Infective Endocarditis

Prevalence:

Infective endocarditis (IE) accounts for 0.5 to 1 of every 1000 hospital admissions, excluding postoperative endocarditis.

Pathogenesis:

1. Two factors are important in the pathogenesis of IE: a damaged area of endothelium and bacteremia, even transient. The presence of structural abnormalities of the heart or great arteries, with a significant pressure gradient or turbulence, produces endothelial damage. Such endothelial damage induces thrombus formation with deposition of sterile clumps of platelet and fibrin (nonbacterial thrombotic endocarditis), which provides a nidus for bacteria to adhere and eventually form an infected vegetation. Platelets and fibrin are deposited over the organisms, leading to enlargement of the vegetation.

2. Almost all patients who develop IE have a history of congenital or acquired heart disease. Drug addicts may develop endocarditis in the absence of known cardiac anomalies.

3. All congenital heart defects, with the exception of secundum-type atrial septal defect, predispose to endocarditis. More frequently encountered defects are tetralogy of Fallot, ventricular septal defect (VSD), aortic valve disease, transposition of the great arteries, and systemic-to-pulmonary artery (PA) shunt. Rheumatic valvular disease, particularly mitral insufficiency, is responsible in a small number of patients. Those with a prosthetic heart valve or prosthetic material in the heart are at particularly high risk for developing endocarditis. Patients with mitral valve prolapse (MVP) with mitral regurgitation (MR) and those with hypertrophic obstructive cardiomyopathy are also vulnerable to IE.

4. Any localized infection (e.g., abscess, osteomyelitis, pyelonephritis) can seed organisms into the circulation. Bacteremia frequently results after dental procedures, especially in children who have carious teeth or disease of the gingiva. Bacteremia also occurs with activities such as chewing or brushing the teeth. Chewing with diseased teeth or gums may be the most frequent cause of bacteremia. (Therefore, good dental hygiene is more important in the prevention of IE than antibiotic coverage before dental procedures.)

MICROBIOLOGY:

- α-Hemolytic streptococci (*S. viridans*) are the most common cause of endocarditis in patients who have had dental procedures or in those with carious teeth or periodontal disease.
- . Enterococci are the organisms most often found after genitourinary or gastrointestinal surgery or instrumentation.
- The organisms most commonly found in postoperative endocarditis are staphylococci.
- Intravenous drug abusers are at risk for IE caused by *S. aureus*.

- Fungal endocarditis (which has a poor prognosis) may occur in sick neonates, in patients who are receiving long-term antibiotic or steroid therapy, or after open-heart surgery.

- IE associated with indwelling vascular catheters, prosthetic material, and prosthetic valve is frequently caused by *S. aureus* or coagulase-negative staphylococci.

- Among newborn infants, *S. aureus*, coagulase-negative staphylococci, and *Candida* species are the most common causes of IE.

- Culture-negative endocarditis. A diagnosis of culture-negative endocarditis is made when a patient has clinical and/or echocardiographic evidence of endocarditis but persistently negative blood cultures. The most common cause of culture-negative endocarditis is current or recent antibiotic therapy or infection with a fastidious organism that grows poorly in vitro. Fungal endocarditis and IE caused by other rare organisms are rare causes of culture-negative endocarditis. At times, the diagnosis can be made only by removal of vegetation (during surgery). In the United States, about 5% to 7% of cases are culture-negative endocarditis.

- **CLINICAL MANIFESTATIONS**

History

1. Most patients have a history of an underlying heart defect. However, some patients with bicuspid aortic valve may not have been diagnosed with the defect before the onset of the endocarditis.

2. A history of a recent dental procedure or tonsillectomy is occasionally present, but a history of toothache (from dental or gingival disease) is more frequent than a history of a procedure.

3. Endocarditis is rare in infancy; at this age, it usually follows open-heart surgery.

4. The onset is usually insidious with prolonged low-grade fever and somatic complaints, including fatigue, weakness, loss of appetite, pallor, arthralgia, myalgias, weight loss, and diaphoresis.

Physical Examination

1. Heart murmur is universal (100%). The appearance of a new heart murmur and an increase in the intensity of an existing murmur are important.
2. Fever is common (80% to 90%). The temperature fluctuates between 101°F and 103°F (38.3°C and 39.4°C).
3. 3. Splenomegaly is common (70%).

4. Skin manifestations (50%) (either secondary to microembolization or as an immunologic phenomenon) may be present in the following forms:

A-Petechiae on the skin, mucous membranes, or conjunctivae are the most frequent skin lesions.

