Pediatric Infective Endocarditis: A Clinical Update

Daniel A. Cox, DO*, Lloyd Y. Tani, MD

KEYWORDS

• Antibiotic • Echocardiography • Endocarditis • Infection • Pediatric • Valve

KEY POINTS

- Infective or bacterial endocarditis is an infectious process that involves the heart valves or cardiovascular structures.
- Endocarditis prophylaxis recommendations are more selective for when and for which patients should receive prophylactic antibiotics.
- Transthoracic and transesophageal echocardiography remains the main imaging modalities that assist in diagnosis of infective endocarditis in pediatrics.
- Bioprosthetic valve endocarditis is becoming a more common source of endocarditis, even in the pediatric population.

INTRODUCTION

Infective endocarditis (IE) is an infection of the endocardium of the heart and vascular endothelium. This process can include the native endocardium of the heart chambers or the endothelium associated with the cardiac valves or prosthetic hardware or material (prosthetic valves, conduits, grafts, patches, or pacemaker generator or leads). IE development is a complex process that involves the susceptibility of a valve or tissue to bacterial adherence, survival of the bacteria on the tissue or associated structure, and propagation of the infected vegetation.[1] Most commonly, IE involves a bacterial infection, but can also include a fungal infection. In the pediatric population of developed countries, a shift away from rheumatic heart disease predisposition has occurred. Prior studies estimated that 30% to 50% of children in the United States who eventually developed IE had prior rheumatic heart disease.[2]

With the decrease in the prevalence of rheumatic heart disease in developed countries, nonrheumatic predisposing conditions such as congenital heart disease are more common. It should be noted that endocarditis complicating rheumatic heart

University of Utah School of Medicine, 81 North Mario Capecchi Drive, Salt Lake City, UT 84113, USA
* Corresponding author.
E-mail address: d.cox@hsc.utah.edu

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disease continues to occur in many patients in parts of the world where rheumatic heart disease continues to be prevalent. With this said, 8% to 10% of pediatric IE cases develop in structurally normal hearts, most commonly being associated with *Staphylococcus aureus*.[3] Between the 1960s and 1980s, it has been estimated that endocarditis was responsible for an estimated 1 in 500 to 1 in 1000 pediatric hospitalizations.[4] More recent studies have estimated there to be 0.43 cases per 100,000 children.[5] This finding differs significantly from the reported incidence in an adult population of 15 cases per 100,000 adults.[6] The infectious process involving the endocardium, and the inflammatory process associated with the infection, carries significant risk of morbidity and mortality if not identified early with implementation of effective treatment. Updates published over the past several years take into account the change in pathogenic variance as well as patient-related changes.[7] Although guidelines have been written for pediatric IE, the majority of recommendations are extrapolated from adult studies and guidelines. Diagnostic criteria have been proposed and modified over the past several decades, including the Beth Israel criteria and the Duke criteria.[8,9] More recently, a set of modified Duke criteria has been more readily used to aid in diagnosis: **Box 1**.[10] These criteria help to define definitive IE, possible IE, or rejection of a diagnosis of IE.[10] Certain bacteria or infectious processes, such as that seen with *Staphylococcus*, have become more commonly associated with IE, and have also affected outcomes. However, there has been an increase in streptococcal IE seen in pediatric populations, more commonly with underlying cardiac conditions.[5] Unfortunately, despite medical and surgical advances, outcomes have not been greatly affected over the past few decades.[4]

SOURCE OF INFECTION

Variable sources of IE have been identified, as have the potential cardiovascular structures involved. Commonly involved structures include native cardiac valves, prosthetic valves (bioprosthetic or mechanical), nonvalvar cardiovascular structures (unrepaired ventricular septal defects, patent ductus arteriosus), prosthetic materials (patches, shunts, conduits, stents), implanted devices (pacemaker, leads, ventricular assist devices). Treatment strategies differ based on the structures involved. In adult populations, intravenous drug use remains a common source of IE with the incidence continuing to increase nationally.[11] Although less common in the pediatric population, intravenous drug use should not be excluded as a potential source of infection, especially when right-sided IE is identified. Central lines, implanted devices, synthetic shunts or grafts, increasing numbers of children with cyanotic heart disease, and general immunodeficiencies also contribute to the shifting etiologies associated with IE. In children with an underlying congenital heart condition, the incidence of IE has been estimated at 6.1 per 1000 children with 34% occurring in cyanotic cardiac conditions. In addition, children who had undergone cardiac surgery in the prior 6 months are more than 5 times more likely to develop IE compared with those who had not undergone a cardiac surgery or intervention.[12] The most common associated bacteria include gram-positive organisms (staphylococci, streptococci, enterococci) and less commonly gram-negative bacteria such as the HACEK organisms (*Haemophilus aphrophilus* [more recently identified as *Aggregatibacter aphrophilus* and *Aggregatibacter paraphrophilus*], *Actinobaccillus actinomycetemcomitans* [more recently identified as *Aggregatibacter actinomycetemcomitans*], *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella kingae*). Culture-negative endocarditis can also occur (discussed in the section on Diagnostic Modalities). Fungal IE most commonly occurs with candida or *Aspergillus* species.

