Hospital-Acquired Methicillin-Resistant *Staphylococcus aureus*: Status and Trends

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*Methicillin-resistant Staphylococcus aureus* (MRSA) has been a pathogen of serious concern to both the health care and public health communities since the 1960s. This article focuses on the most serious strains of MRSA, hospital-acquired/health care–associated MRSA. Signs and symptoms of MRSA infection are described, in addition to the modes of transmission, laboratory techniques for identifying MRSA, and treatment options. Global MRSA rates are presented and prevention technologies are discussed. Finally, multiagency suggestions for eradicating MRSA are presented, such as strict adherence to standard contact precautions and hand hygiene practices within the medical community.

After completing this article, the reader should be able to:
- Discuss MRSA and its role in hospital-acquired/health care–associated infections (HAIs).
- Identify the mechanisms of antimicrobial resistance in bacteria generally and MRSA specifically.
- Explain how bacteria acquire resistance.
- Describe how MRSA is identified.
- List the signs and symptoms of MRSA infection and its risk factors.
- State the transmission mechanisms for MRSA.
- Summarize current epidemiological data on MRSA infection.
- Discuss treatment options for MRSA, including antibacterials, microphages, and topical honey.
- Outline techniques for preventing MRSA infection, such as hand washing and the use of hydrogen peroxide vapor and antimicrobial copper.

Hospital-acquired/health care–associated infection (HAI) is of tremendous concern to health care providers as HAI is ranked as one of the top 5 causes of death in the United States.¹ The Centers for Disease Control and Prevention (CDC) estimate that 1 in 20 hospitalized patients will contract an HAI.² The World Health Organization estimates, on average, 8.7% of hospitalized patients worldwide have HAIs at any one time, with the highest frequencies being reported in the Eastern Mediterranean and Southeast Asia regions (11.8% and 10.0%, respectively).³ In the United States, HAIs are contracted by an estimated 1.7 million patients annually, accounting for nearly 99,000 deaths⁴ and imposing additional health care costs of $35.7 to $45 billion.⁵ HAI, also known as *nosocomial infections*, are infections acquired by a patient upon admittance to a hospital that were not present in the patient prior to hospitalization. Infection is said to occur within 48 to 72 hours of admittance or within 10 days of discharge from the hospital.⁶ HAIs can be caused by viral, bacterial, or fungal pathogens and can occur in adults and children.⁷ The most frequent HAIs are those involving infections of surgical wounds, bloodstream infections, urinary tract infections, and lower respiratory tract infections, with the highest prevalence of HAIs occurring in intensive care units (ICUs) and in acute surgical and orthopedic wards.⁸ Patients with lowered immune system functioning, the elderly, and those with underlying disease are the most susceptible to
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HAIs. The use of invasive devices such as catheters and certain procedures increase the risk of acquiring an infectious disease during hospital treatment. Infections associated with these invasive devices include central line–associated bloodstream infections, catheter-associated urinary tract infections, and ventilator-associated pneumonia. These types of infections account for an estimated two-thirds of all HAIs.

Although many pathogenic microorganisms cause HAIs, increasingly to blame are microorganisms resistant to the antimicrobials traditionally used to treat them. In fact, 16% of all HAIs are caused by antimicrobial-resistant pathogens. Not only are these infectious agents resistant to a single antimicrobial drug, but some also are resistant to multiple drugs or even entire classes of antimicrobial drugs. This makes these pathogens of particular interest to clinicians and public health agencies, as the pathogens pose significant treatment and transmission challenges, particularly in health care settings.

An HAI of significant concern for more than 50 years is methicillin-resistant Staphylococcus aureus (MRSA). Staphylococcus aureus (S aureus) ranks as the leading causative agent of HAIs, with a high proportion of these being caused by MRSA.

What Is MRSA?

MRSA is a bacterium labeled a “superbug” because of its acquired resistance to a multitude of antibiotics. MRSA is resistant to antibiotics in the class beta-lactams (β-lactams), which include, but are not limited to, methicillin, penicillin, and amoxicillin. β-lactams work by inhibiting bacterial cell wall synthesis and are among the most widely used antibiotics globally.

By the late 1950s, approximately 10% of S aureus isolates had become resistant to penicillin yet remained susceptible to penicillinase-stable penicillins, in particular oxacillin and methicillin. However, S aureus strains began turning up that were no longer susceptible to oxacillin and methicillin. Shortly after methicillin’s introduction as a treatment option, MRSA was identified.

While methicillin has been replaced by oxacillin for the treatment of MRSA, the acronym MRSA still is used and is interchangeable with oxacillin-resistant Staphylococcus aureus (ORSA). Each year in the United States, approximately 126,000 people are hospitalized with MRSA infections and 19,000 deaths result; 86% of these are from hospital-acquired/health care–associated MRSA (HA-MRSA). More deaths occur from MRSA than from HIV.

Staphylococcus

Staphylococcus is a genus of gram-positive bacteria comprising 40 species, of which most are harmless, asymptomatic colonizers of the skin and mucus membranes of numerous organisms, including humans. However, some Staphylococcus species are opportunistic pathogens that produce complex toxins, leading to severe infections that can sometimes be fatal. As an evolutionary adaptation, they also can exhibit frequent and multiple resistance to antimicrobials. Staphylococcus aureus is the foremost representative of the staphylococci and is among the most ubiquitous bacteria on earth.

Staphylococcus aureus grows in grapelike clusters termed cocci and frequently is found in the human axilla, groin, nose, and throat. It is estimated that approximately 1 in 3 people are colonized by S aureus (ie, they are carriers with no signs or symptoms of infection). Staphylococcus aureus causes staph infections, which

Figure 1. This colorized electron micrograph (magnification 4780X) shows multiple clumps of methicillin-resistant Staphylococcus aureus bacteria. Public domain image courtesy of the Centers for Disease Control and Prevention.
cultures of bacteria are routinely subjected to antibiotic susceptibility tests in which an agar plate containing a bacterial culture (ie, E coli) receives applications of various antimicrobials to determine their effect on that specific bacteria. If a bacteria is susceptible to a particular antibiotic, the application area and a reaction zone (often termed a halo) will be voided of bacteria on the agar plate (see Figure 2). However, if a bacteria is resistant to the applied antibiotic, there will be no effect on its growth pattern and no halo will be present.

Bacterial resistance is of tremendous concern to both the health care and public health communities because resistant bacteria are both prevalent and pervasive within health care facilities as well as in the community. Resistant bacteria make treatment difficult and often ineffective and sometimes lead to “superbugs” that are unresponsive to most common treatment options. Antimicrobial resistance also increases health care costs. Patients infected by an antimicrobial-resistant pathogen incur costs $6000 to $30 000 higher than

Microbiology of Antibiotic Resistance

Antimicrobial agents operate by 1 of 5 mechanisms: interference with cell wall synthesis (eg, β-lactams, vancomycin); inhibition of protein synthesis (eg, clindamycins, tetracyclines); interference with nucleic acid synthesis (eg, fluoroquinolones, rifampin); inhibition of a metabolic pathway (eg, sulfonamides); and disruption of bacterial membrane structure (eg, polymixins).

Almost as soon as antimicrobials were discovered, penicillin being the first in the late 1920s, bacteria began manifesting various forms of resistance against antimicrobials. And as drug development progressed, bacteria’s resistance mechanisms evolved. When antibiotics were introduced, scientists assumed that the evolution of antibiotic resistance was unlikely because mutation rates were believed to be negligible. The ability of bacteria to interchange genes was quite unexpected, and it was later discovered that bacterial resistance had actually begun even before penicillin was used in medical treatment, with the discovery of a β-lactamase in Escherichia coli (E coli). In order to determine a bacteria’s resistance or susceptibility to antibiotics,
costs for patients with infections caused by antimicrobial-susceptible pathogens. The CDC suggested that in the United States, antibiotic resistance accounts for an additional $20 billion in health care costs, $35 million in societal costs, and an additional 8 million days spent in hospitals each year.

