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## Infectious Endocarditis: A Comprehensive Review for Emergency Physicians

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*Infectious endocarditis (IE), an infection of internal structures of the heart, has undergone many changes since the pre-antibiotic era. Recent case reviews have shown the overall incidence of IE to range from 1 to 6.2 cases per 100,000 per year[1,2] and accounts for ~10,000-20,000 new cases per year.[2-4] This makes IE the fourth leading life-threatening infectious disease following urosepsis, pneumonia, and intra-abdominal sepsis.[3]*

*To acquire this infectious syndrome, the etiologic organism can adhere to endocardial structures. This typically occurs through an initial injury to the endocardium. Historically, rheumatic fever was the most commonly noted initiating event worldwide. Although this continues to be a problem in underdeveloped countries, in industrialized nations the predisposing factors are much more varied. Patients with congenital or acquired heart diseases are living longer. The geriatric and immunosuppressed populations are growing due to improved medical and surgical management. Each year an increasing number of prosthetic heart valves are being placed with improved patient survival. Such medical interventions have resulted in an increase in the mean age of patients affected by IE from younger than 30 years of age in the pre-antibiotic era to approximately 50 years in the present era.[5] Not all patients with new onset IE are found to have predisposing endocardial lesions. Many are seen to have a cause for repeat episodes of bacteremia. These include the intravenous drug user (IVDU), burn victims, and patients with intravascular devices such as indwelling catheters and vascular shunts.*

*Organisms responsible for IE have also changed considerably since the pre-antibiotic era. Historically, the most commonly noted was* Streptococcus viridans. *Changes in the patient populations infected are also reflected in changes in the microbiologic spectrum. Most notable is the emergence of staphylococcal species as a major etiologic organism. In addition, causative organisms have shifted from predominantly community acquired to include gram-positive and -negative nosocomial infections. To complicate matters, many etiologic organisms are now resistant to conventional antibiotic therapy. This has resulted in the advent of new antibiotic therapies and combined drug regimens to treat infection adequately.*

*In this review, the authors summarize the evolution of IE, clinical presentation, treatment, and diagnosis. Focus is primarily directed at IE in the emergency department setting. As the patient populations affected have changed, so has the disease. Numerous articles have been published in the last five years discussing these*

*new patient groups. The authors discuss these myriad clinical presentations. Another active issue regards the clinical diagnosis of IE. This has been stimulated by proposals of the Duke criteria in 1994, which emphasize clinical findings and echocardiographic techniques. In 1998, the American Heart Association endorsed the Duke Criteria for the Diagnosis of IE. Comparisons between the Duke criteria and the older Beth Israel Criteria for the Diagnosis of IE are outlined, with a focus on their implementation in the emergency department. Treatment strategies for prophylaxis and the eradication of vegetative infections are also highlighted.*

*— The Editor*

## Introduction

IE, although relatively rare, presents a challenge to the emergency department clinician. A definitive diagnosis can be straightforward when pathologic or histologic evidence is combined with a history of risk factors for IE (preexisting endocardial lesions, a history of previous IE, and cause for repeat episodes of bacteremia). Unfortunately, most presentations for IE range from vague findings with one or two risk factors to variable or non-specific symptoms. Since definitive diagnoses often require serial blood cultures and echocardiographic findings, confirming IE rarely occurs in the emergency department. Consequently, patients suspected of IE are routinely admitted until blood cultures and echocardiography exclude endocardial infection. Of these cases, the majority will be ruled out and discharged with an alternate diagnosis.

The current tactic of admission for "rule out" reflects a conservative approach that reflects the high mortality rate associated with a missed diagnosis. Hence, the diagnostic stratification rules described in this paper were developed with high sensitivity in mind. Improved specificity, although less important from a conservative standpoint, is also beneficial to avoid the high costs of numerous false-positive admissions that hospitals must endure to capture those with IE.

## Epidemiology

IE has undergone considerable epidemiological changes in the last three decades, especially in patient populations at risk for developing IE. Although the incidence has only slightly increased, modern medicine has resulted in a more varied spectrum of patients susceptible to this disease. In the pre-antibiotic era, rheumatic heart disease was the primary culprit for IE, but now this condition rarely occurs in industrialized nations. Today, predisposing lesions are much more varied. Patients with congenital or acquired heart diseases and immunocompromised patients are living longer due to medical and surgical advancements. Other, higher risk patient groups that have emerged include the intravenous drug user (IVDU), burn victims, and patients with intravascular devices such as indwelling catheters and vascular shunts.

In two separate reviews of IE cases, native valve IE accounted for 59-70%, IVDU related cases for 11-16%, and prosthetic valve recipients for 14-30%.[1,6] The incidence between reports varies based on the degree of predisposition and the patient population studied. For example, inner city hospitals may see as many as 40% IVDU-related IE patients.[7] The incidence of endocarditis among IVDUs without a previous cardiac lesion is as high as 5% annually and is estimated to be considerably higher in the presence of a previous cardiac lesion.[8] For prosthetic valve recipients, it has been estimated that, per year, 3-6% of these patients are likely to develop IE.[9]

For pediatric patients, IE accounts for 1-2 hospital admissions per 1000.[10] Of these, 59% are associated with previous congenital heart disease, and 69% with indwelling central vascular catheters.[11] Neonates are even more frequently infected with IE than older children. The incidence of IE in neonates born at less than 34 weeks gestation has been shown to be 4.3%. In addition, the incidence of combined infectious and non-infectious endocarditis in hospitalized neonates may exceed 5%.[12] Such a high rate in these patients is thought to be due to either surgical interventions or the universal use of intravascular prosthetic devices. Such interventions result in either episodes of bacteremia or endocardial trauma.

Recurrence rates among those with IE also vary. For example, reports show a recurrence rate of 41% for IVDUs compared to 2.5% for non-IVDUs.[13,14] This is most likely due to the continuation of high-risk behavior and the nature of the residual endocardial lesion.



