**TABLE 155-4 ANTIBIOTIC TREATMENT FOR INFECTIVE ENDOCARDITIS CAUSED BY COMMON ORGANISMS[a] (*CONTINUED*)**

| Organism | Drug (Dose, Duration) | Comments |
|---|---|---|
| ***Coxiella burnetii*** | | |
| | • Doxycycline (100 mg PO q12h) *plus* hydroxychloroquine (200 mg PO q8h), both for 18 (native valve) or 24 (prosthetic valve) months | Follow serology to monitor response during treatment (antiphase I IgG and IgA decreased 4-fold and IgM antiphase II negative) and thereafter for relapse. |
| ***Bartonella* spp.** | | |
| | • Ceftriaxone (2 g IV q24h) *or* ampicillin (2 g IV q4h) *or* doxycycline (100 mg q12h PO) for 6 weeks<br>***plus***<br>Gentamicin (1 mg/kg IV q8h for 3 weeks) | If patient is highly allergic to β-lactams, use doxycycline. |

[a]Doses are for adults with normal renal function. Doses of gentamicin, streptomycin, and vancomycin must be adjusted for reduced renal function. Ideal body weight is used to calculate doses of gentamicin and streptomycin per kilogram (men = 50 kg + 2.3 kg per inch over 5 feet; women = 45.5 kg + 2.3 kg per inch over 5 feet). [b]MIC, ≤0.1 μg/mL. [c]Vancomycin dose is based on actual body weight. Adjust for trough level of 10–15 μg/mL for streptococcal and enterococcal infections and 15–20 μg/mL for staphylococcal infections. [d]Aminoglycosides should not be administered as single daily doses for enterococcal endocarditis and should be introduced as part of the initial treatment. Target peak and trough serum concentrations of divided-dose gentamicin 1 h after a 20- to 30-min infusion or IM injection are ~3.5 μg/mL and ≤1 μg/mL, respectively; target peak and trough serum concentrations of streptomycin (timing as with gentamicin) are 20–35 μg/mL and <10 μg/mL, respectively. [e]Netilmicin (4 mg/kg qd, as a single dose) can be used in lieu of gentamicin. [f]MIC, >0.1 μg/mL and <0.5 μg/mL. [g]MIC, ≥0.5 μg/mL and <8 μg/mL. [h]Antimicrobial susceptibility must be evaluated; see text. [i]Rifampin increases warfarin and dicumarol requirements for anticoagulation.

***Abbreviations:*** MIC, minimal inhibitory concentration; MRSA, methicillin-resistant *S. aureus*; MSSA, methicillin-sensitive *S. aureus*.

of nephrotoxicity with ampicillin-ceftriaxone therapy, this regimen may also be preferred in patients who are at increased risk for aminoglycoside nephrotoxicity.

If the enterococcal isolate is resistant to all of the commonly used agents, suppression of bacteremia followed by surgical treatment should be considered. The role of newer agents potentially active against multidrug-resistant enterococci (quinupristin/dalfopristin [*E. faecium* only], linezolid, and daptomycin) in the treatment of endocarditis has not been established.

***STAPHYLOCOCCI*** The regimens used to treat staphylococcal endocarditis (Table 155-4) are based not on coagulase production but rather on the presence or absence of a prosthetic valve or foreign device, the native valve(s) involved, and the susceptibility of the isolate to penicillin, methicillin, and vancomycin. All staphylococci are considered penicillin-resistant until shown not to produce penicillinase. Similarly, methicillin resistance has become so prevalent among staphylococci that empirical therapy should be initiated with a regimen that covers methicillin-resistant organisms and should later be revised if the isolate proves to be susceptible to methicillin. The addition of 3–5 days of gentamicin to a β-lactam antibiotic or vancomycin to enhance therapy for native mitral or aortic valve endocarditis has not improved survival rates and may be associated with nephrotoxicity. Neither this addition nor the addition of fusidic acid or rifampin is recommended.

