

# Infective Endocarditis

Team notes are in **BLUE**

Important points mentioned by the doctor  
are in **RED**

**Done By**

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## **Objectives**

- Definition
- Patho-physiology
- The risk factors
- Clinical features
- Diagnosis
- Treatment
- Complication
- Prevention

## **Definition:**

Infection of endothelium surface of heart either of

1. Heart valves .
2. Septal defects.
3. Chordae tendinea .
4. A.V shunt.

It remains a life-threatening disease with significant mortality (about 20%) and morbidity.

## **Pathogenesis of IE**

**remember this: something wrong in the heart + bacteria in the blood = vegetation**

The IE is the net result of the complex interaction between the bloodstream pathogen with matrix molecules and platelets at sites of endocardial cell damage.

The following sequence of events is thought to result in IE:

- Formation of nonbacterial thrombotic endocarditis (NBTE) on the surface of a cardiac valve or elsewhere that endothelial damage occurs,
  - bacteremia,
    - Adherence of the bacteria in the bloodstream to NBTE,
      - Proliferation of bacteria within a vegetation.

## **Formation of NBTE** (nonbacterial thrombotic endocarditis)

Turbulent blood flow produced by certain types of congenital or acquired heart disease, such as flow from a high- to a low-pressure chamber (backflow from the left ventricle to the left atrium 2ry to regurgitation of mitral valve) or across a narrowed orifice, traumatizes the endothelium ( endocardium (any partvalves) is injured and thrombus will form from PLT aggregation and accumulation subsequently RBCs accumulate and form thrombus, then bacteria infects the thrombus “infected thrombus” )

This creates a predisposition for deposition of platelets and fibrin on the surface of the endothelium, which results in NBTE.

Invasion of the bloodstream with a microbial species that has the pathogenic potential to colonize this site can then result in IE.

Summary: Congenital or acquired heart disease → altered homeodynamics → turbulent blood flow → trauma to the endothelium → fibrin and platelets → NBTE

## **Transient Bacteremia**

Mucosal surfaces are populated by a dense endogenous microflora. (Normal flora (NF) of the body ex. GI, urogenital, nose, sinus, throat, skin)

Trauma to a mucosal surface like

Gingiva around teeth,

Oropharynx,

GI tract,

urethra,

Vagina,

This will release many different microbial species transiently into the bloodstream which will leads to

Transient bacteremia caused by

organism e,g viridans group streptococci (it's NF that could be found in the mouth)

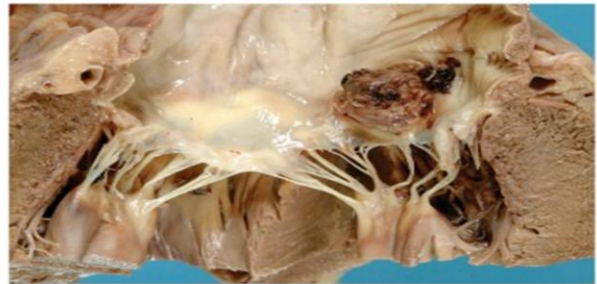
\*N.B: NF enters circulation and causes bacteremia, then goes to the injured endocardium, besides of this, the microorganism releases toxins that produce Ag-Ab complex “immunocomplex” then immunocomplex ( related to organism) & structural (related to vegetation) manifestations of the disease appear

**Endothelial damage**

b/c of

1. *High velocity jet*
2. *Flow from high pressure to low pressure chamber*
3. *Flow across narrow orifice of high velocity*

**Platelet-fibrin thrombi  
(Nonbacterial Thrombotic  
endocarditis)**



Microorganism adherence (BTE)

**Local vegetation**

**EXTENSION(P.V) , Perivalvular ,Destructive valve , FISTULA and embolization.**

## Pathogenesis of Infective Endocarditis

With underlying cardiac disease

No underlying cardiac disease

Valvular endothelium

Mucous membranes - other  
peripheral tissue

*Congenital abnormalities,  
turbulent blood flow*

*Trauma - damage at  
tissue surface*

Nonbacterial thrombus,  
Native valves

Transient  
bacteremia

Adherence and colonization

Platelet adherence, fibrin  
deposition - vegetation  
formation

Elaboration of bacterial  
enzymes, proteases

## **Structural cardiac conditions that make adults and children at risk ([more susceptible](#))**

- Acquired valvular heart disease with stenosis or regurgitation
- Valve replacement ([prosthetic valve](#))
- Structural congenital heart disease
- Hypertrophic cardiomyopathy
- Previous infective endocarditis
- IV drug abuser.

