Chapter 1

Infective Endocarditis

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Outline

Introduction

Infectious endocarditis (IE) is a difficult diagnosis to make in the emergency setting. Early diagnosis and management requires an understanding of endocarditis risk factors, typical and atypical clinical presentations, and current diagnostic and empiric treatment strategies.

Epidemiology and Microbiology

In developed countries, the incidence of IE is roughly 5 cases per 100,000 persons per year. It more commonly affects males (2:1). Well-recognized risk factors for IE include presence of a prosthetic heart valve (which carry an annual incidence of approximately 1%), congenital heart disease, endocardiac devices, injection drug use (see Chapter 61), and a prior history of endocarditis. Rheumatic heart disease is now an uncommon predisposing risk factor in the United States. However, in modern series, there is no easily identifiable risk factor for underlying valve damage in approximately 50% of endocarditis cases. Such cases are believed to be due to age-related degenerative valve disease and subtle immunosuppresion from diabetic endocarditis and other factors. Health-care associated cases, often in the elderly, account for a growing proportion of endocarditis in the United States.

Infective endocarditis occurs when circulating pathogens adhere to damaged endothelium and form a vegetation, usually on or around a cardiac valve. Abnormal turbulent flow and damaged endothelium lead to fibrin and platelete deposition which presents a nidus for bacterial infection during bacteremia. In the setting of frequent bacteremia, such as intravenous drug use and dental infection, IE may occur even without an identifiable pathologic valvular lesion. Growth of the infected vegetation eventually leads to valve destruction and impaired function, typically regurgitation, and eventually heart failure. Invasion of the myocardium can lead to paravalvular abscess and heart block. Large, mobile vegetations are associated with embolization and metastatic infection (see below).

The list of pathogens that have been reported to cause IE is enormous and includes fungi and protozoa. The most common etiolgies, however, are gram-positive cocci, including *Staphylococcus* species, both *S. aureus* and coagulase negative *Staphylococcus*, and Streptococcal species, particularly viridans Streptococci and group D *Streptococcus*. *S. aureus* is both the most common etiology and the pathogen most often associated with metastatic complications. *Enterococcus* is common in the elderly. The clinical setting may suggest the pathogen involved: *S. aureus* is the most common in injection drug users, viridans Streptococci in patients with recent dental procedures, and gram-negative bacilli in patients that have undergone invasive genitourinary procedures.

Pathogens that are less commonly implicated in IE include the "HACEK" (*Haemophilus aphrophilus*, *Haemophilus paraphrophilus*, *Haemophilus parainfluenzae*, *Actinobacillus actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens*, *and Kingella kingae*) group of fastidious bacteria, *Bartonella*, chlamydia, *Legionella*, and fungi. Infections with these organisms may be difficult to detect because they do not always grow in routine blood cultures.

Clinical Features

The presentation of IE (see Table 1.1 and Figure 1.1) ranges from the well-appearing patient with non-specific symptoms to the toxic patient in severe septic shock with multi-organ failure. Symptoms are often frustratingly non-specific, and may include low-grade fever, malaise, myalgias, headache, and anorexia. Patients with mild symptoms are often misdiagnosed as having a viral syndrome. Approximately 80% of patients with IE will have a fever during their initial emergency department stay. The presence of a new murmur may be helpful;

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Table 1.1 Clinical Features: Infective Endocarditis

Pathogens	*Staphylococcus aureus* *Staphylococcus epidermidis* Viridans *Streptococcus bovis* *Enterococcus* spp. HACEK Immuno-compromised: fungal, rickettsial, protozoan
Signs and symptoms	Fever, malaise, weight loss, night sweats, myalgias, headache, chest/neck/back pain, cough, dyspnea, hepatosplenomegaly, hematuria, arthritis, edema, neurologic symptoms, jaundice, rash.
Laboratory and radiologic findings	**Duke Clinical Criteria:** 2 Major *or* 1 Major + 3 Minor *or* 5 Minor **Major (microbiology):** Typical organisms × 2 blood cultures (*S. viridans*, *S. bovis*, HACEK, *S. aureus*, or *Enterococcus*) Persistent bacteremia (≥ 12 hours) 3/3 or 3/4 positive blood cultures **Major (valve):** Positive echocardiogram New valve regurgitation **Minor:** Predisposing heart condition or IDU Fever ≥ 38 °C (100.4 °F) Vascular phenomenon (arterial embolism, mycotic aneurysm, intracerebral bleed, conjunctival hemorrhage, Janeway lesions) Immune phenomenon (glomerulonephritis, Osler node, Roth spot, rheumatoid factor) Positive blood culture not meeting above criteria Echocardiogram – abnormal but not diagnostic

IDU – intravenous drug use.

however, the high prevalence of a baseline murmur in older adults makes this finding non-specific.

