Overview of Methicillin-Resistant *Staphylococcus aureus* Bacteremia
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Learning Objectives

• Demonstrate knowledge of methicillin-resistant *Staphylococcus aureus* (MRSA) bacteremia pathogenesis

• Outline the epidemiology of MRSA bacteremia

• Describe a tiered approach to MRSA bacteremia prevention
The Organism

Methicillin-Resistant *Staphylococcus aureus* (MRSA)

- Gram-positive cocci bacteria that form clusters under gram staining
- Approximately 30% of people are colonized with *S. aureus* in their nose
- MRSA is coagulase-positive
- Some MRSA are resistant to almost all antibiotics related to penicillin/beta-lactams
  - Oxacillin is commonly used to detect resistance

Understanding MRSA Bacteremia

MRSA Bacteremia

*S. aureus* cultured from the blood that is oxacillin-resistant, cefoxitin-resistant or methicillin-resistant or a FDA-approved laboratory test detects MRSA

- Most cases of MRSA bacteremia develop secondary to another site of infection
  - However, in up to 25% of cases, no initial site of infection is identified

- Primary/initial site of infection can include:
  - Vascular catheter-related infection
  - Skin and soft tissue infection
  - Pneumonia
  - Surgical site infection
  - Endocarditis

*(Multidrug-Resistant Organism & Clostridium difficile Infection (MDRO/CDI) Module, CDC, 2016; Klevens RM, JAMA, 2007)*
Evolution of Drug Resistance in *S. aureus*

- **S. aureus**
  - Penicillin-resistant *S. aureus* [1950s]
  - Methicillin-resistant *S. aureus* (MRSA) [1970s]
  - Vancomycin-resistant *S. aureus* [1990s]
  - Vancomycin intermediate-resistant *S. aureus* (VISA) [1997]
  - Vancomycin-resistant enterococci (VRE) [2002]
  - Community-associated MRSA: No prior exposure to health care
Why Are We Concerned About MRSA?

Mortality among those with MRSA bacteremia ranges between 15-50%.

(Image Source: Antibiotic Resistance Threats in the United States, CDC, 2013)
HAIs Caused by *S. aureus* are Frequently Resistant to Methicillin

Percent of *S. aureus* isolates resistant to methicillin

(Wiener LM, Infect Control Hosp Epidemiol, 2016)
MRSA Colonization

Infected

Colonized

(McKinley L, Am J Infect Control, 2016)
Factors that Influence Acquisition of MRSA and Other MDROs

(Harris AD, McGregor JC, Furuno JP. What infection control interventions should be undertaken to control multidrug-resistant gram-negative bacteria? Clin Infect Dis. 2006; 43: S57–61.)
Routes of MRSA Transmission

• Most commonly transmitted to patients via contaminated hands of health care personnel

• Hospitalized patients may also acquire MRSA from contaminated environmental surfaces

• Community-associated MRSA is commonly transmitted by direct contact with a colonized or infected individual

(Anderson DJ, UpToDate, 2016)
MRSA Bacteremia Prevention

Protect patients from antibiotic-resistant infections.

Surgeries and single-use catheters help treat patients, but they can be pathways for bacteria to enter the body.

Bacteria can be spread when appropriate infection control actions are not taken.

Antibiotics save lives, but poor prescribing practices puts patients at risk.

Combine infection control actions with every patient to prevent infections in health care.

Prevent infections from catheters and after surgery.

Prevent bacteria from spreading.

Improve antibiotic use.

Source: CDC Vital Signs, March 2016

(Making Health Care Safer, CDC Vital Signs, 2016)
# Tiers of MRSA Bacteremia Prevention Practices

## Tier 1 Standardize Supplies, Procedures and Process
*(complete all interventions: review and audit compliance with Tier 1 measures prior to moving to Tier 2)*

<table>
<thead>
<tr>
<th>Activity</th>
<th>Description</th>
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<tbody>
<tr>
<td>Conduct basic MRSA Risk Assessment</td>
<td>for facility infection burden and transmission risk.</td>
</tr>
<tr>
<td>Conduct case reviews of NHSN HO MRSA bacteremia LabID events (cases)</td>
<td>to guide source-specific interventions.</td>
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<tr>
<td>Monitor and alert staff of patients with MRSA.</td>
<td></td>
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<tr>
<td>Promote and monitor hand hygiene compliance.</td>
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<tr>
<td>Initiate Contact Precautions for both colonized and infected patients</td>
<td>and monitor adherence.</td>
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<tr>
<td>Assess effectiveness of cleaning and disinfection of environment of care and reusable patient care equipment.</td>
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*(if MRSA bacteremia rates remain elevated, start with MRSA Guide to Patient Safety (GPS) and then proceed with additional interventions)*