## **Determining Risk**

- Cardiac conditions
- Type of Procedure ([cardiac pt. having a dental procedure](#))

## **Cardiac conditions which predispose pt for IE**

- Based on risk of progression to severe endocarditis with substantial morbidity and mortality (not simply risk of developing IE)
- Classified into

<i>HIGH risk</i>	<i>prophylaxis</i>
<i>MODERATE risk</i>	<i>prophylaxis</i>
<i>NEGLIGIBLE risk</i>	<i>no prophylaxis</i>

### **1. Cardiac Conditions – High Risk<sup>1</sup> [IMPORTANT](#)**

- **Prosthetic Valves (400x risk<sup>2</sup>)**
- Previous endocarditis
- Congenital
  - Complex cyanotic dz (Tetralogy, Transposition, Single Vent)
  - Patent Ductus Arteriosus
  - VSD ([ventricular septal defect](#))
  - Coarctation
- Valvular:
  - Aortic Stenosis/ Aortic Regurg
  - **Mitral Regurgitation**
  - Mitral Stenosis with Regurg
- Surgically constructed systemic pulmonary shunts or conduits

## **2. Cardiac Conditions - Moderate Risk<sup>1</sup>**

### **❑ Valvular**

- MVP + regurg and/or thickened leaflets
- Pure Mitral Stenosis
- TR/TS
- Pulmonic Stenosis
- Bicuspid AV/ Aortic Sclerosis
- degenerative valve dz in elderly

### **■ Asymmetric Septal Hypertrophy/HOCM**

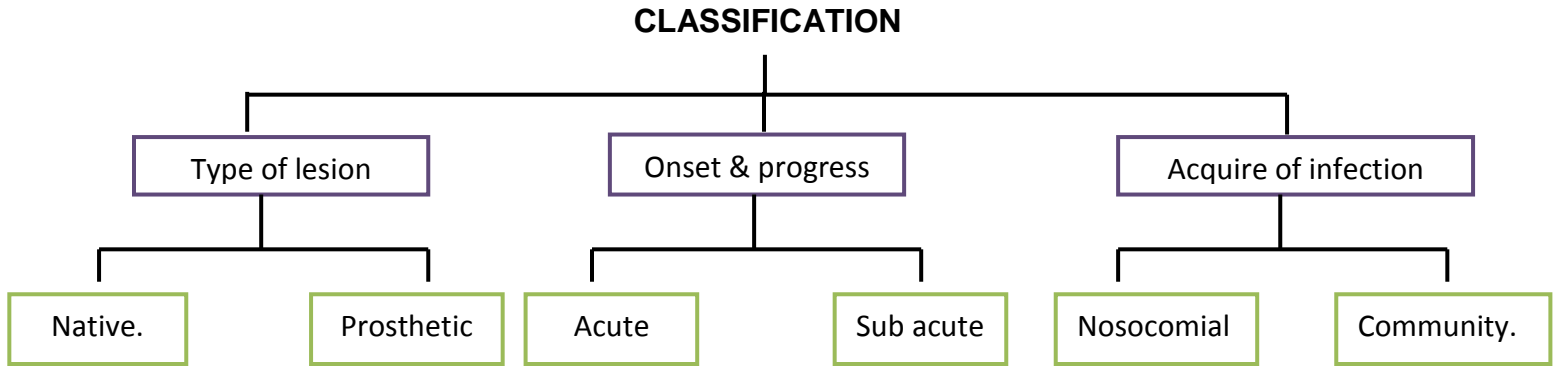
### **■ surgically repaired intracardiac lesions w/o hemodynamic abnormality, < 6 mos after surg**

## **3. Negligible Risk (no prophylaxis)**

- MVP (mitral valve prolapsed) no regurgitation ( young thin women are more likely to have MVP )
- Physiologic/innocent murmur ( pregnant women with murmur & it's usually secondary to their anemia )
- Pacemaker/ICD (implanted cardiovascular defibrillator ) – because pacemakers are outside
- Isolated Secundum ASD ( atrial septic defect )
- prev CABG
- surgical repair ASD/VSD/PDA , no residua > 6mos then it doesn't need prophylaxis

