Cellulitis, Skin Abscesses, and Community-Acquired Methicillin-Resistant *Staphylococcus Aureus*

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ABSTRACT

PURPOSE: To review the clinical features and treatment of common bacterial infections of the skin and soft tissue, the increasing prevalence of community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA), and its impact on treatment decisions.

EPIDEMIOLOGY: Skin and soft-tissue infections account for about 7% to 10% of hospitalizations in North America, and upwards of 2.5% of primary care office visits. MRSA is a common cause of bacterial infection in hospitals, accounting for 40% to 70% of total *S aureus* infections. Traditionally a hospital pathogen, MRSA has become increasingly common in community settings. CA-MRSA has been seen both sporadically and in local outbreaks.

REVIEW SUMMARY: The increasing prevalence of MRSA has had a considerable impact, however clinicians cannot often reliably anticipate CA-MRSA. CA-MRSA tends to affect children and younger adults with an emphasis on skin and soft-tissue infections whereas hospital-acquired MRSA is more common among the older adult population, typically causing bacteremia and deep infections. The approach to pharmacologic therapy of these infections may require modification of the historical long-term reliance upon β-lactam antibiotics, instead using different drugs while increasing the emphasis upon incision and drainage.

TYPE OF AVAILABLE EVIDENCE: Randomized controlled trials, randomized studies, prospective and retrospective cohort studies, unstructured reviews, and conference proceedings/presentation slides.

GRADE OF AVAILABLE EVIDENCE: Good.

CONCLUSION: Pharmacologic treatment of skin and soft-tissue infections, especially in the community setting, may require consideration of drugs targeting MRSA, though whether this needs to be empiric or based on culture results is subject to debate. Incision and drainage of cutaneous abscesses including culturing of material have become particularly important for proper management.

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Bacterial infections of the skin and soft tissues are among the most common reasons for people to seek medical advice.[1] These infections are frequently seen in primary care practice, where cellulitis and impetigo alone account for 2.5% of office visits. However, these infections can be serious enough to require hospitalization. In fact, acute skin and soft-tissue infections account for approximately 7% to 10% of total hospitalizations in North America.[1-4]

Bacterial skin and soft-tissue infections are subdivided into 3 categories: 1) the primary pyodermas, which include cellulitis, impetigo, erysipelas, folliculitis, furuncles and carbuncles, lymphangitis, and abscesses; 2) complicated infections, which are secondary to pre-existing conditions and include surgical wounds, trauma,

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Off-Label Product Discussion: The author of this article does not include discussion of off-label/unapproved use of products.

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bites, and infections related to decubitus and diabetic foot ulcers; and 3) necrotizing infections of soft-tissue structures such as necrotizing fasciitis.[2] Whereas primary pyoderma usually is due to a single pathogen, most commonly *Staphylococcus* or *Streptococcus* species, complicated and necrotizing infections usually are polymicrobial and often involve anaerobes.

In years past, the treatment of primary pyoderma was relatively straightforward; it was the complicated infections that presented the greater therapeutic challenge. However, tides have shifted with the emergence and increasing prevalence of community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA).[1,5-7] Whereas MRSA skin and soft-tissue infections traditionally caused infections seen primarily in hospitals, skilled nursing facilities, and intensive care units (ICUs),[5,6] accounting for 40% to 70% of all *S aureus* infections,[5,8,9] growing numbers of reports since the late 1990s confirm that MRSA infections are becoming more common in community settings.[6,10,11] One such report found that the proportion of MRSA skin and soft-tissue infections in patients seeking treatment at a Los Angeles area emergency room rose from 29% in 2001-2002 to 64% in 2003-2004.[6] Zetola et al[5] argue that the increasing presence of MRSA in the community is a public health problem that warrants increased attention, particularly with regard to the diagnosis and treatment of patients with confirmed and suspected staphylococcal infections.

Against this backdrop, this article first reviews the clinical features, causative pathogens, and therapy of several common skin and soft-tissue infections. It follows with a discussion of antibiotic resistance of staphylococci, risk factors for MRSA, and the emergence of CA-MRSA and its treatment.

