Treatment of skin and soft tissue infections due to methicillin-resistant Staphylococcus aureus in adults

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INTRODUCTION — Methicillin resistance in Staphylococcus aureus is defined as an oxacillin minimum inhibitory concentration (MIC) ≥4 mcg/mL. Isolates resistant to oxacillin or methicillin are also resistant to all beta-lactam agents including oxacillin, dicloxacillin, and cefazolin [1,2].

The treatment of MRSA skin and soft tissue infections in adults will be reviewed here. The treatment of invasive MRSA infections, the mechanisms of antibiotic resistance, epidemiology of MRSA infection, and general issues related to skin and soft tissue infections are discussed separately. (See "Treatment of invasive methicillin-resistant Staphylococcus aureus infections in adults" and "Microbiology of methicillin-resistant Staphylococcus aureus" and "Epidemiology of methicillin-resistant Staphylococcus aureus infection in adults" and "Cellulitis and erysipelas" and "Skin abscesses, furuncles, and carbuncles" and "Impetigo" and "Folliculitis".)

APPROACH TO TREATMENT — Given the increasing prevalence of methicillin-resistant Staphylococcus aureus (MRSA) as both a nosocomial and community-associated pathogen, beta-lactam antibiotics are no longer reliable empiric therapy for skin and soft tissue infections [3]. Familiarity with local antibiotic patterns is important for selecting empiric antibiotic therapy, and culture with susceptibility data is critical for tailoring treatment. (See "Epidemiology of methicillin-resistant Staphylococcus aureus infection in adults".)

The approach to treatment is guided by the type of skin and soft tissue infection and the severity of clinical presentation. Empiric antibiotic therapy should include MRSA coverage if it is suspected based upon local epidemiology; risk factors or the clinical features are not sufficient to make this determination [4-6]. Although many patients with MRSA infection have nasal colonization with the same strain that is responsible for the infection, the predictive value of screening for colonization in the outpatient setting is not known [7].

Patients with fluctuant or purulent skin and soft tissue infections should undergo incision and drainage, and debrided material should be sent for culture and susceptibility testing [8]. Incision and drainage alone may be sufficient for abscesses smaller than 5 cm [9,10]. This was illustrated in a randomized trial of 166 patients with uncomplicated skin abscesses at risk for community-associated MRSA (CA-MRSA) who were managed with cephalexin or placebo following incision and drainage of skin and soft tissue abscesses; the cure rates were similar in the two groups (84 and 90 percent, respectively) [10]. Among the isolates tested, 88 percent were MRSA; because cephalexin does not have activity against MRSA, the cephalexin arm was also a functional placebo arm in this group. (See "Technique of incision and drainage for skin abscess".)

Patients with larger abscesses and/or systemic signs of infection should be managed with incision and drainage plus antimicrobial therapy [9]. Important considerations in antibiotic selection include baseline susceptibility testing prior to antibiotic administration and individual patient circumstances including the type of infection, underlying comorbidities, and other concurrent medications [11].

Oral therapy — The optimal oral antibiotic therapy for empiric treatment of skin and soft tissue infection when MRSA is known or suspected is unclear [12]. Reasonable antibiotics for treatment of MRSA include older agents (clindamycin, trimethoprim-sulfamethoxazole, and tetracyclines such as doxycycline or minocycline) and a newer agent, linezolid (table 1). Use of the older agents is supported by susceptibility testing and clinical experience, but their efficacy for treatment of skin and soft tissue infections due to MRSA has not been rigorously evaluated or compared in clinical trials [13].

Clindamycin (300 to 450 mg every six to eight hours) has good activity against MRSA and is also capable of inhibiting bacterial production of toxins including Panton-Valentine leukocidin and other virulence factors [14]. Careful monitoring of local clindamycin resistance rates is important; some advocate avoiding empiric clindamycin therapy when local MRSA resistance rates exceed 10 to 15 percent [12]. In addition, isolates that appear susceptible to clindamycin and resistant to erythromycin by standard susceptibility testing techniques may be capable of inducing resistance to clindamycin in the presence of the drug [15]. Clinicians should confer with their microbiology laboratory to request evaluation of such isolates for inducible clindamycin resistance with D testing prior to treatment with clindamycin [16,17]. (See "Overview of antibacterial susceptibility testing", section on 'D test'.)

Trimethoprim-sulfamethoxazole (two double-strength tablets twice daily) has been suggested for treatment of skin and soft tissue infections due to MRSA, although data for its efficacy are limited to observational and retrospective reports [18-22]. Trimethoprim-sulfamethoxazole is a reasonable antibiotic choice in the setting of MRSA with known susceptibility to the drug, although it is not advisable for empiric management of soft tissue infections that may be due to group A streptococci [23]. In such cases, some favor combination therapy using a beta-lactam antibiotic with activity against streptococci together with trimethoprim-sulfamethoxazole for empiric MRSA coverage (figure 1) [12]. There is a theoretic concern that clinical failure with this agent may occur due to thymidine released from damaged host tissues, which may bypass the metabolic blockades of trimethoprim and sulfamethoxazole by acting downstream of their target enzymes in the folate synthesis pathway [24].

