

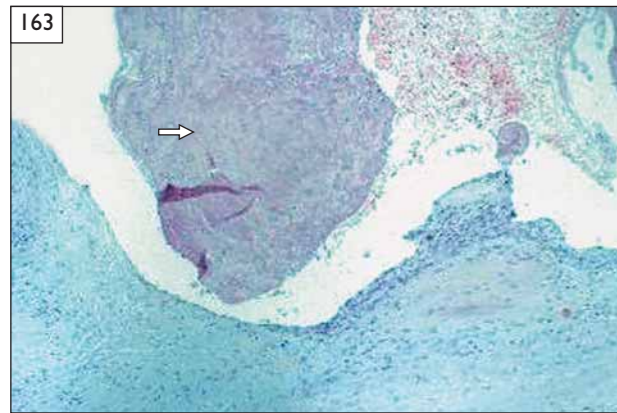
Pathophysiology

Endocarditis generally begins with damage to the endothelial lining of the heart, most commonly the valves, but any endothelial surface may be involved. Jets of abnormal blood flow are usually responsible for the endothelial damage, but any intravascular trauma may initiate the process. The combination of endothelial disruption and a hypercoagulable state produces foci of platelet and fibrin deposition. These foci constitute nonbacterial thrombotic endocarditis and serve as the milieu for bacterial attachment and proliferation (163).

The mitral valve, followed by the aortic valve, is most commonly affected. Characteristically, vegetations form on the downstream side of regurgitant

flow (i.e. the atrial surface of mitral valves and the ventricular surface of aortic valves) (Patel and Steckelberg, 2000). Bacteria vary in their ability to attach and resist host defenses which explains, in part, the prevalence of the specific organisms mentioned earlier.

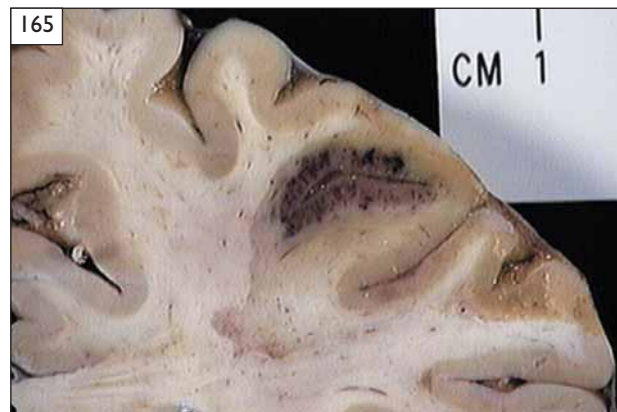
This seemingly superficial infection causes severe morbidity and mortality by several mechanisms including valve regurgitation via local tissue destruction (164), malfunction of prosthetic valves, elaboration of cytokines by activated leukocytes, embolic infarcts (165), hematogenous spread to distant organs via continuous bacteremia (166), and remote tissue damage from immune complex deposition (Karchmer, 2001).



163 Microscopic view of a murant endocarditis lesion (arrow). Note the absence of bacteria and inflammatory cells. This consists primarily of thrombin and fibrin. (Courtesy of Nora Ratcliff, MD.)



164 Gross pathology specimen of a large vegetation attached to an aortic cusp (arrow). (Courtesy of Tom Farrell, MD.)



165 Right frontal cerebral infarct that occurred in the context of nonbacterial thrombotic endocarditis and likely represents an embolic phenomenon. (Courtesy of Tom Farrell, MD.)

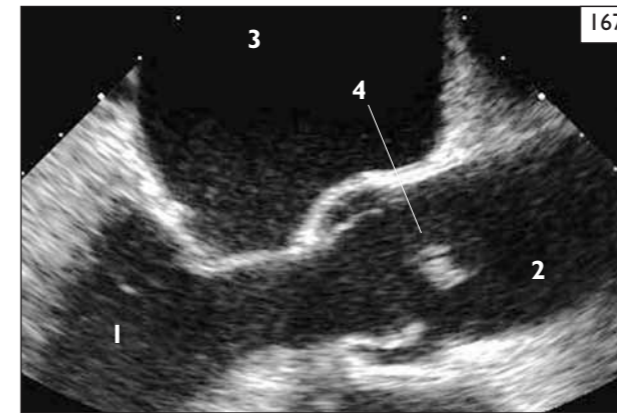


166 Close up view of an embolic splenic abscess in a patient who died of *Staphylococcus aureus* endocarditis. (Courtesy of Tom Farrell, MD.)

