### Infective endocarditis

**Definition**
Infective endocarditis is a disease caused by infection of the heart valves or endocardium.

### Classification

<table>
<thead>
<tr>
<th>Acute endocarditis</th>
<th>Subacute endocarditis</th>
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<tbody>
<tr>
<td>Caused by Staphylococcus aureus, occurs on normal valves</td>
<td>Caused by Streptococcus viridans, occurs on damaged valves</td>
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</table>

### Etiology

Two factors must be present:
1. Infection (Bacteremia)
2. A predisposing cardiac lesion

### Route of entry

After minor surgical operations
1. Dental extraction, other dental maneuvers or even chewing on infected teeth may produce Streptococcus viridans bacteriaemia (most common causative organism)
2. Genitourinary and rectal procedures may cause Streptococcus faecalis bacteriaemia.
3. Cardiac surgery and catheterization may introduce skin organisms as Staphylococcus aureus.

### Predispose cardiac lesions

**Rheumatic heart diseases**
1. Aortic Insufficiency (AR).
2. Aortic Stenosis (AS).

**Prosthetic Valves**
1. Small ventricular septal defects (VSD).
3. Pulmonary stenosis (PS).
5. Coarctation of the aorta.

Rarely, on top of:
1. Mitral valve prolapse (MVP).
2. Mural thrombus in a myocardial aneurysm.

### Pathology

The vegetables are composed of a center of bacteria surrounded by a layer of fibrin and blood cells.

The **clinical manifestation, as well as the complications, of the disease are produced by**:
1. Toxemia
2. Secondary autoimmune changes
   - The bacteria in the vegetables stimulate the body's immune system to produce a generalized increase in gamma-globulins.
   - The excess antigen, antibodies and serum complement join together to make immune complexes.
   - These pass through capillary walls into the sub endothelial tissues and induce damage.
   - Autoimmune changes are seen in sub acute and not acute infections
3. Embolization (of detached vegetations)
4. Cardiac damage.

### Symptoms

**General signs**
Marked pallor and toxaemia, elevation of the temperature

**Hands**
- Pale clubbing.
- Osler nodes: intracutaneous tender purplish nodules in the palms of fingers.
- Splinter haemorrhages below nails.
- Janeway nodules in acute bacterial endocarditis, painless red-blue, dermal, on the palms or soles.

**Lower limbs**
- Reveal the same physical signs present in the upper limbs;
- The dorsalis pedis artery may be absent due to occlusion by an embolus.

**Pulse**
- Tachycardia.
- Absent pulsation may result from embolization.
- Mycotic aneurysms may be present due to weakening of the arterial wall by embolization of the vasa vasaorum.

**Eyes**
- Petechiae in the conjunctiva.
- Sudden blindness due to embolism of the central retinal artery.
- The fundus exhibits what is described as snow white retina.
- Roth spots which are white centered petechiae in the retina.

**Spleen**
- Is enlarged and tender in 80% of cases from the toxemia.
- Sudden severe pain and splenic rub may develop if an embolus causes splenic infarction and peri-splenitis.

**Kidney**
- Acute diffuse glomerulonephritis: probably through an autoimmune mechanism.
- It presents clinically as acute nephritic syndrome → nephrotic syndrome → ends in Chronic Renal Failure (CRF).
- Focal embolic glomerulonephritis: flea-bitten kidney; or
- Renal infarction giving rise to pain and tenderness in the renal angles as well as haematuria.

**Nervous system**
- Embolic hemiplegia
- Encephalopathy from multiple minute embolization or
- Subarachnoid haemorrhage due to rupture of a mycotic aneurysm in the circle of Willis

**Chest**
- Recurrent pulmonary infarctions & Chest infections if the vegetations are on the Right Side of the heart:
- VSD.
- Tricuspid valve disease.
- Pulmonary Stenosis.
- PDA.
## Cardiac examination
1. Signs and symptoms of the predisposing lesion
2. Alterations in the character of the already present murmurs and development of new ones because of further valvular damage
3. Heart failure is a frequent and important complication due to
   a. Toxic myocarditis.
   b. Increased valvular damage

## Common presentations
- Prolonged fever + cardiac murmurs.
- Emboli and vascular accidents
- Nephritis and renal failure
- Congestive heart failure
- Acute Heart Failure due to acute Aortic or Mitral incompetence

## Investigations
- Complete blood picture
  - Not characteristic & shows:
    a. Normochromic, Normocytic Anemia
    b. Monocytosis and Leucopenia
    c. Leucocytosis if embolization occurs

- Echocardiography
  - Two-dimensional echocardiography can detect vegetations in 80% of cases.
  - For each culture an adequate amount of blood 20 - 30 cc is needed.
  - Culture has to be made on both fluid and solid media under both aerobic and anaerobic conditions.
  - Penicillinase is added if the patient is receiving penicillin.
  - The cultures if properly done are positive in 90% of cases.
  - Culture negative endocarditis occurs in:
    a. Fungal endocarditis,
    b. Prior use of antibiotics
    c. Other causative organisms as
    d. Mycobacteria,
    e. Q fever &
    f. Chlamydia.