Microbes such as bacteria, viruses, fungi, and parasites evolve over time by adjusting to their environmental conditions, just as other organisms do. However, microbes evolve much more rapidly than more complex organisms such as humans. This is a consequence of their short generation time, which in some species is on the order of minutes, as in E coli (20 minutes) and S aureus (30 minutes). Short generation times allow for significant genetic changes to occur with each new generation. In the exponential or logarithmic (log) phase of bacterial growth, cells replicate rapidly. Initially, growth is doubled, followed by a logarithmic (exponential) multiplying. The time it takes for bacterial cells to double in number defines the generation time. To further illustrate bacterial replication rates, imagine that a single S aureus bacterial cell gets into an open skin wound. In 10 generations, that single bacterial cell will have grown into a colony of more than 1000 cells (2\(^{10}\) = 1024). Add another 10 generations and that colony will have grown to more than 1 million cells (2\(^{20}\) = 1 048 576). Considering the generation time of about half an hour, it takes only 12 hours for a single original cell to grow into a colony of more than 1 million.

Bacteria manifest resistance to antimicrobial drugs through an assortment of methods. Some bacterial species are innately resistant to more than one class of antibacterial drugs, and in these cases all strains within the species are resistant to all antimicrobials within that class. The more distressing resistance is acquired resistance, in which bacteria that are susceptible to antibiotics are exposed to an antimicrobial or class of antimicrobials, and resistance develops during treatment with that antimicrobial. This form of resistance is acquired through a variety of mutation, selection, and genetic transfer (horizontal gene transfer) mechanisms. For example, the bacterium might acquire a gene or genes that encode an enzyme or enzymes targeted to destroy the antimicrobial before it has an effect. Or, the bacterium might acquire efflux pumps that eradicate the antimicrobial agent from the bacterial cell before it has an effect. Another possibility is that several genes might be acquired that alter cell wall membranes and exclude antimicrobial binding sites. Also, the bacterium might acquire mutations, either spontaneously or through horizontal gene transfer, that limit access of antimicrobial agents to the target site within the cell.

Resistance conferred through chromosomal mutation, selection, or both is termed vertical evolution, while resistance conferred through the acquisition of genetic material from another organism is termed horizontal evolution. Genetic transfers can occur between the same or different species or even genera of bacteria. Transposons, classes of genetic elements that can “jump” to different places within the genome, facilitate genetic transfer between organisms. Resistance genes can be conferred upon the bacterium’s genome or into plasmids (circular DNA molecules in bacterial cells that replicate independently) and can occur through conjugation, transduction, or transformation. The mechanism of conjugation differs between gram-negative and gram-positive bacteria. Gram-negative bacteria transfer resistance genes, contained on plasmids, through an elongated protein structure called a pilus that joins the bacteria during genetic transfer. In gram-positive bacteria, donor and recipient organisms produce sex pheromones that join the 2 organisms during genetic transfer. Transduction, a rather rare event, involves the use of an intermediary, a bacteriophage or bacterial virus, during the genetic transfer. Transformation, on the other hand, involves bacteria incorporating genetic elements found within their environment that have been released from other bacterial cells that have been destroyed.

New mutations in bacteria lead to resistance in a variety of ways. For example, mutations can alter a target protein or proteins to which the antimicrobial binds through changes in the protein binding site. Mutations also can result in adding genes that encode for enzymes that disable the antimicrobial by altering the outer cell membrane (protein channel) that the antimicrobial uses to enter the cell, thereby disrupting drug entry. Finally, mutations can up-regulate mechanisms that expel the antimicrobial from the bacterial cell.
Mechanism of Antimicrobial Resistance in Staphylococcus aureus

The genome of S. aureus was first sequenced in 2001. Since then, there have been at least 18 annotated whole-genome sequences and many more partially sequenced strains of S. aureus, with more expected to be deposited in GenBank, a database of publicly available DNA sequences. The S. aureus genome can essentially be broken down into 3 components: a highly (97%) conserved set of core genes; a group of more than 700 core variable (CV) genes spread throughout the conserved core genes that are variably distributed and whose distribution pattern defines S. aureus lineages; and the mobile genetic elements (MGEs), which show frequent genetic transfer and, on occasion, recombination. Traits that confer antimicrobial resistance in staphylococci are most commonly located on MGEs on the genome. MGEs are large pieces of discrete DNA that encode mobilization functions and can mediate their own transfer to new host (bacterial) cells as well as mediate their own replication autonomously or via integration with host DNA. MGEs constitute more than 20% of the S. aureus genome and encode many recognized virulence factors and antimicrobial resistance elements. Horizontal gene transfer of MGEs in S. aureus results in strains with increasing pathogenesis, a higher level of antibiotic resistance, and a wider range of hosts. Selective pressure from the environment pushes for attainment and propagation of specific genes that promote fitness and survival in organisms, therefore making MGEs especially valuable in terms of their ability to enhance survival of the bacterium. MGEs thus provide an element of plasticity to the bacterium, allowing adjustment to new niches and changing environmental factors.

Microbiology of MRSA

Etiology

The first case of antibiotic (methicillin) resistance in S. aureus was identified in 1961 in the United Kingdom shortly after methicillin was introduced into clinical treatment. Seven years later, in 1968, after its emergence in Japan, Europe, and Australia, the United States had its first case of MRSA at Boston City Hospital in Massachusetts. Three-quarters of S. aureus infections in U.S. intensive care units (ICUs) are identified as methicillin-resistant, according to the CDC. The mortality rate associated with MRSA infections in U.S. hospitals is estimated at 20%.

Mechanism of Resistance

Resistance to methicillin in S. aureus occurs from the acquisition of the mecA gene that codes for a modified penicillin-binding protein (PBP2a), which confers resistance to methicillin and other semisynthetic penicillinase-resistant β-lactams. To be defined as methicillin-resistant, S. aureus must possess this gene sequence. The mecA gene is absent in susceptible strains and present in resistant strains. The mecA gene is part of a larger Staphylococcus cassette chromosome (SCCmec) gene configuration, of which there are several variations, and it is this gene (mecA) that determines whether MRSA is hospital-acquired/health-care-associated (HA-MRSA) or community-acquired/community-associated (CA-MRSA) in origin. CA-MRSA is caused by new strains of MRSA found in community settings such as locker rooms, soldiers’ barracks, prisons, and child-care and long-term care facilities.