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## Table 1. Predisposing Conditions to the Development of IE

A. CARDIAC CONDITIONS

- High risk
  - Prosthetic cardiac valves
  - Previous bacterial endocarditis
  - Complex cyanotic congenital disease
  - Prosthetic shunts or conduits
- Moderate risk
  - Other congenital cardiac malformations*
  - Acquired valvular dysfunction
  - Hypertrophic cardiomyopathy
  - Mitral valve prolapse (High risk with cardiac dysfunction)

B. RECURRENT BACTEREMIC STATES

- Intravenous drug use
- Intravascular prosthesis
- Hemodialysis shunts
- Infected central line catheters
- Extensive burn injury
- Significant dental infection

* Low risk lesions are not listed here. For a thorough description, refer to Dajani et al. 1997.[60]

## Mortality

The overall mortality rate associated with IE approaches 40%[15] but varies among patient groups. Variation is based on underlying medical illnesses, which structures of the heart are infected, and what organism(s) is responsible. Mortality ranges from 16% to 27% in native valve disease where the best predictor of a poor prognosis is accompanying congestive heart failure (CHF).[6] In prosthetic valve recipients, mortality rates vary from 30% to 80% for the early form of the disease (< 60 days following surgery) to 20-40% for the late form (> 60 days post surgery).[9] Mortality in IVDU is lower than that of native valve in part due to a lower mortality rate of right-sided disease (8%) compared to left-sided disease (18%).[7] For IVDUs, HIV seropositivity does not appear to be a predictor of a poor outcome. However, a clear negative correlation is seen with patients who have CD4 counts less than 200. The mortality rate of of IVDUs with CD4 counts of less than 200 was 56%, whereas those with a count higher than 200 had a mortality rate of 6-9%.[7]

Another contributing factor to mortality is the specific organism(s) involved, although the degree of contribution is hard to gauge in light of the various comorbid conditions in each patient. Often, patients will succumb secondarily to associated morbidity, such as cardiac dysfunction and/or cerebral vascular events. It has been shown that the rate of peripheral embolization is related to the etiologic organism.[16] What is certain is that the more virulent organisms, such as *S. aureus*, mixed floral infections, and pseudomonal species, result in more rapid and extensive structural damage to the endocardial structures, which is associated with an increased mortality in the patients affected.

## Pathophysiology

IE is an infection of the internal structures of the heart. Any structure can be affected but more common sites include the valvular leaflets, papillary muscles, membranous septum, and the valvular rings. IE can be divided into those arising from native valves (native valve endocarditis [NVE]) or those arising from prosthetic valves (prosthetic valve endocarditis [PVE]). The endothelial lining of native structures naturally resists the adhesion of microorganisms. Infections typically begin when an initial insult to the endothelium results in the formation and adhesion of a sterile thrombus-platelet vegetation. Subsequent septic events lead to seeding of the thrombus by microorganisms. As the vegetation evolves, microorganisms become embedded in the fibrin clot and thereby evade both cellular and humoral host defenses. Predisposing conditions to the development of IE are summarized in Table 1.

Prosthetic valves are much more susceptible to infection since the foreign materials used are less resistant to the adhesion of microorganisms. Risks of developing endocarditis have been shown to be similar for both mechanical and bioprosthetic valves.[9] Sites of microbial adhesion include graft surfaces, suture lines, and supporting structures disrupted during the operative procedure. Graft infections are considered to be more progressive since infection occurs at the valvular annulus as opposed to the valvular leaflets, therefore it is more likely to progress to abscess.[17] A previous endocardial lesion need not be present for PVE. Extremely virulent organisms such as *S. aureus, S. pneumoniae*, and pseudomonal species have the ability to invade uninjured valvular grafts.[18]

NVE usually results from two predisposing conditions: a previous endocardial lesion and/or episodes of bacteremia. Contrary to classical belief, a previous lesion is not absolutely necessary. One study of 80 cases of NVE showed 55% have a previous endocardial lesion and 45% to have no previous lesion. Likewise, only 46% were shown to have predisposing conditions for bacteremia.[6]

Causes of endothelial injury that predispose to IE can be either congenital or acquired. In either case, endothelial damage results from high-pressure gradients and turbulent flow. Common predisposing lesions include congenital heart disease, mitral valve prolapse, rheumatic valvular disease, degenerative disease, mechanical injury, and a history of endocarditis. Case analysis of pediatric IE showed that the most common predisposing lesions were congenital in nature. These included ventricular septal defects (19%), pulmonary atresia (11%), transposition of the great arteries (9%), coarctation of the aorta (8%), tetralogy of Fallot (8%), and pulmonary valve stenosis (8%).[19] Rheumatic heart disease was noted in only 2% of these cases.[19]

Acquired heart disease predisposing to IE is often degenerative in nature and is seen more commonly in the elderly. Commonly reported predisposing lesions in adult cases of NVE include calcific aortic stenosis stemming from a bicuspic valve (15%), mitral valve prolapse (13%), rheumatic heart disease (11%), and congenital heart disease (9%).[6] Other immunologically mediated and degenerative changes that result in endothelial damage and predispose to IE include systemic lupus erythematosus, hypertrophic cardiomyopathy, and Marfan's syndrome. Endocardial damage resulting in IE may also be procedure related, which is most often seen in neonatal IE. One study noted that 7 out of 11 reviewed neonatal IE cases had venous catheters with radiographic evidence of endocardial contact.[12] Vascular prosthesis, hemodialysis shunts, and any intravascular prosthetic device or conduits, such as a central line catheter, will predispose a patient to IE. In addition, severe burns, distant soft tissue infections, dental infections, and surgical procedures involving mucosal membranes are also considered significant predisposing factors for the development of IE.

IVDUs, with the exception of those having a previous case of IE, rarely have a history of predisposing endocardial lesions.

## Table 2. Causative Organisms in Separate Patient Groups¶

| Organisms | Patient groups (% involvement) | | | | | |
|---|---|---|---|---|---|---|
| | Native | Prosthetic | | IVDU | Pediatrics | Neonates |
| | | early | late | | | |
| *Staphylococcus aureus* | 30 | | 20 | 63 | 24 | 9 |
| Coagulase (-) Staphylococcus | 3 | 67 | 20 | | 11 | 18 |
| *Streptococcus viridans* | 16 | | 2 | 12 | 27 | |
| *Streptococcus bovis* | 6 | | | | 3 | |
| Pneumococcus | 2 | | | 4 | 5 | |
| Non-viridans Streptococcus | 42 | | 32 | 9 | 10 | |
| Enterococci | 7 | | 8 | 2 | 3 | |
| Serratia species | | | | < 1 | 1 | 9 |
| Pseudomonas | 1 | | | 1 | | |
| HACEK* | 4 | | 2 | | 4 | |
| Fungi** | 1 | | | 1 | 4 | 9 |
| Polymicrobial | 2 | | 2 | 2 | 9 | 18 |
| *E. coli* | 1 | | | | 2 | |
| Klebsiella | < 1 | | | < 1 | 3 | 27 |
| Culture negative | 6 | 33 | 8 | 5 | 3 | 0 |

¶ The causative organisms in previously reported cases of infectious endocarditis are shown. Determinations were based on culture results. Percentages were obtained by compiling published reports.

* HACEK = *Haemophilus parainfluenzae, Haemophilus aphrophilus, Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenella* species, and *Kingella* species

** Fungi = Candida, Histoplasma, and an unidentified fungi

Data for NVE was obtained from Sandre et al (80 cases), and Gagliardi et al (108 cases).

IVDU-IE: Sandre et al (15 cases), Pulvirenti et al (102 cases), and Mathew et al (122 cases).