Patients with a more indolent or subacute presentation may display physical findings that result from the deposition of immune complexes in end-vessels throughout the body. These findings include the classic stigmata of IE: *Roth spots* (exudative lesions on the retina), *Janeway lesions* (painless erythematous lesions on the palms and soles), and *Osler nodes* (painful violet lesions on the fingers or toes), as well as hematuria (due to glomerulonephritis), subungual splinter hemorrhages, or petechiae of the palate and conjunctiva. These subtle signs of IE should be sought on examination; however, they are actually quite uncommon and their absence does not rule out IE.

In left-sided endocarditis, arterial embolization may occur in any organ system. The central nervous system is the most common location. Infections that initially appear to be focal or localized, particularly when due to *S. aureus*, may actually be the result of septic emboli from IE. Examples include stroke and spinal cord syndromes, mycotic aneurysms, osteomyelitis, epidural abscesses, septic arthropathies, necrotic skin lesions, and cold, pulseless extremities. Mycotic aneurysms may cause meningitis, headaches, or focal neurological deficits. Destruction of the mitral or aortic valve can cause acute respiratory failure and cardiogenic shock. Right-sided endocarditis may present with septic pulmonary emboli, which cause respiratory symptoms that may be mistaken for pneumonia or pulmonary embolism. Mechanical failure of the pulmonic or tricuspid valves can cause signs and symptoms of acute right-sided heart failure.

Other serious sequelae of endocarditis include intravascular hemolysis, and disseminated intravascular coagulation. Abscesses around the annulae of the cardiac valves may result in conduction blocks and bradydysrhythmias. Ventricular wall rupture may lead to cardiac tamponade or hemorrhagic shock, and extension into the coronary arteries may cause acute coronary syndrome.

Differential Diagnosis

The differential diagnosis of IE includes both acute and chronic infections, malignancies, and a wide spectrum of inflammatory and autoimmune disorders. However, IE should be suspected in any febrile patient with the following risk factors:

- injection drug use
- rheumatic heart disease
- valvular insufficiency
- indwelling catheter
- pacemaker

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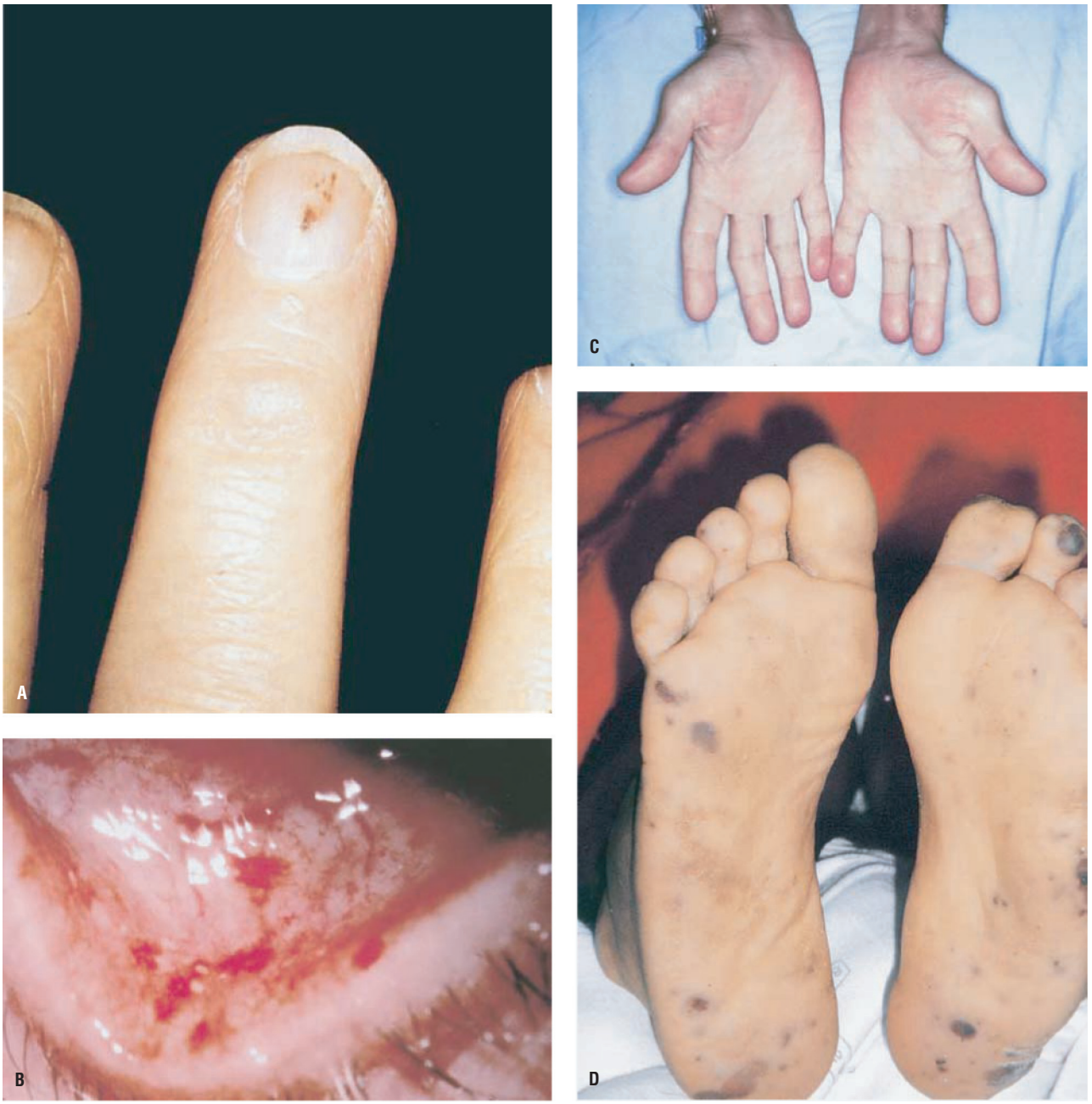

