

# Infective Endocarditis

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# Learning objectives

- ✓ Differentiate the causes and development of infective endocarditis (IE)
- ✓ Identify the clinical presentation and laboratory evaluation for IE
- ✓ Assess diagnostic criteria used to evaluate a patient suspected of having IE
- ✓ Describe the most likely causative organisms of IE
- ✓ Develop appropriate pharmacologic treatment recommendations for patients with IE
- ✓ Define appropriate patient populations requiring prophylactic treatment, and differentiate

# Introduction

- **Endocarditis** is an inflammation of the endocardium, the membrane lining the chambers of the heart and covering the cusps of the heart valves.
- More commonly, endocarditis refers to infection of the heart valves by various microorganisms
- Although it typically affects native valves, it also may involve nonvalvular areas or implanted material

## Cont....

- IE could be
- Native Valve IE
  - Community acquired
  - Nosocomial IE
  - Intravenous drug abuse (IVDA) IE
- Prosthetic Valve IE
- IE also classified as **acute** or **subacute** (old classification)

# Classification

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- **Acute**

- Affects normal heart valves
- Rapidly destructive
- Metastatic foci
- Commonly Staph.
- If not treated, usually fatal within **6 weeks**

- **Subacute**

- Often affects damaged heart valves(VHD)
- Indolent nature
- Caused by less virulent org (**S.viridans**)
- If not treated, usually fatal by **one year**

# Epidemiology and Etiology

- Infective endocarditis is uncommon, in US.
- Male-to-female ratio is approximately 2:1
- Most cases occur in those older than 50 years (>50%)
- **Common bacteria**
  - *S. aureus*
  - Streptococci (viridans)
  - Enterococci
- **Not so common**
  - Fungi
  - Pseudomonas
  - HACEK (*Haemophilus*, *Actinobacillus*,  
*Cardiobacterium*, *Eikenella*, and *Kingella*)

## Cont....

- The incidence of *S. aureus*, continues to increase and it surpassed viridans streptococci
- *S.viridans* cause IE in patient with community acquired disease and underlying cardiac abnormalities (MVP, RHD)
- *S.aures* are most common cause of prosthetic valve endocarditis and intravenous drug abusers
- *Enterococcus* more common in individual who undergo genitourinary manipulation or obstetric procedures
- Subacute IE tend to involve **mitral valve**, whereas acute often involve **aortic valve**

# Risk factors

1. Presence of a prosthetic valve (highest risk)
2. Previous endocarditis (highest risk)
3. Healthcare-related exposure (high risk)
4. Congenital heart disease
5. Chronic intravenous access
6. Diabetes mellitus
7. Acquired valvular dysfunction (e.g, RHD)
8. Cardiac implantable device
9. Chronic heart failure
10. Mitral valve prolapse with regurgitation
11. IVDA



# Pathophysiology

- The most common route is via **hematogenous** spread
  1. For IE to occur there must be alteration of endothelial surfaces of heart valve to allow organism attachment
- These alterations may be produced by an inflammatory process such as rheumatic heart disease or by injury from turbulent blood flow
  2. Platelets and fibrin now deposit on the damaged valves, forming a nonbacterial thrombotic endocarditis (**NBTE**).

## Cont....

3. Bacteria through hematogenous spread (i.e., bacteremia) adhere to and colonize the **site of infection** forming a vegetation
- Bacteremia is the result of trauma to a mucosal surface with a high concentration of resident bacteria
  - such as the oral cavity and GI tract
  - Transient bacteremia commonly follow certain dental, GI, urologic, and gynecologic procedures
- Further deposits of platelets and fibrin cover the bacteria, providing a protective coating for organisms

## Cont....

- staphylococci, S.viridans and enterococci are most likely to adhere to NBTE
  - because of production of specific adherence factors such as **dextran** by some oral streptococci and **glycocalyx** by staphylococci.
- Gram-negative bacteria rarely adhere to heart valves and are uncommon causes of infective endocarditis

## Hemodynamic Factors

Abnormal valve → a turbulent jet of blood flow



Turbulent jets of blood damage endocardium



Platelets and fibrin adhere to damaged endocardium  
(non-bacterial thrombotic endocarditis)



Microbes in bloodstream adhere  
to platelets and fibrin



Large, friable vegetation on mitral valve

**Vegetation**

## Cont....

- Acquisition of PVE differs in early stages, where direct inoculation may occur during surgery
- Causative organisms in early PVE are nosocomial, with increased likelihood of being drug resistant
- However, in late PVE, the process of colonization and vegetation is similar to that of native-valve IE
- The vegetations seen in IE may be single or multiple and vary in size
- Bacteria within the vegetation grow slowly and are protected from antibiotics and host defenses