Box 1
The modified Duke criteria for the diagnosis of IE

Definitive IE
Pathologic criteria
- Micro-organisms demonstrated by culture or histologic examination of vegetation, vegetation that has embolized, or an intracardiac abscess specimen; or
- Pathologic lesions; vegetation or intro cardiac abscess confirmed by histologic examination showing active endocarditis.

Clinical criteria
- Two major and 0 minor criteria; or
- One major and 3 minor criteria; or
- No major and 5 minor criteria.

Major criteria
- Positive blood culture positive for IE
  - Typical endocarditis organism from 2 separate blood cultures
    - Viridans streptococci or *Streptococcus bovis*
    - HACEK organisms
    - *Staphylococcus aureus*
    - Community-acquired enterococcus in absence of primary focus
  - Micro-organisms consistent with IE from persistently positive blood cultures:
    - Two separate blood cultures from samples drawn greater than 12 hours apart
    - Three, or a majority of 4 or more, separate blood cultures (first and last sample drawn 1 hour apart)
    - Single positive blood culture for *Coxiella burnetii* or an antiphase I IgG antibody titer of greater than 1:800
- Evidence of endocardial involvement
- Echocardiogram positive for IE
  - Oscillating intracardiac mass on valve or supporting structures, in the path of regurgitant jets, or on implanted material in the absence of an alternative anatomic explanation; or
  - Abscess; or
  - New partial dehiscence of prosthetic valve or new valvular regurgitation.
- New valvular regurgitation (worsening or changing of preexisting murmur not sufficient)

Minor criteria
- Predisposing heart condition or intravenous drug use
- Fever, temperature greater than 38° C (100.4° F)
- Vascular phenomena: major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial bleed, conjunctival hemorrhages, Janeway lesions
- Immunologic phenomena: glomerulonephritis, Osler nodes, Roth spots, rheumatoid factor
- Microbiological evidence: positive blood culture, but does not meet a major criterion as noted or serologic evidence of an active infection with organism consistent with IE (excluding single positive culture for coagulase-negative staphylococci and other common contaminants)

Possible IE
Clinical criteria
- One major criterion and one minor criterion; or
- Three minor criteria

Rejected diagnosis
- Firm alternative diagnosis explaining evidence of IE; or
- Resolution of IE syndrome with antibiotic therapy for less than or equal to 4 days; or
- No pathologic evidence of IE at surgery or autopsy, with antibiotic therapy for less than or equal to 4 days; or
- Does not meet criteria for possible IE, as described

Adapted from 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(4):633-638; with permission.

RISK FACTORS FOR ENDOCARDITIS

For IE to occur, 2 factors are required: bacteremia (or less commonly fungemia) and disruption of the endocardium or endothelial lining. With an increasing number of children with complex congenital heart disease surviving past infancy, the number of IE cases is shifting from pediatric patients with no structural heart conditions to those with structural heart conditions.

IE commonly develops on areas exposed to blood flow from a high-pressure system through a narrow orifice with the site of infection being in the low-pressure area distal to the narrowing. It is theorized that this area of lower pressure may predispose the tissue to hypoxia and poor metabolic perfusion, and in turn lead to deformation of the valve or vessel wall leading to a propensity to develop IE. In turn, tricuspid and mitral valve vegetations are commonly identified on the atrial surface adjacent to the line of closure. Aortic and pulmonary valve vegetations more commonly occur on the ventricular surface, with aortic insufficiency-related IE also potentially involving the anterior leaflet of the mitral chordae and muscular attachments. IE associated with a ventricular septal defect commonly occurs on the right ventricle side (**Fig. 1**).[13]

