# MRSA: What wound care professionals need to know

## This dangerous pathogen has extended beyond the hospital to become an even greater threat.

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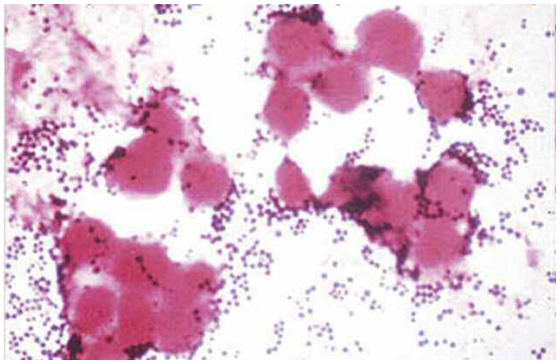
*Staphylococcus aureus* is one of the most feared human pathogens, causing a wide range of infections. Most wound care professionals can expect to frequently encounter patients with *S. aureus* infections. Soft-tissue infections caused by *S. aureus* include impetigo, cellulitis, and cutaneous abscesses, as well as such life-threatening processes as necrotizing fasciitis and pyomyositis (a hematogenous intramuscular abscess). Serious non-soft-tissue infections include septic arthritis, osteomyelitis, pneumonia, endocarditis, and sepsis.

### Why is *S. aureus* such a nasty bug?

*S. aureus* produces various cellular and extracellular factors involved in the pathogenesis of infection. *S. aureus* protein A, an important surface protein, helps the organism resist phagocytosis. Also, *S. aureus* produces several cytotoxins and enzymes that contribute to infection spread and severity. In addition, some strains produce toxins (including toxic shock syndrome toxin-1) that function as superantigens—molecules that nonspecifically trigger release of large amounts of cytokines, leading to a sepsislike condition. Taken together, such factors combine to make *S. aureus* a dangerous pathogen.

### MRSA emergence

When penicillin was introduced in the 1940s, virtually all *S. aureus* isolates were



sensitive to that drug. But soon thereafter, *S. aureus* strains that produced a β-lactamase enzyme capable of inactivating penicillin became widespread. During the 1950s, outbreaks of penicillin-resistant *S. aureus* occurred in many U.S. hospitals. Introduction of penicillinase-resistant antibiotics, such as methicillin and oxacillin, temporarily restored the ability to treat all strains of this pathogen using penicillin antibiotics. The first strain of methicillin-resistant *S. aureus* (MRSA) was described in 1961 shortly after introduction of penicillinase-resistant antibiotics.

The mechanism of methicillin resistance involves a mutation in one of the bacterial cell-wall proteins to which penicillins must bind to kill the bacterium. This mutation renders the organism resistant to all penicillins and penems and almost all cephalosporins.

MRSA incidence has increased steadily to the point where it currently constitutes up to 60% of *S. aureus* isolates in many

## Strains of antibiotic-resistant *S. aureus*

Over the years, *Staphylococcus aureus* (*S. aureus*) has developed a variety of ways to become antibiotic resistant.

| Phenotype | Mechanism | Year described | Frequency |
|---|---|---|---|
| Penicillin resistance | β-lactamase enzyme | 1942 | Ubiquitous (more than 90% of *S. aureus* isolates) |
| Methicillin-resistant *S. aureus* (MRSA) | Penicillin-binding protein mutation | 1961 | 50% to 60% of *S. aureus* isolates in some hospitals |
| Vancomycin-intermediate *S. aureus* (VISA) | Thickened cell wall, leading to diminished antibiotic penetration | 1997 | Rare |
| Vancomycin-resistant *S. aureus* (VRSA) | Vancomycin cell-wall binding site mutation | 2003 | Extremely rare |

U.S. hospitals. These organisms commonly carry genetic material that makes them resistant to various non-β lactam antibiotics as well, leading some to suggest that the term MRSA should stand for **m**ultiply **r**esistant ***S***. ***a****ureus*.

*S. aureus* has continued to mutate in the face of persistent antibiotic pressure. Vancomycin-intermediate *S. aureus* (VISA) was described in 1997; vancomycin-resistant *S. aureus* (VRSA), in 2003. Fortunately, these two strains remain rare and haven't become established pathogens. (See *Strains of antibiotic-resistant* S. aureus.)

