

Infective Endocarditis

:Objectives

- .Define infective endocarditis and its prevalence.1
- .identify pathogenesis of infective endocarditis.2
- .Recognise the pathology of infective endocarditis.3
- Describe major and minor criteria for diagnosis of infective.4
- .endocarditis
- .Recognise risk factors for infective endocarditis.5
- Identify clinical manifestations and physical signs of infective.6
- .endocarditis
- .Recognise investigations for diagnosis of infective endocarditis.7
- Describe the management and prophylaxis for infective.8
- .endocarditis

Infective Endocarditis

Infective endocarditis is a microbial infection of the endocardial (endothelial) surface of the heart. Native or prosthetic heart valves are the most frequently involved sites. Endocarditis also can involve septal defects, the mural endocardium, or intravascular foreign devices such as intracardiac patches, surgically constructed shunts, and intravenous catheters. Infective endarteritis is a similar clinical illness involving arteries, including the ductus arteriosus, the great vessels, aneurysms, or arteriovenous shunts

Prevalence

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

Pathogenesis

Two factors are important in the pathogenesis of IE: (1) a damaged area of endothelium and (2) 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 thrombus). Prosthetic valves or prosthetic materials used in surgery also promote deposition of sterile thrombus, occurrence of a transient bacteremia, adherence of these bacteria to the NBTE, and subsequent proliferation of the bacteria within a vegetation.

All congenital heart defects (CHDs), with the exception of.2
secundum-type atrial septal defect (ASD), predispose to
endocarditis. More frequently encountered defects are tetralogy of
Fallot (TOF), ventricular septal defect(VSD), aortic valve disease,
transposition of the great arteries (TGA), and systemic-to-PA shunt
Bacteremia resulting from dental procedures can cause IE.. 3
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 very important in the prevention
. of IE

RELATIVE RISK OF ENDOCARDITIS FOR VARIOUS CARDIOVASCULAR AND UNDERLYING CONDITIONS

High risk

Prosthetic valves

Previous episode of endocarditis

Complex cyanotic congenital heart disease (e.g., single ventricle states, transposition of the great arteries, tetralogy of Fallot)

Surgically constructed systemic artery to pulmonary artery shunts

Injection drug use

Indwelling central venous catheters

Moderate risk

Uncorrected patent ductus arteriosus

Uncorrected ventricular septal defect

Uncorrected atrial septal defect (other than secundum)

Bicuspid aortic valve

Mitral valve prolapse with regurgitation

Rheumatic mitral or aortic valve disease

Other acquired valvar diseases

Hypertrophic cardiomyopathy

Pathology

Vegetation of IE is usually found on the low-pressure side of the defect, either around the defect or on the opposite surface of the defect where endothelial damage is established by the jet effect of the defect. For example, vegetations are found in the PA in patent ductus arteriosus (PDA) or systemic-to-PA shunts, on the atrial surface of the mitral valve in MR, on the ventricular surface of the aortic valve and mitral chordae in aortic regurgitation (AR), and on the superior surface of the aortic valve or at the site of a jet lesion in the aorta in patients with aortic stenosis (AS).

Virtually all vegetations occur in areas where there is a pressure gradient with resulting turbulence of blood flow. Turbulent blood flow produced by certain types of congenital or acquired heart disease, such as flow from a high- to low-pressure chamber or across a narrowed orifice (for example, where a jet through a small ventricular septal defect hits the right ventricular wall) traumatizes the endothelium

Microbiology

In the past, *Streptococcus viridans*, enterococci, and *Staphylococcus aureus* were responsible for more than 90% of the cases. In recent years, this frequency has decreased to 50% to 60%, with a concomitant increase in cases caused by fungi and HACEK organisms (*Haemophilus*, *Actinobacillus* *Cardiobacterium*, *Eikenella*, and *Kingella* spp.). HACEK organisms are particularly common in neonates and immunocompromised children accounting for 17% to 30% of cases.

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 (GI) surgery or instrumentation.

The organisms most commonly found in postoperative endocarditis are staphylococci.