There seems to be a bimodal distribution of IE cases with a peak during infancy and another during late adolescence. IE in neonates has increased over the past decades and is often associated with indwelling lines and right-sided vegetations.[14]

Additionally, prosthetic valves are becoming a more common source of infection in the pediatric population. There seems to be a propensity to IE with bovine jugular vein valves, including the Contegra surgical valve and the Melody transcatheter valve (Medtronic Inc, Minneapolis, MN), when compared with other valve types. The transcatheter valves are used more frequently in the pediatric and adolescent populations as experience with the valves and number of implanted valves increase. One systematic review of IE in bioprosthetic valves in the pulmonic position reported a 5.4% incidence in the bovine jugular vein valves regardless of mode of implantation, compared with 1.2% in other valve types.[15] Additional studies have indicated that IE associated with the transcatheter Melody valve implanted in the pulmonary position may also be higher with an incidence of 3.2% to 25% with an annualized incidence rate of 1.3% to 9.1% per patient-year.[16]

CLINICAL FINDINGS AND SYMPTOMS OF INFECTIVE ENDOCARDITIS

In pediatrics, higher risk symptoms and physical examination findings should raise suspicion for IE. Unexplained and persistent fevers without a potential source in a patient who carries a high risk for IE should be evaluated thoroughly. Nonspecific findings commonly include new-onset fatigue, night sweats or chills, generalized malaise, and weight loss. With IE associated with a cardiac valve, a murmur will likely become evident. It can be challenging to differentiate a new pathologic murmur from an innocent murmur in times of illness, but can be potentially differentiated by a skilled provider with good auscultation. A new diastolic murmur or an abnormal systolic murmur (often regurgitant or holosystolic) should raise suspicion in a patient without a history of structural heart disease. In patients with bioprosthetic valves, a new diastolic murmur or a rapidly changing or progressive systolic ejection murmur should also raise high suspicion.

As the infectious process proceeds, progressive heart failure symptoms related to valve insufficiency or stenosis may become more evident, as may embolic events. In addition to the infectious process that occurs in relation to IE, the inflammatory and immune response will often contribute to the associated clinical findings and symptoms. This response may include myalgias, neurologic changes, dermatologic