The SCC element is a genomic island that captures foreign DNA segments that are ubiquitous within staphylococci. All methicillin-resistant S. aureus possess the determinant for methicillin-resistance, mecA, making the SCC element SCCmec. Sequencing of numerous SCCmec elements has revealed that elements possess structural differences, which are used in epidemiological studies to discern MRSA strains. HA-MRSA bacteria possess types I, II, and III of the SCCmec gene, while CA-MRSA bacteria possess type IV or V of the SCCmec gene. Types I, II, and III are large genes with additional elements on the gene that impart resistance to other antibiotic classes, such as macrolides, lincosamides, aminoglycosides, fluoroquinolones, tetracyclines, and sulfonamides. Types IV and V, on the other hand, are smaller genes with fewer additional resistance features. This distinction between SCCmec types might explain the susceptibility of CA-MRSA to some antibiotics to which HA-MRSA is unresponsive. HA-MRSA genetic elements, because of their large size, cannot be incorporated into a bacteriophage intermediary; therefore, transfer of genetic material
cannot occur via transduction.\textsuperscript{44} It has been suggested that these larger genetic elements might impair the growth and fitness of HA-MRSA, and it is only the selective pressure of antibiotics that makes HA-MRSA viable and sustaining.\textsuperscript{44} In contrast, CA-MRSA SCC\textit{mec} types IV and V are small enough to be transferred efficiently by bacteriophage or transposon into methicillin-susceptible \textit{Staphylococcus aureus} (MSSA) strains, leading to bacteria that were once only susceptible to \textit{β}-lactams but are now resistant to \textit{β}-lactams.\textsuperscript{58}

Empirical evidence confirms the transfer of resistance from another bacterial genera to \textit{S aureus}. In 2002, a strain of MRSA resistant to vancomycin was cultured from a dialysis patient’s foot ulcer.\textsuperscript{60} This strain was examined, and it was later determined that resistance to vancomycin was conferred upon this \textit{S aureus} strain through transfer of genetic resistance material on the plasmid of another bacteria, namely \textit{Enterococcus faecalis}.\textsuperscript{60}

\textbf{Evolution of Resistance}

Antibiotic resistance in \textit{S aureus} began in the mid-1940s, with increasing numbers of infections caused by penicillin-resistant \textit{S aureus} in hospitals.\textsuperscript{61,62} Penicillin-resistant \textit{S aureus} strains produced a plasmid encoding penicillinase, an enzyme that hydrolyzes the \textit{β}-lactam ring of penicillin, rendering the antibiotic ineffective.\textsuperscript{61,62} Penicillin-resistant strains, mainly \textit{S aureus} clone phage-type 80/81,\textsuperscript{63-65} then became prevalent in the community, leading to widespread infection by the early 1950s and 1960s.\textsuperscript{61,62} The emergence of penicillin-resistant \textit{S aureus} led to the development of methicillin for treatment.\textsuperscript{24} \textit{Staphylococcus aureus} phage-type 80/81 infections became inconsequential with the introduction of methicillin.\textsuperscript{66}

Shortly after the introduction of methicillin, \textit{S aureus} isolates were documented as resistant to this antibiotic as well.\textsuperscript{43} The mechanism of resistance to methicillin is different from that of penicillin resistance in that penicillin resistance is narrow in its spectrum, only acting on penicillin itself, whereas methicillin resistance is more broadly based and includes resistance to the entire \textit{β}-lactam class of antibiotics.\textsuperscript{44} These strains circulated through hospitals in Europe throughout the 1970s,\textsuperscript{67} but by the 1980s they disappeared for unknown reasons.\textsuperscript{44} Emerging strains appeared in U.S. hospitals in the late 1970s and were endemic worldwide by the mid-1980s.\textsuperscript{68,69} They still are present today.\textsuperscript{41} Although endemic, MRSA was confined to hospitals and health care facilities. As a last resort, vancomycin was introduced as the final line of defense against MRSA.\textsuperscript{70} The widespread use of vancomycin to treat burdensome MRSA infections in hospitals and health care facilities provided selective pressure for vancomycin-intermediate (VISA) and vancomycin-resistant (VRSA) strains.

The first VISA MRSA strain was documented in 1996 in an infant aged 4 months,\textsuperscript{71} and in 2002 the first VRSA MRSA strain was documented.\textsuperscript{60,72} Both have since been documented worldwide.\textsuperscript{73} Fortunately, the number of occurrences still is comparatively low. From 2002 to 2006 only 7 cases of VRSA were reported in the United States\textsuperscript{74} and, as of October 2010, all VISA and VRSA isolates have been susceptible to other antimicrobials recommended by the U.S. Food and Drug Administration (FDA).\textsuperscript{75}

\textbf{HA-MRSA vs CA-MRSA}

MRSA is divided into 2 subcategories, depending on where the infection was acquired. If the infection was obtained in a hospital or health care facility while a person was a patient, this form of MRSA is termed hospital-acquired/health care–associated MRSA (HA-MRSA). If the infection was obtained outside of a hospital or health care facility, this type of MRSA is labeled community-acquired/community-associated MRSA (CA-MRSA). Since its discovery in 1961 and into the mid-1990s, MRSA was almost exclusively found in health care settings (HA-MRSA).\textsuperscript{76,77} By the mid-1990s, however, MRSA infections began appearing in individuals who had no previous health care–related associations or risk factors.\textsuperscript{76,77} Around this same time, reports of CA-MRSA also began emerging in other countries, such as Canada, Australia, and New Zealand, primarily in the form of necrotizing pneumonia and skin and soft-tissue infections among native peoples, athletes, and prisoners.\textsuperscript{57,58,78,79}

CA-MRSA isolates differ in many ways from HA-MRSA isolates. One difference is that while CA-MRSA isolates are resistant to the actions of \textit{β}-lactams and erythromycin, they are susceptible to many non-\textit{β}-lactam antibiotics. HA-MRSA isolates, on the other hand, are typically multidrug
resistant, particularly to the action of all β-lactams as well as many non-β-lactams, including erythromycin, clindamycin, and tetracycline. MRSA strains that show partial or full resistance to vancomycin have been reported since 1996. CA-MRSA isolates also are different in that they contain the SCCmec type IV or V genetic elements and numerous toxins, such as the exotoxin Panton-Valentine leukocidin (PVL), which causes leukocyte destruction and tissue necrosis, while HA-MRSA carries SCCmec type I-III genetic elements and does not typically produce toxins. In addition, CA-MRSA exhibits a different pulsed-field gel electrophoresis pattern than HA-MRSA isolates. Growth rates also differ between HA-MRSA and CA-MRSA, with CA-MRSA exhibiting much more rapid growth than HA-MRSA. This difference might confer a selective advantage to CA-MRSA, allowing it to spread globally. Evidence from molecular typing indicates CA-MRSA strains evolved spontaneously, rather than transferring from hospitals to communities. Some of the earliest cases of CA-MRSA occurred in the 1990s in aboriginal populations in western Australia. The first well-documented CA-MRSA cases in the United States occurred from 1997 to 1999 in healthy children with no known health issues who died from their infections. Despite the susceptibility of these particular CA-MRSA strains to antibiotics, they were resistant to β-lactams, which these patients were initially treated with. The delay in treatment with antibiotics that their infections were susceptible to might have contributed to the children’s deaths. Even though these children lost their lives to their infections, CA-MRSA strains were susceptible to most antibiotics.

When CA-MRSA emerged within communities, the genotypes were unrelated to those of HA-MRSA. For example, in the United States, the predominant CA-MRSA causative strains were USA 300 and USA 400, with USA 400 most prevalent until 2001, when USA 300 became dominant. Data from a multistate study indicated that 59% of purulent skin and soft-tissue infections were caused by MRSA, and 97% of these infections were due to CA-MRSA strain USA 300.

The epidemiology of MRSA has become quite complex because of the intermingling of HA-MRSA and CA-MRSA infections in the community and health care facilities, making it increasingly difficult to discern strain origins. Outbreaks of CA-MRSA occur worldwide with similar epidemiology, and clones continually emerge that vary with geography. However, CA-MRSA genotypes still are affected by antibiotics that are ineffective on HA-MRSA strains.

MRSA has even become an emerging problem in animals, affecting livestock, horses, and household pets. Transmission of MRSA between humans and animals is a concern, and evidence indicates that children in households with cats, dogs, or both have become infected with CA-MRSA. However, whether the infection was transmitted from human to animal or vice versa is unclear.