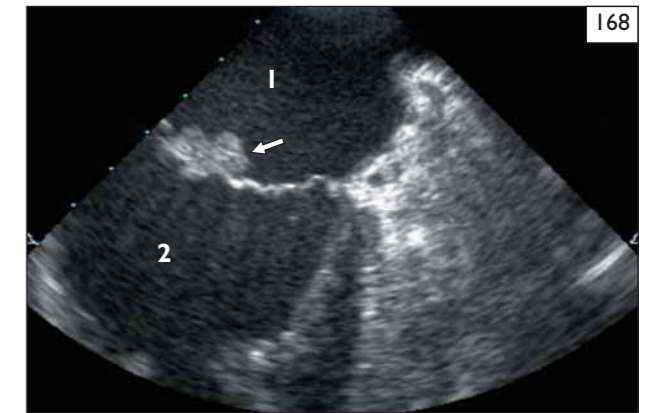
Clinical presentation

As one might expect from the variety of pathologic mechanisms, the clinical manifestations are diverse. They often include systemic symptoms (chills, sweats, anorexia, malaise, confusion) coupled with physical exam findings of fever and embolic phenomena (neurologic deficits, Roth's spots, Osler's nodes, petechiae, and Janeway lesions). A new or changing murmur is present in only 10–40% of patients. Splenomegaly and glomerulonephritis suggest immune complex disease.

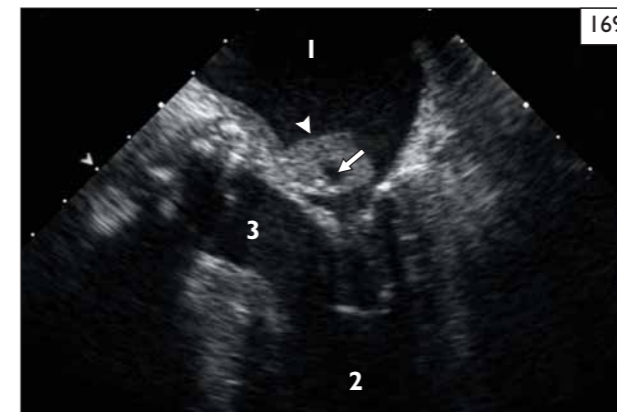
Aerobic and anaerobic culture of three to six sets of blood specimens, each obtained 1 hour or more apart, is the most valuable diagnostic test. However, they may be negative in partially treated or culture-negative endocarditis. Transesophageal echocardiography (TEE) may confirm the diagnosis by demonstrating vegetations but cannot exclude the diagnosis (167–170). Care must be taken not to



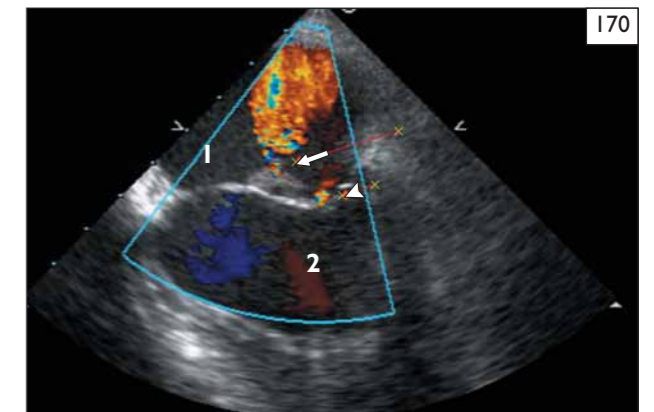
167 Transesophageal view of a large vegetation attached to the undersurface of one of the aortic cusps. During diastole, the vegetation swung into the left ventricular outflow tract (1). 2: aorta; 3: left atrium; 4: vegetation. (Courtesy of Tim A. Beaver, MD.)