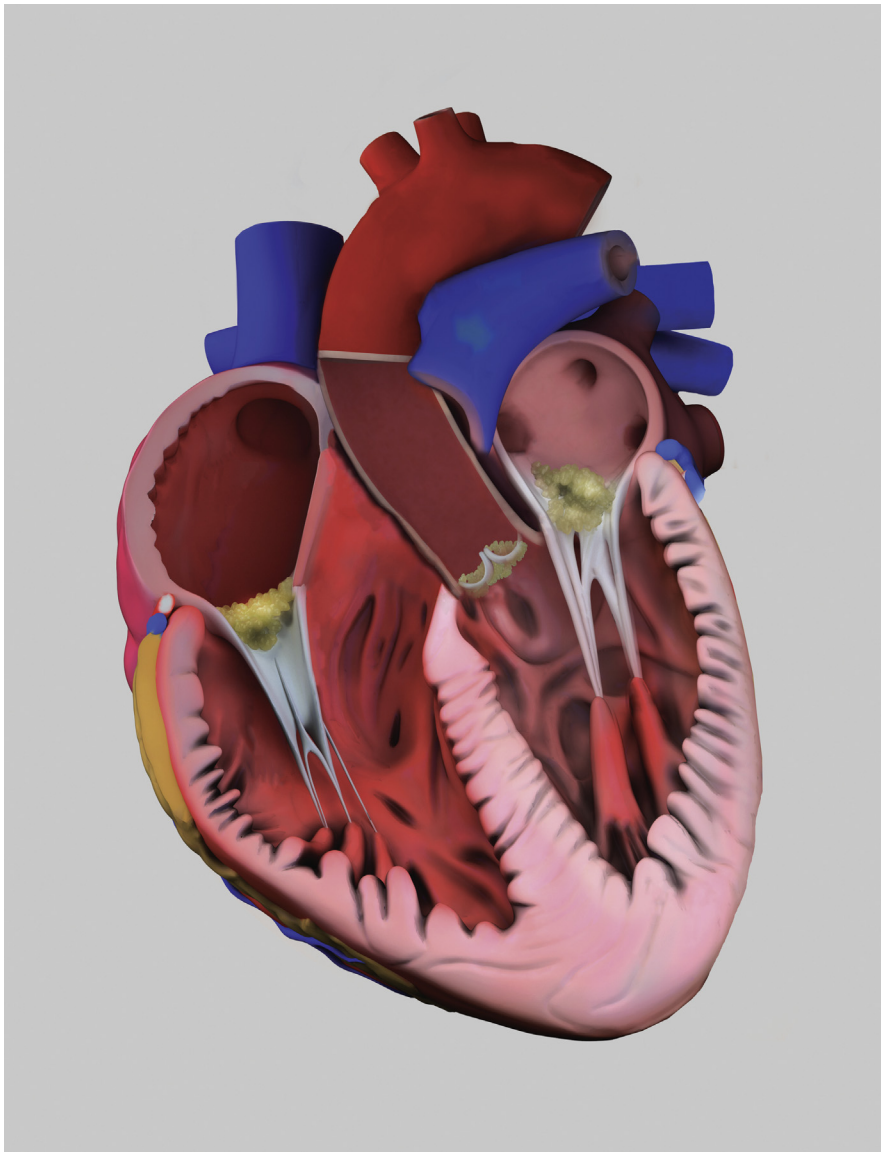

Fig. 1. Representation of common areas of endocarditis, including the atrial side of the tricuspid and mitral valve, ventricular side of the aortic valve.

findings such as splinter hemorrhages, Roth spots (retinal hemorrhagic lesions), Janeway lesions (painless hemorrhagic lesions of the distal extremities), or Osler nodes (painful nodules of the distal extremities). The skin manifestations, if present, are associated with an increased risk of complications. Servy and colleagues[17] noted in a population-based study in 2008 that 11.9% of patients with definite IE had skin manifestations consisting of purpura in 8.0%, Osler nodes in 2.7%, and Janeway lesions in 1.6%. These patients carried a 32.8% risk of cerebral emboli, compared with 18.4% of those without skin manifestations, with Janeway lesions correlating with a 75.0% risk

of cerebral emboli. In addition, patients with purpura had larger vegetations (18.1 mm vs 13.7 mm).[17]

Visual changes such as a sudden or complete loss of vision in 1 eye or eye pain should prompt an ophthalmologic evaluation to look for retinal or ophthalmic artery occlusion or associated endophthalmitis.

DIAGNOSTIC MODALITIES

The modified Duke criteria for diagnosis of IE incorporate pathologic and clinical criteria to assist in the diagnosis of IE (see **Box 1**)[10] Major and minor criteria have been recommended to stratify patients into 3 categories: definitive IE (positive pathologic criteria, 2 major and no minor criteria, 1 major and 3 minor criteria, or no major and 5 minor criteria), possible IE (1 major and 1 minor criteria, or no major and 3 minor criteria), and rejected diagnosis of IE (alternative diagnosis, resolution of IE syndrome with antibiotic therapy for less than or equal to 4 days, no pathologic evidence of IE at the time of surgery or autopsy and having received less than 4 days of antibiotic therapy, or not meeting the other criteria for IE). Major criteria include pathologic findings of micro-organisms demonstrated by culture or histologic examination from a collected specimen showing active infection. They also include a positive blood culture with a typical endocarditis micro-organism from 2 separate blood cultures, persistently positive blood cultures with micro-organisms consistent with IE, evidence of endocardial involvement, an echocardiogram positive for findings consistent with IE, and new valve regurgitation. Minor criteria include a predisposing heart condition, intravenous drug use, a febrile illness with a temperature of greater than 38° C, vascular phenomena, immunologic phenomena, microbiological evidence of IE that does not meet a major criterion, or serologic evidence of an active infection with an organism that is consistent with IE.[10]

Blood cultures are the mainstay of diagnosis. It is not necessary to obtain blood cultures at the time of fever because the bacteremia associated with IE is continuous. Ideally, 3 cultures drawn from separate sites should be obtained before administering empiric antibiotic therapy. Even in the setting where blood culture sampling occurs in a correct manner, 5% to 10% of cases of IE remain culture negative. With suspected endocarditis in patients who have been treated for fewer than 4 days without a prior blood culture, cessation of antibiotic therapy can be considered to potentially identify a pathogen if the patient is clinically stable.[4] Acute phase reactants such as an erythrocyte sedimentation rate, C-reactive protein, or an abnormal platelet count may support a diagnosis, but are not included in diagnostic criteria because they are generally nonspecific findings related to inflammatory processes. Other molecular or polymerase chain reaction techniques may be of benefit in select situations where a bacterial source has not been detected.