Pediatric IE: Stockheim et al (129 cases) and Del Pont et al (38 cases).

Early and late PVE: Watanakunakorn et al (2 and 7 cases, respectively), and Sandre et al (27 and 33 cases, respectively).[1,6,7,19,11,23,24]

Organisms not included above were Serratia, Bacillus, Salmonella, Enterobacter, diptheroids, and Corynebacterium. They all entailed < 1% involvement.

Rather, the cause of endothelial injury is thought to be either the result of adjunctive compounds (e.g., talc and other particulates that are injected along with the elicit drug)[20] or direct invasion by highly virulent organisms. The major source of organisms is skin flora that inoculates the blood stream during injection. Other sources include pseudomonal species from washing needles in contaminated water[21] and *Neisseria sicca* from licking needles prior to their use.[22]

Regions of the heart affected vary based on the initiating events. Acquired and congenital lesions typically affect the left side of the heart. This is the result of high turbulent left-sided flow that results in endocardial damage. The aortic valve is the most common valve affected in NVE (39%), followed by mitral valve infection (29%).[6] Aortic valve involvement in the elderly is often the result of degenerative changes. Mitral valve involvement can be seen secondary to an existing mitral valve prolapse or rheumatic heart disease.

Right-sided lesions are almost invariably the result of intravenous drug use, but may occur in right heart catheterization and urosepsis. Here, the tricuspid valve is most commonly affected (60%) and often is accompanied by left-sided involvement (13%).[6,23] The structures involved in prosthetic valve recipients are defined by site of the graft but may extend to involve adjacent structures.

## Etiologic Organisms

Organisms responsible for IE have changed considerably over the past several decades. The organism responsible for IE was once predominantly *Streptococcus viridans*, but now commonly includes non-viridans streptococci, a variety of coagulase positive and negative staphylococci, and nosocomial organisms including fungi. Other commonly seen organisms are enterococci, the HACEK group (*Haemophilus parainfluenzae, Haemophilus aphrophilus, Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenella* species, and *Kingella* species), pseudomonas, and enteric organisms. Table 2 summarizes commonly seen organisms responsible for IE separated by patient groups.

The most common organisms reported in NVE were non-viridans streptococci (42%, collectively), *S. aureus* (30%), viridans streptococci (16%), and enterococcus (7%). Of the streptococcal species *S. viridans* was reported as the most common (16%), followed by *S. bovis* (6%), *S. pneumoniae* (1%), and Groups A, B, and others (each < 1%).[6,24]

Recent reports on the etiologic organisms in IVDU-associated IE by Sandre et al (15 cases), Pulvirenti et al (102 cases), and Mathew et al (122 cases) are also summarized in Table 2.[6,7,23] *Staphylococcus aureus* remains the most common organism (50-80%) responsible for IE in IVDUs, followed by streptococcal species such as *S. viridans* (12%), non-viridans streptococci (9%, collectively), *S. pneumoniae* (4%), *S. pyogens* (1%), and β-hemolytic Streptococcus (< 1%). Other organisms include enterococcus (2%) and various gram-negative organisms, including pseudomonas (1%), fungal (1%), and polymicrobial (2%) organisms.

The etiologic organisms responsible for PVE vary significantly between the early and late forms of the disease. Early infection (< 60 days post surgery) tends to be hospital acquired and caused by common nosocomial pathogens specific to the institution. Table 2 summarizes causative organisms in early (7 cases and 2 cases) and late (27 cases and 33 cases) PVE as reported by Sandre et al and Watanakunakorn et al, respectively.[6,1] Organisms reported in the late form of the disease were more varied. In early onset PVE, coagulase-negative staphylococci were responsible for six of the nine cases and the remainder were culture negative. The etiology of late onset PVE tends to reflect that of NVE as is also seen in Table 2.[25]

The causative organisms in 167 pediatric cases of IE were reported by Stockheim et al (129 cases) and Del Pont et al (38

## Table 3. Clinical Features of IE

**SYMPTOMS**
- Fever
- Chills
- Arthralgia/myalgia
- Back pain
- Pleuritic chest pain
- Malaise/weight loss
- Mental confusion
- Symptoms of CHF

**SIGNS**
- Temperature > 38°C
- New or changing murmur
- Pneumonia
- Vascular phenomena:
  - Janeway lesions
  - conjunctival hemorrhage
- Immunologic phenomena:
  - Osler's nodes
  - Roth's spots
- Petechiae
- Hepatomegaly
- Splenomegaly
- Clubbing
- Splinter hemorrhages
- CNS manifestations

**LABORATORY FINDINGS***
- Persistently positive blood cultures
- Positive serologic studies (organisms typical of IE)
- Anemia (Hb ≤ 10 g/dL*)
- Elevated ESR (> 30 mm/hr*)
- Elevated WBC (> 10,000 cells/$mm^3$*)
- Positive rheumatoid factor
- Hematuria (gross or microscopic)
- Pyuria
- Proteinuria
- Renal insufficiency
- Chest x-ray:
  - congestive heart failure
  - septic emboli
  - pneumonia

**ECHOCARDIOGRAPHY**
- Vegetation
- Valvular thickening
- Endocardial abscess
- Valvular dehiscence
- Cardiac dysfunction

**CNS ABNORMALITIES**
- Intracranial hemorrhage
- Arterial embolism
- Aseptic meningitis
- Mycotic aneurysm

* Specific laboratory thresholds were derived from prior case studies that carried significant differences between IE and non-IE cases.

cases).[11,19] These are also summarized in Table 2 and include most commonly *S. viridans* (27%) and *S. aureus* (24%). In addition, 11 cases of neonatal IE were reported by Pearlman et al.[12] The most common organisms seen were Klebsiella, *S. aureus*, and polymicrobial infection. *(See Table 2.)*

## Clinical Presentation: Overview

Patients with IE have been traditionally categorized as either subacute or acute based on their initial presentation and clinical course. Subacute IE is more consistent with the classical Oslerian description of vascular and embolic phenomena and is typical of disease caused by *Streptococcus viridans.* This form of the disease has an insidious onset and may mimic other systemic illnesses with low-grade fever, night sweats, fatigue, malaise, weight loss, and symptoms of cardiac dysfunction. Acute IE is more characteristic of rapidly progressing symptoms, which causes patients to present for care prior to manifestation of vascular or immunologic phenomena. These individuals may appear rather toxic, with fulminant symptoms including hypotension, widespread metastatic infections, high fever, and sudden valvular insufficiency. Organisms known to be associated with acute IE are *S. aureus, Streptococcus pneumoniae, Neisseria gonorrhoeae,* and enterococcal species. Unfortunately, the presentation of IE as a syndrome is highly varied and may be better thought of as a spectrum between these two extremes. Findings consistent with IE are summarized in Table 3.