- Urine
  - This is an important investigation for the diagnosis and monitoring the disease.
  - Two-dimensional echocardiography can detect vegetations in 80% of cases.
  - Vegetations of only 2 mm in size can be visualised but failure to image them does not exclude the diagnosis.
  - It provides information about the pre-existing cardiac defect.
  - It will also show perivalvular abscesses.
  - Doppler echocardiography is particularly useful in the diagnosis of a perivalvular leak in a patient with dehiscence of a prosthetic heart valve.
  - Serial examinations will demonstrate any increase in size of the cardiac chambers.
  - Sequential studies of cardiac function help in making decisions on the necessity and timing of surgery.

- CXR
  - (a) Evidence of early CHF.
  - (b) Multiple small patchy infiltrates in the lungs suggest septic pulmonary infarction due to embolisation from a right side infection commonly on the TV in IV drug addicts.
  - (c) Fluoroscopy demonstrates abnormal motion of an infected prosthetic valve

- Blood culture
  - Two to five blood cultures done on 2 - 3 successive days.
  - For each culture an adequate amount of blood 20 - 30 cc is needed.
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- ESR
  - It is always elevated except when heart failure occurs

## Complications
- Increase of valvular damage and toxic myocarditis leading to congestive heart failure.
- Kidney involvement ending in CRF
- Systemic and pulmonary embolization.
- Complications of treatment.

## How to diagnose:
**Definite IE:** 2 major or 1 major and 3 minor or all 5 minor criteria (if no major criterion is met).

<table>
<thead>
<tr>
<th>Minor criteria</th>
<th>Major criteria</th>
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<tr>
<td>1) Predisposition (cardiac lesion; IV drug abuse)</td>
<td>• Positive blood culture:</td>
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<tr>
<td>2) Fever &gt;38°C</td>
<td>o Typical organism in 2 separate cultures or</td>
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<tr>
<td>3) Vascular/immunological signs</td>
<td>o Persistently +ve blood cultures, eg 3, &gt;12h apart (or majority if ≥4)</td>
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<tr>
<td>4) / 5) Positive blood culture/or echocardiogram that do not meet major criteria</td>
<td>• Endocardium involved:</td>
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<tr>
<td></td>
<td>o Positive echocardiogram (vegetation, abscess, dehiscence of prosthetic valve) or</td>
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<td>o New valvular regurgitation (change in murmur not sufficient).</td>
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## Diagnosis
- **Rheumatic fever**
  - Present
- **Infective endocarditis**
  - Absent

### RF vs IE
- **Rheumatism marginatum**
  - Present
- **Petechiae**
  - Absent
- **Haematuria**
  - Present
- **Clubbing**
  - Negative
- **Spleen enlargement**
  - May be positive
- **Embolization**
  - Culture
### Infective endocarditis treatment

<table>
<thead>
<tr>
<th>Endocarditis prophylaxis</th>
<th>Recommended</th>
<th>Not recommended</th>
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| High risk | 1. Prosthetic cardiac valves, including bioprosthetic and homograft valves  
2. Previous bacterial endocarditis, even in the absence of heart disease  
3. Complex cyanotic congenital heart disease (e.g., tetralogy of Fallot)  
4. Surgically constructed systemic-pulmonary shunts or conduits | 1. Isolated secundum ASD.  
2. Surgical repair without residua beyond 6 mo of secundum ASD, VSD, and PDA.  
3. Previous CAGB.  
4. Mitral valve prolapase without valvular regurgitation.  
5. Physiologic, functional, or innocent heart murmurs.  
6. Previous rheumatic fever without valvular dysfunction.  
7. Cardiac pacemakers and implanted defibrillators | 1. Rheumatic and other acquired valvular dysfunction, even after valvular surgery.  
2. Hypertrophic cardiomyopathy.  
3. Mitral valve prolapse with valvular regurgitation and/or thickened leaflets.  
4. Most other congenital cardiac malformations (other than the above and below) |

| Prophylaxis | For patients with predisposing cardiac lesions undergoing procedures known to cause bacteremia.  
• Correction of predisposing cardiac lesions if possible.  
• Good oral hygiene.  
• For gastrointestinal or genitourinary procedure: high risk regimen. | For dental, oral or upper respiratory procedures:  
• Low risk:  
  a) Amoxicillin 2 g PO, one hour before procedure.  
  b) Clindamycin 600 mg PO, one hour before procedure.  
• High risk:  
  a) Ampicillin 2 gm IV plus gentamicin 1.5 mg/kg IV (maximum 80 mg), ½ hour before and 6 hours after procedure.  
  b) Vancomycin, 1 gm IV, one hour before if allergic to penicillin. |