**Necrotizing Fasciitis**

MRSA is one of the bacteria considered to be “flesh-eating,” although the bacteria do not actually eat the flesh of infected individuals. So-called flesh-eating bacteria produce and emit toxins that destroy (or necrotize) the tissue they infect. Medically, this condition is known as necrotizing fasciitis (NF), a “severe bacterial infection of the fascia, the tissues that line and separate muscles, that causes extensive tissue death.” NF is a rare but serious bacterial infection that can be caused by several bacteria, including group A Streptococcus, Klebsiella, Clostridium, E coli, S aureus, and Aeromonas hydrophila. While MRSA infection can lead to NF, MRSA is not the most common causative agent of this type of infection. NF is most commonly caused by group A Streptococcus. However, more cases are being reported in which MRSA is the causative agent. For example, during a 5-year period from 2001 to 2006 at a large urban hospital, there were 74 reported and investigated cases of NF, of which 39% were caused by MRSA that resulted in a 15% mortality rate.

Most cases of NF result from bacteria entering the body through a break in the skin, and NF often is associated with other health problems that tend to weaken the body’s immune system. Most healthy people have a very low probability of contracting NF. Once a person is infected, NF spreads rapidly, often within hours of contact with the infectious agent, infecting the fascia (layers of connective tissue surrounding muscles, nerves, fat, and blood vessels).
Symptoms of NF can be confusing and often lead infected patients to delay seeking medical treatment. Often, the infected person complains of pain or soreness similar to a pulled muscle. The skin might be red, swollen, and warm to the touch. Pain at the infection site might be severe and out of proportion to the appearance of the infected area. A black spot often appears on the skin, with ulcers or blisters at or near the infection site. Treatment involves immediate antibiotic therapy as well as surgical removal of dead tissues because antibiotics might not effectively reach all infected tissue. Techniques for preventing NF include covering open wounds with clean, dry bandages until healed; promptly seeking first aid for even minor, noninfected wounds, including minor breaks in the skin; avoiding hot tubs, swimming pools, and whirlpools if you have an open wound (even if it is contained); and washing hands often with soap and water or an alcohol-based cleaner when soap and water are unavailable.

Clinical Identification
Detecting MRSA is complicated by several factors that necessitate rapid, accurate, and sensitive testing methods in routine diagnostic laboratories. One of these factors is that methicillin/oxacillin resistance is heterogeneous in most strains of \textit{S. aureus}, meaning that susceptible cells and highly resistant cells reside within a MRSA isolate.

Clinicians use several conventional laboratory tests to determine whether an \textit{S. aureus} infection is in fact MRSA. Microbiological tests include the cefoxitin disk screen test, the latex agglutination test for PBP2a, and a Mueller–Hinton agar plate supplemented with oxacillin. When used correctly, broth- and agar-based screening methods usually can detect MRSA, with the cefoxitin disk test available for additional verification. Oxacillin rather than methicillin is used as a screening agent for several reasons. First, methicillin is no longer commercially available as a treatment agent in the United States. Second, the integrity of oxacillin’s antimicrobial action when maintained under storage is greater than that of methicillin. Third, oxacillin is a better detecting agent for heteroresistant strains.

In recent years, molecular-based screening methods have become the gold standard for MRSA detection. Molecular nucleic acid amplification testing methods involve isolation of the \textit{mecA} gene through polymerase chain reaction (PCR). As discussed previously, the \textit{mecA} gene confers oxacillin/methicillin resistance in \textit{S. aureus}.

In 2011 the FDA approved the use of a rapid-detection method for MRSA and methicillin-sensitive \textit{S. aureus} (MSSA). The KeyPath MRSA/MSSA Blood Culture Test (MicroPhage Inc) is a phenotypic test of cefoxitin susceptibility and resistance and can distinguish between MRSA and MSSA in a blood sample within 5 hours after bacterial growth is first detected in the sample with 98.9% and 99.4% accuracy, respectively.

A 2013 study compared performance of the KeyPath MRSA/MSSA BC test to conventional identification and susceptibility methods and found that the KeyPath MRSA/MSSA BC test produced diagnostic results a median of 30 hours faster than conventional methods.

In June 2013 the FDA approved another rapid blood culture testing method, the Xpert MRSA/SA Blood Culture (BC) test (Cepheid) for use in the rapid detection and identification of MRSA and MSSA. Cepheid’s Xpert MRSA/SA BC test is a molecular-based test that allows for identification of MRSA or MSSA in a blood sample determined to be gram-positive cocci clusters or singles within 1 hour of culturing. This approval comes 3 years after a class I recall was issued by the FDA to Cepheid regarding false negatives generated by the Xpert MRSA/SA BC test.

Clinical Signs and Symptoms
Because MRSA is a form of staph infection, the signs and symptoms of MRSA are similar to those for other types of staph infection. MRSA infections can start as small red bumps that resemble pimples, boils or spider bites. The infected area might be red, swollen, pustilled, warm to the touch, extremely painful (more painful than would be expected for the minimal appearance of the sore) or a combination of these (see Figure 3). MRSA skin infections can occur anywhere on the body but are commonly found on the back of the neck, the legs, groin, or buttocks. As the infection continues, fever might develop and the infection might spread from the original site. If not addressed soon after symptoms develop,
early stages, MRSA infections can become severe and complications such as sepsis, necrotizing fasciitis, and death can ensue.\textsuperscript{105}

**Risk Factors**

Because HA-MRSA and CA-MRSA infections occur in different settings, the risk factors associated with each are different.\textsuperscript{106} However, a person does not need to be infected to transmit either type; people who are colonized and thus are carriers also can transmit the infection.\textsuperscript{106}

**HA-MRSA**

The risk of developing HA-MRSA is a concern in most hospitals because of the vulnerability of hospitalized patients. HA-MRSA risk increases in the elderly and people with weakened immune systems.\textsuperscript{106} Risk of infection also increases if a patient has a medical device inserted into his or her body, such as a catheter or intravenous line.\textsuperscript{106} HA-MRSA also is prevalent in long-term care facilities such as nursing homes because of the close person-to-person contact between patients and the declining health status of most patients, who might have impaired immune systems.\textsuperscript{106}

**CA-MRSA**

According to epidemiological data, groups at highest risk of contracting CA-MRSA in the United States are those in areas with high concentrations of people where risk of cross-infection is high, such as schoolchildren, poor and homeless young adults, military personnel, athletes, and day-care center personnel and clients.\textsuperscript{39,81} Athletes are at risk of infection from close contact with others while participating in sports as well as contact in locker rooms and shower facilities.\textsuperscript{106}

Transmission

**Hospital Settings**

MRSA is transmitted to patients via human hands, mainly those of health care personnel, according to the CDC.\textsuperscript{107} If appropriate hand hygiene is not practiced, either through the use of soap and water or an alcohol-based hand cleaner, MRSA bacteria can spread from health care personnel to patients, resulting in serious infection.\textsuperscript{107} Transmission also can occur when invasive

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**Figure 3.** A. Cutaneous abscess caused by MRSA on the knee. B. Cutaneous abscess caused by MRSA on the hip that began to drain spontaneously. Public domain images courtesy of the Centers for Disease Control and Prevention.
Medical devices are used that have been in contact with MRSA, either through direct contact with an infected or colonized person or from contact with a contaminated surface or person who has not appropriately sanitized his or her hands.

**Skin Infections**

MRSA skin infections can be transmitted from person to person if there is close skin-to-skin contact where there are openings in the skin tissue such as abrasions, cuts, lesions, or boils. MRSA also can contaminate surfaces outside the body when someone with an infection touches that surface with contaminated hands or other body parts where the bacteria reside. Once MRSA enters the body, it can spread to the blood, joints, bones, or any other organ.