For treatment of endocarditis caused by *methicillin-resistant S. aureus* (MRSA), vancomycin, dosed to achieve trough concentrations of 15–20 μg/mL, is recommended, with the caveat that this regimen may be associated with nephrotoxicity. Although resistance to vancomycin among staphylococci is rare, reduced vancomycin susceptibility among MRSA strains is increasingly encountered. Isolates with a vancomycin MIC of 4–16 μg/mL have intermediate susceptibility and are referred to as *vancomycin-intermediate S. aureus* (VISA). Isolates with an MIC of 2 μg/mL may harbor subpopulations with higher MICs. These *heteroresistant VISA* (hVISA) isolates are not detectable by routine susceptibility testing. Because of the pharmacokinetics/pharmacodynamics of vancomycin, killing of MRSA with a vancomycin MIC of >1.0 μg/mL is unpredictable, even with aggressive vancomycin dosing. Although not approved by the U.S. Food and Drug Administration for this indication, daptomycin (6 mg/kg [or, as some experts prefer, 8–10 mg/kg] IV once daily) has been recommended as an alternative to vancomycin, particularly for left-sided endocarditis caused by VISA, hVISA, or isolates with a vancomycin MIC of >1.0 μg/mL. These isolates should be tested to document daptomycin susceptibility. Daptomycin activity against MRSA—even against some isolates with reduced daptomycin susceptibility—is enhanced by the addition of nafcillin or ceftaroline. Case reports suggest that either the latter combinations or ceftaroline alone (600 mg IV q8h) may be effective in recalcitrant MRSA endocarditis. Nevertheless, a discussion of treatment of endocarditis in which MRSA bacteremia persists despite therapy is beyond the scope of this chapter and requires consultation with an infectious disease specialist. The efficacy of linezolid for left-sided MRSA endocarditis has not been established. Although not widely adopted by other groups, the recommendation of the British Society for Antimicrobial Chemotherapy is that a second drug be added to vancomycin (rifampin) or to daptomycin (rifampin, gentamicin, or linezolid) for the treatment of NVE due to MRSA.

Methicillin-susceptible *S. aureus* endocarditis that is uncomplicated and limited to the tricuspid or pulmonic valve can often be treated with a 2-week course that combines oxacillin or nafcillin (but not vancomycin) with gentamicin. However, patients with prolonged fever (≥5 days) during therapy or multiple septic pulmonary emboli should receive standard-duration therapy. Vancomycin plus gentamicin for 2 weeks as treatment for right-sided endocarditis caused by MRSA yields suboptimal results; thus this entity is treated for 4 weeks with vancomycin or daptomycin (6 mg/kg as a single daily dose).

Staphylococcal PVE is treated for 6–8 weeks with a multidrug regimen. Rifampin is an essential component because it kills staphylococci that are adherent to foreign material in a biofilm. Two other agents (selected on the basis of susceptibility testing) are combined with rifampin to prevent in vivo emergence of resistance. Because many staphylococci (particularly MRSA and *Staphylococcus epidermidis*) are resistant to gentamicin, the isolate's susceptibility to gentamicin or an alternative agent should be established before rifampin treatment is begun. If the isolate is resistant to gentamicin, then another aminoglycoside, a fluoroquinolone (chosen on the basis of susceptibility), or another active agent should be substituted for gentamicin.

***OTHER ORGANISMS*** In the absence of meningitis, endocarditis caused by *Streptococcus pneumoniae* isolates with a penicillin MIC of ≤1 μg/mL can be treated with IV penicillin (4 million units every 4 h), ceftriaxone (2 g/d as a single dose), or cefotaxime (at a comparable dosage). Infection caused by pneumococcal strains with a penicillin MIC of ≥2 μg/mL should be treated with vancomycin. If meningitis is suspected or present, treatment with vancomycin plus ceftriaxone—at the doses advised for meningitis—should be initiated until susceptibility results are known. Definitive therapy should then be selected on the basis of meningitis breakpoints (penicillin MIC, 0.06 μg/mL; or ceftriaxone MIC, 0.5 μg/mL). *P. aeruginosa* endocarditis is treated with an antipseudomonal penicillin (ticarcillin or piperacillin) and high doses of tobramycin (8 mg/kg per day in three divided doses). Endocarditis caused by Enterobacteriaceae is treated with a potent β-lactam antibiotic plus an aminoglycoside. Corynebacterial