## Symptoms

Because of the vascular and embolic nature of IE, multiple organ systems are often affected, which, in turn, leads to a varied clinical presentation. Classic Oslerian findings, such as an active endocardial process, vascular embolic phenomena, and persistent bacteremia, are seen more often in subacute than acute presentations, but are usually absent in the majority of cases. Often, patients will present with rather vague, non-specific and otherwise misleading complaints. *(See Table 3.)* Common non-specific complaints often include fever/chills, arthralgia/myalgia, nausea/vomiting, weight loss, cough, pleuritic chest pain, headache, and low back pain. Subjective fever is the most common of these complaints but this may be absent in certain patient subgroups such as those with renal disease, CHF, prior antibiotics, and in patients presenting with a ruptured mycotic aneurysm.[26]

Pulmonary symptoms such as pleuritic chest pain are most commonly reported in IVDU-IE (33%) as compared to NVE (13%).[6] Arthralgias and myalgias are more often seen in PVE (61-71%) than in NVE (25%), IVDU-IE (20%),[6] or pediatric patients (13%).[11] The most common constitutional complaint in pediatric patients are malaise and weight loss (39%).[11] Cardiovascular symptoms stem directly from the invading organism and valvular dysfunction. Patients may present with angina or symptoms suggestive of new or worsening CHF. Vascular embolic events may affect any organ system giving rise to headache, mental status changes, stroke, myocardial ischemia secondary to coronary embolization, hemoptysis, back pain, abdominal pain, or hematuria.

## Physical Examination

Physical findings associated with IE are highly variable. Individual presentations depend upon the duration of symptoms, the endocardial structures affected, underlying conditions, and the etiologic agent. These signs are summarized in Table 3. The most commonly reported sign in IE, although non-specific, is fever greater than 38°C which occurs in 63-77% of NVE,[1,6] 42-78% of IVDU-related IE,[1,6,23] 50-71% of early onset PVE, 70-71% of late onset PVE,[1,6] and 78-97% of pediatric IE.[11,19]

Cardiac findings, although less consistent, are just as common. These include a new or evolving murmur that may or may not be regurgitant in nature. The predominance of a murmur, irrespective of its nature, varies from 24% to 95% in recent reports.[1,6,11,19,23] Damage to the endocardial structures with resultant valvular dysfunction can produce signs of CHF such as dependent edema, pulmonary edema, and hypoxia. Reports have shown a slightly lower rate of CHF for IVDU-related IE (21%) compared to other patient groups (32-52%).[1,11] This is most likely due to the higher incidence of right-sided heart disease in IVDU-related IE. Mural involvement can also result in arrhythmia, fistula formation, and pericardial effusions that in turn can lead to cardiogenic shock or sudden death.

Vascular phenomena specific to endocarditis, if present, can be very helpful in formulating a diagnosis. Vascular findings with IE are more often seen in subacute disease and late onset PVE where there has been a longer duration of symptoms, and are less common in acute onset disease, early onset PVE, and disease isolated to the right side of the heart. In addition, the rate of peripheral embolization is dependent on the etiologic organ-

ism.[16] Vascular phenomena specific to IE include Janeway lesions, conjunctival hemorrhages, major arterial emboli, septic pulmonary infarcts, and mycotic aneurysm. Each of these is found in less than 10% of patients. Generally speaking, left-sided disease results in systemic vascular involvement and right-sided disease results in pulmonary vascular involvement. Septic pulmonary emboli is a hallmark of right-sided IE and, as evidenced by radiography, is present in 28% of IVDU-related IE.[23] One should keep in mind that up to one in five of the cases of right-sided IE has accompanying left-sided disease and may therefore have concurrent systemic embolic phenomena.

Other non-specific vascular phenomena that are seen in IE include intracranial hemorrhage, splinter hemorrhages, and a petechial rash. Late findings include splenomegaly resulting from emboli or abscess, hepatomegaly, and clubbing. Immunologic phenomena are also shown in Table 3. These include immune complex glomerulonephritis presenting with proteinuria and/or microscopic hematuria.

The cornerstone of the laboratory evaluation of IE continues to be the demonstration of a persistent bacteremia. Culture results permit identification of the etiologic organism and determination of the antibiotic susceptibility profile. IE is characterized by a continuous bacteremia with a high frequency of positive blood cultures. Early reports have shown that 95% of blood samples drawn from culture positive cases of IE yielded the causative organism and that all cultures were positive in 91% of these cases.[27] However, the incidence of culture negative IE has been increasing.[28] Causes of culture negative IE include infection with non-bacterial or highly fastidious bacterial organisms, poor technique, and recent antimicrobial therapy. Because early signs of IE are often vague and non-specific, many patients are treated with antimicrobials for presumed minor upper respiratory or urinary tract infections. Prior antimicrobial therapy has been shown to decrease the yield of blood cultures by up to 40%.[28,29] For this reason, past and present diagnostic criteria have suggested that three sets of blood cultures (with a set including an aerobic and anaerobic bottle) be drawn prior to the administration of antibiotics, with at least one hour of time spanning the first and last sample.[30,31]

Specific blood culture criteria for the diagnosis of IE is outlined in the section on diagnostic criteria. For continued culture negative results, the AHA recommends that serologic or polymerase chain reaction (PCR) studies for the detection of fastidious organisms known to cause IE (*Coxiella burnetii, Brucella, Bartonella*, chlamydia, or *Tropherema whipelli)* be considered.[3]

Other common laboratory findings include anemia, an elevated white blood cell count, an elevated erythrocyte sedimentation rate, and an elevated serum rheumatoid factor. Routine laboratory screening can also reveal evidence of renal involvement. This stems from either embolic events or immune complex glomerulonephritis resulting in laboratory findings of azotemia, elevated blood creatinine levels, proteinuria, and either gross or microscopic hematuria.

