33 Infective Endocarditis

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Infective endocarditis (IE) is a rare, but important diagnosis to consider in children with a predisposing cardiac lesion or history of cardiac surgery. Targeted prolonged IV antibiotics are the mainstay of therapy, with aggressive early surgery intervention being warranted in certain situations.

Pathophysiology

Turbulent blood flow from cardiac lesions results in injury to the endocardial surface and subsequent thrombus formation. The injured endocardial surface and thrombus become infected secondary to transient bacteremia, which occurs routinely in otherwise healthy children. Noncardiac complications from IE occur as a result of either embolic or immune-mediated phenomena.

Although a variety of microorganisms can cause IE, Gram-positive bacteria are by far the most common. Streptococcal species, especially Viridans-group Streptococci, are the most common bacteria identified in children with CHD. *Staphylococcus aureus* is also an important cause of IE in children with and without CHD, and frequently results in a more fulminant clinical presentation. Other organisms that cause IE include HACEK organisms (*Haemophilus* species, *Aggregatibacter* species, *Cardiobacteria hominis*, *Eikenella corrodens*, and *Kingella kingae*). More unusual pathogens include *Bartonella* species, *Coxiella burnetti*, *Brucella* species, and *Mycoplasma* species. IE can also be caused by *Candida* species, particularly in infants.

Table 33-1. Microorganisms identified in 67 children with IE at TCH, 2011-2016

Microorganism	CHD patients N=51	Non-CHD patients N=16	p-value
Staphylococci species	**9 (18%)**	**8 (50%)**	<0.01
Methicillin-resistant *S. aureus*	0	6	
Methicillin-susceptible *S. aureus*	7	1	
Coagulase-negative Staphylococcus	2	1	
Streptococci species	**28 (55%)**	**6 (38%)**	<0.05
Viridans-group Streptococci	24	2	
Gemella spp.	1	1	
Granulicatella adiacens	1	1	
Streptococcus pneumoniae	1	1	
Group A/G Streptococcus	1	1	
HACEK species	**6 (12%)**	**1 (6%)**	NS
Haemophilus spp.	3	1	
Aggregatibacter spp.	2	0	
Cardiobacteria hominis	1	0	
Other	**2 (4%)**	**1 (6%)**	NS
Neisseria gonorrhoeae	0	1	
Enterococcus faecalis	1	0	
Candida tropicalis	1	0	

Table 33-2. AHA Guidelines for the Prevention of Infective Endocarditis (Wilson et al. 2007)

Cardiac conditions warranting antibiotic prophylaxis prior to dental procedures (involving manipulation of gingival tissue or perforation of the oral mucosa) *or* surgical procedures involving infected skin or musculoskeletal tissue

- Prosthetic cardiac valve, prosthetic material used for cardiac valve repair
- Previous occurrence of IE
- Certain types of CHD
  - Unrepaired cyanotic CHD, including palliative shunts and conduits
  - Completely repaired CHD with prosthetic material or device (placed by surgery or interventional cath) during the initial 6 months postprocedure
  - Repaired CHD with residual defects at the site or adjacent to the site of a prosthetic patch or prosthetic device
- Cardiac transplantation recipients who develop cardiac valvulopathy
 	
Prophylaxis is not indicated:
- Prior to dental radiographs, routine anesthetic injections through noninfected tissue, placement or removal of orthodontic appliances, shedding of deciduous teeth, and bleeding from trauma to the lips or oral mucosa.
- Prior to genitourinary or GI tract procedures, including diagnostic endoscopy

Table 33-1 shows the microorganisms identified in our patient population based on a recent review of cases at TCH from 2011 to 2016.

Prevention

The most important step in the management of IE is prevention. For this reason, any patient with a history of CHD must adhere to vigilant dental hygiene and routine dental visits. The 2007 AHA Guidelines for the Prevention of Infective Endocarditis (Table 33-2) were designed to ensure appropriate use of antibiotic prophylaxis in certain high-risk groups while minimizing unnecessary use in those for whom the risk does not warrant prophylaxis.

Clinical Presentation and Diagnosis

The clinical presentation of IE in children with CHD is variable, and depends on a number of factors such as the microorganism involved, the degree of local cardiac disease, and whether noncardiac embolic or immune-mediated complications are present. Children with IE typically have either a subacute or acute clinical presentation.