**Biofilm**

A biofilm is a community of microbial cells that can include MRSA. The cells adhere to each other and to a surface material that is embedded into an extracellular polymeric substance (EPS) matrix that protects the MRSA from antibiotics and host immune defenses (see Figure 4). Dr. Timothy Lu, a leading biofilm researcher, likened a biofilm to “fruit Jell-O,” in which pieces of fruit represent microbial cells and the gelatin is like the protective EPS-type matrix. Biofilms form on both biotic (living) and abiotic (nonliving) surfaces, such as catheters and implanted medical devices, and can persist and form infection that is difficult to eradicate. Biofilms might prolong the duration of MRSA infections and promote colonization.

**Epidemiology**

**Surveillance**

Since 1995, the CDC Emerging Infections Program (EIP) has used active bacterial core surveillance (ABCs) to track invasive bacterial pathogens significant to public health. This surveillance system uses both laboratory and population-based data to track invasive bacterial pathogens in the populace. Each incidence of bacterial infection within the 10 current EIP sites, patient demographic information, and cultures of the infectious agent are provided to the CDC and independent reference laboratories for analysis. Surveillance sites include California, Colorado, Connecticut, Georgia, Maryland, Minnesota, New Mexico, New York, Oregon, and Tennessee, with a representation of 41 million people. Currently, the CDC tracks 6 pathogens using group A and group B Streptococcus (GAS, GBS), Haemophilus influenzae, Neisseria meningitis, Streptococcus pneumoniae, and MRSA.

Among its many accomplishments, ABCs has contributed to the development and implementation of a program designed to assist state and local health departments in tracking MRSA occurrence. ABCs has shown that the proportion of health care-associated Staphylococcal infections due to MRSA has increased since the 1970s, with 2% in 1974, 36% in 1992, and 64% in 2003 (3% increase annually). However, more recent estimates have revealed a downward trend in MRSA infections since the 2000s:

- Central line–associated MRSA bloodstream infections decreased 50% to 70% between 2001 and 2007.
- All MRSA-related bloodstream infections decreased 34% between 2005 and 2008.
- Invasive MRSA infections acquired in hospitals declined 54% from 2005 through 2011.
- Data from 2011 show a decrease of 25.92% in MRSA infections overall, including both...
community- and health care–associated types, from a baseline established in 2007 to 2008. MRSA infections also are monitored at participating hospitals through the National Nosocomial Infections Surveillance System and the National Healthcare Safety Network (NHSN). The CDC’s NHSN is the most widely used HAI tracking system in the United States and provides data to national, state, and local organizations, including health care facilities, to help measure progress in prevention efforts and identify problem areas in HAI prevention. The NHSN also aids health care facilities in tracking blood safety errors and health care personnel infection control adherence rates. Currently, more than 11 000 medical facilities use NHSN.

In addition to federal tracking of MRSA cases, many state health departments also track the occurrence of MRSA in health care facilities. However, tracking and reporting vary among states. For example, the Texas Department of State Health Services reported that 55% of S aureus infections occurring in Texas in 2012 were sensitive to oxacillin/methicillin, (45% of MRSA cases were not susceptible to oxacillin/methicillin) while the Mississippi State Department of Health simply reported that it has not found a significant increase or an unusual number of MRSA cases in the state.

A study published in 2012 by researchers at the University of Chicago Medicine (UCM) and the University Healthcare Consortium (UHC) estimated that rates of MRSA in U.S. academic medical centers doubled between 2003 and 2008. This contradicts CDC findings that show MRSA infections in hospitals are declining. This might be because the CDC looked only at invasive infections (those found in the blood, spinal fluid, or deep tissue) and excluded skin infections, which the UCM-UHC study included. The UCM-UHC results estimated that hospitalizations for MRSA increased from 21 out of every 1000 patients in 2003 to 42 out of every 1000 patients in 2008. Researchers attributed this overall increase to CA-MRSA infections, while also noting that HA-MRSA cases generally are declining. Interestingly, the UCM-UHC researchers reported that the number of MRSA-infected patients far exceeded those hospitalized with AIDS and influenza combined in each of the last 3 years of the survey (ie, 2006, 2007, and 2008).

A study published in 2011 analyzing changes in the epidemiology of HA-MRSA bloodstream infections (MRSA-BSI) at a tertiary 900-bed university hospital from 1990 through 2008 noted that 524 patients developed HA-MRSA-BSI. Investigators divided this 19-year study into 4 consecutive periods: 1990-1994, 1995-1999, 2000-2004, and 2005-2008. While no significant trend in infection rate was observed over the 19-year period, investigators did identify significant upward trends in patient age and comorbidities, health care–associated acquisition of MRSA, and nonintravascular catheter sources between the 4 periods. The first and second periods were dominated by one type of MRSA clone (ST247/SSCmecI), while the third and fourth periods were dominated by a clonal complex (ST125/SCCmecIV and ST228/SCCmecI). No significant differences were found in regard to mortality rates across the 4 periods, with mortality reaching about 29% for all patients after 30 days of infection throughout the 19-year period.

Global Occurrence

The global status of HA-MRSA differs widely among regions and even between countries within a region, according to epidemiological data from various health agencies and medical laboratories. In East Asia, Southeast Asia, North America, and South America, the situation is rather severe, and within these regions, the situation differs from country to country. In East Asia, for example, prevalence rates in Japan and Korea are more than 50%, whereas rates are 25% to 50% in other East Asian countries. In Southeast Asia, Indonesia and Singapore have the lowest prevalence rates at 25% to 50%, while rates in other Southeast Asian countries are greater than 50%. In Western Europe, most countries report prevalence rates of 10% to 25%, although Spain, Great Britain, Italy, and Portugal’s rates are 25% to 50%. In North America, the majority of the United States has rates greater than 50%, except for Alaska, where rates are 25% to 50%. In Canada the rate is 5% to 10%, and in Mexico it is 10% to 25%. Most South American countries also exhibit

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rates greater than 50%, with the exception of Paraguay, Panama, and Columbia, where rates are 25% to 50%. Australia and Africa (North and South Africa only; Middle Africa epidemiological data is absent) have prevalence rates of 25% to 50%; the Middle East is at 10% to 25%; and Northern Europe has the lowest rate at less than 5%. The lower rate in Northern Europe might be the result of strict surveillance measures, antibiotic control, and eradication measures.

**MRSA in the Environment**

*Staphylococcus aureus* has been reported in marine environments since the early 1990s. It is well known that *S aureus* is not susceptible to the action of salts, owing to its ability to survive in natural fresh and saltwater environments. While MRSA has been identified in environmental waters, the reported incidence is low. An analysis of MRSA in seawater and sand samples during summer months at 3 Southern California beaches showed a low incidence of MRSA in both seawater (1.6%) and sand (2.7%) samples. Another study showed that of 350 seawater samples collected at a recreational subtropical beach, 22 MRSA isolates were identified, 17 of which were clonally related to CA-MRSA strain USA 300. A study examining the survivability of HA-MRSA and CA-MRSA isolates in pool, seawater, and river water showed that all HA-MRSA and CA-MRSA survived in the seawater and river water inoculations but were unculturable after 24 hours in the pool water, indicating that both seawater and river water can be reservoirs for both HA-MRSA and CA-MRSA if they become contaminated. The CDC reported that there are no known cases of people being infected with MRSA from recreational waters at facilities; however, they caution that MRSA can be spread at recreational water facilities through direct and indirect contact with people, infected objects, or surfaces.