### Healthcare- versus community-acquired MRSA

Although MRSA initially arose and spread within healthcare settings (chiefly acute-care hospitals), a community-based variant was described in 1998. Called community-acquired MRSA (CA-MRSA), this variant differs from healthcare-associated MRSA (HCA-MRSA) in more ways than the acquisition site. CA-MRSA occurs predominately in otherwise healthy children and young adults. It most commonly presents as recurrent cutaneous abscesses, although life-threatening infections (such as necrotizing fasciitis and pneumonia) also have occurred. The propensity to cause cutaneous abscesses isn't fully understood but may relate partly to production of the Panton-Valentine toxin by many CA-MRSA isolates.

In contrast, HCA-MRSA afflicts mainly older patients, particularly those with chronic illnesses, including chronic wounds. It typically causes wound infections, urinary tract infections, pneumonia, and bacteremia.

Besides these epidemiologic and clinical differences, many CA-MRSA isolates derive from a single clone, known as clone USA 300, whereas HCA-MRSA is composed of multiple non-USA 300 clones. Finally, many CA-MRSA isolates are sensitive to non-β lactam antibiotics, whereas most HCA-MRSA isolates resist multiple antibiotics. More recently, the distinction between CA-MRSA and HCA-MRSA has been blurred as evidence emerges that CA-MRSA now is being transmitted in healthcare settings as well as in the community.

### *S. aureus* carrier state

Staphylococci are frequent colonizers of humans. Common colonization sites include the skin, anterior nares, axillae, and inguinal

regions. Individuals can be colonized continuously or transiently, with nasal carriage rates varying from 20% to 40%. Most *S. aureus* infections result from the strain carried by the infected patient.

Three patterns of *S. aureus* carriage exist in humans:

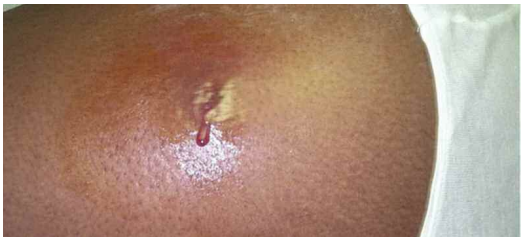
- 20% of individuals are *continuously colonized*.
- 30% of individuals are *intermittently colonized*.
- 50% of individuals are *never colonized*.

The highest carriage rates occur in patients receiving frequent injections (such as insulin-dependent diabetics, hemodialysis patients, and I.V. drug users) and those with chronic skin conditions (for instance, psoriasis or eczema). In the general population, MRSA carriage rates have increased to 1% or 2%, with clinical consequences hinging on the colonizing strain (CA-MRSA versus HCA-MRSA) and host characteristics. The most consistent carriage site is the anterior nares, but many other sites may carry this pathogen, including the axillae, inguinal regions, and perirectal area.

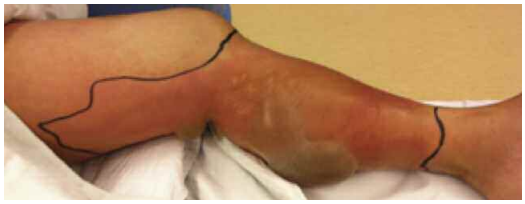
## MRSA treatment

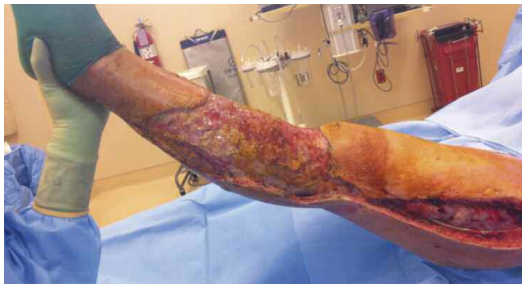
Therapy for MRSA infection depends on the infection location and antibiotic sensitivity of the infecting strain.

- *Cutaneous abscesses* (see below) are treated by incision and drainage; antibiotics play a secondary role to adequate drainage.

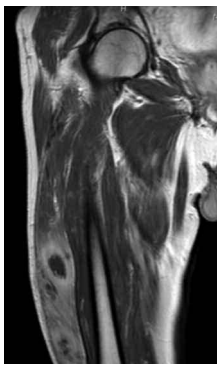


- Therapy for *necrotizing fasciitis* caused by MRSA involves aggressive debridement with removal of all necrotic tissue, plus adequate antibiotic therapy. Typically, patients require serial debridement (see images below: necrotizing fasciitis before and after debridement) followed by subsequent careful wound care, often with eventual skin grafting.