Children with *subacute* IE can present with long-standing (weeks to months) low-grade fever and nonspecific somatic complaints including fatigue, weakness, myalgias, arthralgias, weight loss, night sweats, rigors, and exercise intolerance. Subacute IE is more likely to be associated with immune-mediated noncardiac complications, such as glomerulonephritis, Roth spots, and Osler nodes, although these findings are less common in children compared with adults. Children with Viridans-group Streptococci typically have a more subacute presentation. In addition, infections associated with the bovine jugular RV-PA valved conduits have also been described as having a more indolent, subacute presentation.

In contrast, children with *acute* IE usually have more severe symptoms and can

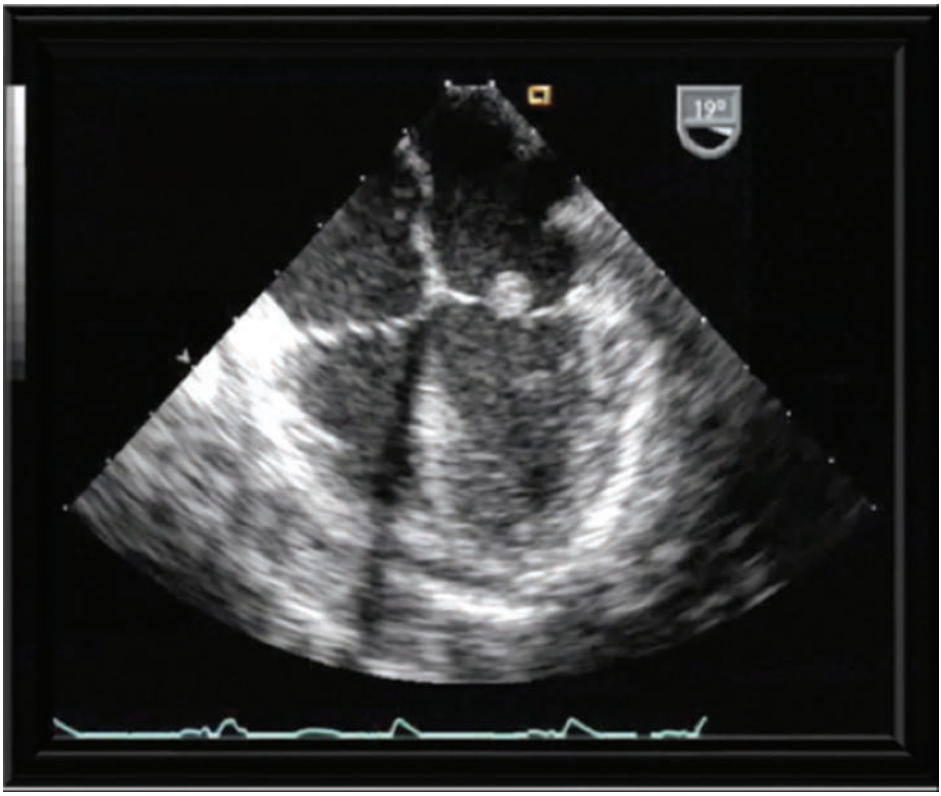

Figure 33-1. Large mass on the anterior leaflet of the mitral valve by TEE.

experience a rapid clinical deterioration requiring emergent intensive care interventions. Symptoms include high fevers, tachycardia, and overall ill appearance. These infections are associated with more aggressive local disease in the heart (including larger vegetations) as well as noncardiac embolic disease, which can result in stroke/neurologic injury, pulmonary embolism/pneumonia, osteomyelitis, kidney injury, and GI injury. Organisms that are associated with an acute presentation of IE and large vegetations include *S. aureus*, *Streptococcus pneumoniae*, and fungal pathogens.

The modified Duke criteria (Table 33-3) are used for diagnosis of IE. Clinical signs are supplemented by imaging with echocardiography (Figure 33-1, Figure 33-2, and Figure 33-3) or CT (Figure 33-4).

For children who are clinically stable, every attempt should be made to obtain 3 sets of blood cultures prior to the initiation of antimicrobial therapy (over 24-48 hours). To maximize blood culture sensitivity, it is essential that each blood culture bottle is inoculated with the appropriate blood volume based on patient weight. Blood-culture sets should include aerobic and anaerobic cultures when clinically feasible.