Intravenous (IV) drug abusers are at risk for IE caused by infection. 5
.with *S. aureus*

Fungal endocarditis (which has a poor prognosis) may occur in sick. 6
neonates, in patients who are on long-term antibiotic or steroid
therapy, or after open heart surgery. Fungal endocarditis is often
.associated with very large friable vegetations

IE associated with indwelling vascular catheters, prosthetic material,. 7
and prosthetic valves is frequently caused by *S. aureus* or coagulase-
.negative staphylococci

Among newborn infants, *S. aureus*, coagulase-negative staphylococci,. 8
.and *Candida* spp. are the most common causes of IE

A diagnosis of culture-negative endocarditis is made when a patient. 9
has clinical or echocardiographic evidence of endocarditis but
persistently negative blood culture results. The most common cause of
culture-negative endocarditis is current or recent antibiotic therapy or
infection caused by a fastidious organism that grows poorly in vitro.
Fungal endocarditis is a rare cause of culture-negative endocarditis

Clinical Manifestations

History

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

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

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

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

Physical Examination

Heart murmur is universal (100%). 1

Fever is common (80%–90%). Fever fluctuates between 101° and 103°F (38.3° and 39.4°C). 2

Splenomegaly is common (70%). 3

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

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) also are rare



Osler's nodes in fingers



Embolic or immunologic phenomena in other organs are present. 5
: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 (CNS) (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 fewer than 5% of patients

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

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

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

Endocarditis involving the left side of the heart frequently results in peripheral embolization, leading to ischemia, infarction, or mycotic aneurysms. In these cases, specific clinical findings depend on the localization of the emboli. In children, embolization from the right heart may be no less frequent, but such emboli are not as easily appreciated clinically because of filtration by the lungs. However, large pulmonary emboli may complicate endocarditis of the tricuspid valve

Laboratory Studies

Positive blood cultures are found in more than 90% of patients in the absence of previous antimicrobial therapy. Antimicrobial pretreatment reduces the yield of positive blood culture to 50% to 60%.

A complete blood cell count shows anemia, with hemoglobin levels lower than 12 g/100 mL (present in 80% of patients), and leukocytosis with a shift to the left. Patients with polycythemia preceding the onset of IE may have normal hemoglobin. The sedimentation rate is increased unless there is polycythemia. Microscopic hematuria is found in 30% of patients.

Echocardiography

Two-dimensional echocardiography is the main modality for.1 detecting endocardial infection . It detects the site of infection, extent of valvular damage, and cardiac function.2. TEE may be superior to TTE in identifying vegetations on prosthetic valve

The absence of vegetations on echocardiography does not in itself. 3 rule out IE. Both TTE and TEE may produce false-negative results if vegetations are small or have already embolized, and they may miss initial perivalvular abscess. Repeat examinations are indicated if suspicion exists without diagnosis of IE or worrisome clinical course .during early treatment of IE

Conversely, a false-positive diagnosis is possible. An echogenic mass. 4 represent a sterile thrombus, sterile prosthetic material, normal anatomic variation, an abnormal uninfected valve

Diagnosis

Recently, the American Heart Association has recommended the modified Duke Criteria in the .diagnosis and management of IE

Definition of Infective Endocarditis According to the Modified Duke Criteria

Definite Infective Endocarditis

A. Pathological criteria

Microorganisms demonstrated by culture or histologic examination of a. 1
vegetation, a vegetation that has embolized, or an intracardiac abscess specimen *or*
Pathological lesions; vegetation or intracardiac abscess confirmed by histologic. 2
examination showing active endocarditis

B. Clinical criteria

Two major criteria *or*. 1

One major criterion and three minor criteria *or*. 2

Five minor criteria. 3

Possible Infective Endocarditis

One major criterion and one minor criterion *or*. 1

Three minor criteria. 2

Rejected

Firm alternative diagnosis explaining evidence of IE *or*. 1

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

No pathological evidence of IE at surgery or autopsy with antibiotic therapy for. 3
. <4 days *or* 4. Does not meet criteria for possible IE

Major Criteria

A. Blood culture positive for IE

Typical microorganisms consistent with IE from two separate blood. 1 cultures: Viridans streptococci, *Streptococcus bovis*, HACEK group, *Staphylococcus aureus*; or community-acquired enterococci in the absence of a primary focus *or*

Microorganisms consistent with IE from persistently positive blood. 2 cultures defined as follows: at least two positive cultures of blood samples drawn >12 h apart or all of three or a majority of four or more separate cultures of blood (with first and last sample drawn at least 1 h apart)

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Single positive blood culture for *Coxiella burnetii* or anti-phase. 3
1 IgG antibody titer >1:800

B. Evidence of endocardial involvement

Echocardiogram positive for IE (TEE is 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

Oscillating intracardiac mass on valve or supporting structures,. 1
in the path of regurgitant jets, or on implanted material in the
absence of an alternative anatomic explanation *or*

Abscess *or*. 2

New partial dehiscence of prosthetic valve *or*. 3

New valvular regurgitation (worsening or changing *or*. 4
preexisting murmur not sufficient)

Minor Criteria

Predisposition, predisposing heart condition, or injection drug. 1
users

Fever, temperature $>38^{\circ}\text{C}$. 2

Vascular phenomena: major arterial emboli, septic pulmonary. 3
infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival
hemorrhages, and Janeway's lesions

Immunologic phenomena: glomerulonephritis, Osler's nodes,. 4
Roth's spots, and rheumatoid factor

Microbiologic evidence: positive blood culture but does not meet. 5
a major criterion as noted above or serologic evidence of active
infection with organism consistent with IE

Management

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

a. Usually three blood cultures 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. 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

.

