INTERNATIONAL SOCIETY FOR INFECTIOUS DISEASES

GUIDE TO INFECTION CONTROL IN THE HOSPITAL

Staphylococcus Aureus

Author
Jacob Pierce, MD, Michael Edmond, MD, MPH, Michael Stevens, MD, MPH

Chapter Editor
Michelle Doll, MD, MPH

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KEY ISSUE

Staphylococcus aureus is a major human pathogen that commonly causes healthcare-associated and community-acquired infections. It is a highly virulent organism that exhibits significant antibiotic resistance.

KNOWN FACTS

- Colonization with *S. aureus* is common. A national, population-based study of non-hospitalized persons in the U.S. found 32% of persons to be colonized with methicillin-susceptible *S. aureus* (MSSA) and 1% colonized with methicillin-resistant *S. aureus* (MRSA).
- *S. aureus* is a major cause of healthcare-associated infections (HAIs), accounting for 12% of all HAIs in the United States.
- Regarding antimicrobial resistance, *S. aureus* is typically characterized by its susceptibility patterns to penicillinase-resistant penicillins (e.g., methicillin) and vancomycin.
- The *mecA* gene encodes for penicillin binding protein 2a(PBP2a) which confers resistance to beta-lactam antibiotics.
- Over half of all *S. aureus* strains acquired in U.S. healthcare facilities are resistant to methicillin.
- Historically, MSSA strains were mostly acquired in the community, whereas MRSA strains were typically acquired in healthcare facilities.

However, community-associated MRSA (CA-MRSA) is now the predominant cause of purulent skin and soft tissue infections in the outpatient setting. MRSA isolates with the CA-MRSA phenotype are now commonly encountered in hospital settings, as well.

- Classification of MRSA strains into community-associated and hospital-associated based on exposure to the healthcare setting is no longer reliable.
- CA-MRSA tends to differ from traditional hospital-acquired MRSA in that community-associated strains are more likely to be susceptible to TMP/SMX and tetracyclines.
- CA-MRSA often manifests as skin and soft tissue infections and may be misdiagnosed as a “spider bite.” CA-MRSA is responsible for the majority of purulent skin and soft tissue infections presenting to U.S. emergency rooms.
- Many community-associated strains contain the Panton-Valentine leukocidin (PVL) gene which is associated with lysis of white blood cells and tissue necrosis. These strains characteristically cause skin and soft tissue infections, often in healthy children and young adults, as well as a severe, multilobar, necrotizing pneumonia that often occurs with or following influenza.
- Risk factors for staphylococcal colonization and infection include disruptions of the skin (insulin injections, hemodialysis, allergy therapy, IV drug use, eczema, burns), underlying diseases (respiratory infections, HIV infection), prolonged hospitalization, and exposure to other infected or colonized individuals. However, in many patients with CA-MRSA infections, these risk factors are not present.
- >80% of cases of *S. aureus* bacteremia are caused by endogenous strains (i.e., a strain colonizing the patient is responsible for invasive infection).
- The most common sources of *S. aureus* bloodstream infection are catheters (46%), skin/soft tissue/bone (27%), lower respiratory tract (11%), and urinary tract (10%).

- Vancomycin intermediate *S. aureus* (VISA), vancomycin resistant *S. aureus* (VRSA), and heteroresistant *S. aureus* (hetero-VRSA) have all been reported.
- The Clinical and Laboratory Standards Institute defines staphylococcal vancomycin minimum inhibitory concentrations (MICs) of ≤2 μg/mL as susceptible, 4–8 μg/mL as intermediate, and ≥16 μg/mL as resistant. Generally speaking, vancomycin should be avoided for severe infections where the staphylococcal isolate has an MIC of ≥2 μg/mL due to the risk of treatment failure.
- Hetero-VRSA are defined as strains of *S. aureus* that contain subpopulations of vancomycin-resistant daughter cells but for which the MICs of the parent strain are only 1–4 μg/mL. These subpopulations typically have MICs 2–8 fold higher than the original clinical isolate.
When grown in the absence of vancomycin, the subpopulation of cells reverts back to the lower MIC of the parent strain.
- In 2002, two strains of *S. aureus* with high levels of resistance to vancomycin (VRSA) were reported in the United States. These strains have MICs ≥16 μg/ml. As of February 2015, 14 patients in the U.S. had been identified with infections due to VRSA.
- Patients who develop infection with VISA and VRSA often have serious comorbid disease states such as renal failure and diabetes, a previous history of infections with MRSA, recent vancomycin use, the presence of foreign material (including intravenous catheters and prosthetic devices) and recent hospitalizations.
- Major route of transmission for *S. aureus* is direct or indirect contact; airborne transmission is uncommon.
- Colonized healthcare workers may be the source of outbreaks in the hospital setting.