Clinical Features and Treatment

The clinical features and treatment of several common bacterial skin and soft-tissue infections in the primary pyoderma category are described below.

Impetigo

The predominant nonbullous form of impetigo is characterized by superficial intraepidermal vesicles with exudate. The lesions rupture, become "weepy," and eventually form a honey-colored crust (Figure 1). This usually occurs in young children, and poor hygiene frequently is a contributing factor. Fever and other systemic signs typically are absent.

The less common bullous form presents as a thin-walled bulla, 2 cm to 5 cm in size, containing serous yellow fluid. Rupture results in a partially or completely denuded area within the ring or arc of the bulla that remains.[2]

Historically, *Streptococcus pyogenes* accounted for the majority of cases of impetigo, with the immunologic sequela glomerulonephritis a potential concern, and penicillin was favored as the treatment of choice. However, recent evidence has shown that *S aureus* is now the more common pathogen,[12] and penicillin is therefore no longer an appropriate empiric agent. Antibiotic selection for impetigo should include both streptococcal and staphylococcal coverage with drugs such as cefazolin, dicloxacillin, or other agents with a similar spectrum. Systemic therapy may not be required as topical therapy with mupirocin (Bactroban®) ointment is as effective as a course of oral antibiotics.[13] Indeed, with limited areas of disease, topical therapy usually is all that is required to treat impetigo. Prevention and limiting spread within families can be best accomplished by advising frequent hand washing and laundering of clothing, towels, and bed linens.

Erysipelas

Erysipelas, also known as St Anthony's fire, is a deeper and more serious infection than impetigo. It affects the upper layer of the skin and is considered the most superficial form of cellulitis. Unlike impetigo, erysipelas is most common in older adults, although children occasionally are affected, as well. It is characterized by intense erythema and edema with sharply demarcated borders and most commonly occurs on the face (Figure 2 can be viewed on the New Zealand Dermatological Society's Web site at: www.dermnetnz.org) or arms. Fever may be present, particularly with facial erysipelas, which may require hospitalization and intravenous (IV) antibiotics. Less serious cases can be adequately treated with oral antibiotics. Because nearly all cases of erysipelas are caused by *S pyogenes*, with *S aureus* only rarely confirmed as the causative organism, erysipelas is one of the few skin infections for which penicillin is recommended.

Cellulitis

Cellulitis is one of the most common skin and soft-tissue infections for which patients may need to be hos-

Figure 1. Impetigo

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pitalized. It is a painful, erythematous infection involving the dermis, epidermis, and subcutaneous tissue, and is characterized by redness and warmth of the affected area with tenderness and induration (Figure 3). Unlike erysipelas, the borders of bacterial cellulitis are not sharply demarcated, but blend in with the surrounding skin. Infection commonly occurs near breaks in the skin—such as those associated with surgical wounds, trauma, tinea infections, and ulcerations—and may spread rapidly. Additional risk factors include systemic conditions such as diabetes mellitus and alcohol abuse and anatomically localizing factors such as venous or lymphatic insufficiency. Fever often is present, and the white blood cell count also may be elevated.[2]

Figure 3. Cellulitis

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Table 1. Antibiotic Therapy for Cellulitis

	Parenteral	Oral
Default drugs	Oxacillin, cefazolin	Cephaloxin, dicloxacillin
Penicillin allergic	Clindamycin, vancomycin	Clindamycin, fluoroquinolones
Erysipelas	Penicillin	Penicillin, macrolide
Concern for MRSA	Vancomycin, linezolid, clindamycin	Linezolid, clindamycin, TMP/SMX, doxycycline
Neutropenia, cirrhosis, poorly controlled diabetes*	Piperacillin/tazobactam, cefazolin + fluoroquinolones	Amoxicillin/clavulanate, levofloxacin
Fresh water exposure	Oxacillin/cefazolin + fluoroquinolones	Fluoroquinolones
Salt water exposure	3rd generation cephalosporin + doxycycline	Doxycycline
Bites†	Ampicillin/sulbactam	Amoxicillin/clavulanate

*Gram-negative or polymicrobial-associated cellulitis possible; †requires anaerobic coverage.
MRSA = methicillin-resistant *Staphylococcus aureus*; TMP/SMX = trimethoprim/sulfamethoxazole.