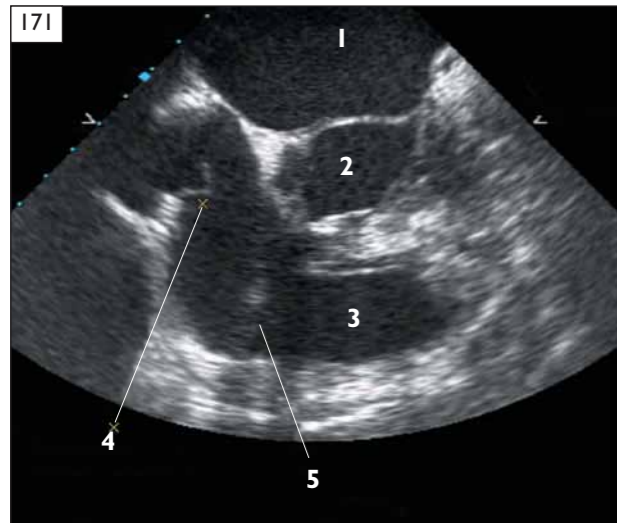
168 Magnified echocardiography view of a large vegetation with a central echolucency consistent with abscess adherent to the atrial surface of the anterior mitral valve leaflet (arrow). 1: left atrium; 2: left ventricle.



169, 170 Mitral valve vegetation. **169** 2D transesophageal view of a large vegetation adherent to the mid portion of the anterior mitral leaflet (the A₂ segment). **170** Doppler color flow display suggesting the presence of a leaflet perforation. Note the flow through the perforation diverging above the vegetation (arrow) and the smaller jet of regurgitant flow through the leaflet coaptation site (arrowhead). 1: left atrium; 2: left ventricle; 3: left ventricle outflow.



mistake normal anatomic variations (e.g. Eustachian valves, nodules of Arantius, Lambl's excrescences) with vegetations (171). Both Von Reyn *et al.* (1981) and the Duke Endocarditis Service (Durack *et al.*, 1994) have published diagnostic criteria for IE. The Duke criteria incorporate echocardiographic findings (Table 24).



171 A transesophageal view of a prominent Eustachian valve which lies at the junction of the inferior vena cava and the right atrium. This normal structure is sometimes mistaken for a vegetation of infective endocarditis. 1: left atrium; 2: aortic valve; 3: right ventricle; 4: Eustachian valve; 5: tricuspid valve.

Medical management

Prompt treatment with appropriate IV doses of antibiotics is essential to minimizing morbidity and mortality in these patients. The choice of antimicrobial agent depends on the etiologic organism, the nature of the infected valve (prosthetic or native),

Table 24 Duke criteria for clinical diagnosis of infective endocarditis

Major criteria

Persistently positive blood cultures
 Typical organisms for endocarditis: *Streptococcus viridans*, *S. bovis*
 'HACEK' group, community-acquired *Staphylococcus aureus* or enterococci in the absence of primary focus
 Persistent bacteremia: ≥ 2 positive cultures separated by ≥ 12 hours or ≥ 3 positive cultures ≥ 1 hour apart, or 70% blood culture samples positive if ≥ 4 are drawn

Evidence of endocardial involvement

Positive echocardiogram
 Oscillating vegetation
 Abscesses
 Valve perforation
 New partial dehiscence of prosthetic valve
 New valvular regurgitation

Minor criteria

Predisposing heart condition
 Mitral valve prolapse, bicuspid aortic valve, rheumatic or congenital heart disease, intravenous drug abuse

Fever

Vascular phenomena
 Major arterial emboli, septic pulmonary emboli, mycotic aneurysm, intracranial hemorrhage, Janeway lesions

Immunologic phenomena

Glomerulonephritis, Osler's nodes, Roth spots, rheumatoid factor
 Positive blood cultures: not meeting major criteria
 Echocardiogram: positive but not meeting major criteria