Data on the efficacy of long-acting tetracyclines for treatment of skin and soft tissue infections due to MRSA are limited to observational and retrospective reports [18-21]. As with trimethoprim-sulfamethoxazole, a tetracycline is a reasonable antibiotic choice in the setting of MRSA with known susceptibility to this agent, although it is not advisable for empiric management of soft tissue infections that may be due to group A streptococci [23]. In such cases, some favor combination therapy using a beta-lactam antibiotic with activity against streptococci together with a tetracycline for empiric MRSA coverage (figure 1) [12].

Linezolid has activity against both MRSA and streptococci and has been shown to be as effective as vancomycin for the treatment of skin and soft tissue infection [25]. Its use is limited by cost, toxicity, and potential for resistance. It should be reserved for those who do not respond to or cannot tolerate an older agent. (See "Treatment of invasive methicillin-resistant Staphylococcus aureus infections in adults", section on 'Linezolid'.)

Fluoroquinolones should NOT be used to treat skin and soft tissue infections due to MRSA; resistance to ciprofloxacin has been observed to develop readily during therapy, and widespread MRSA fluoroquinolone resistance is already prevalent in many regions [18,26]. There is also concern that resistance may emerge during therapy even for fluoroquinolones with enhanced antistaphylococcal activity such as levofloxacin and moxifloxacin [26].

Rifampin has excellent activity against MRSA and may be used in combination with one of the above agents for treatment of skin and soft tissue infections due to MRSA, although data supporting this approach are lacking [12]. Use of rifampin alone is contraindicated given rapid development of resistance to this agent.

Follow-up — Repeat evaluation after 24 to 48 hours of outpatient empiric oral antibiotic therapy is prudent to verify clinical response [3]. The appropriate duration of therapy is one to two weeks; the clinical response to therapy should guide antibiotic duration. Lack of response may be due to infection with resistant pathogens or a deeper, more serious infection than previously realized.

Parenteral therapy — Parenteral therapy should be considered for patients with extensive soft tissue involvement, fever or other signs of systemic illness, or patients with diabetes or other immunodeficiency [12]. Such patients should also be evaluated for evidence of invasive disease. (See "Epidemiology of methicillin-resistant Staphylococcus aureus infection in adults" and "Treatment of invasive methicillin-resistant Staphylococcus aureus infections in adults" and "Treatment of Staphylococcus aureus bacteremia in adults" and "Complications of Staphylococcus aureus bacteremia".)

Vancomycin remains the antibiotic of choice for treatment of invasive MRSA infection, although there is increasing concern regarding the rise in S. aureus MICs to this antibiotic [27]. Dosing is 30 mg/kg per 24 hours in two divided doses, not to exceed 2 g per 24 hours unless serum concentrations are inappropriately low. (See "Vancomycin dosing and serum concentration monitoring in adults".)

For patients who fail to respond or cannot tolerate vancomycin, the optimal alternative parenteral agent is not known (table 1). Among the newer agents, linezolid, daptomycin, tigecycline, telavancin and quinupristin-dalfopristin all have FDA approval for treatment of skin and soft tissue infections. If continued outpatient antibiotic therapy is expected, linezolid (600 mg every 12 hours) is an appropriate choice given the capacity for parenteral or oral administration with good bioavailability [25]. Daptomycin (4 mg/kg once daily) and tigecycline (100 mg IV once, followed by 50 mg IV every 12 hours) are reasonable alternatives. Telavancin (10 mg/kg every 24 hours), although noninferior to vancomycin in clinical studies, has a higher rate of toxicity and substantially higher cost. Use of quinupristin-dalfopristin is limited by adverse effects. Supportive data for the use of these drugs in the management of MRSA infections are presented separately. (See "Treatment of invasive methicillin-resistant Staphylococcus aureus infections in adults".)

Among the older agents, data on parenteral use for treatment of MRSA are limited. Parenteral clindamycin may be given in regions where the likelihood is resistance is low [12]. Parenteral trimethoprim-sulfamethoxazole was less effective than vancomycin in a randomized trial of intravenous drug users with serious S. aureus infections [28].

The appropriate duration of therapy is one to two weeks; clinical response to therapy may guide antibiotic duration.

INFORMATION FOR PATIENTS — Educational materials on this topic are available for patients. (See "Patient information: Methicillin-resistant Staphylococcus aureus (MRSA)".) We encourage you to print or e-mail this topic review, or to refer patients to our public web site, www.uptodate.com/patients, which includes this and other topics.