For children who are more seriously ill, 3 sets of blood cultures from 3 separate

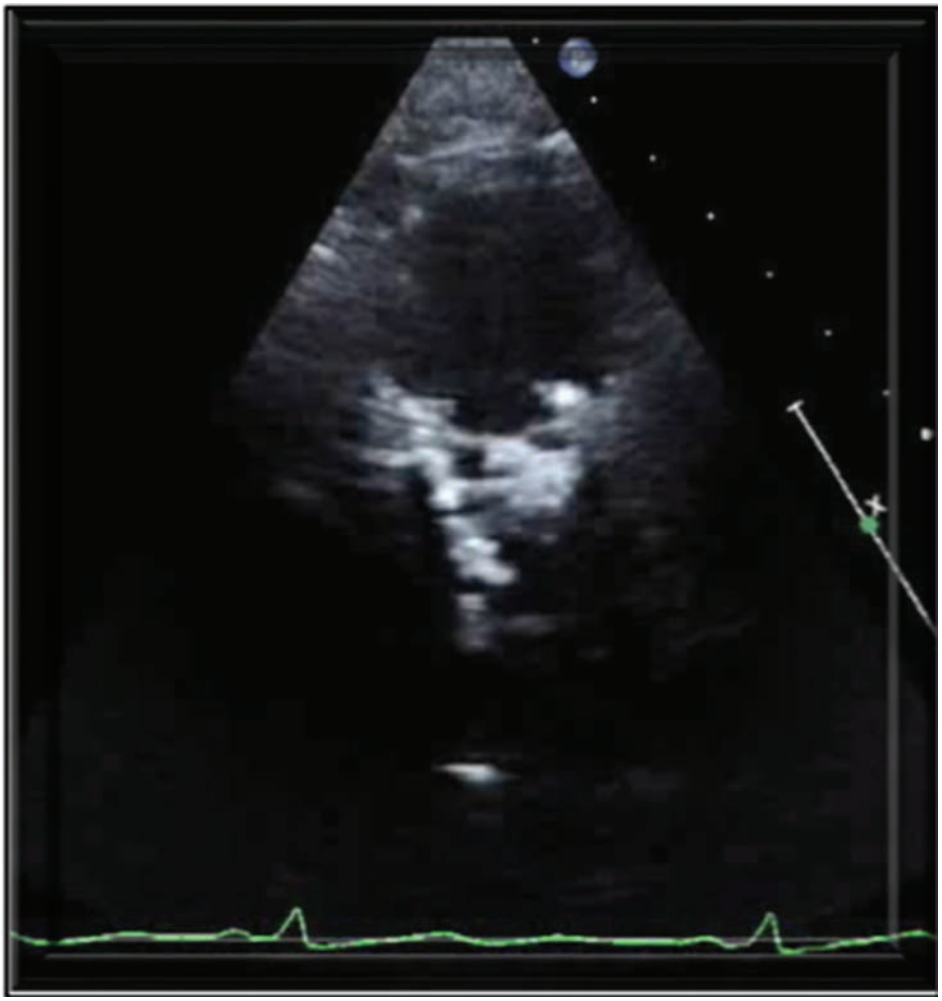

Figure 33-2. Vegetation within a bovine jugular RV-PA conduit.

venipuncture sites should be obtained as soon as clinically feasible (within an hour) and empirical antibiotic therapy should be started as soon as possible.

All patients with suspected IE should also receive an echocardiogram. In children, TTE is usually adequate, but in older children or in children who are overweight, TEE may be required. TEE may also be prefered in children with grafts/conduits or suspected aortic valve lesions.

At TCH, children undergoing evaluation for IE may also undergo head imaging (CT or MRI with contrast) and chest/abdominal imaging (high-resolution CT of the chest, abdominal CT with contrast, or abdominal ultrasound) to evaluate for septic emboli. Ophthalmology may be consulted to complete a funduscopic exam looking for Roth spots. Laboratory evaluation may include complete blood count with differential (CBC