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## Tier 2 Enhanced Practices

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<thead>
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<th>Practice</th>
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<tr>
<td>Implement daily chlorhexidine bathing for populations at risk for</td>
<td>developing MRSA bacteremia.</td>
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<tr>
<td>Consider decolonization for those patients colonized with MRSA and at</td>
<td>high risk of infection.</td>
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<tr>
<td>Active Surveillance Testing (AST) for high-risk patient populations.</td>
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<tr>
<td>Consider gowns and gloving for all intensive care unit (ICU) patients.</td>
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*Image: CDC*
Tier 1: First Steps to MRSA Bacteremia Prevention

- Complete MRSA Risk Assessment
  - Primary source of infection, risk factors, etc.
- Have prospective monitoring and reporting of cases
- Provide detailed review of cases
  - Consider using the Team STEPPS learned from defects tool
- Promote and monitor hand hygiene adherence
- Use Contact Precautions for both infected and colonized patients
- Assess quality and thoroughness of cleaning and disinfection of environment of care
Tier 2: Enhanced Practices

- Perform Hospital Onset (HO) MRSA bacteremia needs assessment using Guide to Patient Safety (GPS)
- Provide daily chlorhexidine gluconate bathing for populations at risk for developing MRSA bacteremia
- Consider decolonization for those patients colonized with MRSA and at high risk of infection
- Consider Active Surveillance Testing (AST) for high risk patient populations
- Consider gowned and gloved for all intensive care units (ICU) patients
Summary

• MRSA bacteremia is a serious and life-threatening healthcare-associated infection

• MRSA bacteremia is often secondary to an initial site infection

• Prevention strategies need to be identified by an in-depth review of cases to understand the epidemiology of these infections at the facility
**References**

References (continued)

Speaker Notes
Welcome to the module titled “Overview of Methicillin-Resistant *Staphylococcus aureus* Bacteremia.” Methicillin-resistant *Staphylococcus aureus* or MRSA, are strains of *Staphylococcus aureus* that are multidrug-resistant. This module will focus on bacteremia caused by MRSA. We will take a look at how health care personnel can work together to prevent this infection.
This module was developed by national infection prevention experts devoted to improving patient safety and infection prevention efforts.
This module will describe the pathogenesis and outcomes of MRSA bacteremia. It will also cover how people develop MRSA bacteremia and then review a tiered strategy to prevent MRSA bacteremia. MRSA bacteremia is one of the more severe forms of MRSA infection. Diagnosis requires blood cultures that verify MRSA is present in the blood, indicating a systemic infection.
MRSA refers to particular strains of gram-positive bacteria *Staphylococcus aureus* (*S. aureus*) that are resistant to methicillin. *S. aureus* is common and frequently present in or on human skin. It also colonizes areas in or on the body, meaning that it can be detected, but may not be causing an acute infection. Up to 30 percent of people are colonized with *S. aureus* in their nose, but this bacteria can also colonize other sites like the axilla, groin and lower gastrointestinal tract. Methicillin is a semi-synthetic penicillin used to test susceptibility of bacterial isolates to antibiotics; currently oxacillin or a first generation cephalosporin is more commonly used in the microbiology laboratory.
MRSA strains are uniformly resistant to beta-lactam antibiotics, which include both penicillin and cephalosporin. Some strains of MRSA also have been shown to have increased resistance to vancomycin. The image at the top left side of this slide is an electron micrograph magnified 20,000 times from one of the first MRSA isolates in the U.S. In addition to uniform resistance to beta-lactams, S. aureus bacteria including MRSA produce coagulase, which distinguishes them from other Staphylococci, such as *S. epidermidis*, which do not produce coagulase.
While most strains of *S. aureus* present in a person’s nose are not MRSA, this colonization can change, in other words, you can develop MRSA colonization if you have a frequent need for hospitalization or use of antibiotics. Patients with those risk factors, nasal colonization rates are between 9 to 15 percent. MRSA from colonized individuals can easily spread within the health care setting if proper hand hygiene and personal protective equipment are not followed. For example, the image at the bottom left shows the growth of MRSA bacteria detected on an agar plate (left side) from a hand print of a health care provider who has just done an abdominal exam on a patient who is colonized with MRSA.
The agar plate on the right is after that individual applied alcohol-based hand rub for the proper amount of time and put their hand back on the agar plate. And you can see almost complete removal of MRSA from this provider’s hand.
Health care facilities report MRSA bacteremia cases to the CDC’s National Healthcare Safety Network (NHSN) and they categorize these infections into two different categories. The first is hospital-onset and the other is community-onset. MRSA bacteremia cases are reported as hospital-onset when the positive blood culture is detected after day three of hospitalization. Community-onset is when the blood culture is positive within the first three days of hospitalization. Most cases of MRSA bacteremia develop from a primary site of infection, such as those around a vascular catheter, skin or soft tissue infection, pneumonia, or surgical site infection or potentially endocarditis.
In 2007, Klevens and colleagues investigated MRSA epidemiology and found that hospital-onset cases often involved a primary infection at a surgical site, occurred in those who are on dialysis or in residents of long-term care facilities. Community-onset cases, on the other hand, often developed from localized skin or soft tissue infections. Despite the prevalence of a documented primary site infection, up to 25 percent of all MRSA bacteremia cases do not identify a primary site of infection. MRSA surveillance will be discussed in more detail in the following modules. Fortunately, MRSA has so far remains rare and predominantly affects patients such as those with chronic renal failure and diabetic foot disease.
Before we dig deeper into MRSA bacteremia and how it can be prevented, let's take a few minutes to explore how antibiotic resistance arose in *S. aureus*. And interestingly, almost as soon as penicillin was discovered by Scottish scientist and Nobel laureate, Sir Alexander Fleming in 1928, strains of *S. aureus* began to develop resistance.