## Diagnostic Challenges

Most cases of IE cannot be definitively diagnosed in the ED setting. A definitive diagnosis requires serial blood cultures and positive echocardiographic findings.[32] The classic Oslerian presentation is rare. The diagnostic dilemma exists with patients who have a predisposition to the development of IE and present with vague, non-specific symptoms. Early recognition of IE is crucial; one must keep a high clinical suspicion when dealing with any patient who may be at increased risk for the development of IE. Consequently, high-risk patients are admitted for intravenous antibiotics until culture results and echocardiography can exclude IE as the diagnosis.[32,33] This has led to a number of trials attempting to develop a predictive score for IE, with limiting success.[17,28,34,35] Each of these studies was unable to establish a set of clinical rules to consistently diagnose IE on the basis of clinical signs and symptoms alone. Diagnosis still depends on culture results and echocardiographic findings, with the gold standard being tissue biopsy.[3,6]

**Echocardiography.** Echocardiography is a primary diagnostic modality in IE and is second only to histologic findings. Direct imaging of the internal structures of the heart yields valuable information about the underlying cardiac lesion and its severity. These findings help the clinician develop management strategies and, in some cases, provide prognosis. For this reason, an echocardiogram should be performed in all patients suspected of having IE.[30]

Observed lesions that are considered specific for IE include an oscillating intracardiac mass located at sites where vegetation typically occurs, findings consistent with intracardiac abscess, and a new partial dehiscence of a prosthetic valve.[30] Other associated findings helpful in management include locating areas of turbulence, valvular regurgitation, papillary muscle dysfunction, and wall motion abnormalities.[36]

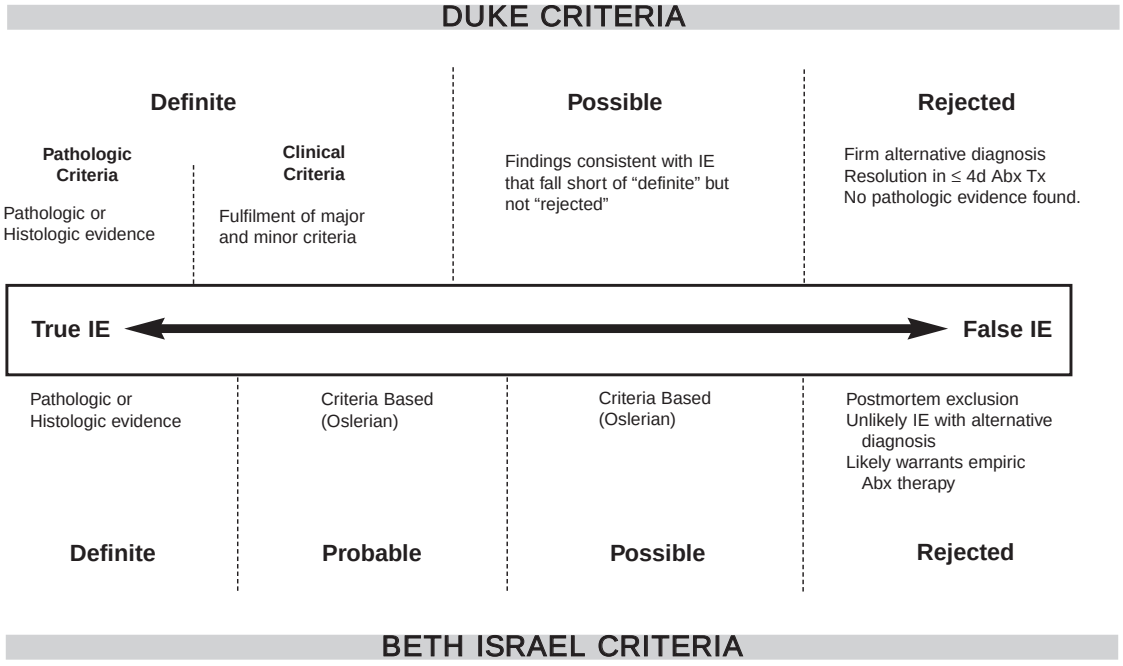
Two modalities are utilized for the diagnosis of IE: transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE). TEE has been shown in a number of comparison studies to be superior to TTE, with sensitivities of 90-100% compared to 28-63%, respectively.[37,38,39,40] TEE is also more effective in detecting abscesses and valve perforation as complications of IE.[41,42] One exception might be in cases of right-sided IE where TTE has been shown to be as effective as TEE in identifying valvular vegetations, but it remains less precise than TEE.[43] The benefit of TEE is most dramatic in patients with prosthetic valves where the sensitivity of TTE drops considerably due to shadowing effects imparted by the prosthetic devices. TEE is more costly, time-consuming, and more invasive, and therefore it is not the primary method utilized in most institutions. Generally speaking, current practice is to perform TTE first because it is less costly and easier to perform.[3,32]

In December of 1998, the AHA reported recommendations for the approach to the diagnostic use of echocardiography in IE.[3] Initial TTE is recommended for low risk patients. TEE would then follow in those cases with a negative and/or technically inadequate TTE study in which there is a high clinical suspicion of IE. In those patients where TTE reveals high-risk features, TEE should follow to determine and characterize associated complications. High-risk patients or those which are predicted to be difficult imaging candidates should undergo TEE as the initial study.

## Diagnostic Classification Schemes

The classic Oslerian manifestations of IE (the presence of persistent bacteremia or fungemia, the presence of active valvulitis, the occurrence of large-vessel embolic events, and the presence of immunologic vascular phenomena) remain specific predictors of the disease. Historically, these signs have remained the crux of the clinical diagnosis; however, 20-30 years ago an increasing number of atypical presentations began to appear in the literature. This has been attributed to increasing mean age of

## Figure 1. Diagnostic Evaluation Criteria for Infective Endocarditis




patients with IE, a shifting in the microbiologic spectra from predominantly streptococcal to staphylococcal species, and an increasing population of new predisposing conditions such as intravenous drug use and those with prosthetic valve placement.

This wide range of presentations has led to the proposal of diagnostic strategies to characterize IE. The high mortality of IE mandates a sensitive means of diagnosis. The first of these criteria was proposed in 1981 by von Reyn (the Beth Israel criteria), which categorized IE into "definite," "probable," "possible," and "rejected."[31] *(See Figure 1.)* Inclusion into the definite category requires the "gold standard" of either tissue histology or microbiologic evidence acquired from autopsy or surgery. The probable and possible categories required fulfillment of various criteria that consisted of classic manifestations specific to IE. At the time of its proposal, the Beth Israel criteria effectively standardized the diagnostic criteria for IE.

During the last three decades, both the organisms and etiologies responsible for IE, as well as the technologies available to identify IE have changed. These resulted in a number of problems when applying the Beth Israel criteria.[30] First, echocardiographic imaging was not utilized in the stratification process and has since become a very effective tool for the diagnosis of IE. Second, there have been an increasing number of cases of acute IE that do not manifest vascular phenomenon. Third, medical management has improved, resulting in less than one of three patients undergoing surgery in the acute phase. These patients would therefore not meet criteria for "definite" IE. Lastly, intravenous drug use, an increasing problem in infectious endocarditis, was not recognized as a significant predisposing condition. These patients have a higher proportion of atypical presentations and would therefore fail to meet Oslerian-based criteria for IE.