Although echocardiographic imaging plays an important role, the initiation of treatment after obtaining blood cultures in highly suspicious cases should not be delayed before obtaining echocardiographic imaging.

Echocardiographic imaging should be performed on any patient with suspected endocarditis to assist in diagnosis. Echocardiographic imaging of intracardiac masses, noninfectious thrombus, and vegetations associated with IE may be indistinguishable (**Fig. 2**). Without additional clinical findings, echocardiographic imaging alone is insufficient to diagnose IE and is inappropriate to use as a screening test. In the pediatric population, transesophageal echocardiographic imaging has not been shown to increase the diagnostic potential. In a majority of cases, transthoracic imaging is sufficient for the initial evaluation of suspected IE. In cases where

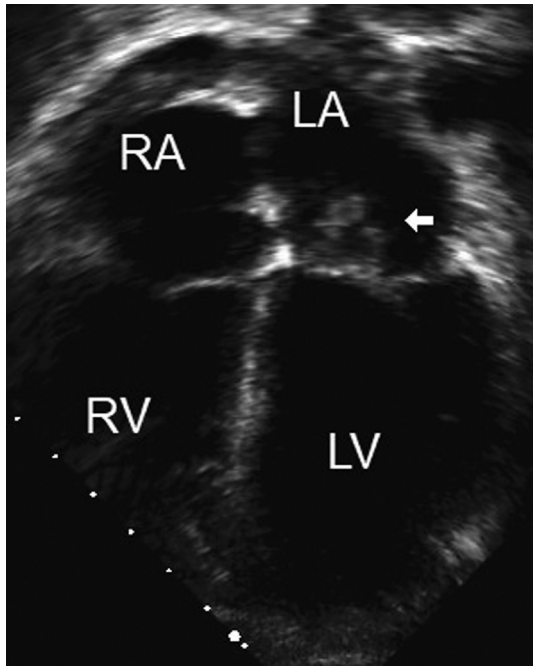

Fig. 2. Transthoracic echocardiogram 4-chamber view with large vegetation (*arrow*) associated with the anterior leaflet of the mitral valve. LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

transthoracic windows for imaging are poor with incomplete visualization of higher risk structures, transesophageal imaging should be considered. These factors may include patients with a prominent lung artifact, a larger body habitus, or a prosthetic valve or material that is positioned behind the sternum or other location not well-visualized by transthoracic imaging. In addition, persistent bacteremia or a high clinical suspicion for IE with normal transthoracic imaging should prompt consideration of transesophageal echocardiographic imaging. In the younger pediatric patient, transesophageal imaging can be challenging to perform without general anesthesia. In a controlled setting with older children, transesophageal echocardiography can be performed with conscious sedation. A negative echocardiogram does not mean that the patient does not have endocarditis. In some cases, repeat imaging may be indicated. Serial imaging studies can also provide valuable information in regard to therapy success or progressive disease.

Other imaging modalities such as computed tomography scans, MRI, and cardiac PET may be used in select situations. The use of these modalities are increasing in utility in the setting of concern for prosthetic valve IE or abscess formation not identified by echocardiographic imaging. An electrocardiogram, in general, is not helpful in the diagnosis of IE, but a new conduction abnormality or bundle branch block should raise concern for abscess formation affecting the conduction system.

MANAGEMENT OF INFECTIOUS ENDOCARDITIS

Treatment of IE requires a multidisciplinary approach. The subspecialty teams involved commonly include cardiology, infectious disease, and cardiothoracic

surgery, with other providers involved on an as-needed basis. An infectious disease consultation is strongly recommended to assist in guidance of appropriate antibiotic therapy early in the workup and treatment of IE. Successful management includes the diagnosis, early initiation of appropriate antibiotic therapy, and surveillance for, identification of, and management of complications, along with determining the need for and potential timing of surgery. Antibiotic therapy is the mainstay of treatment with an attempt to clear the associated bacteremia and sterilize the infected source. The course of antibiotic therapy varies based on the pathogen and the site(s) involved in the primary infectious process and any potential embolic sites. Owing to the complexity of potential antibiotic therapies, this topic will not be addressed in detail in this article. A common duration of antibiotic therapy consists of 4 to 6 weeks of treatment, depending on the organism identified, antibiotic susceptibility, and native versus prosthetic valve IE.[4] Transitioning from inpatient to outpatient therapy can be considered for part of the antibiotic course in lower risk patients with close outpatient monitoring. Because a higher risk of complications generally exists during the first 2 weeks of antibiotic therapy, outpatient therapy during this time is generally discouraged. Outpatient therapy may be considered for lower risk patients after the initial 2 weeks of antibiotic therapy. This includes patients who are medically stable, free of systemic symptoms, have negative blood culture results, have a stable electrocardiogram, have a stable home environment, have an appropriate monitoring plan in place, and have acute care access readily available.[18] Outpatient antibiotic treatment is not recommended in high-risk patients with unstable hemodynamics or symptoms, sepsis or ongoing bacteremia, perivalvar abscess, new conduction abnormalities, vegetations greater than 10 mm in diameter, or other serious complications.[18]