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. 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

The final selection of antibiotics depends on the organism isolated and the

.results of an antibiotic sensitivity test

a. Streptococcal IE

In general, patients with native cardiac valve IE caused by a highly sensitive *S. viridans* can be successfully treated with IV penicillin (or ceftriaxone given once daily) for 4-6 weeks, combined with gentamicin for .2 weeks

b. Staphylococcal endocarditis

The drug of choice for native valve IE by methicillin-susceptible) 1(staphylococci is one of the semisynthetic β -lactamase-resistant penicillins (nafcillin, oxacillin, or methicillin) for a minimum of 6 .weeks

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

Enterococcus-caused native valve endocarditis usually requires a combination of IV penicillin or ampicillin together with gentamicin for 4 to 6 weeks. If patients are allergic to penicillin, vancomycin combined with gentamicin for 6 weeks is required

Patients with prosthetic valve endocarditis should be treated for 6 weeks based on the organism isolated .and the results of the sensitivity test

Fungal Endocarditis

Fungal endocarditis is a relatively new syndrome and is often a complication of medical and surgical advances. Its incidence in children is reported to have increased significantly in recent years. The prognosis is poor, with high mortality and morbidity. Treatment of fungal endocarditis with antifungal agents alone is almost always unsuccessful, particularly in older patients. Surgical replacement of the infected valve (native or prosthetic) and excision of infected tissue are usually required in conjunction with antifungal agents.

Amphotericin B remains the most effective antifungal agent. A test dose of 0.1 mg/kg of amphotericin B (maximum 1 mg) is initially administered. If this is well tolerated, it is followed by a dose of 0.5 mg/kg for 1 day and then 1 mg/kg/day as the maintenance dose. Minimum duration of therapy should be 6 to 8 weeks. Renal function and serum potassium concentration should be carefully monitored.

Indications for operative intervention include significant valvular obstruction, progressive heart failure secondary to valvular insufficiency or dehiscence, fungal endocarditis, persistently positive blood cultures after appropriate antibiotics for 10 to 14 days, bacteriologic relapse after an appropriate course of therapy, and recurrent major emboli. Less definite indications for surgery include a single major embolus, echocardiographic demonstration of a large vegetation, and extension of infection to an annular abscess or a myocardial abscess

Prevention

The estimated frequency of bacteremia during routine daily activities. 1 (e.g., chewing, toothbrushing, flossing, use of toothpicks, use of water irrigation devices, and other activities) far exceeds that occurring during dental procedures. For example, tooth brushing and flossing result in bacteremia 20% to 40% of the time and chewing food results in bacteremia 7% to 51% of the time

Therefore, an emphasis should be on maintaining good oral hygiene.2 and eradicating dental disease to decrease the frequency of bacteremia from routine daily activities. Note that prophylaxis is no longer recommended for routine bronchoscopy; it is recommended for).tonsillectomy and adenoidectomy only in high-risk patients Prophylaxis is no longer recommended for GI or genitourinary procedures, such as diagnostic esophagogastroduodenoscopy or .colonoscopy

CARDIAC CONDITIONS ASSOCIATED WITH THE HIGHEST RISK OF ADVERSE OUTCOME FROM ENDOCARDITIS FOR WHICH PROPHYLAXIS WITH DENTAL PROCEDURES IS RECOMMENDED

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 endothelialization)

Cardiac transplantation recipients who develop cardiac valvulopathy

Procedures for Which Endocarditis Prophylaxis is Recommended

Dental procedures. 1

All dental procedures that involve manipulation of gingival tissue of the periapical region of teeth or perforation of the oral .mucosa

Respiratory tract procedures. 2

a. Prophylaxis is recommended for the procedures that involve incision or biopsy of the respiratory mucosa, such as .tonsillectomy and adenoidectomy

b. Prophylaxis is not recommended for bronchoscopy (unless it .involves incision of the mucosa, such as for abscess or empyema)

GI or GU procedures. 3

a. No prophylaxis is used for diagnostic .esophagogastroduodenoscopy or colonoscopy

b. Skin, skin structure, or musculoskeletal tissue

Prophylaxis is recommended for surgical procedures that involve infected skin.regimen for prophylaxis is single dose of amoxicillin 30-60 min.before procedure

Patients who undergo cardiac surgery: A careful preoperative dental evaluation is recommended so that required dental treatment may be completed whenever possible before cardiac valve surgery or replacement or repair of a CHD