Diagnosis

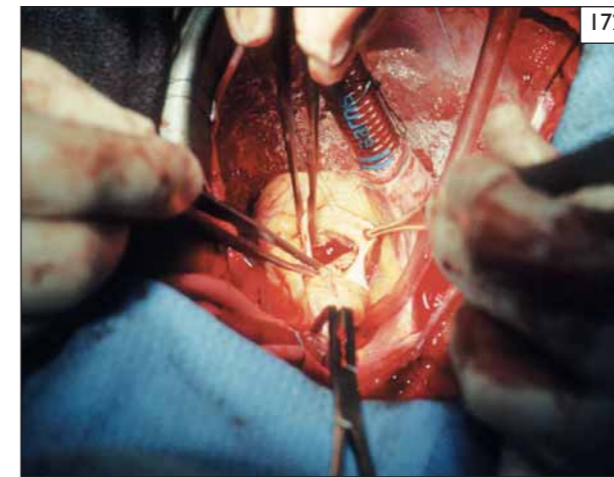
2 major criteria or
 1 major criterion plus 3 minor criteria or
 5 minor criteria

(Adapted from Bonow RO, Carabello B, de Leon AC Jr, *et al.* (1998). ACC/AHA guidelines for the management of patients with valvular heart disease. *Journal of the American College of Cardiology* 32:1486–1588.)

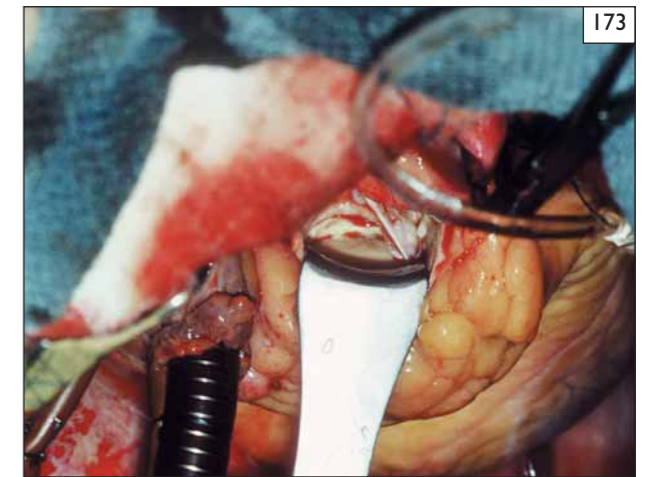
and the immune status of the patient. The recommended duration of therapy ranges from 2 to 6 or more weeks (Bonow *et al.*, 1998). Current recommendations may be obtained from the American Heart Association on their website: www.americanheart.org (accessed 11/14/04).

Surgical intervention

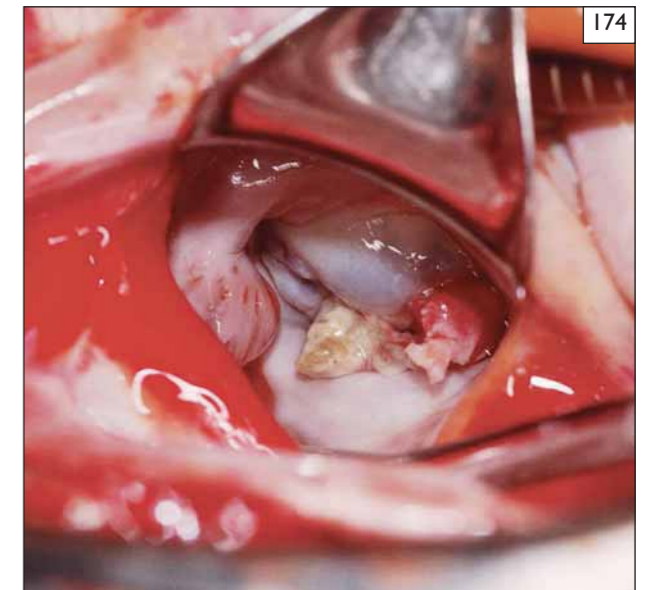
Excision of an infected valve and implantation of a prosthetic valve is recommended in the setting of severe congestive heart failure or cardiogenic shock, providing existing complications (e.g. severe central nervous system damage, multiorgan failure) do not preclude meaningful recovery (172–174). Less urgent