By the 1950s, penicillin-resistant *S. aureus* was a major threat in hospitals and especially in newborn nurseries. And with each new class of anti-Staphylococcal antibiotics, new resistant strains of *S. aureus* began to emerge.

By the 1970s, as you can see here, methicillin-resistant *S. aureus* was widespread, encouraging the extensive use of vancomycin.
In the 1990s, vancomycin-resistant enterococci emerged and rapidly spread as well in health care settings.

Later in the 1990s, MRSA skin and soft tissue infections emerged in the community notably without prior exposure to health care facilities and many times these emerged in pediatric populations in particular.

At the end of the century, the first *S. aureus* strains with reduced susceptibility to vancomycin was initially documented.

And unfortunately, you can see in June 2002, the first case of vancomycin-resistant *S. aureus* was detected.
So, why should we be concerned about MRSA? As of the 2013 CDC threat report, over 80,000 severe MRSA infections (serious MRSA infections) occur every year and among those with a severe MRSA infection, over 11,000 do not survive. Second, as previously mentioned, *S. aureus* is often present on skin and up to 40 percent of surgical site infections have been shown to be caused by *S. aureus*. Lastly, antibiotics effective against MRSA are limited, they often require the use of central lines to administer and can cause adverse effects. These reasons have led the Centers for Disease Control and Prevention, the CDC, to classify MRSA as a serious threat.
Another reason to focus on MRSA prevention, is that *S. aureus* is frequently the cause of other healthcare-associated infections (HAIs). According to the data reported in the CDC’s NHSN in 2014, *S. aureus* ranks as the second most common pathogen for all HAIs. It is the number one cause of surgical site infections (SSI) and ventilator-associated pneumonias (VAPs) and the second most common cause of central line-associated blood stream infections (CLABSI). More than 40 percent of all *S. aureus* isolates reported to NHSN were methicillin-resistant *S. aureus* strains. So, preventing MRSA will help to prevent other types of HAIs.
To prevent MRSA, it is important to understand the impact of bacterial colonization. Like the iceberg on this slide, which is mostly below the surface of the water and not visible, there are many more individuals that carry MRSA than are documented with active infection. Patients who have active MRSA infection are just the “tip of the iceberg.” Without proper infection prevention practices, MRSA can be spread from colonized patients to other patients, health care personnel and the environment. Particularly troubling with MRSA colonization is its connection to other multidrug-resistant organisms (MDROs). A recent study cited here by McKinley in two Wisconsin Veterans Affairs facilities found that individuals colonized with one MDRO were more likely to be colonized by other MDROs.
The figure on this slide by Harris and colleagues highlights how patients admitted to a health care facility can become colonized or infected with MRSA. Non-infected patients, as seen on the left, enter the facility and their risk of becoming colonized or infected really depends on their individual characteristics and then the facility-level factors.