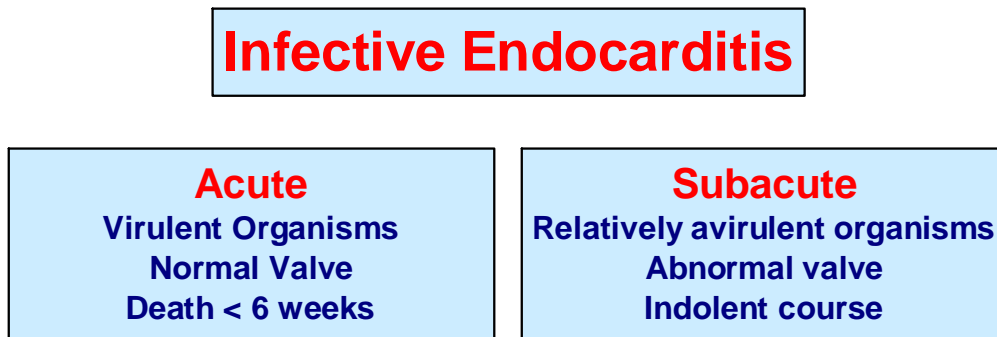
## **Procedures:**

- *Highest* risk oral/dental b/c mouth contain a lot of bacteria while brain doesn't have organisms that's why Brain procedures are sterile and it's away from any source of bacteremia
- *Intermediate* risk GU(genitourinary ) /Pulm (pulmonary)
- *Low* risk GI



\*Nosocomial : inside the hospital

**ORIGINAL CLASSIFICATION (Prior to Antibiotic era) :**



**Clinical Features :**

Onset usually within 2 weeks of infection

› Indolent course

- fever
- **Malaise**
- **Fatigue**
- **Night sweats**
- **Anorexia**
- **Weight loss**

› Explosive course

- CCF ,murmur new onset or changing characters,
- S/o severe systemic sepsis

### Other Clinical Features :

- ☐ Splenomegaly ~ 30%
- ☐ Petechiae 20 - 40%
  - Conjunctivae
  - Buccal mucosa
  - Palate
  - skin in supraclavicular regions
- ☐ Osler's Nodes 10 - 25%
- ☐ Splinter Haemorrhages 5 - 10%
- ☐ Roth Spots ~ 5%
- ☐ Musculoskeletal (arthritis)

### Diagnosis tests :

- ✓ C.B.C : Leukocytosis , thrombocytopenia or thrombocytosis may occur
- ✓ ESR : ↑
- ✓ Blood cultures: 1. At least 3 sets of blood cultures 2. Taken at different times 3. Taken from different locations (different veins)
- ✓ RFT: (renal function test )
- ✓ URINE: microscopic haematuria, proteinuria
- ✓ ECG : T/Q wave changes due to the complications, show evidence of MI or conduction defect .
- ✓ CXR: shows complications of IE :( chest x-ray) may show embolization of the lung / cardiomegaly/ pulmonary odema secondary to heart failure
- ✓ ECHO: Goal of diagnosis , we can see the vegetation and its advantages 1- helps in diagnosis 2- evaluation of the presence or absence of structural heart disease 3- and help in the management of the patient .

### Most important : ECHO & Blood culture !!!!!!!

#### A. Native Valve Endocarditis Microbiology:

1. » Streptococci 50 - 70%  
**Viridans Streptococci** (50% of all Strep)
2. » Staphylococci ~ 25%  
Mostly Coagulase +ve Staph. Aureus  
Staph. Epidermidis
3. » Enterococci ~ 10%

#### 4. HACEK rare

*Haemophilus species, Actinobacillus Actinomycetemcomitans, Cardiobacterium hominis, Eikenella, Kingella)*

blood culture for these organisms takes from 3-4 weeks takes long time in treatment and usually involve the immunocompromised patients .

Fastidious organisms: 1. Hard to Treat 2. Hard to detect in culture



## **B. IE in IV Drug Abusers :**

- Skin most predominant source of infection
- Also contamination of drugs and paraphernalia
- 70 - 100% of Rt. sided IE results in pneumonia and septic emboli
- Microbiology

— <b>Staph aureus</b>	~60%
— Streptococci and Enterococci	~20%
— Gram -ve bacilli	~10%
— Fungi (Candida and Aspergillus) ***	~5%

## **C. Prosthetic Valve Endocarditis :**

It's dangerous because :

-Organisms may make this valve not functioning and then the valve will be damaged

- the blood doesn't reach the metal b/c there is no blood supply for metallic valve unlike the original valve and the antibiotic won't reach there , so we need to prolong the therapy and if there's any complication we have to take the patient immediately for surgery .