B-Osler's nodes (tender, pea-sized red nodes at the ends of the fingers or toes) are rare in children.

C-Janeway's lesions (small, painless, hemorrhagic areas on the palms or soles) are rare.

D-Splinter hemorrhages (linear hemorrhagic streaks beneath the nails) are also rare.

5. Embolic or immunologic phenomena in other organs are present in 50% of cases:

A-Pulmonary emboli may occur in patients with VSD, PDA, or a systemic-to-PA shunt.

B- Seizures and hemiparesis are the result of embolization to the central nervous system (20%) and are more common with left-sided defects such as aortic and mitral valve disease or with cyanotic heart disease.

C-Hematuria and renal failure may occur.

d. Roth's spots (oval, retinal hemorrhages with pale centers located near the optic disc) occur in less than 5% of patients.

6. Carious teeth or periodontal or gingival disease is frequently present.

7. Clubbing of fingers in the absence of cyanosis develops rarely in more chronic cases.

8. Signs of heart failure may be present as a complication of the infection.

9. The clinical manifestations in a neonate with IE are nonspecific (respiratory distress, tachycardia) and may be indistinguishable from septicemia or congestive heart failure (CHF) from other causes. Embolic phenomena (such as osteomyelitis, meningitis, pneumonia) are common. There may be neurologic signs and symptoms (seizures, hemiparesis, apnea).

- Definition of infective endocarditis according to the modified duke criteria
- DEFINITE INFECTIVE ENDOCARDITIS

A. Pathologic criteria

1. Microorganisms demonstrated by culture or histologic examination of a vegetation, a vegetation that has embolized, or an intracardiac abscess specimen

or 2. Pathologic lesions; vegetation or intracardiac abscess confirmed by histologic examination showing active endocarditis

B. Clinical criteria

1. Two major criteria
2. or One major criterion and three minor criteria
3. or Five minor criteria

- POSSIBLE INFECTIVE ENDOCARDITIS

1. One major criterion and one minor criterion
2. or Three minor criteria

- Rejected

1. Firm alternative diagnosis explaining evidence of IE

or 2. Resolution of IE syndrome with antibiotic therapy for <4 days

or 3. No pathologic evidence of IE at surgery or autopsy, with antibiotic therapy for <4 days

or 4. Does not meet criteria for possible IE as above

- **MAJOR CRITERIA**

A. Blood culture positive for IE

1. Typical microorganisms consistent with IE from two separate blood cultures: viridans streptococci, *Streptococcus bovis*, HACEK group, *Staphylococcus aureus*, or community-acquired enterococci in the absence of a primary focus; or
2. Microorganisms consistent with IE from persistently positive blood cultures defined as follows: at least two positive cultures of blood samples drawn >12 hours apart; or all of three or a majority of four separate cultures of blood (with first and last samples drawn at least 1 hour apart)
3. Single positive blood culture for *Coxiella burnetii* or anti-phase 1 IgG antibody titer >1:800

B. Evidence of endocardial involvement

Echocardiogram positive for IE (TEE recommended for patients with prosthetic valves, rated at least "possible IE" by clinical criteria, or complicated IE [paravalvular abscess]; TTE as first test in other patients) defined as follows:

1. 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
2. Abscess; or
3. New partial dehiscence of prosthetic valve; or
4. New valvular regurgitation (worsening or changing or preexisting murmur not sufficient)

- **MINOR CRITERIA**

- 1. Predisposition, predisposing heart condition, or injection drug users.
- 2. Fever, temperature >38°C
- 3. Vascular phenomena: major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, and Janeway's lesions
- 4. Immunologic phenomena: glomerulonephritis, Osler's nodes, Roth's spots, and rheumatoid factor
- 5. Microbiologic evidence: positive blood culture but does not meet a major criterion as noted above or serologic evidence of active infection with organism consistent with IE

- MANAGEMENT

1. Blood cultures are indicated for all patients with fever of unexplained origin and a pathologic heart murmur, a history of heart disease, or previous endocarditis.

a. Usually, three blood culture samples are drawn by separate venipunctures over 24 hours, unless the patient is very ill. In 90% of cases, the causative agent is recovered from the first two cultures.

b. If there is no growth by the second day of incubation, two more may be obtained. There is no value in obtaining more than five blood cultures over 2 days unless the patient received prior antibiotic therapy.

c. It is not necessary to obtain the cultures at any particular phase of the fever cycle.

d. An adequate volume of blood must be obtained; 1 to 3 mL in infants and young children and 5 to 7 mL in older children are optimal.

e. Aerobic incubation alone suffices because it is rare for IE to be due to anaerobic bacteria.