Because most cases of cellulitis are caused by *S aureus* and β-hemolytic streptococci (such as *S pyogenes*, also known as Group A β-hemolytic streptococci), therapy consists of antibiotics that target these pathogens.[1,2,7] Elevation of an affected limb to speed resolution of the infection also is indicated. Specific treatment of several distinctive forms of cellulitis, as well as cellulitis in special populations, is outlined in Table 1.

Cutaneous infections arising from animal or human bites tend to be polymicrobial and include both aerobic and anaerobic flora.[14] Aerobes include *Pasteurella multocida, S aureus, Staphylococcus intermedius*, β-hemolytic streptococci, *Capnocytophaga canimorsus, Eikenella corrodens, Haemophilus* species, and other members of the oral flora. Anaerobic bacteria are present in approximately one third of bite wounds and are associated with the formation of abscesses and with relatively serious infections. Human bites more frequently than animal bites tend to be serious.

In the absence of definitive studies comparing oral therapy at home with IV therapy in the hospital, the decision to hospitalize a patient with routine cellulitis depends upon clinical judgment. However, a recent randomized controlled trial comparing IV therapy of cellulitis at home with IV therapy in the hospital found similar clinical outcomes with either treatment venue and a strong patient preference for at-home care.[15] Only 5% of patients treated at home stated a preference for in-hospital treatment versus 33% of hospitalized patients who stated a preference for at-home care. The findings of this study, which was conducted in New Zealand of nearly 200 patients with a very low prevalence of MRSA, suggest that home-based IV therapy for cellulitis is feasible as long as MRSA is not a concern.

Recurrent cellulitis (ie, 2 or more episodes per year) is not uncommon. Once the skin has been affected by cellulitis, it appears to become predisposed to additional episodes. One series has suggested that 20% to 50% of patients who have had 1 episode will have another within 2 years' time.[16]

Recurrent cellulitis is usually due to Group A β-hemolytic *Streptococcus* and often is associated with chronic skin conditions such as tinea pedis, psoriasis, onycholysis, other nail problems, venous insufficiency, and/or lymph-edema. Therapy consists of treating the underlying infection with an appropriate antibiotic along with prevention of recurrent episodes. Preventive measures include treatment of chronic skin conditions so that the skin is not breached. Wearing a compression stocking or sleeve to prevent microabrasions of the skin is recommended for patients with lymphedema. Occasionally, chronic

antibiotic prophylaxis with amoxicillin or clindamycin may be required for patients suffering frequent and/or severe recurrences of cellulitis.[17,18] This should only be undertaken in special circumstances, ideally in consultation with an infectious disease specialist.

Cellulitis that does not seem to resolve should prompt 2 responses: a review of the antibiotics chosen for treatment and whether they were appropriate, and a review of conditions that can mimic cellulitis. These mimickers include contact dermatitis, insect and spider bites, superficial or deep thrombophlebitis, cutaneous drug reactions, erythema nodosum (especially if discrete nodules are present on the shins), Sweet's syndrome (acute febrile neutrophilic dermatosis), eosinophilic cellulitis or fasciitis, hidradenitis suppurativa, gout, lupus, relapsing polychondritis, and sarcoidosis.[19]

Lymphangitis

Bacterial lymphangitis is an infection of the deep lymphatic channels. It is characterized by erythematous streaks along the lymphatic channels often from an area of cellulitis. Treatment for lymphangitis is the same as that for cellulitis. It is most commonly caused by *S pyogenes*; occasionally, mixed pathogens are responsible for the infection. However, there have been reports that lymphangitis rarely may be caused by herpes simplex inflammation.[20]

Skin Abscesses

Cutaneous abscesses are localized collections of pus that cause soft-tissue swelling surrounded by erythema. Usually, they follow minor trauma and often are seen as folliculitis, furuncles, and carbuncles.[2] Accompanying features may include local cellulitis, lymphangitis, lymphadenopathy, fever, and leukocytosis. Organisms isolated from cutaneous abscesses typically are those residing on the skin of the involved area.