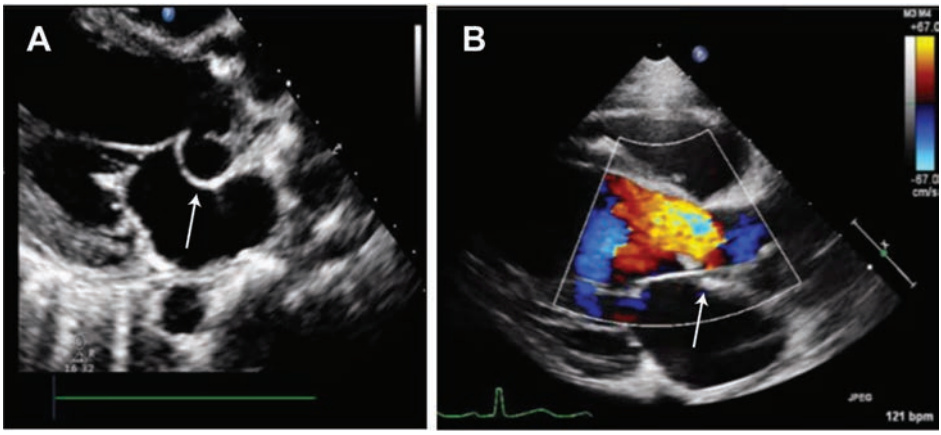

Figure 33-3. Parasternal long axis view (2D and color Doppler) demonstrating a periaortic root abscess. (arrow) with severe AI. Images courtesy of Dr. Josh Kailin, www.pedecho.org.

with differential), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), rheumatoid factor, complement levels, and urine analysis.

Children who require surgical management should also have diagnostic specimens sent from the OR. Vegetations and other infected material should be sent for aerobic, anaerobic, fungal, and possibly mycobacterial cultures. In addition, newer techniques such as broad-range bacterial (16S rRNA) and fungal (28S rRNA) PCR should be considered, especially if preliminary culture results are negative.

Medical Management

Children with IE typically require a prolonged course of IV antibiotic therapy. Antibiotic choice, dosage, and duration depends on the microorganism responsible for the infection as well as whether the infection involves prosthetic material. Updated recommendations for medical management of IE were published in 2015 (Baddour et al. 2015). Most children with IE will require placement of a PICC for long-term access to complete their antibiotic therapy. Placement of PICC lines should be delayed until the patient has had 48-72 hours of negative blood cultures.

Children receiving prolonged antibiotic therapy for IE should be closely monitored. At TCH, weekly blood work typically includes CBC with differential, CRP, and ESR. Kidney function should also be monitored 1 or more times per week depending on the risk of nephrotoxicity from the antibiotic regimen. In addition, children who are receiving therapy with aminoglycosides (and possibly vancomycin) should have troughs checked weekly.

Indications / Timing for Intervention

IE carries a significant mortality risk and the extent of disease is usually underappreciated by imaging. As such, early surgical intervention is generally favored at TCH.

Table 33-3. Modified Duke criteria for diagnosis of IE (Li et al. 2000).

Modified Duke Criteria for Diagnosis of IE	
Major criteria	Minor criteria
1. Positive blood culture for IE A) Typical microorganism consistent with IE from ≥2 blood cultures: - Viridans strep, Strep bovis, or HACEK group or - Community-acquired Staph aureus or enterococci, in the absence of a primary focus B) Microorganisms consistent with IE from persistently positive blood cultures, defined as: - 2 positive cultures of blood samples drawn >12 h apart or - All of 3 or a majority of ≥4 blood cultures (irrespective of the timing) or - 1 positive blood culture for Coxiella burnetti or antiphase-I Immunoglobulin G antibody titer >1:800 2. Evidence of endocardial involvement A) Positive echocardiogram - Oscillating intracardiac mass on valve or supporting structures, in the path of regurgitant jets (Figure 33-1), or on implanted material (Figure 33-2) in the absence of an alternative anatomic explanation or - Abscess (Figure 33-3) or - New partial dehiscence of a prosthetic valve B) New valvar regurgitation	1. Predisposing heart condition or IV drug use 2. Fever ≥38°C 3. Vascular phenomena • Janeway lesions • Intracranial hemorrhage • Conjunctival hemorrhages • Septic pulmonary infarcts • Major arterial emboli • Mycotic aneurysm 4. Immunologic phenomena • Osler nodes • Roth spots • Glomerulonephritis • Rheumatoid factor 5. Positive blood cx not meeting major criteria Definite IE Pathological criteria - Culture positive vegetation / abscess or - Vegetation / abscess confirmed by history showing active endocarditis Clinical criteria - 2 major criteria or - 1 major + 3 minor criteria or - 5 minor criteria Possible IE Findings consistent with IE that fall short of "definite" but not "rejected"