In 1994, Durack et al proposed a new diagnostic criteria (the Duke criteria).[30] The Duke criteria included intravenous drug use as a predisposing factor for IE and used echocardiography in the stratification process. Cases were divided into "definite," "possible," and "rejected." The "definite" category was broadened to not only include the pathologic confirmation of the Beth Israel criteria but also to include specific clinical parameters. Thus, the Duke criteria allowed for the categorization of cases as "definite" based on clinical criteria alone. Those classified as clinically "definite" were required to meet a number of major or minor criteria. Here, specific echocardiographic findings were listed as major criteria, along with the important diagnostic parameters used in the Beth Israel criteria, namely persistent bacteremia or fungemia, new cardiac murmurs, and vascular phenomena. "Possible" IE was listed simply as those falling short of "definite" but not "rejected." "Rejected" cases were defined as those that either had been excluded by biopsy, to which a firm alternate diagnosis existed, or in which the symptoms resolved after a short course of antibiotics (< 4 days). *(See Tables 4 and 5.)*

Since the proposal of the Duke criteria, multiple separate studies (~1700 total cases) have been conducted to directly compare these two criteria.[11,19,24,28,30,44-48] Cases analyzed included a variety of patient groups ranging from pediatrics to the elderly to IVDUs. Each of these studies suggested that the Duke criteria had higher sensitivity with a greater number of "definite" cases and fewer "rejected" cases. In addition, the Duke criteria were shown to be in close agreement (71-99%) to infectious disease experts who were blinded to underlying infectious endocarditis risk factors.[49] The negative predicted value was estimated to be at least 92 by prospectively following 52 consecutive "rejected" cases.[45] Evaluating specificity of the Duke criteria has received less attention. One retrospective study conducted on 100 patients at low risk for IE showed a specificity of 99%.[50] This has yet to be evaluated in high risk patients.

Modifications have also been suggested for the Duke "minor" criteria. This suggested adding diagnostic findings of elevated erythrocyte sedimentation rate, C-reactive protein,

newly diagnosed clubbing, splenomegaly, and microscopic hematuria. Including these minor criteria in the analysis of 118 consecutive cases of endocarditis resulted in an increase in the number of confirmed cases in the "definite" category by 10% without a loss in specificity.[51]

Critics suggest that the Duke criteria overemphasize sensitivity in a disease that is difficult to prove clinically. Misdiagnosing patients as "definite IE" would require long-term immediate management and once diagnosed would require life-long prophylactic measures. Another criticism that merits review is the undefined nature of the Duke "possible" IE. This category is defined simply as "cases consistent with IE that fall short of 'definite' but not 'rejected' and that require at least four days of antibiotic therapy." One suggestion states that "possible" IE would require a minimum of one major or three minor criteria.[3] This may serve to clarify the distinction between "possible" and "rejected" and to reduce the number of cases assigned to the former. On the other hand, narrowing the focus of the "possible" category would increase the number of true positives falsely rejected. A potential solution may be to add a fourth category of equivocal cases as in the Beth Israel criteria. The fourth category may prove worthwhile, especially with the increasing incidence of culture negative IE, in which the offending organism is not readily cultivated on routine culture media (*Coxiella burnetii*, Brucella, *Bartonella quintana*, chlamydia, or *Tropherema whipelli.)*[1,5,6] Combining specific serologic tests with culture results in the minor criteria would serve to better define these cases.

## Management

Hemodynamic stability is always the first priority. Presenting symptoms such as sepsis, shock, CHF, and embolic events should be dealt with promptly. Additionally, attention must be directed toward antibiotic coverage and other diagnostic studies helpful in determining long-term care needs. Cardiac surgery may be necessary for patients with destructive lesions or symptoms of cardiac dysfunction. Indications for surgical intervention include symptoms of CHF, arrhythmia, repeat infection, myocardial abscess, or continued embolic events.

Blood cultures should always be drawn prior to the initiation of antibiotic therapy. Thereafter, the goal of antibiotic therapy is to eradicate microorganisms from endocardial structures. This requires long courses of antibiotics and these patients may eventually require to cardiac surgery and valvular replacement. Antibiotic coverage should be directed at the most likely causative organism until culture results are known. Recommended antibiotic regimens adapted from the American Heart Association Guidelines are summarized in Table 5.[52]

For patients who present with a suspicion of community-acquired subacute IE, are non-toxic appearing and have no risk factors, initiation of immediate antibiotic coverage may not be necessary. However, if the diagnosis is evident and all cultures have been obtained, therapy can be initiated with treatment directed toward streptococcal species. Since most of these organisms are exquisitely sensitive to penicillin, recommended treatment includes penicillin (12-18 million units IV per day divided q4), and gentamicin (1.0 mg/kg IV q8h).

For patients presenting with acute IE, immediate treatment should be directed toward *S. aureus* using an anti-staphylococ-

### Table 4. Criteria for the Diagnosis of IE: Duke Criteria

**MAJOR CRITERIA**

- Positive blood culture for Infective endocarditis
  Typical microorganism for IE from two separate blood cultures in the absence of a primary focus.*
  Persistently positive blood culture defined as recovery of a microorganism consistent with IE from:
  Blood cultures drawn more than 12 hours apart, *or*,
  all of three or a majority of four or more separate blood cultures, with first and last drawn at least 1 hour apart
- Positive echocardiogram for IE
  1) Oscillating intracardiac mass, on valve or supporting structures, or in the path of regurgitant jets, or on implanted graft in the absence of an alternative anatomic explanation, or
  2) abscess, or
  3) new partial dehiscence of prosthetic valve, or new valvular regurgitation (increase or change in preexisting murmur not sufficient).

**MINOR CRITERIA**

- Predisposing heart condition or intravenous drug use
- Fever: > 38.0°C (100.4°F)
- Vascular phenomena: major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, Janeway lesions
- Immunologic phenomena: glomerulonephritis, Osler's nodes, Roth spots, rheumatoid factor
- Positive blood culture but not meeting major criterion† or sero logic evidence of active infection with organism consistent with IE
- Echocardiogram: consistent with infective endocarditis but not meeting major criterion

**ADDITIONAL MINOR CRITERIA¶**

- Newly diagnosed splenomegaly
- Newly diagnosed clubbing
- Splinter hemorrhages
- Petechiae
- Elevated ESR‡
- Elevated C-reactive protein level (> 100 mg/L)
- Microscopic hematuria§
- Central nonfeeding venous lines
- Peripheral venous lines

* Viridans and nutritional variant streptococci, *Streptococcus bovis*, HACEK group (Ha*emophilus parainfluenzae, Haemophilus aphrophilus, Actinobacillus actinomycetemcomitans, Cardiobacterium hominis*, *Eikenella* species, and *Kingella* species), community-acquired *Staphlococcus aureus*, enterococci, in the absence of a primary focus.

† Excluding single positive cultures for coagulase-negative staphylococci and organisms that do not cause endocarditis.

‡ ESR > 30 mm/h for patients < 60 years of age; > 50 mm/h for patients > 60 years of age.

§ Hematuria disregarded for patients with other likely causes of the finding.