Folliculitis. Folliculitis is a superficial skin infection in and around the hair follicles, usually presenting without fever. It is characterized by small pustules around the hair (Figure 4). Although most cases of folliculitis are due to *S aureus*, other organisms can be implicated in certain settings such as whirlpool or "hot tub" folliculitis (*Pseudomonas aeruginosa*), folliculitis in ICU patients (*Candida albicans*), and patients with HIV/AIDS (eosinophilic folliculitis associated with *Demodex* mites).[21] As with impetigo, there is an inclination to prescribe systemic antibiotics. However, though not well studied, general measures such as showering with soap or with a product containing chlorhexidine or hexachlorophene every day are sufficient to treat and also to decolonize the skin.[22] If the infection is being transmitted from one member of the household to another, or if the infection persists in a given patient, antibacterial washes are appropriate with consideration of a course of an oral antistaphylococcal antibiotic.

Furuncles and Carbuncles. Furuncles are small boils that develop from folliculitis (Figure 5). They range from <1 cm to 2 cm in size, and may or may not be accompanied by fever. Carbuncles are larger boils, >2 cm in size, with multiple "heads" that result from the coalescence of furuncles (Figure 6). They are more likely than furuncles to be accompanied by fever. Both types of boils are more prevalent in hot weather when individuals perspire more heavily, and they tend to occur more frequently in heavier-set individuals—occurring most commonly around the neck, under the arms, or in the groin—and in those with diabetes or who are on corticosteroid therapy.

S aureus is the causative pathogen, and primary therapy consists of incision to achieve drainage of pus. Antibiotics with activity against *Staphylococcus* are unnecessary in many cases, as uncomplicated furuncles and carbuncles often resolve spontaneously as they come to a head and drain on their own. However, if systemic symptoms exist or significant cellulitis sur-

Figure 4. Folliculitis

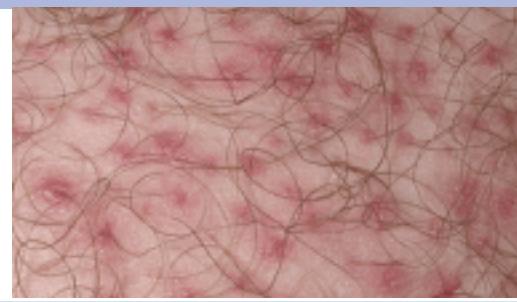

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Figure 5. Furunculosis

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rounds the boil, antibiotics become necessary. At present, pus should be cultured mainly to assess for the presence of MRSA, even if antibiotics are not initially considered necessary, in case systemic symptoms later develop and require therapy.

Recurrent furuncles and carbuncles may require decolonization strategies if measures to improve hygiene (ie, taking daily showers or baths with soap, laundering towels, bed sheets, and clothing in hot water) fail.[23] However, randomized studies have shown that prophylactic decolonization has not been proven effective, except perhaps in patients on renal dialysis who have high rates of staphylococcal infections.[24,25] In these studies, topical therapy with intranasal mupirocin 2% for 5 days decreased the incidence of recurrent staphylococcal infections by targeting the major risk factor for acquiring *S aureus* infection—nasal carriage and subsequent autoinoculation.