Early surgery should be considered in patients with CHF or severe valve involvement, suspicion of periannular involvement or abscess, left-sided vegetations at risk for embolization (>1 cm, mobile) especially if evidence of a previous systemic emboli, virulent organisms (*S. aureus* or fungi), presence of heart block (usually indicating invasion into the conduction system between the aortic and tricuspid valves), prosthetic valve endocarditis, previous endocarditis, or poor response to antimicrobial therapy.

A difficult question is the optimal timing of intervention in patients with IE and a stroke from embolization. There are no adequate studies to address the risk of hemorrhagic conversion of a stroke with the heparinization needed for CPB. In general,

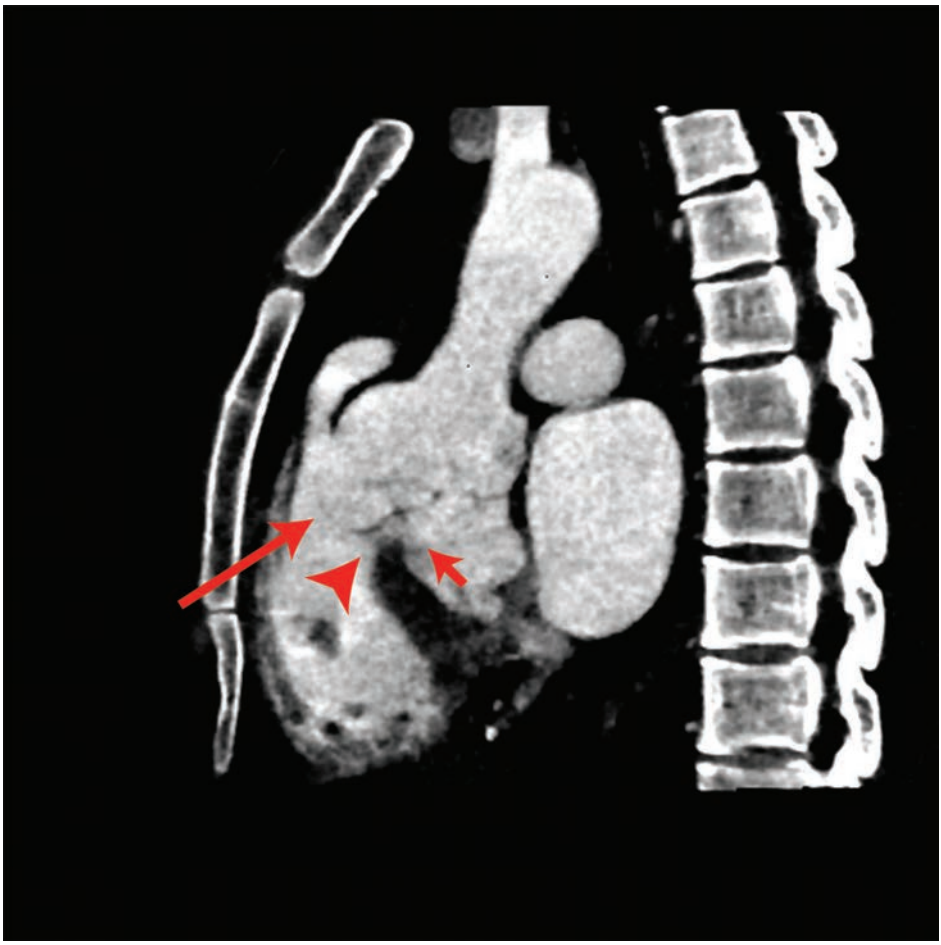

Figure 33-4. CT on a patient with a doubly-committed juxta-arterial VSD, mitral and aortic valve endocarditis, and severe AI. Images show a prolapsing right coronary leaflet (long arrow) through the VSD (arrowhead) and irregular masses consistent with vegetations on the ventricular side of the aortic valve leaflets (short arrow).

patients with a small stroke and a significant indication for early intervention should undergo surgical intervention. In patients with a large ischemic stroke and no evidence of hemorrhage, surgery may be delayed for 2-4 weeks, if possible. Similarly, for stable patients with intracerebral hemorrhage, surgery should be delayed for 4 weeks, if possible. However, the clinical status of the patient may mandate early surgical intervention regardless of the presence of a stroke or intracerebral hemorrhage. In these cases, surgery is performed with the understanding that the risk of neurologic deterioration is likely higher than if delay was possible.