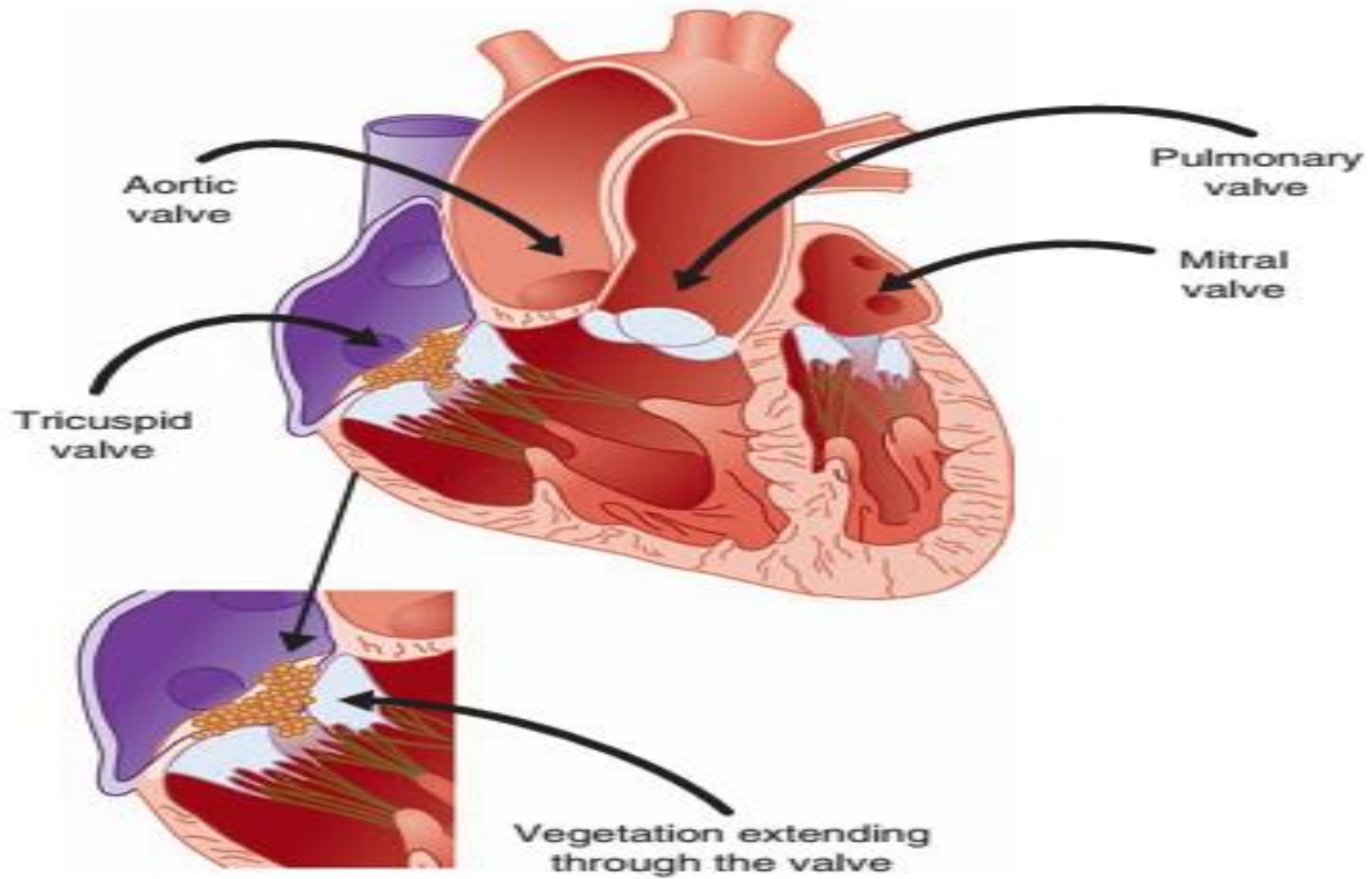
# Complication of IE

- Adverse effects of IE and the resulting lesions include
  - local perivalvular damage,
  - embolization of septic fragments with potential hematogenous seeding of remote sites, and
  - Formation of antibody complexes
- Vegetations may destroy valvular tissue, & continued destruction lead
  - Acute heart failure via perforation of the valve leaflet,
  - Rupture of the chordae tendineae or papillary muscle,
  - For patients with PVE, valve dehiscence
- Vegetations may be friable, and released downstream leading to septic emboli