Other studies evaluating various drug therapies for the treatment of these infections do not provide any clear answers except that resistance tends to emerge.[26] Nevertheless, intranasal therapy with mupirocin solution (or mupirocin ointment applied within the nostrils) and/or chlorhexidine 4% solution body washes may provide a reduction in the staphylococcal carriage that leads to these infections. Systemic therapy with trimethoprim/sulfamethoxazole, tetracycline, minocycline, and doxycycline (some in combination with rifampin) for decolonization has been less well studied. Short-term treatment appears to be effective, but little is known about longer-term use.[26] One caveat regarding rifampin is that it not be used to treat or prevent recurrent staphylococcal infections as monotherapy because of a quick emergence of resistance.[27]

Antibiotic Resistance of Staphylococci

The impact of antibiotic resistance on clinical practice is considerable. Drug resistance also is a major public health concern. Drugs that were once used with great success to treat various infections have become less effective, a circumstance that prompts consideration as to whether a revised approach to customary pharmacologic therapy is necessary.

Figure 6. Carbuncle

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A Brief History

In the case of *S aureus*, a virulent pathogen that coagulates plasma and inhibits phagocytosis, its resistance to penicillin was first reported in the 1940s; by the 1950s it was widespread. MRSA first emerged in the 1960s, with increasingly numerous reports appearing throughout the 1970s. By the 1980s MRSA had become common in hospitals, and occurrences were reported in communities during the 1990s.[28] In 2002, antibiotic resistance intensified with the first US report of vancomycin-resistant *S aureus*, or VRSA, in a man with renal failure who was treated with vancomycin for more than a year because of a foot ulcer; he also was known to be colonized with vancomycin-resistant enterococci.[29] A recent additional case now brings us to 4 additional cases of VRSA since its initial description [J. Jernigan, personal communication].

Methicillin-Resistant Staphylococcus Aureus *in the Community*

As previously noted, MRSA is a major nosocomial pathogen. Risk factors for MRSA infections in hospitalized patients include a prolonged hospital stay—usually in excess of 14 days—preceding antimicrobial therapy, surgical procedure(s), a stay in the ICU or burn unit, and proximity to a known case of MRSA.[30] In patients residing in long-term care facilities, the risk factors are recent hospitalization, decubitus ulcer, indwelling catheter, and a high level of dependency.[30]

Both the high prevalence of nosocomial MRSA and the identification of risk factors raise questions about the prevalence of CA-MRSA and whether it too has identifiable risk factors. Prompted by its own report of 4 deaths in children with CA-MRSA,[31] the Centers for Disease Control and Prevention drafted a strict definition of CA-MRSA to assist with determining its prevalence: diagnosis of MRSA infection is made in previously nonhospitalized persons or within 48 hours of hospital admission; there is no prior history of MRSA or hospitalization, nursing home admission, surgery, or dialysis within the previous 12 months, and there is no history of catheter use.

One of the first studies to examine prevalence and risk factors found that the rate of CA-MRSA among children in Chicago rose from 10/100 000 during 1988-1990 to 259/100 000 during 1993-1995.[32] Of those with CA-MRSA without identifiable risk factors, 12 had cellulitis, 6 had skin abscesses, 3 had pneumonia, and none had bacteremia. By comparison, there were 4 cases of bacteremia and 4 skin and tissue infections in those with nosocomially acquired MRSA, reflecting a shift in the type of infection caused by CA-MRSA.

A more recent study prospectively examined the

distribution of CA-MRSA and healthcare-associated MRSA (ie, in hospitals and other healthcare facilities) among 100 patients differentiated by age and found that those with CA-MRSA were significantly younger (median age, 30 years vs 70 years; $P < .001$).[33] The distribution of MRSA infection in both groups by decade of age is shown in Figure 7. The study also found that skin and soft-tissue infections predominated in CA-MRSA, whereas bacteremia and genitourinary infections predominated in healthcare-associated MRSA.

Published studies over the past few years also have found regional differences in the incidence of CA-MRSA depending on age and race, regional differences in hospitalization rates, and evidence that these new strains of CA-MRSA behave differently. Risk groups among adults and adolescents have included drug users, military recruits, men who have sex with men, prison inmates, and contact sport players.[5]

In one such study, overall case rates in Atlanta, Georgia, were similar for children under 2 years of age and for adults between the ages of 19 and 64, lowest in those 2 to 18 years of age, highest in those over age 64, and more common in African Americans regardless of age group.[34] By comparison, overall case rates in Baltimore, Maryland, were highest in children under 2 years of age and lowest in adults over age 64 with a paralleling decline in rates in African Americans according to age.

