on May 3, 2014. On June 1, MRSA was cultured from blood and a skin abscess from the patient. The isolate was typed as ST22 at Statens Serum Institut, Copenhagen, as part of the national surveillance of MRSA. MRSA ST22 was isolated from a diagnostic sample from another patient at the ward on June 4, and patients and staff members were screened for MRSA. MRSA ST22 was isolated from additional 6 individuals, including 1 mother and 2 staff members. Infection control interventions included, among other measures, an audit in infection control at the ward focused on reinforcing standard precaution measures, replacement of worn utensils and equipment, and thorough cleaning and disinfection of parts of the ward. No MRSA ST22 were isolated from patients, relatives, or staff members after June 16. On July 12, MRSA ST22 was cultured from a patient, previously admitted to the affected ward concomitant with the index patient. No further transmission was observed.

We included isolates of MRSA ST22 (1) from 9 individuals suspected of being infected during the outbreak, (2) from 9 individuals from the same area collected over the preceding 7 years, and (3) from 27 individuals from the neighboring hospital area in the same year as the suspected outbreak. One isolate was analyzed from each individual. WGS was performed on a Miseq (Illumina, San Diego, CA).[4]

The genome sequences confirmed all isolates as MRSA ST22 carrying the resistance genes *blaZ* and *mecA*. One isolate was typed as a recombinant sccmec type, while all other isolates were sccmec type IV. Genes encoding Panton–Valentine leucocidin, toxic shock syndrome toxin, and exfoliative toxins were not detected. All isolates had 1 or more mutations associated with resistance to ciprofloxacin (Fig. 1). No other genetic markers of resistance to antibiotics were detected in the outbreak isolates. The

Author for correspondence: Michael Kemp, E-mail: mkemp@regionsjaelland.dk.
Cite this article: Slott Jensen ML, *et al.* (2022). Whole-genome sequence analyses by a new easy-to-use software solution support the suspicion of a neonatal ward outbreak of methicillin-resistant *Staphylococcus aureus* (MRSA) and transmission between hospitals. *Infection Control & Hospital Epidemiology*, 43: 947–949, https://doi.org/10.1017/ice.2021.123