Initial empirical therapy is started with the following antibiotics while awaiting the results of blood cultures.

a. The usual initial regimen is an antistaphylococcal semisynthetic penicillin (nafcillin, oxacillin, or methicillin) and an aminoglycoside (gentamicin). This combination covers against *S. viridans*, *S. aureus*, and gram-negative organisms. Some experts add penicillin to the initial regimen to cover against *S. viridans*, although a semisynthetic penicillin is usually adequate for initial therapy.

b. If a methicillin-resistant *S. aureus* is suspected, vancomycin should be substituted for the semisynthetic penicillin.

c. Vancomycin can be used in place of penicillin or a semisynthetic penicillin in penicillin-allergic patients.

The final selection of antibiotics depends on the organism isolated and the results of an antibiotic sensitivity test.

a. Streptococcal IE

1). In general, native cardiac valve IE caused by a highly sensitive *S. viridans* can be successfully treated with intravenous (IV) penicillin (or ceftriaxone given once daily) for 4 weeks. Alternatively, penicillin, ampicillin or ceftriaxone combined with gentamicin for 2 weeks may be used.

2). For IE caused by penicillin-resistant streptococci, 4 weeks of penicillin, ampicillin, or ceftriaxone combined with gentamicin for the first 2 weeks are recommended.

b. Staphylococcal endocarditis

1). The drug of choice for native valve IE caused by methicillin-susceptible staphylococci is one of the semisynthetic β-lactamase-resistant penicillins (nafcillin, oxacillin, and methicillin) for a minimum of 6 weeks (with or without gentamicin for the first 3 to 5 days).

2). Patients with methicillin-resistant native valve IE are treated with vancomycin for 6 weeks (with or without gentamicin for the first 3 to 5 days).

C. For culture-negative endocarditis,

treatment is directed against staphylococci, streptococci, and the HACEK organisms using ceftriaxone and gentamicin. When staphylococcal IE is suspected, nafcillin should be added to the preceding therapy.

- Patients with prosthetic valve endocarditis should be treated for 6 weeks based on the organism isolated and the results of the sensitivity test. Operative intervention may be necessary before the antibiotic therapy is completed if the clinical situation warrants (such as progressive CHF, significant malfunction of prosthetic valves, persistently positive blood cultures after 2 weeks of therapy). Bacteriologic relapse after an appropriate course of therapy also calls for operative intervention.

- Amphotericin B is the most effective agent for most fungal infections

- **PROGNOSIS**

The overall recovery rate is 80% to 85%; it is 90% or better for *S. viridans* and enterococci and about 50% for *Staphylococcus* organisms. Fungal endocarditis is associated with a very poor outcome.

Prophylaxis

Prosthetic cardiac valve

Previous IE

Congenital heart disease (CHD)

Unrepaired cyanotic CHD, including palliative shunts and conduits

Completely repaired congenital heart defect with prosthetic material or device, whether placed by surgery or by catheter intervention, during the first 6 months after the procedure

Repaired CHD with residual defects at the site or adjacent to the site of a prosthetic patch or prosthetic device (which inhibit endotheliazation)

Cardiac transplantation recipients who develop cardiac valvulopathy

Prophylactic Regimens for Dental, Oral, Respiratory Tract

- ✓ Standard general prophylaxis Amoxicillin Children: 50 mg/kg orally 1 hr before procedure Adults: 2 g orally 1 hr before procedure
- ✓ Unable to take oral medications
- Ampicillin Children: 50 mg/kg IM or IV within 30 min before procedure Adults: 2 g IM or IV within 30 min before procedure
- ✓ Allergic to penicillin Clindamycin, or cephalexin or cefadroxil, or azithromycin or clarithromycin
- Clindamycin: children, 20 mg/kg; adults, 600 mg orally 1 hr before procedure
- Cephalexin or cefadroxil: children, 50 mg/kg orally; adults, 2 g orally 1 hr before procedure
- Azithromycin or clarithromycin: children, 15 mg/kg orally; adults, 500 mg orally; 1 hr before procedure
- ✓ Allergic to penicillin and unable to take oral medications Clindamycin or cefazolin
- Clindamycin: children, 20 mg/kg IM or IV; adults, 600 mg IM or IV within 30 min before procedure
- Cefazolin: children, 25 mg/kg IM or IV; adults, 1 g IM or IV within 30 min before procedure