**Treatment**

**Antimicrobials**

While vancomycin is still used to treat MRSA infections, many other FDA-approved drug alternatives to vancomycin are used. These include antimicrobials such as linezolid, daptomycin, tigecycline, quinupristin/dalfopristin, ceftaroline, and tefavancin. Investigational compounds not yet approved by the FDA that exhibit in vitro action against MRSA include ceftobiprole, dalbavancin (currently in phase III clinical trial), oritavancin (also in phase III clinical trial), and iclaprim.

With antibiotic-resistant organisms on the rise, medical researchers and drug companies are racing to develop the next antibiotic to treat serious infections. Researchers at the University of Illinois and the University of California San Diego are investigating the use of undecaprenyl diphosphate synthase (UPPS) inhibitors as a new form of antibacterial drug. UPPS is an enzyme essential in early-stage cell wall synthesis. Because humans do not make UPPS (human cells do not contain cell walls), it is a potential target for new drug development.

In 2011, the Infectious Diseases Society of America provided new recommendations on treatment options and antibiotic dosing requirements to treat various types of MRSA. The management of clinical syndromes presented by MRSA infection is discussed, as are recommendations to physicians and other health care providers regarding usage and dosing with vancomycin, as well as the use of alternate therapies for treating MRSA infections caused by vancomycin-resistant strains and strains treated with vancomycin that have failed to respond favorably.

**Bacteriophages**

While antibiotics are the historical treatment for bacterial infections, they are not the only treatment option. Many novel treatment approaches have been suggested to overcome antibiotic resistance. The development, mass-production, and wide availability of antibiotics are crowning achievements of the 20th century; however, over the past 30 years, we have seen a serious decline in the number of newly approved antibiotics in the United States. We now recognize many inherent problems in the use of antibiotics beyond the development of antibiotic-resistant microbes. For example, broad-spectrum antibiotics can have a deleterious effect on the human body’s natural communities of beneficial bacteria, which are essential to health and immunity. Economic factors
also make developing new antibiotics unprofitable, time-
consuming, and therefore undesirable in a free market. 
These problems with antibiotics have led to a need for
alternative treatments.

One such alternative treatment that has been in 
use for more than 90 years globally is phage therapy.137
Phage therapy is the use of viruses as a biological con-

trol agent against pathogenic or invasive bacteria.138
Phages are viruses that only attack bacteria and specifi-
cally attack only the types of bacteria they are capable
of infecting, which is called their host range.139

Phages were discovered by Felix Twort in 1915
and then, independently, by Felix d’Hérelle in 1917.139
D’Hérelle is credited with the discovery because he purs-
ued investigation into the nature of bacteriophages and
their use as anti-infective agents.139 D’Hérelle first used
phage therapy in 1919 to cure a young boy of dysentery;
however, phage therapy was not used by other practi-

tioners until the late 1920s or early 1930s.132,139 Even
then, its use was short-lived once antibiotics came onto
the scene.132 Most likely, the decline in phage therapy
was the result of misuse of phages by practitioners who
had a poor understanding of phage biology and lacked
expertise in administering them.132

Bacteriophage therapy is proving to be an important
alternative to antimicrobial treatment in the face of
invasive, multidrug-resistant pathogenic bacteria such
as MRSA. However, in the Western world, we are still
far from using phages as viable treatment mechanisms.
An opinion article, based on a scientific meeting on
viruses of microbes in Europe and appearing in a spe-
cial issue of the journal Virology, addressed the current
status of and hurdles to phage therapy in the West, as
well as the need for a coordinated effort within the
public health sector to evaluate the use of phage therapy
as an adjunct to antibiotics.139 According to this article,
the FDA supports use of phage therapy, has stated its
interest in phage therapy as a treatment option, and
favors developing regulatory guidance for using phages.
However, this is not a new development.139 The FDA
cited specific advantages to using phages for treatment,
noting phages’ specificity, ability for high-purification,
nontoxicity, and effectiveness where other treatments
have failed.138 The FDA also cited negative aspects to
using phages, including phages’ specificity (the bacterial
pathogen must be identified for effective phage use) and
possible development of bacterial resistance against phag-
es.138 Attendees at the conference cited regulatory hurdles
and development costs as high for the medical applica-
tion of phages.138 While Western countries are hesitant to
approve phage therapy, other countries have been using
phage therapy as a treatment option for decades.

Phages are similar to antibiotics in that both have
remarkable antimicrobial activity via lysis (cell break-
down), but phages possess several therapeutic advan-
tages over antibiotics.140 For example, treatment with
phages results in fewer, if any, adverse effects compared
with antibiotics.140 Also, because of phage specificity,
only the target bacteria are affected, thus eliminating or
reducing the risk of secondary infection.140 Phages rep-
licate at the site of infection, making them more avail-
able as treatment progresses.142 Phage-resistant bacteria
remain susceptible to other phages with the same host
target range, and selection of new phages is fast, often
taking days or weeks.140 Finally, phages have been more
successful than antibiotics in treating certain infections
in humans.143

using phage therapy in treatment revealed success
rates of 80% to 95% with few adverse effects, as well
as several studies showing significant effectiveness
of phages against many multidrug-resistant bacteria,
including S aureus.144

Topical Honey

Honey, specifically honey produced by Apis mellifera
(the Western or European honeybee145), has been used
to treat infection for centuries.146 Modern research-
ers have reported that natural, nonheated honey has
broad-spectrum antibacterial action against pathogenic
bacteria.147 The antibacterial activity in most types
of honey is the result of the enzymatic production of
hydrogen peroxide. However, a honey that has been
found to be very effective in the treatment of MRSA
infections, manuka honey, is considered a nonperoxide
honey, meaning it maintains its antibacterial activity
even in the absence of hydrogen peroxide.148 Manuka
honey is derived from honeybees consuming nectar
from the New Zealand flowering plant Leptospermum
scoparium.149
A 2012 study to identify the antimicrobial activity of manuka honey showed that treatment with this type of honey resulted in a significant decrease in the bacterial growth rate and the down-regulation and up regulation of several proteins. Another study reported that fewer proteins were identified in MRSA cells treated in the lab with manuka honey for 4 hours than cells left untreated and that one of the missing proteins, FabL, a protein necessary for fatty acid biosynthesis, might explain the mode of action of manuka honey against MRSA.

Microbial resistance to honey has never been reported, making it extremely promising as a treatment in the new era of antimicrobial resistance. Presently, the use of honey as an antimicrobial treatment is limited in the United States to an FDA-approved topical wound and burn treatment (MediHoney, Derma Sciences) for management of light-to-moderately exuding wounds and treatment of first- and second-degree burns. Most honey treatment in the United States is used only in an alternative medicine branch called apitherapy.

MRSA Prevention

The CDC provides recommendations to health care providers to help prevent MRSA infections (see Box 1). Epidemiologists and researchers agree that HAIs, including MRSA, can be prevented through proper hand-washing practices, medical equipment sterilization, and eliminating the use of unnecessary catheter lines in patients.

Breaking the Chain of Infection

The chain of infection is the mode of transmission of infectious disease from one person or object to another. In this chain, there are many links that must be intact and in sequential order for infection to be transmitted. While many factors make the chain of infection difficult to break, it is not impossible. Health care professionals, including radiologic technologists, can prevent tens of thousands of infections annually by breaking a single link. Radiologic technologists and other health care workers must be diligent in following standard precautions and hand hygiene, and these must be used for every patient in the health care facility. Standard precautions also include proper cleaning and disinfection of hospital equipment before use on every patient. In the radiology suite, pieces of equipment used daily and on multiple patients are of particular importance for proper disinfection, as each can be a source of infection transmission. These include examination tables, x-ray tubes, the upright Bucky, and exposure switch.