CONTROVERSIAL ISSUES

- The effectiveness of routine surveillance cultures to detect MRSA colonized patients followed by isolation of the patient in order to reduce MRSA infection and colonization in high prevalence settings is probably not effective.
- The role of decolonizing agents in the non-outbreak setting remains undefined. In particular, use of mupirocin for all patients in the ICU setting (universal decolonization), raises concerns for the development of high rates of resistance. Resistance to chlorhexidine is also a concern (but appears to occur to a much less frequent extent).
- Use of contact precautions (gloves and gowns) in non-outbreak settings continues to be recommended by major organizations. However, increasing evidence (in resource rich environments) indicates that this may not be universally necessary.

SUGGESTED PRACTICE

MSSA

- Use standard precautions

MRSA/VISA

- Use contact precautions (gloves and gowns).
- Emphasize handwashing with antiseptic agents (chlorhexidine gluconate or alcohol-based products).
- Consider private room or cohorting the infected or colonized patient with other MRSA patients.
- Offer decolonization with intranasal mupirocin and chlorhexidine bathing for patients with recurring infections and for colonized personnel.
- If the MRSA patient is transferred, notify the receiving healthcare facility.
- No special precautions for home discharge are required; emphasize good hand washing.
- Universal chlorhexidine bathing of ICU patients can have a major impact on reducing MRSA infections.

VRSA

- Contact precautions, including a private room, are recommended.
- Minimize the number of people in contact with or caring for the patient.
- Educate all healthcare personnel about the epidemiology of VRSA and the appropriate infection control precautions.
- Daily chlorhexidine bathing should be considered while an inpatient.
- Initiate epidemiologic and laboratory investigations with the assistance of the public health department.
- Consult with the public health department before transferring or discharging the patient.

SUGGESTED PRACTICE IN UNDER-RESOURCED SETTINGS

- In resource limited settings compliance with guidelines can be inconsistent; low nurse-to-patient staffing ratios, insufficient infection prevention training of healthcare workers, poor access to medical supplies, and hospital overcrowding can all contribute.
- Infection prevention training for healthcare workers is critical; strict compliance with handwashing should be emphasized.
- The other infection prevention strategies outlined above should be deployed whenever possible.

SUMMARY

• In the community, *S. aureus* is best known as the cause of furuncles and soft tissue infections. In the hospital environment, *S. aureus* may cause life-threatening infections, such as pneumonia, bloodstream, or surgical site infections, and is considered one of the most important hospital-acquired pathogens.

• The nares are the usual reservoir for *S. aureus*, but other locations such as moist or hairy body areas, skin defects, wounds, and burns also can become colonized. Methicillin-resistant *S. aureus* carriage may be

eradicated with application of topical mupirocin to the anterior nares, although recolonization often occurs. This therapy should be limited to patients with recurring MRSA infections, to select pre-operative patients who have documented nares MRSA colonization, and to colonized hospital personnel to prevent the development of resistance.

- The most common mode of *S. aureus* transmission is direct contact of body surface to body surface. Sexual transmission of MRSA has been described and manifests as folliculitis or abscesses of the pubic, vaginal or perineal areas. The airborne route is less efficient but may occur in patients with *S. aureus* pneumonia or large burn wounds. It has been shown that colonized individuals with viral upper respiratory tract infections may shed *S. aureus* into the air. Transmission via indirect contact with inanimate objects such as instruments can occur, and *S. aureus* can be detected on many surfaces in hospitals, including stethoscopes and laboratory coats.

- Strategies for the management of *S. aureus* and especially MRSA colonization or infection must focus on the type of spread. Epidemic outbreaks are successfully handled with prompt application of infection control measures. Application of precautions such as patient isolation, handwashing with antiseptic agents, and glove use can interrupt the chain of transmission and control the outbreak. Institutions with repeated introduction of MRSA from the community or other facilities are unlikely to be able to eradicate this pathogen.

- Vancomycin remains the mainstay of therapy for systemic MRSA infections. For MRSA-associated necrotizing pneumonia some experts recommend the addition of an antibiotic active at the ribosomal level (such as clindamycin) to terminate toxin production. For relatively minor skin infections, the use of doxycycline or trimethoprim/sulfamethoxazole (TMP/SMX) is typically recommended in addition to incision and drainage

of abscesses.

- Fortunately, infections due to VISA and VRSA have remained uncommon. In the United States, there have been fourteen cases ascribed to VRSA. Importantly, strict compliance with infection control guidelines is necessary to minimize cross transmission within healthcare facilities. When identified, public health departments should be involved in the management of these cases.

- Treatment options for VISA and VRSA are few, and clinical experience is limited. Quinupristin-dalfopristin and linezolid are bacteriostatic for VISA/VRSA. Other potential therapies include daptomycin, ceftaroline, ceftobiprole, telavancin, tedizolid, and tigecycline. Susceptibility of VISA/VRSA has also been reported to chloramphenicol, minocycline, tetracycline, doxycycline, and TMP/SMX. Expert consultation with an infectious disease specialist should be sought for the management of VISA and VRSA cases.

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