TABLE 172-3 ANTIMICROBIAL THERAPY FOR STAPHYLOCOCCAL INFECTIONS[a]

Sensitivity/Resistance of Isolate	Drug of Choice	Alternative(s)	Comments
Parenteral Therapy for Serious Infections			
Sensitive to penicillin	Penicillin G (4 mU q4h)	Nafcillin or oxacillin (2 g q4h), cefazolin (2 g q8h), vancomycin (1 g q12h[b])	Fewer than 5% of isolates are sensitive to penicillin. The clinical microbiology laboratory must verify that the strain is not a β-lactamase producer.
Sensitive to methicillin	Nafcillin or oxacillin (2 g q4h)	Cefazolin (2 g q8h), vancomycin (15–20 mg/kg q8–12h[b])	Patients with penicillin allergy can be treated with a cephalosporin if the allergy does not involve an anaphylactic or accelerated reaction; desensitization to β-lactams may be indicated in selected cases of serious infection when maximal bactericidal activity is needed (e.g., prosthetic-valve endocarditis[c]). Type A β-lactamase may rapidly hydrolyze cefazolin and reduce its efficacy in endocarditis. Vancomycin is a less effective option.
Resistant to methicillin	Vancomycin (15–20 mg/kg q8–12h[b]), daptomycin (6 mg/kg IV q24h[b,d]) for bacteremia, endocarditis, and complicated skin infections	Linezolid (600 mg q12h PO or IV), ceftaroline (600 mg IV q12h)	Sensitivity testing is necessary before an alternative drug is selected. For some serious infections, higher doses of daptomycin have been used. Quinupristin/dalfopristin is bactericidal against methicillin-resistant isolates unless the strain is resistant to erythromycin or clindamycin. The efficacy of adjunctive therapy is not well established in many settings. Both linezolid and quinupristin/dalfopristin have had in vitro activity against most VISA and VRSA strains. See footnote for treatment of prosthetic-valve endocarditis.[c]
Resistant to methicillin with intermediate or complete resistance to vancomycin[e]	Daptomycin (6 mg/kg q24h[b,d]) for bacteremia, endocarditis, and complicated skin infections	Same as for methicillin-resistant strains; check antibiotic susceptibilities *or* Ceftaroline (600 mg IV q12h) Newer agents include tedizolid (200 mg administered once daily either IV or orally) or dalbavancin (two IV doses: 1000 mg followed in 1 week by 500 mg). Both drugs are approved only for the treatment of skin and soft tissue infections.	Same as for methicillin-resistant strains; check antibiotic susceptibilities. Ceftaroline is used either alone or in combination with daptomycin.
Not yet known (i.e., empirical therapy)	Vancomycin (15–20 mg/kg q8–12h[b]), daptomycin (6 mg/kg q24h[b,d]) for bacteremia, endocarditis, and complicated skin infections	—	Empirical therapy is given when the susceptibility of the isolate is not known. Vancomycin is recommended for suspected community- or hospital-acquired *Staphylococcus aureus* infections because of the increased frequency of methicillin-resistant strains in the community.
Oral Therapy for Skin and Soft Tissue Infections			
Sensitive to methicillin	Dicloxacillin (500 mg qid), cephalexin (500 mg qid)	Minocycline or doxycycline (100 mg q12h[b]), TMP-SMX (1 or 2 ds tablets bid), clindamycin (300–450 mg/kg tid), linezolid (600 mg PO q12h), tedizolid (200 mg PO q24h)	It is important to know the antibiotic susceptibility of isolates in the specific geographic region. All drainage should be cultured.
Resistant to methicillin	Clindamycin (300–450 mg/kg tid), TMP-SMX (1 or 2 ds tablets bid), minocycline or doxycycline (100 mg q12h[b]), linezolid (600 mg bid) or tedizolid (200 mg once daily)	Same options as under "Drug of Choice"	It is important to know the antibiotic susceptibility of isolates in the specific geographic region. All drainage should be cultured.

[a]Recommended dosages are for adults with normal renal and hepatic function. [b]The dosage must be adjusted for patients with reduced creatinine clearance. [c]For the treatment of prosthetic-valve endocarditis, the addition of gentamicin (1 mg/kg q8h) and rifampin (300 mg PO q8h) is recommended, with adjustment of the gentamicin dosage if the creatinine clearance rate is reduced. [d]Daptomycin cannot be used for the treatment of pneumonia. [e]Vancomycin-resistant *S. aureus* isolates from clinical infections have been reported.

Abbreviations: ds, double-strength; TMP-SMX, trimethoprim-sulfamethoxazole; VISA, vancomycin-intermediate *S. aureus;* VRSA, vancomycin-resistant *S. aureus.*

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Although the quinolones are active against staphylococci in vitro, the frequency of staphylococcal resistance to these agents has increased progressively, especially among methicillin-resistant isolates. Of particular concern in MRSA is the possible emergence of quinolone resistance during therapy. Therefore, quinolones are not recommended for the treatment of MRSA infections. Resistance to the quinolones is most commonly chromosomal and results from mutations of the topoisomerase IV or DNA gyrase genes, although multidrug efflux pumps may also contribute. Although the newer quinolones exhibit increased in vitro activity against staphylococci, it is uncertain whether this increase translates into enhanced in vivo activity.

Tigecycline, a broad-spectrum minocycline analogue, has bacteriostatic activity against MRSA and is approved for use in skin and soft tissue infections as well as intraabdominal infections caused by *S. aureus*. Other antibiotics, such as minocycline and trimethoprim-sulfamethoxazole, have been used successfully to treat MRSA infections in cases of vancomycin toxicity or intolerance.

Combinations of antistaphylococcal agents have been used to enhance bactericidal activity in the treatment of serious infections such as endocarditis or osteomyelitis. In selected instances (e.g., right-sided endocarditis), drug combinations are also used to shorten the duration of therapy. Among the antimicrobial agents