When a valve is directly involved, progressive stenosis or insufficiency may ensue. Depending on the rate of progression and the ability to clear the potential infectious process, heart failure management may be required in an acute or chronic setting, and surgery is often indicated in these cases.

Blood culture–negative IE is a complicated situation when a micro-organism cannot be identified by blood culture, but there is clinical or imaging concerns for IE, or pathologic examination of a valve or tissue after surgery. This situation may occur for several reasons that include antibiotic therapy before blood cultures are obtained, improper sampling or laboratory evaluation of samples, IE associated with a fastidious bacteria or nonbacterial micro-organism, or right-sided IE. With the administration of antibiotic therapy before blood cultures, the recovery rate of bacteria may be decreased by up to 40%.[19] This scenario emphasizes the importance of cultures being obtained before antibiotic administration, unless the clinical context warrants immediate administration of antibiotics in patients at risk.

Fungal IE presents a challenging situation because the complications may be compounded, with larger vegetations often being present, an increased risk of embolic events, and a high risk of perivalvar abscess formation. Antifungal therapies, including amphotericin B, have a poor ability to penetrate infected material and surgery is commonly required if complications arise. Antifungal therapy using oral fluconazole, because a long-term suppressive therapy has been reported for uncomplicated IE related to fungal infection, with the mortality rate no worse than those receiving combined medical and surgical therapy.[20]

The timing of potential surgical intervention relies on many associated factors that may occur in isolation or in combination. The decision about surgical intervention should be individualized in the pediatric patient. These determinants include the tolerance of associated symptoms such as heart failure symptoms necessitating surgery in 60% of patients with IE, the size and location of a vegetation in 48%, inability to clear

the infection or refractory sepsis in 40%, or embolic episodes in 18%.[21] Surgical intervention, including debridement or extraction of any involved tissue, valve repair, or valve replacement, often becomes a necessity in the setting of IE. Surgery may be required in up to 25% of acute infections and 40% of subacute or chronic cases.[22]

Perioperative risks remain high with the complexity of intervention and potential for multiorgan involvement with reports of a 6% to 25% risk of perioperative mortality with long-term survival of approximately 70% in adult studies.[22] Note that these studies include many older patients with additional comorbidities.

The potential need for, or timing of, any intervention can be challenging. Determining factors include left-sided IE versus right-sided IE, vegetations that are progressively increasing in size while on appropriate antibiotics, or significant mobility of the vegetation. Prior studies have attempted to recommend indications for surgical removal of a vegetation based on its size. Although these recommendations should be considered, they should not be used as definitive indications to intervene because they do not carry good confirmatory evidence and these indications remain controversial, even more so in the pediatric patient. Echocardiographic features that have been described in the adult literature in regard to the timing of potential surgical intervention include persistent vegetation after systemic embolization, anterior mitral valve leaflet vegetation size of greater than 10 mm, 1 or more embolic events during the first 2 weeks of antimicrobial therapy, 2 or more embolic events during or after antimicrobial therapy, or an increase in vegetation size after 4 weeks of antimicrobial therapy. Surgery should be considered with valvular dysfunction contributing to signs of ventricular decompensation associated with aortic or mitral valve insufficiency with heart failure that is unresponsive to medical therapy. Finally, perivalvar extension that includes valve perforation, dehiscence, rupture, or fistula creation as well as new heart block, or a large abscess with extension despite antimicrobial therapy, are indications for surgical intervention in select patients (**Box 2**). Although indicated for other reasons (eg, mechanical prosthetic valve), anticoagulation is not indicated in IE. In some situations, such as IE associated with mycotic aneurysms or other high-risk intracranial complications, anticoagulation may be contraindicated.[19]