- *Pyomyositis* (shown in MRI at right) treatment entails drainage of the muscle abscess (which sometimes can be done with percutaneous tube placement instead of open drainage), plus appropriate antibiotic therapy.



Vancomycin has been the mainstay of I.V. therapy for MRSA for decades, but some clinicians are concerned that its effectiveness may be declining due to slowly increasing minimum inhibitory concentrations (the minimum concentration of an antibiotic needed to inhibit pathogen growth). Other parenteral options have emerged in the last few years. (See *I.V. drugs used to treat MRSA*.) Several oral antibiotics also are available for MRSA treatment. (See *Oral agents used to treat MRSA*.)

Knowing the antibiotic sensitivity pattern of the infecting MRSA strain is crucial to ensuring that the patient receives an appropriate antibiotic. Treatment duration for soft-tissue infections usually ranges from 7 to 14 days, but bacteremia and bone or joint infections call for more prolonged therapy.

## I.V. drugs used to treat MRSA

This chart shows major advantages and drawbacks of each I.V. agent used to treat methicillin-resistant *Staphylococcus aureus* (MRSA) infection.

| Antibiotic | Advantages | Disadvantages |
|---|---|---|
| Ceftaroline | • Cephalosporin antibiotic | • Little clinical data available on severe infections |
| Daptomycin | • Good toxicity profile<br>• Once-daily dosing | • Expensive<br>• Weekly creatinine kinase levels required |
| Linezolid | • Also available orally | • Expensive<br>• May interact with selective serotonin reuptake inhibitors to cause serotonin syndrome<br>• May cause cytopenias and neuropathy |
| Telavancin | • No drug blood levels required<br>• Once-daily dosing | • May cause renal failure<br>• May have teratogenic effects |
| Tigecycline | • Broad-spectrum coverage | • Expensive<br>• Concerns about efficacy<br>• May cause nausea |
| Vancomycin | • Long track record<br>• Inexpensive | • Periodic drug blood levels required<br>• Possible decreasing efficacy |

### Efforts to eradicate MRSA carriage

Because the carrier state increases the risk of subsequent *S. aureus* infection, efforts have been made to eradicate carriage. Unfortunately, this has proven to be difficult. A commonly used regimen involves 5 days of twice-daily mupirocin nasal ointment with either chlorhexidine gluconate showers or immersion up to the neck in a dilute bleach solution. However, success in eliminating carriage is limited, although the bleach bath seems to improve eradication rates better than other modalities.

MRSA is one of the most problematic pathogens.

### Controlling MRSA in hospitals

How best to control MRSA spread within hospitals is controversial. Some experts advocate an aggressive, "search and destroy" approach involving screening all patients for nasal carriage on admission and initiating contact precautions with subsequent decolonization efforts. Others focus on improving the overall level of hand hygiene and other general infection-control measures, arguing that nasal screening misses at least 20% of MRSA-colonized patients and thus gives an unwarranted sense of security.

Many hospitals use a mixed approach, screening patients suspected to be at high risk for MRSA carriage (such as those admitted from extended-care facilities or to the intensive care unit), while simultaneously trying to improve hand hygiene and general infection-control measures. Recent data suggest MRSA colonization and infec-

## Oral agents used to treat MRSA

Most oral antibiotics used to treat methicilliln-resistant *Staphylococcus aureus* (MRSA) infections are older drugs that may be useful for less severe infections, particularly those caused by community-acquired MRSA.

| Antibiotic | Advantages | Disadvantages |
|---|---|---|
| Clindamycin | • Also covers group A streptococci | • Expensive<br>• Resistance may develop |
| Doxycycline, minocycline | • Inexpensive<br>• Well absorbed | • Little published efficacy data available |
| Linezolid | • Well absorbed | • Expensive<br>• May interact with selective serotonin reuptake inhibitors to cause serotonin syndrome<br>• May cause cytopenias and neuropathy |
| Sulfamethoxazole-trimethoprim | • Inexpensive<br>• Well absorbed | • May cause rash and renal failure |

tion rates have stopped increasing and are beginning to decline.

MRSA is one of the most problematic pathogens encountered on a regular basis, and among the most dangerous pathogens we face. While some MRSA infections are relatively mild, many are serious or life-threatening. Severe soft-tissue infections, such as necrotizing fasciitis and pyomyositis, require surgical debridement or drainage, appropriate antibiotic therapy, and assistance from a wound-care professional to achieve optimal outcomes. ■

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