endocarditis is treated with a penicillin plus an aminoglycoside (if the organism is susceptible to the aminoglycoside) or with vancomycin, which is highly bactericidal for most strains. Therapy for *Candida* endocarditis consists of amphotericin B plus flucytosine and early surgery; long-term (if not indefinite) suppression with an oral azole is advised. Echinocandin treatment of *Candida* endocarditis has been effective in sporadic cases; nevertheless, the role of echinocandins in this setting has not been established.

Empirical Therapy In designing therapy (largely with antimicrobials and doses from Table 155-4 to target putative microorganisms) to be administered before culture results are known or when cultures are negative, clinical clues (e.g., acute vs. subacute presentation, site of infection, patient's predispositions) as well as epidemiologic clues to etiology must be considered. Thus empirical therapy for acute endocarditis in an injection drug user should cover MRSA and gram-negative bacilli. Treatment with vancomycin plus gentamicin, initiated immediately after blood samples are obtained for culture, covers these organisms as well as many other potential causes. Similarly, treatment of health care–associated endocarditis must cover MRSA. In the treatment of culture-negative episodes, marantic endocarditis must be excluded and fastidious organisms sought by serologic testing. In the absence of prior antibiotic therapy, it is unlikely that *S. aureus*, CoNS, or enterococcal infection will present with negative blood cultures; thus, in this situation, recommended empirical therapy targets not these organisms but rather nutritionally variant organisms, the HACEK group, and *Bartonella* species. Pending the availability of diagnostic data, blood culture–negative subacute NVE is treated with gentamicin plus ampicillin-sulbactam (12 g every 24 h) or ceftriaxone; doxycycline (100 mg twice daily) is added for enhanced *Bartonella* coverage. For culture-negative PVE, vancomycin, gentamicin, cefepime, and rifampin should be used if the prosthetic valve has been in place for ≤1 year. Empirical therapy for infected prosthetic valves in place for >1 year is similar to that for culture-negative NVE. If cultures may be negative because of confounding by prior antibiotic administration, broader empirical therapy may be indicated, with particular attention to pathogens that are likely to be inhibited by the specific prior therapy.

CIED Endocarditis Antimicrobial therapy for CIED endocarditis is adjunctive to complete device removal. The antimicrobial selected is based on the causative organism and should be used as recommended for NVE (Table 155-4). Bacteremic CIED infection may be complicated by coincident NVE or remote-site infection (e.g., osteomyelitis). A 4- to 6-week course of endocarditis-targeted therapy is recommended for patients with CIED endocarditis and for those with bacteremia that continues during ongoing antimicrobial therapy after device removal. Although *S. aureus* bacteremia (and persistent CoNS bacteremia) in patients who have a CIED in place is likely—in the absence of another source—to reflect endocarditis and should be managed accordingly, not all bloodstream infections in these patients indicate endocarditis. If evidence suggesting endocarditis is lacking, bloodstream infection due to gram-negative bacilli, streptococci, enterococci, and *Candida* species may not indicate device infection. However, in the absence of another source, relapse after antimicrobial therapy increases the likelihood of CIED endocarditis and warrants treatment as such.

Outpatient Antimicrobial Therapy Fully compliant, clinically stable patients who are no longer bacteremic, are not febrile, and have no clinical or echocardiographic findings that suggest an impending complication may complete therapy as outpatients. Careful follow-up and a stable home setting are necessary, as are predictable IV access and use of antimicrobial agents that are stable in solution. Recommended regimens should not be compromised to accommodate outpatient therapy.

Monitoring Antimicrobial Therapy Measurement of the serum bactericidal titer—the highest dilution of the patient's serum during therapy that kills 99.9% of the standard inoculum of the infecting organism—is not recommended for assessment of standard regimens but may be useful for assessment of the treatment of endocarditis caused by unusual organisms. Serum concentrations of aminoglycosides and vancomycin should be monitored and doses adjusted to avoid or address toxicity.

Antibiotic toxicities, including allergic reactions, occur in 25–40% of patients and commonly arise after several weeks of therapy. Blood tests to detect renal, hepatic, and hematologic toxicity should be performed periodically.

Blood cultures should be repeated daily until sterile in patients with endocarditis due to *S. aureus* or difficult-to-treat organisms, rechecked if there is recrudescent fever, and performed again 4–6 weeks after therapy to document cure. Blood cultures become sterile within 2 days after the start of appropriate therapy when infection is caused by viridans streptococci, enterococci, or HACEK organisms. In *S. aureus* endocarditis, β-lactam therapy results in sterile cultures in 3–5 days, whereas in MRSA endocarditis, positive cultures may persist for 7–9 days with vancomycin or daptomycin treatment. MRSA bacteremia persisting despite an adequate dosage of vancomycin may indicate infection due to a strain with reduced vancomycin susceptibility and therefore may point to a need for alternative therapy. When fever persists for 7 days despite appropriate antibiotic therapy, patients should be evaluated for paravalvular abscess, extracardiac abscesses (spleen, kidney), or complications (embolic events). Recrudescent fever raises the possibility of these complications but also of drug reactions or complications of hospitalization. Vegetations become smaller with effective therapy; however, 3 months after cure, 50% are unchanged and 25% are slightly larger.

SURGICAL TREATMENT

Intracardiac and central nervous system complications are important causes of morbidity and death due to infective endocarditis. In some cases, effective treatment for these complications requires surgery. The indications for cardiac surgical treatment of endocarditis **(Table 155-5)** have been derived from observational studies and expert opinion. The strength of individual indications varies; thus the risks and benefits as well as the timing of surgery must be individualized **(Table 155-6)**. From 25% to 40% of patients with left-sided endocarditis undergo cardiac surgery during active infection, with slightly higher surgery rates for PVE than NVE. Intracardiac complications (which are most reliably detected by TEE) and CHF are the most commonly cited indications for surgery. The benefit of surgery has been assessed primarily in studies comparing populations of medically and surgically treated patients matched for the necessity of

TABLE 155-5 INDICATIONS FOR CARDIAC SURGICAL INTERVENTION IN PATIENTS WITH ENDOCARDITIS

Surgery Required for Optimal Outcome
Moderate to severe congestive heart failure due to valve dysfunction
Partially dehisced unstable prosthetic valve
Persistent bacteremia despite optimal antimicrobial therapy
Lack of effective microbicidal therapy (e.g., fungal or *Brucella* endocarditis)
S. aureus prosthetic valve endocarditis with an intracardiac complication
Relapse of prosthetic valve endocarditis after optimal antimicrobial therapy
Surgery to Be Strongly Considered for Improved Outcome[a]
Perivalvular extension of infection
Poorly responsive *S. aureus* endocarditis involving the aortic or mitral valve
Large (>10 mm in diameter) hypermobile vegetations with increased risk of embolism, particularly with prior embolic event or with significant valve dysfunction
Persistent unexplained fever (≥10 days) in culture-negative native valve endocarditis
Poorly responsive or relapsed endocarditis due to highly antibiotic-resistant enterococci or gram-negative bacilli

[a]Surgery must be carefully considered; findings are often combined with other indications to prompt surgery.