Surgical Intervention

Surgical treatment is individualized for each particular patient based on anatomy and extent of infection. Surgical intervention for IE is best described as two separate processes: *debridement* and *reconstruction*. Debridement involves removal of all infected tissue and should be the main priority of surgical intervention. This may entail partial or complete removal of valve leaflets, debridement of valve annuli or aortic wall, removal of subvalvar chordal apparatus for mitral or tricuspid valves, etc. Once all tissue is debrided, reconstruction proceeds. Patch material, in particular autologous pericardium, is used to repair small or moderate defects in valve tissue, VSDs, defects on the free wall of the atria or ventricles, or the aortic root. Some particular scenarios include:

- **Aortic valve endocarditis.** If the infection is confined to a small portion of an aortic valve leaflet, especially in children, the defect may be reconstructed with autologous pericardium. However, it is not uncommon to have significant involvement of the aortic valve or aortic root, precluding an adequate and durable reconstruction. In those cases, aortic valve replacement should be entertained. Aortic homograft valves are favored, although replacement with a bioprosthetic or mechanical prosthesis may be appropriate in older children or adults with no involvement of the aortic root. If the aortic root is partially involved, it may be reconstructed with a patch to allow placement of a prosthesis. Alternatively, the patient may undergo an aortic root replacement with an aortic homograft. A Ross procedure may be a possible alternative although in many cases the long cross-clamp period due to the added debridement may preclude it at this time.
- **Mitral valve endocarditis.** Reconstruction of the mitral valve may be feasible, especially if the process is confined to part of one leaflet. Excised mitral chords may be treated by different techniques such as chordal transfer, artificial chords, or leaflet anchoring to surrounding leaflet tissue, depending on the situation. It is important to assess the integrity of the AV junction. If compromised, the area may need placement of a patch prior to replacing the valve. If needed, the valve is usually replaced with a mechanical prosthesis although placement of a bioprosthesis is also an option.
- **Tricuspid valve endocarditis.** It is extremely rare to have to replace the tricuspid valve, especially in children. Reconstruction may include patch material and other surgical techniques. Some degree of tricuspid regurgitation is usually well tolerated.

Statistics

In a recent 15-year retrospective review conducted at TCH involving 76 cases of IE, 46 (61%) patients required surgical intervention within 6 weeks of diagnosis (Shamszad et al. 2016). Median age at presentation was 8.3 years. The main organisms involved were *S. aureus* (24%), *Streptococcus* (22%), and coagulase-negative *Staphylococcus* (10%). Among surgical patients, median interval to surgery was 3 days. There was 1 perioperative mortality on a patient that had a significant stroke from a previous embolus. Of the 38 patients with native-valve involvement that underwent surgery, 50% had valve repairs and 50% had valve replacements:

- 12 aortic (8 aortic homograft, 3 Ross, 1 bioprosthetic)

- 5 mitral (4 mechanical)
- 2 pulmonary

Suggested Readings

Baddour LM, Wilson WR, Bayer AS, et al. Infective endocarditis in adults: Diagnosis, antimicrobial therapy, and management of complications: A Scientific Statement for Healthcare Professionals from the American Heart Association. Circulation 2015;132:1435-1486.

Li JS, Sexton DJ, Mick N, et al. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. Clin Infect Dis 2000;30:633-638.

Mery CM, Guzmán-Pruneda FA, De León LE, et al. Risk factors for development of endocarditis and reintervention in patients undergoing right ventricle to pulmonary artery valved conduit placement. J Thorac Cardiovasc Surg 2016;151:432-439.

Shamszad P, Khan MS, Rossano JW, et al. Early surgical therapy of infective endocarditis in children: a 15-year experience. J Thorac Cardiovasc Surg 2013;146:506-511.

Wilson W, Taubert KA, Gewtiz M, et al. Prevention of infective endocarditis: guidelines from the American Heart Association. Circulation 2007;116:1736-1754.