MORBIDITY AND MORTALITY ASSOCIATED WITH INFECTIVE ENDOCARDITIS

Complications related to IE are variable with an emphasis placed on early diagnosis and initiation of antibiotic therapy before clinical decompensation. There are many factors that may predispose pediatric patients to cardiac and noncardiac complications that may require intervention. Complication risks are higher in patients with prosthetic valves, left-sided IE, IE owing to *S aureus* or fungi, prior IE, prolonged clinical symptoms lasting months, cyanotic congenital heart disease, systemic to pulmonary artery shunts, and those with poor clinical response to antimicrobial therapy.[19]

Sepsis can be a late complication after the infectious process has spread, leading to multiorgan failure and shock. Early recognition and standard shock protocols should be used. Embolic events may involve many organ systems, including the brain, lungs, peripheral vasculature, kidneys, and other organs depending on the primary locations of IE. Attempts to predict the risk of embolic events have been difficult, including identification of higher risk groups for which surgery would be recommended to avoid risk of an embolic event. IE associated with staphylococcal or fungal infections, as well as those involving the anterior leaflet of the mitral valve, may carry a higher risk of embolization.[19]

Stroke, meningitis, intracranial abscess, and other neurologic manifestations complicate the course in roughly 30% of patients, with roughly 60% of patients having

Box 2
Criteria to consider in determining surgical indications for IE

Echocardiographic features suggesting potential need for surgical intervention
Vegetation
- Persistent vegetation after systemic embolization
- Anterior mitral valve leaflet vegetation size of greater than 10 mm
- One or more embolic events during the first 2 weeks of antimicrobial therapy
- Two or more embolic events during or after antimicrobial therapy
- Increase in vegetation size after 4 weeks of antimicrobial therapy

Valvular dysfunction
- Acute aortic or mitral insufficiency with sings of ventricular failure
- Heart failure unresponsive to medical therapy
- Valve perforation or rupture

Perivalvular extension
- Valvular dehiscence, rupture, or fistula
- New heart block
- Large abscess or extension of abscess despite appropriate antimicrobial therapy

From Bayer AS, Bolger AF, Taubert KA, et al. Diagnosis and management of infective endocarditis and its complications. *Circulation.* 1998;98(25):2936-2948. Reprinted with permission, Circulation. 1998.98;2936-2948 © 1998 American Heart Association, Inc. All requests to use this information must come through the AHA.

a neurologic finding as their chief complaint or one of the major presenting symptoms.[23] Congestive heart failure is often related to associated valve pathology and can have a great impact on overall prognosis. Heart failure symptoms may develop early in the process of IE owing to rapid degeneration of an infected valve. These symptoms may occur owing to a progressive obstructive or regurgitant process, as well as potential dehiscence of a valve or development of a new intracardiac shunt. Surgical intervention should be strongly considered in these cases complicated by heart failure.

Overall in-hospital mortality related to IE has been estimated to occur in between 1.1% and 5.0% of patients, with staphylococcal IE being associated with increased mortality. Patients with certain congenital heart conditions have an increased risk of mortality, with death occurring in 48% of patients with tetralogy of Fallot and pulmonary atresia and 8% in patients with prosthetic valve IE.[5,14,24] A high risk of mortality also exists in premature infants, occurring in 31% of patients in 1 study.[14]

INFECTIVE ENDOCARDITIS PREVENTION AND PROPHYLACTIC RECOMMENDATIONS

Prevention of IE is of utmost importance. Patients and their families should be made aware of potential risk factors and ways to minimize the risk of acquiring IE. Some procedural risks cannot be avoided, but sterile technique and other infection reduction protocols should be used.

In 2007, the American Heart Association and American College of Cardiology revised the antibiotic prophylactic guidelines to restrict preprocedural antibiotics to a few cardiac conditions that remain at higher risk for adverse outcomes related to IE.[25] The historical rational for, or against, the prophylactic use of antibiotics before certain invasive procedures included the association between bacteremia and IE. It should be noted that bacteremia can occur with daily activities such as teeth brushing, flossing, and chewing. Although certain higher risk procedures may contribute to transient bacteremia, justification for the recommendation to continue to use preprocedural prophylactic antibiotics in select situations has included the following:

Streptococci and Enterococci are a part of the normal flora and carry a higher susceptibility to antibiotics recommended for prophylaxis, previously published cases of IE have had a potential temporal relationship with IE and certain procedures, the risk of antibiotic prophylaxis is overall low, and the potential for complications associated with IE are high.[6] These updated guidelines note that, although these factors remained valid, they did not compensate for the lack of published data to support the use of prophylactic antibiotics. No prospective, randomized, placebo-controlled studies having been published in regard to the efficacy of antibiotic prophylaxis to prevent IE when undergoing dental procedures.