The same study also found regional differences in hospitalization rates despite similar proportions of patients with CA-MRSA skin and soft-tissue infections and wounds.[34] In Atlanta, the hospitalization rate was 27%, whereas in Baltimore the rate was 61%. The proportion of hospitalized patients who required an ICU stay varied between 4% and 8%, depending on location.

Two case studies suggest that CA-MRSA may be responsible for some previously unrecognized associations. One report found that community-acquired strains were responsible for necrotizing fasciitis, a new spectrum of infection for *S aureus*.[35] Another report, which has generated some controversy, described 5 cases of purpura fulminans secondary to *S aureus*.[36] Purpura fulminans usually is associated with coagulation abnormalities in certain hosts. However, in all 5 cases, toxins such as toxic shock protein and enterotoxins were elaborated by the infecting strains of *S aureus*.

Community-acquired outbreaks have been reported in prisoners, IV drug users, members of athletic teams, and other populations in which there is close physical contact or a "closed" environment.[7,10,37] Because it is difficult to differentiate CA-MRSA from healthcare-associated MRSA or methicillin-sensitive *S aureus*, the best recommendation for physicians is that they maintain a high index of suspicion in these populations and make empiric decisions regarding hospitalization and treatment based upon the severity of the infection.

Recurrent CA-MRSA infections that are difficult to eradicate also have been reported in closed environments. In one report, 11 players on a college football team developed these infections over a period of 2 years.[37] Associated risk factors were having a locker near an infected teammate's locker, sharing soap with teammates, and having a cut or other open wound. Infections were brought under control by improved hygiene and daily showers with hexachlorophene instead of soap. In general, efforts to keep locker rooms scrupulously clean also would be helpful.

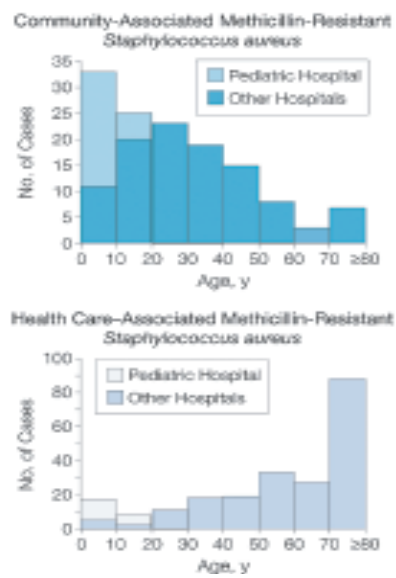
Methicillin-Resistant Staphylococcus Aureus

Genetics and Pathogenesis

Genetic differences between healthcare-acquired and CA-MRSA appear to account for their pathogenetic behavior, resistance, and proclivity to infect different patient populations. Healthcare-acquired MRSA carries a good deal of genetic code for resistance to many antibiotics in a large staphylococcal chromosome cassette (types I-III SCC*mec*) with enough room to contain other resistance alleles.[1,5] However, it is poorly transferred, does not code for Panton-Valentine leukocidin (PVL), and tends to strike older individuals with risk factors for MRSA infection.

By comparison, CA-MRSA carries its genetic code for resistance in a smaller and possibly more mobile cassette (type IV SCC*mec*) with little room for other antibiotic

Figure 7. Community-Associated and Healthcare-Associated Methicillin-Resistant *Staphylococcus Aureus* Infections by Age



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resistance alleles.[1,5] However, the PVL toxin is associated with CA-MRSA strains and tends to infect younger individuals without typical risk factors. PVL kills white cells and neutrophils, a beneficial effect for *S aureus*. PVL also seems to have cytokine effects and is associated with increased levels of toxic shock syndrome toxin-1 and enterotoxins A, C, and K, which are all thought to play some virulence role in the development of necrotizing pneumonia, and severe skin and soft-tissue infections.