SUMMARY AND RECOMMENDATIONS

- Patients with skin and soft tissue infections amenable to debridement should undergo Incision and drainage with culture and susceptibility testing. Debridement alone may be sufficient for abscesses smaller than 5 cm.

- Patients with larger areas of infection and/or systemic signs of infection should be managed with antimicrobial therapy. Susceptibility testing should guide antibiotic selection. It is appropriate for empiric antibiotic therapy to include activity against MRSA.

- For the outpatient management of possible or proven MRSA infection, we suggest oral antibiotic therapy with clindamycin, trimethoprim-sulfamethoxazole or a long acting tetracycline such as minocycline or doxycycline (**Grade 2B**). Linezolid is an acceptable alternative agent; its use is limited by cost, toxicity, and potential for resistance. Appropriate dosing for these agents is as outlined in the Table (table 1).

- Parenteral therapy should be considered for patients with extensive soft tissue involvement, fever or other signs of systemic illness, or patients with diabetes or other immunodeficiency. We suggest parenteral antibiotic therapy with vancomycin (30 mg/kg per 24 h in two divided doses, not to exceed 2 g per 24 hours unless serum concentrations are inappropriately low) (**Grade 2B**). (See "Vancomycin dosing and serum concentration monitoring in adults".)

- For patients who fail to respond or cannot tolerate vancomycin, we suggest linezolid (600 mg every 12 hours) or daptomycin (4 mg/kg once daily) (**Grade 2C**).

- The duration of therapy is usually one to two weeks; the clinical response to therapy may guide antibiotic duration. Treatment may be switched from parenteral to oral therapy with clinical improvement.

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GRAPHICS

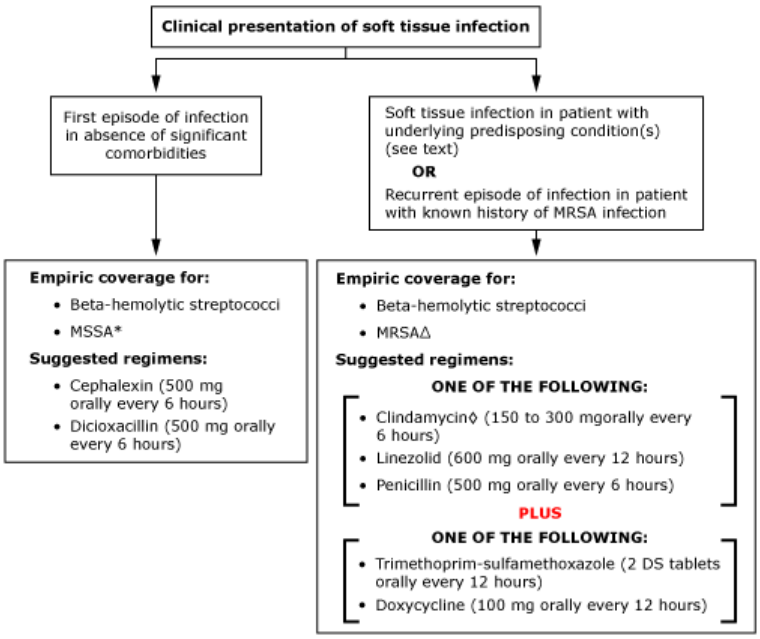
Antimicrobial therapy for infections due to methicillin-resistant Staphylococcus aureus in adults

	Preferred	Alternative
Bacteremia	• Vancomycin (30 mg/kg IV every 24 hours in 2 equally divided doses; not to exceed 2 g/24 hours unless concentrations in serum are inappropriately low)	• Daptomycin (6 mg/kg IV once daily) • Linezolid (600 mg IV or orally twice daily; IV preferred)
Skin and soft tissue infections		
Parenteral therapy	• Vancomycin (30 mg/kg IV every 24 hours in 2 equally divided doses; not to exceed 2 g/24 hours unless concentrations in serum are inappropriately low)	• Daptomycin (4 mg/kg IV once daily) • Linezolid (600 mg IV twice daily) • Tigecycline (100 mg IV once, thereafter 50 mg IV every 12 hours)
Oral therapy	• TMP-SMX (2 double-strength tablets orally twice daily) • Doxycycline or minocycline (100 mg orally twice daily) • Clindamycin* (300 to 450 mg orally every 6 to 8 hours)	• Linezolid (600 mg orally twice daily)

IV: intravenously; TMP-SMX: trimethoprim-sulfamethoxazole.

* D testing required to evaluate for inducible resistance; see text.

Approach to outpatient management of soft tissue infections



DS: double strength.
* MSSA: methicillin-susceptible Staphylococcus aureus.
Δ MRSA: methicillin-resistant Staphylococcus aureus.
◇ Note local prevalence of inducible clindamycin resistance.