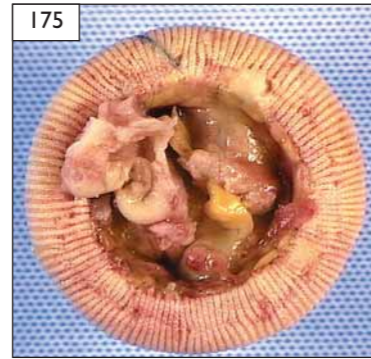
172, 173 Intraoperative view of a patient with acute bacterial endocarditis involving the aortic valve. **172** Preserved valve architecture. **173** Vegetation adherent to the ventricular surface of the valve held in forceps. (Courtesy of John Sanders, MD.)



174 Intraoperative photograph of a patient with endocarditis and vegetations adherent to the mitral valve. (Courtesy of John Sanders, MD.)



indications include perivalvular abscess, aneurysm formation, fever persisting beyond 7–10 days of appropriate antibiotics, fungal infection, prosthetic valve infection (175), and some cases of staphylococcal infection (Bonow *et al.*, 1998). The full AHA/ACC recommendations are outlined in Tables 25, 26.



175 This mitral bioprosthesis became infected and required resection. Note the prominent vegetations and the destruction of the valve leaflets. (Courtesy of Tom Farrell, MD.)

Table 25 Recommendations for surgery for native valve endocarditis*

Indication	Class
Acute AR or MR with heart failure	I
Acute AR with tachycardia and early closure of the mitral valve	I
Fungal endocarditis	I
Evidence of annular or aortic abscess, sinus, or aortic true or false aneurysm	I
Evidence of valve dysfunction and persistent infection after a prolonged period (7–10 days) of appropriate antibiotic therapy, as indicated by presence of fever, leukocytosis, and bacteremia, provided there are no noncardiac causes of infection	I
Recurrent emboli after appropriate antibiotic therapy	IIa
Infection with Gram-negative organisms or organisms with a poor response to antibiotics in patients with evidence of valve dysfunction	IIa
Mobile vegetations >10 mm	IIb
Early infections of the mitral valve that can likely be repaired	III
Persistent pyrexia and leukocytosis with negative blood cultures	III

* Criteria also apply to repaired mitral and aortic allograft or autograft valves. Endocarditis defined by clinical criteria with or without laboratory verification; there must be evidence that function of a cardiac valve is impaired. AR: aortic regurgitation; MR: mitral regurgitation. (Adapted from Bonow RO, Carabello B, de Leon AC Jr, *et al.* (1998). ACC/AHA guidelines for the management of patients with valvular heart disease. *Journal of the American College of Cardiology* 32:1486–1588.)

Case study

A 43-year-old man was brought to the emergency room for evaluation of persistent sweats, chills, weight loss, and recent onset of confusion and drowsiness. His history was provided by one of his companions. Two months prior to admission he had left for Pakistan with a sponsored team of mountaineers to attempt a new climbing route on an 8000 m peak. Approximately 3 weeks prior to admission while fixing rope above camp III at 6500 m he started having mild fever and chills. He attributed this to fatigue and the effects of altitude, but when the symptoms continued at base camp he became a bit more concerned. Not wanting to

jeopardize the expedition and his personal chance to reach the summit, he kept quiet and took ibuprofen on a scheduled basis. Despite this he became weaker and lost what little appetite he had. He gave up his rotation working high on the mountain. Several days later, a teammate discovered his sleeping bag soaked with sweat. Two fellow climbers accompanied him out of the mountains for the trek and long bus trip back to Islamabad, where he intended to fly home for medical care. He was having daily drenching sweats and had lost 9 kg (20 lb) since arriving in Pakistan. At the airport he felt somewhat short of breath at rest, but was able to board the plane without attracting attention. However, on the second