<table>
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<tr>
<th>Curative treatment</th>
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| Streptococci | Benzylpenicillin 1.2g/4h IV + gentamicin, eg 80mg/12h IV.  
If acute, add flucloxacillin 2g/6h IV to cover staphylococci. |
| Enterococci | Amoxicillin 1 g/6h IV + gentamicin, eg 80mg/12h IV for 4wks.  
Monitor gentamicin levels. |
| Staphylococci | Flucloxacillin 2g/6h IV + gentamicin 80mg/12h IV.  
Treat for 6-8wks; stop gentamicin after 1wk |
| Coxiella | Doxycycline 100mg/12h PO indefinitely + co-trimoxazole, rifampicin, or ciprofloxacin. |
| Fungi | Fluconazole 5g/6h IV over 30 minutes  
Followed by fluconazole 50mg/24h PO (a higher dose may be needed).  
Amphotericin if fluconazole resistance or Aspergillus.  
Miconazole if renal function is poor. |

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<tr>
<th>Empiric therapy for IE</th>
<th>Host substrate</th>
<th>Antibiotics</th>
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<tbody>
<tr>
<td>Native valve endocarditis</td>
<td>Acute presentation</td>
<td>Gentamicin, oxacillin or vancomycin</td>
</tr>
<tr>
<td>Subacute presentation</td>
<td>Gentamicin, ampicillin</td>
<td></td>
</tr>
<tr>
<td>Prosthetic valve endocarditis</td>
<td>Early (&lt;60 days postoperative)</td>
<td>Gentamicin, vancomycin</td>
</tr>
<tr>
<td>o Late (&gt;60 days postoperative)</td>
<td>Gentamicin, vancomycin, cephalosporin</td>
<td></td>
</tr>
<tr>
<td>IV drug use endocarditis</td>
<td>Gentamicin, oxacillin, cephalosporin</td>
<td></td>
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| Surgical treatment | Replacement of infected valve or prosthesis:  
a) Refractory heart failure, related to valvular dysfunction.  
b) Myocardial or perivalvular abscess.  
c) Persistent bacteremia.  
d) Fungal infection.  
e) Repeated relapses.  
f) Unstable prosthesis.  
g) Multiple embolic episodes. | Urgent surgery for native valve endocarditis  
• Life-threatening hemodynamic instability due to valvular regurgitation, valvular destruction, or paravalvular extension.  
• Additional factors favoring earlier surgical intervention include significant congestive heart failure, infections resistant to antimicrobial therapy, fungal endocarditis, vegetations larger than 1 cm in diameter (which pose a risk of embolism), and recurrent distal emboli.  
• Even if active bacteremia is still present or if the antibiotic treatment course is ongoing, surgery for endocarditis should not be delayed if surgical criteria are met. |

| Prognosis | 30% mortality with staphylococci. |
|-----------| 15% with bowel organisms. |
| Prognosis | 7.5% with sensitive streptococci. |

| Prognosis | A prosthetic valve whether tissue or mechanical is a highly risky lesion for the development of infective endocarditis.  
• The increased risk is due to the endothelial damage and exposure to bacteriaemia during surgery.  
• Infective endocarditis can occur early after surgery (within 2 months) or later.  
• The incidence of infection has been found to be 2.7% for early endocarditis and the cumulative risk is about 5% at 10 years.  
• The patients are seriously ill and often have rigors.  
• Prompt surgical replacement is indicated in most cases |

| Prophylaxis | Source of infection  
1. Carrier members of staff.  
2. Contamination of the blood by the oxygenator or instruments at operation  
3. Infected sternal wounds.  
4. Postoperative drains and catheters |

| Early Onset Prosthetic Endocarditis | These patients have a mortality rate between 30 and 90%.  
• Staphylococcus epidermidis accounts for 30% of cases and other important organisms are Gram-negative bacilli, staph. aureus and fungi. |

| Late onset prosthetic endocarditis | The microbiological pattern is similar to that found in native valve endocarditis.  
• Most may be initially treated with antibiotics.  
• Valve replacement is often necessary |