## Cont.....

- Septic emboli from right-sided IE (tricuspid and pulmonary) → **pulmonary abscess**
- Left-sided IE (mitral and aortic valves) → embolus travel to any organ system, especially the kidneys, spleen, and brain
- Circulating immune complexes consisting of antigen, antibody, and complement may deposit in organs, producing local inflammation, and organ damage.
  - **Petechiae, Osler nodes, and Janeway lesions, Roth spots** (within the eye ) and **glomerulonephritis**

# Cont....





# Clinical presentation and Diagnosis

- **General**

- Patients typically present with nonspecific and variable sign or symptoms

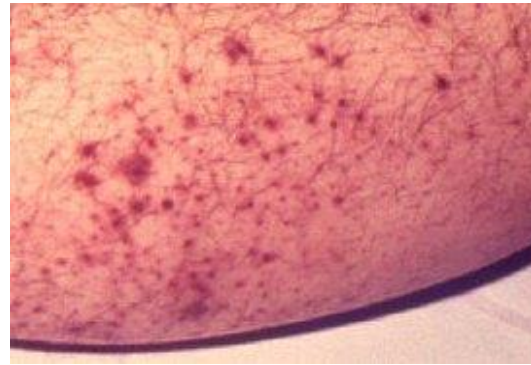
- **Symptoms:**

- Fever, chills, weakness, dyspnea, night sweats, weight loss, and/or malaise.

- **Signs**

- **Fever** is the most common sign of IE.
- New or changing **heart murmur**
- Embolic phenomena (emboli affect the heart, lungs, abdomen, or extremities)
- Vascular phenomena(e.g., petechiae, splinter hemorrhages, Janeway lesions)
- Immunologic phenomena (Osler nodes, Roth spot, glomerulonephritis, +RF)

# Petechiae



1. Nonspecific
2. are very small(<3mm
3. often located on extremities, mucous membranes or conjunctiva



# Splinter Hemorrhages



1. nonspecific
2. small dark streaks beneath the fingernails or toenails
3. occur due to local vasculitis or microemboli
4. usually do NOT extend the entire length of the nail

# Osler's Nodes



1. nonspecific
2. **Painful** and erythematous nodules
3. Located on pads of fingers and toes
4. More common in **subacute** IE

# Janeway Lesions



1. small, painless, hemorrhagic macularPlaque
2. Located on palms and soles
3. More common in **acute** IE

## Cont....

- **Laboratory test**
- Blood cultures are important for persistent bacteremia, which occurs commonly in IE.
- Three blood culture sets should be drawn within the initial 24 hours
- approximately 90% of the first two cultures will yield a positive result.
- WBC may be elevated in acute disease but could be normal in subacute IE

# Cont....

- Nonspecific findings include
  - Hematologic tests for anemia (normochromic, normocytic),
  - thrombocytopenia
  - elevated ESR or CRP
  - proteinuria/microscopic hematuria
- **Other diagnostic test**
- An echocardiogram (TTE with 60% sensitivity or TEE with 95% sensitivity) should be performed on any patient with suspected IE to detect the presence of vegetations.

# Diagnosis criteria for IE (Duke's Criteria)

- **Major criteria**
  - Blood culture positive for IE: Typical microorganisms consistent with IE
  - Evidence of endocardial involvement: Echo
- **Minor Criteria**
  - Predisposition: predisposing heart condition or injection drug use
  - Fever: temperature greater than 38°C (100.4°F)
  - Vascular phenomena: major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, and Janeway's lesions
  - Immunologic phenomena: glomerulonephritis, Osler's nodes, Roth's spots, and rheumatoid factor



## Cont....

- Definitive : 2 major criteria
  - : 1 major and 3 minor criteria
  - : 5 minor criteria
  - : pathology/histology findings
- Possible : 1 major and 1 minor criteria
  - : 3 minor criteria
- Rejected : firm alternate diagnosis
  - : resolution of manifestations of IE with antimicrobial therapy for  $\leq 4$  days

# Treatment

- **Desired outcome**
  - Relieve the signs and symptoms of the disease
  - Decrease morbidity and mortality
  - Eradicate the causative organism with minimal drug exposure
  - Provide cost-effective antimicrobial therapy
  - Indicate appropriate prophylactic antimicrobials for those with high risk

# Cont....

- **General approach to treatment**
- Empirical therapy
  - Should cover MRSA and gram-negative bacilli
    - vancomycin plus gentamicin
- Then;
  - Isolation of the infecting pathogen and determination of antimicrobial susceptibilities,
  - High-dose, parenteral, bactericidal antibiotics for an extended period.