Table 26 Recommendations for surgery for prosthetic valve endocarditis*

Indication	Class
Early prosthetic valve endocarditis (first 2 months or less after surgery)	I
Heart failure with prosthetic valve dysfunction	I
Fungal endocarditis	I
Staphylococcal endocarditis not responding to antibiotic therapy	I
Evidence of paravalvular leak, annular or aortic abscess, sinus or aortic true or false aneurysm, fistula formation, or new-onset conduction disturbances	I
Infection with Gram-negative organisms or organisms with a poor response to antibiotics	I
Persistent bacteremia after a prolonged course (7–10 days) of appropriate antibiotic therapy with noncardiac causes of bacteremia	IIa
Recurrent peripheral embolus despite therapy	IIa
Vegetation of any size on or near the prosthesis	IIb

*Criteria exclude repaired mitral valves or aortic allograft or autograft valves. Endocarditis is defined by clinical criteria with or without laboratory verification. (Adapted from Bonow RO, Carabello B, de Leon AC Jr, *et al.* (1998). ACC/AHA guidelines for the management of patients with valvular heart disease. *Journal of the American College of Cardiology* 32:1486–1588.)

leg of the trip from Frankfurt to Chicago, he suffered the sudden onset of difficulty in speaking and right-sided weakness. The plane was diverted to Boston and the patient was taken from the airport to a large academic hospital.

His past history was remarkable for exceptional good health. He had never had any hospitalizations or operations. He took no medications. He was a lifelong nonsmoker and modest beer drinker (0–2 per day). His family history was unremarkable. Review of systems was remarkable for a dental abscess that had bothered him for a week about 1 month earlier. A team member had removed the tooth with multipurpose pliers he wore on his belt.

On exam he was a longhaired, unshaven, delirious man wearing dirty shorts and a T-shirt. His temperature was 39.2°C (102.5°F), blood pressure was 100/45 mmHg (13.3/6.0 kPa) in both arms, and his pulse rate was 98 bpm. He had splinter hemorrhages and Janeway lesions. His jugular venous pressure was below the level of the sternal angle and his carotid upstrokes were hyperdynamic. His chest exam revealed bibasilar crackles. His point of maximal intensity (PMI) was not displaced, but was hyperdynamic. He had no right ventricular lift. S_1 was normal, but was followed immediately by an ejection sound. S_2 was soft and there was a 2/6 decrescendo diastolic murmur heard along the left sternal border at held end-expiration while leaning forward. His spleen was enlarged. He had difficulty with word finding and mild right-sided weakness.

Urinalysis revealed red blood cell casts and bacteria. He had a leukocytosis, a normochromic, normocytic anemia, and an elevated platelet count. Three sets of blood cultures were collected 1 hour apart. An emergent computed tomography scan of the brain without contrast showed no evidence of intracranial hemorrhage. An urgent transthoracic echocardiogram revealed a hyperdynamic left ventricle with moderate aortic regurgitation (AR), and a vegetation adherent to the ventricular surface of the aortic valve.

He was admitted to the cardiac care unit and given fluids and intravenous antibiotics. The next morning a transesophageal echocardiogram confirmed the AR, the vegetation, but also revealed the presence of a complex echolucency at the base of the aortic valve, consistent with a valve abscess. Later that day the blood cultures grew *Streptococcus viridans*. After consultation with his family and friends, he was taken to the operating room and underwent resection of the aortic valve, debridement of all visible infection, and replacement with a bioprosthetic valve. Following the surgery he defervesced and his delirium cleared. Surveillance cultures grew nothing. He was discharged to a rehabilitation facility on his fourth hospital day, to complete his course of intravenous antibiotics and receive twice daily physical therapy. With this program he gained weight and strength steadily and by 2 weeks he was ambulating independently with the support of a cane. He had only mild word finding difficulties. Six months following discharge he was running 8 miles per day and was rock climbing. To his family's dismay, he was planning a winter climbing trip to Mexico.

COMMENTS

This vignette presents some of the common symptoms, findings, and natural history of infective endocarditis. Because of his remote location and disinterest in seeking prompt medical care he had developed advanced disease by the time of presentation. The presence of a valve abscess provided the indication for surgical valve replacement. The choice of a bioprosthetic valve was influenced by the patient's lifestyle that made warfarin therapy difficult, and by the notion that a bioprosthetic valve may be somewhat more resistant to infection.

References

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