Other neurologic complications include aseptic or purulent meningitis, intracranial hemorrhage due to hemorrhagic infarcts or ruptured mycotic aneurysms, and seizures. (*Mycotic aneurysms* are focal dilations of arteries occurring at points in the artery wall that have been weakened by infection in the vasa vasorum or where septic emboli have lodged.) Microabscesses in brain and meninges occur commonly in *S. aureus* endocarditis; surgically drainable intracerebral abscesses are infrequent.

Immune complex deposition on the glomerular basement membrane causes diffuse hypocomplementemic glomerulonephritis and renal dysfunction, which typically improve with effective antimicrobial therapy. Embolic renal infarcts cause flank pain and hematuria but rarely cause renal dysfunction.

Manifestations of Specific Predisposing Conditions Almost 50% of endocarditis associated with injection drug use is limited to the tricuspid valve and presents with fever but with faint or no murmur and no peripheral manifestations. Septic pulmonary emboli, which are common with tricuspid endocarditis, cause cough, pleuritic chest pain, nodular pulmonary infiltrates, or occasionally pyopneumothorax. Infection of the aortic or mitral valves presents with the typical clinical features of endocarditis, including peripheral manifestations.

If not associated with a retained intracardiac device or masked by the symptoms of concurrent comorbid illness, health care–associated endocarditis has typical manifestations. CIED endocarditis may be associated with obvious or cryptic generator pocket infection and results in fever, minimal murmur, and pulmonary symptoms due to septic emboli. Late-onset PVE presents with typical clinical features. In cases arising within 60 days of valve surgery (early onset), typical symptoms may be obscured by comorbidity associated with recent surgery. In both early-onset and more delayed presentations, paravalvular infection is common and often results in partial valve dehiscence, regurgitant murmurs, CHF, or disruption of the conduction system.

DIAGNOSIS

In order to avoid delayed or missed diagnosis, careful clinical, microbiologic, and echocardiographic evaluation should be pursued when febrile patients have endocarditis predispositions, cardiac or noncardiac features of endocarditis, or microbiologic findings consistent with endocarditis (e.g., a stroke or splenic infarct, multiple positive blood cultures for an endocarditis-associated organism).

The Duke Criteria The diagnosis of infective endocarditis is established with certainty only when vegetations are examined histologically and microbiologically. Nevertheless, a highly sensitive and specific diagnostic schema—known as the *modified Duke criteria*—is based on clinical, laboratory, and echocardiographic findings commonly encountered in patients with endocarditis (Table 155-3). While developed as a research tool rather than for patient management, the criteria can be a helpful diagnostic tool. If the criteria are to be maximally helpful in evaluating patients, appropriate data must be collected. Furthermore, clinical judgment must be exercised in order to use the criteria effectively. Documentation of two major criteria, of one major criterion and three minor criteria, or of five minor criteria allows a clinical diagnosis of definite endocarditis. The diagnosis of endocarditis is rejected if an alternative diagnosis is established, if symptoms resolve and do not recur with ≤4 days of antibiotic therapy, or if surgery or autopsy after ≤4 days of antimicrobial therapy yields no histologic evidence of endocarditis. Illnesses not classified as definite endocarditis or rejected as such are considered cases of possible infective endocarditis when either one major and one minor criterion or three minor criteria are fulfilled. Requiring some clinical features of endocarditis for classification as possible infective endocarditis increases the specificity of the schema without significantly reducing its sensitivity. Unless there are extenuating circumstances, patients with definite or possible endocarditis are treated as such.

The criteria emphasize bacteremia and echocardiographic findings typical of endocarditis. The requirement for multiple positive blood cultures over time is consistent with the continuous low-density bacteremia characteristic of endocarditis. Among patients with untreated endocarditis who ultimately have a positive blood culture, 95% of all blood cultures are positive. The diagnostic criteria attach significance to the species of organism isolated from blood cultures. To fulfill a major criterion, the isolation of an organism that causes both endocarditis and bacteremia in the absence of endocarditis (e.g., *S. aureus*, enterococci) must take place repeatedly (i.e., persistent bacteremia) and in the absence of a primary focus of infection. Organisms that rarely cause endocarditis but commonly contaminate blood cultures (e.g., diphtheroids, CoNS) must be isolated repeatedly if their isolation is to serve as a major criterion.

Blood Cultures Isolation of the causative microorganism from blood cultures is critical for diagnosis and for planning treatment. In patients with suspected NVE, PVE, or CIED endocarditis who have not received antibiotics during the prior 2 weeks, three 2-bottle blood

TABLE 155-3 THE MODIFIED DUKE CRITERIA FOR THE CLINICAL DIAGNOSIS OF INFECTIVE ENDOCARDITIS[a]

Major Criteria

1. Positive blood culture
   - Typical microorganism for infective endocarditis from two separate blood cultures
     - Viridans streptococci, *Streptococcus gallolyticus*, HACEK group organisms, *Staphylococcus aureus*, *or*
     - Community-acquired enterococci in the absence of a primary focus,
     - ***or***
   - Persistently positive blood culture, defined as recovery of a microorganism consistent with infective endocarditis from:
     - Blood cultures drawn >12 h apart; *or*
     - All of 3 or a majority of ≥4 separate blood cultures, with first and last drawn at least 1 h apart
     - ***or***
   - Single positive blood culture for *Coxiella burnetii* or phase I IgG antibody titer of >1:800
2. Evidence of endocardial involvement
   - Positive echocardiogram[b]
     - Oscillating intracardiac mass on valve or supporting structures or in the path of regurgitant jets or in implanted material, in the absence of an alternative anatomic explanation, *or*
     - Abscess, *or*
     - New partial dehiscence of prosthetic valve,
     - ***or***
   - New valvular regurgitation (increase or change in preexisting murmur not sufficient)

Minor Criteria

1. Predisposition: predisposing heart conditions[c] or injection drug use
2. Fever ≥38.0°C (≥100.4°F)
3. Vascular phenomena: major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, Janeway lesions
4. Immunologic phenomena: glomerulonephritis, Osler's nodes, Roth's spots, rheumatoid factor
5. Microbiologic evidence: positive blood culture but not meeting major criterion, as noted previously,[d] *or* serologic evidence of active infection with an organism consistent with infective endocarditis

[a]Definite endocarditis is defined by documentation of two major criteria, of one major criterion and three minor criteria, or of five minor criteria. See text for further details. [b]Transesophageal echocardiography is required for optimal assessment of possible prosthetic valve endocarditis or complicated endocarditis. [c]Valvular disease with stenosis or regurgitation, presence of a prosthetic valve, congenital heart disease including corrected or partially corrected conditions (except isolated atrial septal defect, repaired ventricular septal defect, or closed patent ductus arteriosus), prior endocarditis, or hypertrophic cardiomyopathy. [d]Excluding single positive cultures for coagulase-negative staphylococci and diphtheroids, which are common culture contaminants, or for organisms that do not cause endocarditis frequently, such as gram-negative bacilli.

Source: Adapted from JS Li et al: Clin Infect Dis 30:633, 2000. With permission from Oxford University Press.