Individual factors include: the patient’s antibiotic use, the severity of their current illness, existing colonization among others with multidrug-resistant organisms including MRSA, the quality of their immune system and other comorbid conditions.
Facility-level factors include: frequency with which health care personnel adhere to and use hand hygiene and personal protective equipment, cleanliness of the health care environment, nurse-to-patient ratios and patient crowding, just to name a few. Based on how these factors come together, some patients may develop MRSA infection during or after their hospitalization.
Preventing MRSA transmission within the health care facility is key to reducing the impact and burden of MRSA bacteremia. Transmission of MRSA to patients is most often from carriage of MRSA on the hands of health care personnel – usually related to gaps in hand hygiene. Contaminated surfaces can also be a source of transmission. In fact, several studies demonstrate that the risk of acquiring MRSA is increased if patients are admitted to a room previously occupied by a patient with MRSA. And in the community, MRSA is most often transmitted by direct contact with someone who is colonized or has active infection.
So, how do we prevent and control MRSA and other multidrug-resistant organisms? This infographic from CDC provides a great summary of primary prevention strategies. These include preventing infections from use of devices such as central lines, making sure we, as health care providers, clean our hands and practice antibiotic stewardship. Now, let’s take a closer look at how hospitals can work to prevent MRSA bacteremia.
There are two tiers to MRSA bacteremia prevention. The first tier consists of interventions best supported by the evidence as effective at preventing MRSA bacteremia in the hospital setting. These are activities that all acute care hospitals should be doing. The second tier is composed of interventions to try if the MRSA bacteremia incidences remain higher than desired despite implementation of Tier 1 strategies. Tier 2 interventions are more complex to implement and may be more controversial, but there are reasons to believe they may be helpful in preventing MRSA bacteremia when added on to Tier 1 interventions. Let’s take a closer look at these interventions.
The first step of the Tier 1 interventions involves completing an assessment of the epidemiology of cases of MRSA bacteremia detected in your facility. For example, are risk factors for hospital-onset cases more commonly related to central lines? Patients on dialysis? Or patients who have recently had a surgical site infection?
Next, it’s important to have a system in place to alert care teams to a patient’s MRSA status. Another tactic is to provide an in-depth review of MRSA bacteremia cases. And the final tactic in Tier 1 to prevent MRSA transmission are fundamental strategies like hand hygiene, personal protective equipment use and disinfection of the environment. When applying these strategies, it is important to use local data to tailor and focus implementation strategies.

Now, let’s go to escalating Tier 2 tactics.
If your MRSA bacteremia incidences remain higher than you desire after implementing Tier 1, consider following Tier 2 Enhanced Practices. The next steps are to re-examine your MRSA surveillance data and the barriers to implementation of Tier 1 interventions. The MRSA Guide to Patient Safety, or MRSA GPS, is a tool that can help with this assessment. The tool walks through a number of prevention elements and helps you score their implementation at your facility.

Next, consider cleansing with an antiseptic like chlorhexidine for at-risk patient populations. Newer evidence suggests that decolonization or cleansing with antiseptic can be effective for high-risk groups, like those in intensive care units.
Another element may be active surveillance testing, which can be used to identify those who are colonized with MRSA; the rationale is that there may be as many as five patients colonized for every one case of acute infection like MRSA bacteremia. Finally, gowing and gloving for all high-risk populations, like intensive care unit populations, may help to prevent transmission between patients.
This session has highlighted that MRSA bacteremia is a serious threat to patient safety. It usually develops secondary to a primary site of infection like pneumonia, a vascular catheter or surgical site infection. Prevention involves a combination of understanding the epidemiology of MRSA bacteremia in the population served, a high level of hand hygiene adherence and cleaning and disinfection of the patient environment and patient care equipment. Additional prevention strategies will relate to analysis at the hospital that identifies primary sites of infection at your facility.
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