culture sets, separated from one another by at least 2 h, should be obtained from different venipuncture sites over 24 h. If the cultures remain negative after 48–72 h, two or three additional blood culture sets should be obtained, and the laboratory should be consulted for advice regarding optimal culture techniques. Pending culture results, empirical antimicrobial therapy should be withheld initially from hemodynamically stable patients with suspected subacute endocarditis, especially those who have received antibiotics within the preceding 2 weeks. Thus, if necessary, additional blood culture sets can be obtained without the confounding effect of empirical treatment. Patients with acute endocarditis or with deteriorating hemodynamics who may require urgent surgery should receive empirical treatment immediately after three sets of blood cultures are obtained over several hours.

Non-Blood-Culture Tests Serologic tests can be used to implicate organisms that are difficult to recover by blood culture: *Brucella*, *Bartonella*, *Legionella*, *Chlamydia psittaci*, and *C. burnetii*. Pathogens can also be identified in vegetations by culture, microscopic examination with special stains (i.e., the periodic acid–Schiff stain for *T. whipplei*), or direct fluorescence antibody techniques and by the use of polymerase chain reaction to recover unique microbial DNA or DNA encoding the 16S or 28S ribosomal unit (16S rRNA or 28S rRNA); sequencing of these DNAs allows identification of bacteria and fungi, respectively.

Echocardiography Echocardiography anatomically confirms and measures vegetations, detects intracardiac complications, and assesses cardiac function (Fig. 155-3). Transthoracic echocardiography (TTE) is noninvasive and exceptionally specific; however, it cannot image vegetations <2 mm in diameter, and in 20% of patients it is technically inadequate because of emphysema or body habitus. TTE detects vegetations in 65–80% of patients with definite clinical endocarditis but is not optimal for evaluating prosthetic valves or detecting intracardiac complications. TEE is safe and detects vegetations in >90% of patients with definite endocarditis; nevertheless, initial studies may yield false-negative results in 6–18% of endocarditis patients. When endocarditis is likely, a negative TEE result does not exclude the diagnosis but rather warrants repetition of the study once or twice in 7–10 days. TEE is the optimal method for the diagnosis of PVE, the detection of myocardial abscess, valve perforation, or intracardiac fistulae and for the detection of vegetations in patients with CIED. In patients with CIED and negative blood cultures, a mass adherent to the lead is likely to be a bland thrombosis rather than an infected vegetation.

Because *S. aureus* bacteremia is associated with a high prevalence of endocarditis, routine echocardiographic evaluation (TTE or preferably TEE) is recommended in these patients. Patients with nosocomial *S. aureus* bacteremia are at increased risk of endocarditis if one or more of the following are present: positive blood cultures for 2–4 days, hemodialysis dependency, a permanent intracardiac device, spine infection, nonvertebral osteomyelitis, or an endocarditis-predisposing valve abnormality. Ideally, these patients should be evaluated with TEE. In patients with none of these findings, the risk of endocarditis is low and evaluation with TTE may suffice.

Experts favor echocardiographic evaluation of all patients with a clinical diagnosis of endocarditis; however, the test should not be used to screen patients with a low probability of endocarditis (e.g., patients with unexplained fever). An American Heart Association approach to the use of echocardiography for evaluation of patients with suspected endocarditis is illustrated in (Fig. 155-4).

Other Studies Many studies that are not diagnostic—i.e., complete blood count, creatinine determination, liver function tests, chest radiography, and electrocardiography—are important in the management of patients with endocarditis. The erythrocyte sedimentation rate, C-reactive protein level, and circulating immune complex titer are commonly increased in endocarditis (Table 155-2). Cardiac catheterization is useful primarily to assess coronary artery patency in older individuals who are to undergo surgery for endocarditis.

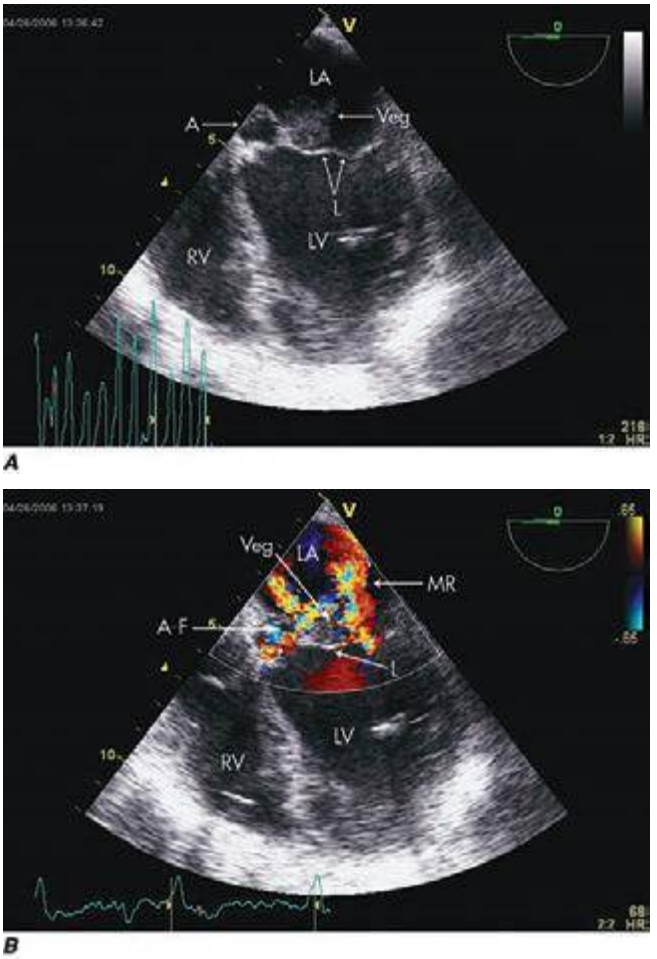

FIGURE 155-3 Imaging of a mitral valve infected with *Staphylococcus aureus* by low-esophageal, four-chamber-view, transesophageal echocardiography (TEE). *A.* Two-dimensional echocardiogram showing a large vegetation with an adjacent echolucent abscess cavity. ***B.*** Color-flow Doppler image showing severe mitral regurgitation through both the abscess-fistula and the central valve orifice. A, abscess; A-F, abscess-fistula; L, valve leaflets; LA, left atrium; LV, left ventricle; MR, mitral central valve regurgitation; RV, right ventricle; veg, vegetation. *(With permission of Andrew Burger, MD.)*

TREATMENT INFECTIVE ENDOCARDITIS

ANTIMICROBIAL THERAPY

To cure endocarditis, all bacteria in the vegetation must be killed. However, it is difficult to eradicate these bacteria because local host defenses are deficient and because the bacteria are largely nongrowing and metabolically inactive and thus are less easily killed by antibiotics. Accordingly, therapy must be bactericidal and prolonged. Antibiotics are generally given parenterally to achieve serum concentrations that, through passive diffusion, result in effective concentrations in the depths of the vegetation. To select effective therapy requires knowledge of the susceptibility of the causative microorganisms. The decision to initiate treatment empirically must balance the need to establish a microbiologic diagnosis against the potential progression of disease or the need for urgent surgery (see "Blood Cultures," earlier). Simultaneous infection at other sites (such as the meninges), allergies, end-organ dysfunction, interactions with concomitantly administered medications, and risks of adverse events must be considered in the selection of therapy.

Although given for several weeks longer, the regimens recommended for the treatment of PVE (except that caused by staphylococci) are similar to those used to treat NVE (Table 155-4). Recommended doses and durations of therapy should be followed