# Cont....

- **Nonpharmacologic therapy**
- Surgery
  - Valvectomy and
  - Valve replacement
- Echocardiographic features that suggest the need for surgery include:
  - Persistent vegetation or an increase in vegetation size after prolonged antibiotic treatment,
  - Valve dysfunction, or
  - Paravalvular extension (e.g., abscess).

# Cont....

- **Pharmacologic therapy**

## **A. Streptococci**

### **1. Penicillin-susceptible streptococci, *S. bovis***

- Penicillin G (12-18mU /day IV q4/6hr for 4 weeks)
- Ceftriaxone (2 g/d IV as a single dose for 4 weeks)

**In beta-lactam allergic patients**

- Vancomycin (30 mg/kg/day i.v. in 2 doses for 4weeks)

# Cont....

## 2. Penicillin-resistant streptococci

- **Penicillin G** (4 mU IV q4h) *or* **ceftriaxone** (2 g IV qd) for 4 weeks **plus** **gentamicin** (3 mg/kg qd IV or IM, as a single dose for 2 weeks)
- **Vancomycin** as noted above for 4 weeks

# Cont....

- **B. Enterococci**
  - **Penicillin G** (4–5 mU IV q4h) plus **gentamicin** (3 mg/kg/d IV/IM in 1 dose), both for 4–6 weeks
  - **Ampicillin** (2 g IV q4h) *plus* **gentamicin** (3 mg/kg/d IV/IM in 1 dose), both for 4–6 weeks
  - **Vancomycin** (15 mg/kg IVq12h) *plus* **gentamicin** (3 mg/kg/d IV/IM in 1 dose), both for 4–6 weeks

# Cont....

- **C. Staphylococci**

1. **Methicillin-susceptible, infecting native valves**

- **Nafcillin or oxacillin** (2 g IV q4h for 4–6 weeks)

**For penicillin-allergic (nonanaphylactoid type)**

- **Cefazolin** (2 g IV q8h for 4–6 weeks)

2. **Methicillin-resistant, infecting native valves**

- **Vancomycin** (15 mg/kg IV q12h for 4–6 weeks)



## Cont....

### 3. Methicillin-susceptible, infecting prosthetic valves

- **Nafcillin or Oxacillin** (2 g IV q4h for 6–8 weeks) *plus*  
**Gentamicin** (3 mg/kg/d IM or IV for 2 weeks) *plus*  
**Rifampicin** (300 mg i.v/ PO q8h for 6–8 weeks)

### 4. Methicillin-resistant, infecting prosthetic valves

- **Vancomycin** (15 mg/kg IV q12h for 6–8 weeks) *plus*  
**Gentamicin** (3 mg/kg/sd IM or IV for 2 weeks) *plus*  
**Rifampicin** (300 mg i.v/PO q8h for 6–8 weeks)

## Cont....

- **D. HACEK Organisms**
  - **Ceftriaxone** (2 g/d IV as a single dose for 4 weeks)
  - **Ampicillin/sulbactam** (3 g IV q6h for 4 weeks)

# Prevention

- For dental procedures
- But not for:
  - Gastrointestinal or
  - Genitourinary tract procedures

## High-Risk Cardiac Lesions for Which Endocarditis Prophylaxis Is Advised before Dental Procedures

Patients with prosthetic heart valves

Patients with prior endocarditis

Unrepaired cyanotic congenital heart disease, including palliative shunts or conduits

congenital heart disease repaired with prosthetic valve, upto 6 month after the procedure

Incompletely repaired congenital heart disease with residual defects adjacent to prosthetic material

Valvulopathy developing after cardiac transplantation

# Empiric antibiotic regimen for prophylaxis

- **Standard oral regimen**
  - Amoxicillin 2 g PO 1 h before procedure
- **Inability to take oral medication**
  - Ampicillin 2 g IV or IM within 1 h before procedure
- **Penicillin allergy**
  - Clarithromycin or azithromycin 500 mg PO 1 h before procedure
  - Cephalexin 2 g PO 1 h before procedure
  - Clindamycin 600 mg PO 1 h before procedure
- **Penicillin allergy, inability to take oral medication**
  - Cefazolin or ceftriaxone 1 g IV or IM 30 min before procedure
  - Clindamycin 600 mg IV or IM 1 h before procedure

THANK YOU