Though research laboratories can look at the staphylococcal cassette type and check for PVL to determine whether an MRSA strain is healthcare acquired or community acquired, clinical laboratories generally cannot. However, because CA-MRSA has a very short genetic code for resistance, its strains generally are sensitive to many of the antibiotics that are not customarily associated with MRSA—namely, fluoroquinolones, trimethoprim-sulfamethoxazole, tetracycline, clindamycin, and erythromycin (Table 2).[33] Thus, antibiotic susceptibility profiles can be used in clinical practice as a rough indicator of whether an MRSA strain is healthcare acquired or community acquired.

A special concern with clindamycin, which is often used to treat streptococcal and staphylococcal infections, is that 15% to 20% of CA-MRSA isolates have an inducible enzyme that yields an initial finding of sensitivity to this drug on the initial microbiology report.[38] However, resistance may quickly develop when patients are exposed to clindamycin. Therefore, clindamycin should not be chosen if it appears susceptible but erythromycin is deemed resistant. To avoid this false-positive result for susceptibility, clinicians should request a D-test, in which an erythromycin disk and a clindamycin disk are used to confirm clindamycin sensitivity without induction of resistance later on. If the D-test shows inducible clindamycin resistance, clindamycin should not be used.

Table 2. Antibiotic Susceptibility Profiles of Community-Associated and Healthcare-Associated Methicillin-Resistant *Staphylococcus Aureus* Isolates

	No. (%) Susceptible*		
Antibiotic	Community Associated (n = 106)	Healthcare Associated (n = 211)	*P* Value†
Oxacillin (methicillin)	0	0	NA
Ciprofloxacin	84 (79)	33 (16)	<.001
Clindamycin	88 (83)	44 (21)	<.001
Erythromycin	47 (44)	18 (9)	<.001
Gentamicin	100 (94)	168 (80)	.001
Rifampin	102 (96)	199 (94)	.64
Tetracycline	98 (92)	194 (92)	.95
TMP/SMX	101 (95)	189 (90)	.13
Vancomycin	106 (100)	211 (100)	NA

NA = not applicable; TMP/SMX = trimethoprim/sulfamethoxazole.
*Tested at the Minnesota Department of Public Health Laboratory by broth microdilution using National Committee for Clinical Laboratory Standards break points.
†Statistical probability that the percentage susceptible among community-associated isolates differed from the percentage susceptible among healthcare-associated isolates ($P = 0.05$).
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Treatment: Then and Now

The traditional approach to treatment of staphylococcal infections was to prescribe cephalexin for outpatients, cefazolin or oxacillin/nafcillin for patients requiring hospitalization, and vancomycin for patients with β-lactam allergies or MRSA. However, with the emergence and increasing prevalence of CA-MRSA, some of these choices may need reconsideration.

Clinicians have always been encouraged to incise and drain any infection that can be drained. Whereas in the past culturing was not deemed essential, now culture of isolates that have been drained can be used to provide antibiotic susceptibility profiles to guide therapy later on, and to consider alternatives to β-lactams as empiric therapy in selected patients.

One recent study of skin and soft-tissue CA-MRSA infections found that neither incision and drainage nor using an initial antibiotic that was inactive was significantly associated with adverse outcomes (eg, follow-up visits to a healthcare provider, subsequent incision and drainage, or subsequent change in antimicrobial therapy).[34] In addition, in a subgroup of patients who did not initially undergo incision and drainage, there were no significant differences in outcomes according to whether the initial therapy was inactive. This study may suggest that even CA-MRSA presenting as localized disease without severe symptoms or toxicity can be treated with traditional measures including β-lactams empirically without adverse outcome. For the unresponsive patient, having culture information in-hand can guide the clinician to proper antibiotic selection (Table 3). Clinicians also should ask patients about close contacts who also may be infected and initiate decolonization measures as appropriate, especially if the infections are recurrent.