¶ Suggested modifications (Adapted from Lamas, et al, 1997).[51]

The Duke Criteria are reprinted with permission from Excerpta Medica Inc.: Durack, et al. New criteria for diagnosis of infective endocarditis: Utilization of specific echocardiographic findings. *Am J Med* 1994;96:200-209.

## Table 5. Suggested Antibiotic Regiments for the Treatment of IE due to Specific Organisms

| Organism | Antibiotic | Alternate Antibiotics |
|---|---|---|
| Streptococci | PCN G 12-18 million U/24 h × 4-6 weeks<br>and<br>Gentamicin 1 mg/kg q8 h × 2 weeks† | Vancomycin 30 mg/kg/24 h × 4 weeks<br>or<br>Ceftriaxone 2g qd × 4 weeks |
| Enterococci | PCN G 18-30 million U/24 h × 4-6 weeks<br>and<br>Gentamicin 1 mg/kg q8 h × 4-6 weeks | Ampicillin 12 g/24 h × 4-6 weeks<br>or<br>Vancomycin 30 mg/kg/24 h × 4-6 weeks<br>and<br>Gentamicin 1 mg/kg q8 h × 4-6 weeks |
| Staphylococci | | |
| (Methicillin-susceptible) | Nafcillin 2 g q4 h × 4-6 weeks<br>and<br>Gentamicin 1 mg/kg q8 h × 3-5 days† | Cefazolin 2 g q8 h × 4-6 weeks<br>and<br>Gentamicin 1 mg/kg q8 h × 3-5 days†<br>or<br>Vancomycin 30 mg/kg/24 h × 4-6 weeks |
| (Methicillin-resistant) | Vancomycin 30 mg/kg/24 h × 4-6 weeks | |
| In the presence of prosthetic material<br>(Methicillin-susceptible)‡ | Nafcillin 2 g q4 h × ≥ 6 weeks<br>and<br>Gentamicin 1 mg/kg q8 h × 2 weeks<br>and<br>Rifampin 300 mg PO q8 h × ≥ 6 weeks | |
| HACEK § | Ceftriaxone 2 g qd × 4 weeks | Other third-generation cephalosporins<br>or<br>Ampicillin 12 g/24 h × 4 weeks<br>and<br>Gentamicin 1 mg/kg q8 h × 4 weeks |

§ HACEK = *Haemophilus parainfluenzae, Haemophilus aphrophilus, Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenella* species, and *Kingella* species.
* Adapted from Wilson et al.[52]
† Gentamicin may be excluded for highly susceptible streptococci and susceptible staphylococci.
‡ Vancomycin should be substituted for nafcillin in cases of resistant organisms in the presence of prosthetic material.

cal beta-lactam (nafcillin 2 gm IV q4) and an aminoglycoside (gentamicin 1.0 mg/kg IV q8h). Addition of an aminoglycoside has been shown to shorten the bacteremic episode and may also shorten the coarse of therapy.[53] For patients allergic to penicillin, vancomycin may be used as a substitution.

Additional considerations are required for patients who may be infected with resistant organisms such as nosocomial organisms, enterococcus, methicillin-resistant *Staphylococcus aureus* (MRSA), and coagulase-negative staphylococcus. Patients who are more likely to have this infection are those with recent antimicrobial therapy, recent hospitalization, valvular prosthesis, and intravenous drug users. For these patients, vancomycin should be used along with gentamicin. *(See Table 5.)* In addition, some authors have advocated the addition of rifampin to the treatment regiment.[52,54,55] Of concern is the emergence of vancomycin resistance such as that seen in vancomycin resistant enterococcus (VRE). One regimen that has shown success against VRE is treatment with the now approved quinupristin/dalfopristin combination along with doxycycline, and rifampin.[56] Additional blood cultures should be obtained 48-72 hours after initiation of antimicrobial therapy. Embolic events are more likely to occur early in the course of therapy. Therefore, patients should be monitored for an adequate clinical response. Persistently positive blood cultures after three days of therapy are an indication for valve replacement.[52]

The duration of treatment needed for complete eradication of organisms from endocardial structures continues to be an area of debate. Conventional therapy dictates continued intravenous antibiotic coverage for 4-6 weeks. Treatment protocols continue to be refined including outpatient management recommendations.[57] One recent study demonstrated that once daily administration of ceftriaxone (2 g IV) alone or in combination with once daily gentamicin (3 mg/kg IV) was as equally effective as long-term therapy for patients with streptococcal IE.[58] For IVDUs with disease isolated to the tricuspid valve, a two week course of cloxacillin alone or in combination with gentamicin was as effective as the standard treatment.[59]

## Prophylaxis

The currently accepted practice is to use antimicrobial medications during known episodes of bacteremia to prevent the development of IE. These prophylactic measures are reserved for significant episodes of bacteremia and for those patients known to be at a higher risk than the general population for the development of IE. Causes of bacteremia are numerous and often spontaneous. Any infection can lead to bacteremic episodes, but those involving mucosal surfaces are much more likely to do so. Some of the more obvious causes include focal infections, pneumonia, cellulitis, and urinary tract infections. In addition, procedures

## Table 6. Prophylaxis of Procedure-Related Infective Endocarditis

| PROCEDURE SITE | RELEVANT ORGANISMS* | PROPHYLACTIC RECOMMENDATIONS** (DIRECTED AT THE MOST COMMON ORGANISM) |
|---|---|---|
| **Dental, oral, esophageal** | Alpha hemolytic Streptococcus (viridans) | Amoxicillin 2.0 g PO (children 50 mg/kg) 1 hour before procedure, or |
| **Respiratory Tract** | Streptococcal species | Clindamycin 600 mg PO (children 20 mg/kg, or First-generation Cephalosporin, or macrolides |
| **Infected tissues** | | |
| genitourinary | gram (-) bacilli | Third-generation cephalosporin, aminoglycosides |
| skin (abscess/cellulitis) | Staphylococcal species<br>Streptococcal species | First-generation cephalosporin |
| **Gastrointestinal Tract and Genitourinary Tract** | enterococcus<br>gram (-) bacilli | High risk: Ampicillin + gentamycin IV or, Vancomycin + gentamycin<br>Moderate risk: Amoxicillin or vancomycin |
| **Cardiac and Specific Vascular surgery[§]** | *S. aureus*<br>Coagulase (-) Staphylococcus<br>Diptheroids<br>Streptococcus spp.<br>gram (-)<br>fungi | Perioperative only—directed toward *Staphylococcus* spp. and institutional specific nosocomial organisms |
| **Cardiovascular procedures** | similar to cardiac surgery, also consider nosocomial organisms | Procedure specific, generally not recommended.** |

* Suggested prophylactic regiments are directed at known procedure-related organisms. Specific treatment choices should always be dealt with on an individual basis.