Figure 1.1 Classic physical examination findings in IE. Splinter hemorrhages (A); conjunctival petechiae (B); Osler nodes (C); and Janeway lesions (D).
Images from E. Mylonakis and S. B. Calderwood, Infective endocarditis in adults. *N. Engl. J. Med.*, 2001; 345(18): 1318–30.

- prosthetic heart valve
- congenital heart disease
- prior endocarditis

In more severe cases, the differential diagnosis will depend on the presenting signs and symptoms:

- severe sepsis with end-organ dysfunction: pneumonia, urinary tract infection, peritonitis, soft-tissue infections, and meningitis
- left- or right-sided heart failure: myocardial infarction, acute myocarditis, decompensated valvular disease, pulmonary embolism, or aortic dissection
- systemic embolization: carotid stenosis, vascular dissection, or cardiac dysrhythmias
- altered mental status with fever: meningitis, encephalitis, brain abscess

Laboratory and Radiographic Findings

Blood cultures are a crucial basis for the definitive diagnosis of IE. Thus, it is important for emergency providers to obtain blood cultures prior to giving antibiotics whenever IE is suspected. At least two and preferably three sets of blood cultures should be drawn with aseptic technique, be of

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sufficient volume (10 mL), and be drawn at multiple sites. The sensitivity of three sets of blood cultures approaches 90% in patients who have not received antibiotics. Serologies for Bartonella, Brucella, and Coxiella Burnetii (Q fever) may be indicated if standard cultures are negative. Other routine blood tests such as inflammatory markers (complete blood count [CBC], erythrocyte sedimentation rate [ESR], C-reactive protein [CRP]) lack specificity.

Endocarditis produces abnormal findings on standard diagnostic tests that can lead the clinician to an incorrect initial diagnosis. For example, an abnormal urinalysis may lead to a diagnosis of cystitis or glomerulonephritis, infiltrates on a chest X-ray may be interpreted as pneumonia, or abnormalities on a lumbar puncture may lead to a diagnosis of primary meningitis.

Electrocardiography (ECG) is seldom helpful in establishing the diagnosis of IE. The most common ECG abnormality in IE is sinus tachycardia. A valve ring abscess can produce heart block, particularly an elongating PR interval. Cardiac ischemia may result if IE extends into a coronary artery lumen.

Like blood cultures, echocardiography is an essential test in establishing the definitive diagnosis of IE. However, its main utility in the emergency setting is in the detection of life-threatening complications such as pericardial effusion, cardiac tamponade, and valvular rupture. Transthoracic echocardiography is useful if positive for a clear-cut vegetation; however, transesophageal echocardiography has higher sensitivity and is generally required in suspected IE if the transthoracic echocardiogram is negative.

The Duke Criteria (see Table 1.1) are a widely accepted, structured diagnostic tool for assisting in the often challenging diagnosis of IE. However, these criteria have limited utility in the emergency setting. Emergency providers must maintain constant vigilance for IE, have a low threshold for obtaining blood cultures and echocardiography in suspicious cases, and must exercise judgment in when to admit patients for empiric therapy.