One proviso regarding treatment of cellulitis where both streptococci and staphylococci cause significant infections is that targeting CA-MRSA with certain drugs may leave insufficient therapy for streptococci. In particular, streptococci display anywhere from a 20% to 45% resistance profile against trimethoprim/sulfamethoxazole and tetracyclines.[39] Clinicians with strong concerns about CA-MRSA may need to use clindamycin or consider alternatives such as combination therapy or use of linezolid or parenteral vancomycin to provide sufficient coverage.

Office treatment of CA-MRSA in patients with severe and less severe infections, and in those with and without healthcare-associated risk factors, is outlined in Table 3.[5] The risk factors that were considered in developing the treatment scheme are: hospitalization within the previous 1 to 24 months; outpatient visit within the previous 12 months; nursing home admission within the previous 12 months; antibiotic exposure within the previous 1 to 12 months; hemodialysis; chronic illness; IV drug use; and close contact with persons with risk factors.

Conclusion

CA-MRSA is different from healthcare-acquired MRSA in several respects. Most CA-MRSA infections affect the skin and soft tissues, and most patients cannot be identified as being at risk by using typical MRSA risk factors as a guide. Moreover, community isolates have different antibiotic susceptibilities such that they are resistant to fewer classes of drugs than is healthcare-acquired MRSA. However, CA-MRSA strains have a novel methicillin-resistance gene and are more virulent than healthcare-acquired strains, which may be owing to the presence of PVL.

Because CA-MRSA infection is not a reportable disease, its actual prevalence is not precisely known. In the setting of CA-MRSA, the older antibiotics may still have good efficacy (eg, vancomycin, tetracyclines, trimethoprim-sulfamethoxazole, and clindamycin) and they may be a less expensive alternative than are newer agents with MRSA activity, such as linezolid, daptomycin, tigecycline, and quinupristin/dalfopristin. Oxacillin/nafcillin should no longer be relied upon for very ill patients with a suspected staphylococcal infection.

The advent of CA-MRSA will require ongoing epidemiological investigations and clinical study to understand whether the traditional algorithms for the treatment of gram-positive skin and skin structure infections will need to change on a wholesale basis. Regarding prevention, further research is needed to study the association between nasal carriage of CA-MRSA and skin and soft-tissue infection to develop decolonization guidelines.

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Table 3. Treatment of Community-Associated Methicillin-Resistant *Staphylococcus Aureus*

Severe Infections			Nonsevere Infections	
	First-Line Agents	*Second-Line Agents*	*First-Line Agents*	*Second-Line Agents*
Patient with healthcare-associated risk factors*	Vancomycin	Linezolid; quinupristin/dalfopristin; daptomycin†	Empiric penicillinase-resistant penicillin‡§; first-generation cephalosporin§‖	Linezolid; co-trimonxazole
	Clindamycin	Tigecycline	Vancomycin¶	Tetracycline#
Patient without healthcare-associated risk factors*	Vancomycin	Linezolid; quinupristin/dalfopristin; daptomycin†; tigecycline	Pencillinase-resistant penicillin‡§; first-generation cephalosporin§‖	Co-trimoxazole; clindamycin
		Penicillinase-resistant penicillin‡§ + 1 of the following: trimethoprim/sulfamethoxazole; clindamycin; tetracycline#		Tetracycline#

*Described in text; †Daptomycin should be avoided in the treatment of methicillin-resistant *Staphylococcus aureus* (MRSA) pneumonia; ‡Oxacillin, nafcillin, dicloxacillin; §Avoid β-lactam in areas with high prevalence of community-acquired MRSA; ‖Cefazolin, cefalexin; ¶Vancomycin should be discouraged as empirical treatment of furuncles and non-severe skin and soft tissue infections; #Minocycline (preferred) or doxycycline.
Adapted with permission from Zetola et al. *Lancet Infect Dis*. 2005;5:275-286.[5]

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