** Exceptions to listed recommendations include drug allergy, previous abx use, intolerance of oral medications, and high risk conditions.

[§] Noncoronary vascular graft may merit antibiotic prophylaxis for the first six months postoperatively.

such as surgical, dental, or any instrumentation of mucosal surfaces are also likely causes of bacteremia. *(See Table 6.)*

The AHA, in conjunction with the American Dental Association, Infectious Disease Society of America, American Academy of Pediatrics, and the American Society for Gastrointestinal Endoscopy released suggested guidelines for prophylactic treatment for the prevention of bacterial IE.[60] These guidelines take into consideration the degree to which the patient's underlying condition creates a risk of endocarditis, the apparent risk of bacteremia with the procedure, adverse reactions to the particular prophylactic regimen, and cost-benefit aspects. Specific cardiac lesions were stratified into high, moderate, and low risk. High and moderate risk lesion are shown in Table 1. Low-risk lesions are numerous and in general are those where no significant valvular dysfunction exists. Please refer to the AHA report for a more detailed discussion.[60]

General considerations in choosing a specific antimicrobial for prophylaxis include the most likely organism associated with the expected procedure, recent antimicrobial therapy, and the likelihood of resistant organisms. Suggested regimens are outlined in Table 6. For dental procedures, prophylaxis with amoxicillin or ampicillin directed at viridans streptococci is recommended. The dose should be given one hour before the procedure. Clindamycin, first-generation cephalosporins, or macrolides are alternates for patients who are allergic to penicillin. The most common organism involved in IE associated with gastrointestinal or genitourinary procedures is enterococcus faecalis.[60,61] Prophylaxis entails dosing 30 minutes before the procedure with ampicillin and gentamycin for high-risk patients and amoxicillin or ampicillin for moderate-risk patients. High-risk patients should receive a second dose six hours later. For patients allergic to ampicillin, vancomycin can be used as the alternative.

High- and moderate-risk patients presenting with soft tissue infections such as cellulitis or abscess should receive appropriate antibiotic coverage prior to manipulations, debridement, or incision and drainage. Dosing should be administered 30-60 minutes prior to the procedure.[62] Coverage here should be directed toward staphylococcal and streptococcal species for which a first-generation cephalosporin is an appropriate choice.

Generally, the most common organisms associated with post cardiac surgery IE are *Staphylococcus aureus,* coagulase negative staphylococcus, and diptheriods. No single antibiotic covers these three organisms. Most hospitals have instituted treatment protocols for patients undergoing cardiac surgery and is based on the organisms typically involved in that institution.

Antibiotics for patients with either previous antibiotic therapy or those with previously isolated drug-resistant organisms should be selected on a case-to-case basis. For serial dental or other procedures, it is generally recommended to allow an interval of 9-14 days to avoid the emergence of resistant organisms and to allow the mucosal surface to repopulate with antibiotic susceptible organisms.[63] If a procedure is performed within a shorter interval, it is generally suggested to chose a different class of antibiotics. For culture-resistant organisms, antibiotics should be directed based on the known susceptibilities of that organism or likely organisms. The use of antibiotic prophylaxis for high risk behavior such as intravenous drug use is controversial and is not recommended. Additionally, physicians with extensive experience managing the IVDU population recognize that many "street-wise"

addicts routinely self administer antibiotics, thus contributing to an increasing incidence of antimicrobial resistance.

## Summary

The syndromes associated with IE have changed considerably over the last 30 years. Today, IE presents an increasing challenge to physicians. Patients at risk are living longer. Cardiac prosthetic devices and intravenous drug users are encountered more frequently. The classic Oslerian findings remain specific but do not always apply to these new patient subgroups. Many of these patients present acutely or with non-specific and misleading complaints.

The specific challenge for the emergency physician is ensuring initial recognition. Most often, a definitive diagnosis is obtained after the patient leaves the emergency department and undergoes further work-up. The delayed definitive diagnosis combined with a highly variable clinical presentation makes IE an ideal disease for the application of diagnostic criteria. Of the two proposed criteria discussed in this review, the Duke criteria have been shown to be the most sensitive and their use has been advocated by the AHA.[3] It allows for the clinical diagnosis of IE based on physical and laboratory findings. Criticism of the Duke criteria focuses on its emphasis of sensitivity with a loss of specificity. Further refinement may be directed at improving specificity while maintaining high sensitivity.

New treatment regimens may allow some patients home therapy instead of the traditional month-long inpatient stay. Regardless, infectious endocarditis remains a difficult clinical entity to recognize, a diagnostic challenge to confirm, and a difficult disease to cure.

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## Physician CME Questions

97. The most common predisposing condition to the development of IE in pediatric patients is:
    A. surgical procedures.
    B. congenital heart disease.
    C. acquired heart disease.
    D. prosthetic cardiac valves.

98. The most common causative organism of infectious endocarditis in intravenous drug users is:
    A. pseudomonal species.
    B. *Staphylococcus epidermidis.*
    C. *Streptococcus viridans.*
    D. *Staphylococcus aureus.*
    .

99. Which comorbid condition is the best predictor of poor patient outcome?
    A. HIV serostatus
    B. Prosthetic valve placement one year prior to presentation
    C. CD4 lymphocyte count higher than 200.
    D. Intravenous drug use
    E. Congestive heart failure (CHF)

100. Which statement is true regarding the pathogenesis of IE?
    A. Intravascular prosthetic devices predispose to infection irrespective of a previous endocardial lesion.
    B. Lesions are more likely to form in low-flow, static areas of the heart.
    C. Mechanical valves are more susceptible than bioprosthetic valves.
    D. Left-sided heart disease is more common than right-sided disease in IVDU.

101. In adults, the most common predisposing condition to the development of IE is:
    A. surgical procedures.
    B. congenital heart disease.
    C. acquired heart disease.
    D. prosthetic cardiac valves.

102. The most common organism involved in gastrointestinal or genitourinary procedure related IE and of which prior antibiotic prophylaxis is directed toward is:
    A. *Escherichia coli.*
    B. Pseudomonal species.
    C. Bacillus.
    D. *Enterococcus faecalis.*

103. Which statement is true when comparing the Duke criteria to the Beth Israel Criteria for the diagnosis of IE?
    A. The Beth Israel criteria do not utilize echocardiography in the stratification process.
    B. The Beth Israel criteria are more sensitive but less specific than the Duke criteria.
    C. The Duke criteria fail to allow definite diagnosis of IE by clinical criteria.
    D. Neither criteria consider IVDU as a predisposing condition to the development of IE.

104. The most common finding in patients who present with IE is:
    A. signs of congestive heart failure (CHF).
    B. hematuria/proteinuria.
    C. CNS changes.
    D. Rash.
    E. Fever higher than 38°C.

**In Future Issues:** Thoracic Abdominal Aneurysm