Treatment and Prophylaxis

Empiric therapy targeting common IE bacterial pathogens is indicated when the diagnosis is strongly suspected. The empiric regimen should be tailored to whether or not there is a prosthetic valve, and, when possible, to the current hospital antibiogram (see Table 1.2). The duration of therapy is typically 4 to 6 weeks. It may be appropriate to withhold antibiotics pending culture results in patients with chronic, intermittent fevers who otherwise appear well, provided that close follow-up is available.

Antibiotic prophylaxis was previously recommended to all patients at risk from IE prior to certain invasive dental, gastrointestinal, and genitourinary procedures; however, this practice has now become controversial, with conflicting guidelines in the United States and Europe. While most procedures routinely performed in the emergency department do not require prophylaxis, prophylaxis should be strongly considered for dental or skin abscess incision and drainage (see Table 1.3) or skin infections (with vancomycin 20mg/kg IV × 1) in very high risk patients: those with a prior history of IE; prosthetic valve; heart transplant with abnormal valve function; repaired congenital heart disease.

Table 1.2 Empiric Treatment for Infective Endocarditis

Patient Category	Empiric Therapy Recommendation*
Adults	**Native valve:** Vancomycin 15–20 mg/kg/dose IV every 8–12 hours *and* Ceftriaxone 2 g IV every 24 hours (alternate: ciprofloxacin 400 mg IV every 12 hours) **Prosthetic valve:** Vancomycin 15–20 mg/kg/dose IV every 8–12 hours *and* Gentamicin 1 mg/kg IV every 8 hours *and* Rifampin 300 mg PO/IV every 8 hours
Children	Vancomycin 15–20 mg/kg/dose IV every 6 hours *and* Gentamicin 1.5–2.5 mg/kg IV every 8 hours
Pregnant women	Vancomycin 15–20 mg/kg/dose IV every 8–12 hours *and* Ceftriaxone 2 g IV every 24 hours *and* Rifampin 300 mg PO/IV every 8 hours (if prosthetic heart valve)
Immunocompromised	As above, depending on age and pregnancy status

* Vancomycin and gentamicin dosing may need to be adjusted based on renal function and ideal body weight. Trough monitoring with both agents is strongly recommended. Rifampin has many clinically important drug–drug interactions and may require other drug-level monitoring.

IV – intravenous.

Complications and Admission Criteria

The treatment of septic and mechanical complications of endocarditis can be challenging. In cases of suspected acute valvular dysfunction with pump failure, emergent echocardiography and consultation with a cardiothoracic surgeon and cardiologist are indicated. Anticoagulation with heparin is not recommended for septic emboli because it does not reduce further embolization and the risk of hemorrhagic transformation is very high. Limb-threatening emboli (e.g. a cold, pulseless extremity) may require revascularization with interventional or surgical techniques, such as the administration of local fibrinolytics.

Patients for whom the diagnosis of IE is suspected should generally be admitted for further work-up and empiric intravenous antibiotics. In selected cases, it may be appropriate to discharge febrile but otherwise well-appearing patients home with blood cultures pending, provided that reliable, urgent

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Table 1.3 Antibiotic Prophylaxis for Invasive Procedures in Highest Risk Patients

Patient Category	Recommended Antibiotic for ED Dental Procedures
Adults	Amoxicillin 2 g PO × 1 *if PCN allergy* Clindamycin 600 mg PO × 1 *Unable to take oral medications:* Ceftriaxone 1 g IV/IM × 1 *if PCN allergy* Clindamycin 600 mg IV/IM × 1
Children	Amoxicillin 50 mg/kg PO × 1 (max. 2 g/dose) *if PCN allergy* Clindamycin 20 mg/kg PO × 1 (max. 600 mg/dose) *Unable to take oral medications:* Ceftriaxone 50 mg/kg IV/IM × 1 (max. 1 g/dose) *if PCN allergy* Clindamycin 20 mg/kg IV/IM × 1 (max. 600 mg/dose)
Pregnant women	As above
Immunocompromised	As above

IM – intramuscular; IV – intravenous; PCN – penicillin; PO – by mouth.

follow-up is available. Patients with septic or mechanical complications of IE should be managed in a closely monitored setting, preferably one in which cardiothoracic surgical intervention is readily available.

Pearls and Pitfalls

1. Endocarditis is important to consider in any febrile patient with a predisposing valve disease or other risk factors.
2. Emergency providers can play an essential role in IE diagnosis by obtaining blood cultures prior to empiric antibiotics.
3. Mechanical complications of IE may require emergent cardiovascular surgery.
4. Do not heparinize patients with septic emboli and endocarditis.

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Additional Readings

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