This updated guideline acknowledges that the effectiveness is unknown, but that it is reasonable to use prophylactic antibiotic therapy only in select situations.[25] Antibiotic prophylaxis is reasonable for dental procedures that may perforate the oral mucosa or involve the gingiva or periapical tooth manipulation, for respiratory tract procedures, and for procedures that involve skin infections, skin structures, or musculoskeletal tissue for those at risk (**Box 3**). Recommendations for antibiotic prophylaxis include a single antibiotic dose 30 to 60 minutes before a procedure (**Table 1**). In the event a dose is not administered before the procedure, it can be administered up to 2 hours after the procedure. If patients are already receiving an antibiotic, a drug from a different class should be considered. Antibiotic prophylaxis is not required for patients undergoing gastrointestinal or genitourinary procedures. With limited data to fully support the use and benefit of antibiotic prophylaxis, emphasis should still be placed on good oral and skin hygiene.

CONTROVERSIES IN MANAGEMENT

In the pediatric population, clear guidelines remain limited and many treatment strategies are inferred from adult guidelines. It is unlikely that large randomized controlled trials will be performed, but population-based or case-control studies could prove useful toward improving recommendations for prophylaxis and infection prevention. The authors of the Modified Duke Criteria have encouraged others to assist in

Box 3
Indications for endocarditis prophylaxis

Prosthetic cardiac valve or prosthetic material used for cardiac valve repair

Previous IE

Congenital heart disease
- Unrepaired cyanotic congenital heart disease, including palliative shunts and conduits
- Completely repaired congenital heart defect with prosthetic material or device, whether placed by surgery or catheter intervention, during the first 6 months after the procedure
- Repaired congenital heart disease with residual defects at the site or adjacent to the site of a prosthetic patch or prosthetic device (which inhibit endothelialization)

Cardiac transplant recipients who develop cardiac valvulopathy

From Wilson W, Taubert KA, Gewitz M, et al. Prevention of infective endocarditis: guidelines from the American Heart Association: a guideline from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group. *Circulation.* 2007;116(15):1736-1754. Reprinted with permission, Circulation.2007;116:1736-1754 ©2007 American Heart Association, Inc. All requests to use this information must come through the AHA.

Table 1
Antibiotic dosing for prophylaxis before procedures carrying increased IE risk

Regimens for a Dental Procedure				
	Antibiotic	**Route**	**Children**	**Adult**
Usual therapy	Amoxicillin	Oral	50 mg/kg	2 g
Unable to take oral medication	Ampicillin	IV or IM	50 mg/kg	2 g
	Cephazolin or ceftriaxone	IV or IM	50 mg/kg	1 g
Allergic to penicillins or ampicillin	Clindamycin or	Oral	20 mg/kg	600 mg
	Cephalexin[a,b] or	Oral	50 mg/kg	2 g
	Azithromycin or clarithromycin	Oral	15 mg/kg	500 mg
Allergic to penicillins or ampicillin and unable to take oral medication	Clindamycin	IV	20 mg/kg	600 mg
	Cefazolin/ceftriaxone	IV or IM	50 mg/kg	1 g

Regimen: single dose 30 to 60 minutes before procedure.

Abbreviations: IM, intramuscularly; IV, intravenous.

[a] Or other first- or second-generation oral cephalosporins in equivalent adult or pediatric dosage.

[b] Cephalosporins should not be used in an individual with a history of anaphylaxis, angioedema, or urticaria with penicillins or ampicillin.

From Wilson W, Taubert KA, Gewitz M, et al. Prevention of infective endocarditis: guidelines from the American Heart Association: a guideline from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group. *Circulation.* 2007;116(15):1736-1754. Reprinted with permission, Circulation.2007;116:1736-1754 ©2007 American Heart Association, Inc. All requests to use this information must come through the AHA.

evaluating additional modifications to these criteria to further improve the diagnostic capability.[10]

More recent studies from adult populations have shown that a change from intravenous antibiotic therapy to early oral antibiotic therapy was not associated with delayed treatment failure for patients whose conditions have stabilized with left-sided endocarditis.[26,27] These results have not been reproduced in pediatrics to date.

DISCLOSURE

The authors have nothing to disclose.

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