Hand Washing

Although it might seem like common sense that hand washing is the most effective tool in the medical toolbox to prevent infection, too many health care professionals still do not adhere to proper hand-washing guidelines (see Figure 5). For decades, hand hygiene

Box 1

Top CDC Recommendations for Preventing MRSA Infections

- Strictly adhere to CDC hand hygiene guidelines.
- Practice contact precautions:
  - If possible, patients with MRSA should be placed in their own room or share a room with someone else who has MRSA.
  - All health care personnel and visitors in contact with a known MRSA-infected patient shall wear gloves and a gown, which are removed upon exiting the room.
  - All persons who have been in contact with MRSA-infected patients should thoroughly clean their hands.
  - A patient on contact precautions should be asked to remain in his or her room as much as possible to prevent spreading the infection.
- Recognize patients previously infected or colonized with MRSA.
- Report MRSA testing results immediately.
- Educate health care providers on MRSA infections.

Also consider:

- Facility participation in active surveillance testing.
- Patient decolonization.
- Chlorohexidine bathing of MRSA-infected patients.

Abbreviations: CDC, Centers for Disease Control and Prevention; MRSA, methicillin-resistant Staphylococcus aureus.
The link between hand washing and infection control was made by a Hungarian physician more than 165 years ago. The physician, Ignaz Semmelweis, noticed that mortality rates between 2 clinics within a maternity hospital were significantly different. In the clinic that had the higher mortality rate, he noticed that personnel went from autopsy rooms to the delivery suite without washing their hands. He theorized the physicians and medical students were carrying germs from the cadavers to mothers and their newborn infants. The physicians began washing their hands with a chlorinated lime solution, and the mortality rate plummeted. The CDC and the World Health Organization provide resources for health care professionals on the proper hand-washing technique (see Box 2).

Alcohol-Based Hand Sanitizers

When soap and water are not available, as in some emergency situations, the CDC recommends using an alcohol-based hand sanitizer containing at least 60% alcohol. It also advises that not all germs are killed with hand sanitizers, and when hands are visibly dirty these rubs are not as effective. The FDA reported some hand sanitizer and antiseptic product manufacturers are falsely claiming that their products prevent MRSA infections. These claims are unproven, as the FDA has not approved any over-the-counter products for preventing MRSA.
Hospital-Acquired Methicillin-Resistant *Staphylococcus aureus*: Status and Trends

**Targeted vs Universal Decolonization**

Results published in the *New England Journal of Medicine* in 2013 from the REDUCE MRSA trial, funded by the Department of Health and Human Services, evaluated the effectiveness of 3 MRSA prevention practices in ICUs: routine care, use of germ-killing soap and ointment on patients infected with MRSA (targeted decolonization), and use of germ-killing soap and ointment on all ICU patients (universal decolonization). Results published in the *New England Journal of Medicine* in 2013 from the REDUCE MRSA trial, funded by the Department of Health and Human Services, evaluated the effectiveness of 3 MRSA prevention practices in ICUs: routine care, use of germ-killing soap and ointment on patients infected with MRSA (targeted decolonization), and use of germ-killing soap and ointment on all ICU patients (universal decolonization). Results published in the *New England Journal of Medicine* in 2013 from the REDUCE MRSA trial, funded by the Department of Health and Human Services, evaluated the effectiveness of 3 MRSA prevention practices in ICUs: routine care, use of germ-killing soap and ointment on patients infected with MRSA (targeted decolonization), and use of germ-killing soap and ointment on all ICU patients (universal decolonization). Patients receiving universal decolonization were bathed daily for the duration of their stay in the ICU with chlorhexidine soap and had mupirocin ointment applied to the insides of their nasal passages for 5 days. The study found that universal decolonization reduced the rate of bloodstream infections by up to 44% and significantly reduced the presence of MRSA in ICUs.

**Hydrogen Peroxide Vapor**

Decontamination of the hospital environment is as essential as health care personnel decontaminating themselves before and after coming into contact with patients, particularly patients colonized or infected with MRSA. Several pathogens linked to HAI can survive for extended periods of time on surfaces and might not be eradicated effectively with conventional cleaning methods. Hydrogen peroxide vapor can be used proactively, to prevent infection, or reactively, to stop outbreaks in the hospital setting. It can be scaled for use in single rooms or used hospital-wide. Hydrogen peroxide vapor currently is used in hospitals worldwide to reduce the transmission of multidrug resistant organism infections. In addition to use in hospital rooms, it also can be used to decontaminate mobile equipment, fixed equipment in high-risk areas, and for prevention in low-risk areas. When hydrogen peroxide vapor was first introduced in the United States, the equipment required specialists to operate it; however, now hospital personnel can be trained on its operation.

Hydrogen peroxide vapor fills the room uniformly, even reaching around corners and behind obstructions, with what ultimately becomes a surface-deposited microcondensation layer of hydrogen peroxide, providing a full 3-D, rapid killing of all microorganisms. Hydrogen peroxide vapor consistently yields higher levels of decontamination than conventional cleaning methods.

**Antimicrobial Copper**

Copper has long been known to possess sanitizing properties and might be useful for environmental control in health care facilities for preventing HAIs. Hard surfaces in health care facilities can be contaminated with microorganisms responsible for HAIs, such as MRSA, and these surfaces serve as ongoing sources of contamination to patients, either through direct contact or indirect contact via health care providers. To reduce hard surfaces as sources of contamination,
copper has been suggested as a surface coating because of its sanitizing properties. The mechanism of copper’s antimicrobial properties has not been fully explained, but it has been suggested that copper ions in contact with cell walls and membranes trigger structural damage, resulting in DNA fragmentation.

One study evaluated the effect of antimicrobial copper implementation on the microbial flora found in an ICU and the use of antibiotics over a nonsequential 1-year period. There was a 95% reduction overall in the microbial flora concentration (measured as colony-forming units per milliliter or CFU/mL), a reduction in the use of antimicrobial drugs (per day per patient) by 30%, and a reduction in hospitalization time and cost per patient. A separate study conducted by the same authors examined the effect of antimicrobial copper on microbial flora in a neonatal ICU and found similar results, with a 90% reduction in microbial flora concentration measured in colony-forming units per milliliter, including reductions in S. aureus.

A literature review of 37 studies analyzing the reduction in microbial flora from copper (both pure copper and copper alloys) showed that all but one examination identified significant reductions in microorganisms when placed in contact with copper, with pure copper providing the best results. The reductions were significant, especially when compared with other metals such as stainless steel, the metal most commonly used in health care facilities because of its anticorrosive properties and its appearance of cleanliness. Studies have shown that microorganisms persist on stainless steel surfaces for long periods of time. In fact, the transmission of infection-causing microbes in hospitals occurs most commonly through health care workers’ direct contact with surfaces. Health care workers then pass the bacteria on to their patients.

The Radiologic Technologist’s Role in Preventing MRSA

Like other health care providers, radiologic technologists learn about standard precautions during their professional education. It is imperative that they remain vigilant and keep implementation of standard precautions at the forefront of their daily activities. It is easy to become complacent about activities that become second nature. However, by skipping one simple but important action, a radiologic technologist could unknowingly create an environment favorable for infection transmission. All health care professionals also must understand the simplicity behind infection transmission to help stop transmission.

The eradication of HA-MRSA begins with each health care provider and facility. By adhering to hand hygiene and surface decontamination protocols, the radiologic technologist plays a valuable role in eradicating not only MRSA but also other HAIs.

Conclusion

Overall, the rate of HA-MRSA infections in the United States is declining. Results from a CDC study published in 2010 showed that invasive (ie, life-threatening) MRSA infections declined 28% between 2005 and 2008, with bloodstream MRSA infections declining even further. NHSN results found that MRSA bloodstream infections in hospitals decreased nearly 50% during the 10-year period from 1997 to 2007.

Although these reports are promising for HA-MRSA and many HAIs, infections caused by Clostridium difficile, another HAI agent, are rising rapidly. In fact, they have tripled within the past decade. Further incentive to reduce and eliminate HAIs such as MRSA comes from the new federal health care law in which hospitals with infection rates that exceeded national averages will lose 1% of their Medicare funding beginning in 2015. Although this might not seem like much, consider that $563 billion in Medicare claims were paid last year in support of 49 million Medicare patients.

The decrease in HA-MRSA is certainly good news for both the health care and public health communities; however, the risk of developing infectious MRSA within a health care setting is still present. More remains to be done to eradicate this disease, and health care workers must remain vigilant in their fight. Radiologic technologists must do their part with frequent and proper hand washing and implementation of standard precautions to break the chain of MRSA infection.

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References


5. Scott II RD. The direct medical costs of healthcare-associated infections in U.S. hospitals and the benefits of prevention. Division of Healthcare Quality Promotion, National Center for Preparedness, Detection, and Control of Infectious Diseases, Coordinating Center for Infectious Diseases, Centers for Disease Control and Prevention; 2009:13.


70. Wootton M, Howe RA, Hillman R, Walsh TR, Bennett PM, MacGowan AP. A modified population analysis


Hospital-Acquired Methicillin-Resistant Staphylococcus aureus: Status and Trends


Hospital-Acquired Methicillin-Resistant *Staphylococcus aureus*: Status and Trends

Read the preceding Directed Reading and choose the answer that is **most correct** based on the article.

1. What is another name for hospital-acquired/health care–associated infections (HAIs)?
   a. beta-lactams
   b. nosocomial infection
   c. mononucleosis
   d. necrotizing fasciitis

2. Most frequently, HAIs involve infections of the:
   1. bloodstream.
   2. urinary tract.
   3. lower respiratory tract.
   a. 1 and 2
   b. 1 and 3
   c. 2 and 3
   d. 1, 2, and 3

3. The use of invasive devices such as catheters **decrease** the risk of acquiring an infectious disease during hospital treatment.
   a. true
   b. false

4. According to the article, what HAI has been of significant concern for more than 50 years?
   a. *Escherichia coli*
   b. methicillin-resistant *Staphylococcus aureus* (MRSA)
   c. *Actinobacter baumannii*
   d. *Clostridium difficile*

5. *Staphylococcus aureus* (*S aureus*) is able to resist an array of adverse environmental conditions including:
   1. complete drying.
   2. high salt concentrations.
   3. temperatures lower than 10°F.
   a. 1 and 2
   b. 1 and 3
   c. 2 and 3
   d. 1, 2, and 3

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6. **Vertical evolution** is the term for resistance conferred:
   a. through chromosomal mutation and/or selection.
   b. through circular replication.
   c. through the acquisition of genetic material from another organism.
   d. from a bacterial virus.

7. All of the following are ways in which new mutations in bacteria lead to resistance except:
   a. altering a target protein.
   b. altering the inner cell membrane.
   c. obtaining genes that encode for enzymes.
   d. upregulation of mechanisms for expulsion of antimicrobials.

8. Which phrase best describes mobile genetic elements?
   a. large pieces of discrete DNA that encode mobilization function
   b. bacteriophages used to transfer DNA to bacteria
   c. genes that travel throughout the body of an infected person
   d. elements that transfer core variable genes

9. The estimated mortality rate associated with MRSA infections in U.S. hospitals is ______%.
   a. 12
   b. 20
   c. 39
   d. 97

10. Community-acquired/community-associated MRSA (CA-MRSA) first appeared in:
    a. the 1960s.
    b. the 1990s.
    c. 2002.
    d. 2010.

11. Necrotizing fasciitis is a rare but serious bacterial infection that can be caused by *S. aureus* and:
    1. *Klebsiella*.
    2. *Clostridium difficile*.
    3. *Escherichia coli*.
    a. 1 and 2
    b. 1 and 3
    c. 2 and 3
    d. 1, 2, and 3

12. Which of the following tests is **not** used to detect MRSA?
    a. cefoxitin disk screen test
    b. latex agglutination test for PBP2a
    c. Mueller-Hinton agar plate supplementation with oxacillin
    d. Mueller-Hinton agar plate supplementation with methicillin

13. Which of the following might be the first sign of MRSA?
    a. fever
    b. nausea
    c. diarrhea
    d. small red bumps

14. Which population is **not** at high risk for CA-MRSA?
    a. schoolchildren
    b. athletes
    c. the homeless
    d. hospital inpatients

15. According to the Centers for Disease Control and Prevention (CDC), what is the **main** way hospital-acquired MRSA (HA-MRSA) is transmitted?
    a. poor hand hygiene
    b. nasal cannulas
    c. dirty hospital gowns
    d. needles

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16. Which is the **most** widely used HAI tracking system in the United States?
   a. National Healthcare Safety Network
   b. Nosocomial Infections Surveillance System
   c. University Healthcare Consortium
   d. Emerging Infections Program

21. Which of the following has been used to treat infections for centuries?
   a. honey
   b. tea
   c. baking soda
   d. alcohol

17. What part of the world has the lowest HA-MRSA rate?
   a. East Asia
   b. Northern Europe
   c. North America
   d. the Middle East

22. Which of the following is **not** a CDC recommendation for preventing HA-MRSA?
   a. proper hand washing
   b. medical equipment sterilization
   c. eliminating the use of unnecessary catheter lines
   d. reducing the number of blood test draws

18. Which of the following can be reservoirs for MRSA if they become contaminated?
   1. pool water
   2. river water
   3. seawater
   a. 1 and 2
   b. 1 and 3
   c. 2 and 3
   d. 1, 2, and 3

23. The chain of infection is:
   a. the way the organism enters the body.
   b. a mechanism of antibacterial resistance transmission.
   c. a mode of transmission of infectious disease from one person or object to another.
   d. a mode of transmission from 2 or more people to another person.

19. Which drug is still used to treat MRSA?
   a. methicillin
   b. vancomycin
   c. oxytocin
   d. alcohol

24. In the radiology suite, which pieces of equipment are particularly important to disinfect properly because they can be sources of infection transmission?
   1. examination table
   2. exposure switch
   3. upright Bucky
   a. 1 and 2
   b. 1 and 3
   c. 2 and 3
   d. 1, 2, and 3

20. Phage therapy is the use of:
   a. viruses as biological control agents.
   b. bacteria as biological control agents.
   c. antibiotics for treatments.
   d. antivirals for treatments.
25. Hungarian physician Ignaz Semmelweis made the connection between hand washing and infection control in a maternity hospital more than 165 years ago. He theorized that hospital staff were transferring germs from ______ to mothers and their newborns.
   a. porous surfaces
   b. surgical equipment
   c. bed linens
   d. cadavers

26. What is the lowest percentage of alcohol the CDC recommends for hand sanitizers?
   a. 10
   b. 50
   c. 60
   d. 75

27. What can be used as a proactive or reactive cleaning mechanism in a hospital setting?
   a. hydrogen peroxide
   b. alcohol
   c. hydrogen peroxide vapor
   d. alcohol vapor

28. Which material has been suggested as an infection preventive surface coating?
   a. copper
   b. aluminum
   c. stainless steel
   d. carbon fiber

29. Where does the eradication of HA-MRSA begin?
   1. health care provider
   2. health care facility
   3. patient
   a. 1 and 2
   b. 1 and 3
   c. 2 and 3
   d. 1, 2, and 3

30. By what percentage has life-threatening MRSA infection declined, according to the CDC?
   a. 10
   b. 28
   c. 49
   d. 50