## **Classification :**

### ☐ Early ( < 60 days ) \*\*

- Reflects perioperative contamination
- Incidence around 1%
- Microbiology
  - Staph (45 - 50%)
    - Staph. Epiderm (~ 30%)
    - Staph. Aureus (~ 20%)
  - Gram -ve aerobes (~20%)
  - Fungi (~ 10%) \*\*\*
  - Strep and Entero (5-10%)

### ☐ Late ( > 60 days ) \*

- After endothelialization
- Incidence 0.2 -0.5 % / pt. year
- Transient bacteraemia from dental, GI or GU
- Microbiology
  - resembles native valve endocarditis

\*For the late infection (more than 2 months after surgery) the etiology of the organism will resemble native valve endocarditis

\*\* For the early infection (2 months or less after surgery) the microbiology resembles IV abusers

\*\*\* Very hard to treat and culture and might require surgery

## **Diagnostic (Duke) Criteria :**

**Duke Criteria: 2 major OR 1 major and 3 minor , 5 minor**

### **❑ Major Criteria**

1. positive **blood** cultures
  - a. Typical organisms for 2 separated blood cultures
  - b. Persist positive blood cultures
  - c. Positive blood culture for **coxiella burneti**
2. Evidence of Endocardial involvement
  - Positive **Echocardiogram**
    - Oscillating intra cardiac mass
    - Abscess
    - Dehiscence of prosthetic valve
    - New Valvular regurgitation

### **❑ Minor criteria**

- predisposition (heart condition or IV drug use)
- fever of 100.4<sup>0</sup>F or higher
- Vascular ( Arterial emboli, septic pulmonary infarcts, intracranial hemorrhage, Osler, Janeway)
- immunologic phenomena ( GN, Osler, Roth spots, Rheumatoid Factor)
- microbiologic or echocardiographic evidence not meeting major criteria **ex: leak with thickening of the valve but no vegetation**

### **➤ Definitive infective endocarditis**

#### **1. pathologic criteria**

- microorganisms or pathologic lesions: demonstrated by culture or histology in a vegetation, or in a vegetation that has embolized, or in an intracardiac abscess

#### **2. clinical criteria (as above)**

- two major criteria, or
- one major and three minor criteria, or
- five minor criteria

### **➤ Possible infective endocarditis**

- Findings consistent of IE that fall short of “definite”, but not “rejected”

### **➤ Rejected**

- Firm alternate Dx for manifestation of IE
- Resolution of manifestations of IE, with antibiotic therapy for  $\leq 4$  days
  - Because this means that this infection was not IE, IE never responds quickly to antibiotics
- No pathologic evidence of IE at surgery or autopsy, after antibiotic therapy for  $\leq 4$  days

## Treatment

1. Medical: antibiotics
2. Surgical: valve replacement , or closing the VSD ...

### Principles of Medical Management

Sterilization of Vegetations with antibiotics

It should be prolonged therapy at least 4 weeks depending on the antibiotic used, high dose and bactericidal to penetrate the thrombus vegetation.

#### Acute onset:

blood culture and start treatment *within 3 hours*.

#### Sub acute onset:

Blood culture then antibiotic can be started *within 3 days* (so we can wait for 3 days, usually it is indolent disease process)

## Indications for Surgery

Left sided native valve endocarditis

- Valvular disruption (*severe valvular incompetence*) leading to severe insufficiency and CCF (*Congestive Cardiac Failure*)
- Extravalvar extension (*mycotic aneurism*)
- Embolization of vegetations
- Failure of medical management
  - Positive blood culture and systemic signs of infection after “adequate” antibiotic therapy
- Resistant organisms
  - such as MRSA, Fungi , Pseudomonas
- Echo detected vegetation > 1 cm (*>10 mm*)?? *likelihood of embolization is high >>> death*

**NB:** *mycotic aneurism is infected embolism from the vegetation.. if it ruptures it causes septicaemia then death.*

## **Complications**

### ➤ **Congestive Cardiac Failure (Commonest complication)** 2ry to:

1. Valve Destruction
2. Myocarditis
3. Coronary artery embolism and MI
4. Myocardial Abscesses

### ➤ **Neurological Manifestations (1/3 cases)**

1. Major embolism to MCA territory ~25%
2. Mycotic Aneurysms (infected embolism) 2 - 10%

### ➤ **Metastatic infections**

- Rt. Sided vegetations
  - Lung abscesses vegetation metastasize & deposit in the low pressure chambers & low pressure valves
  - Pyothorax / Pyopneumothorax (embolisation to the lung causing infection causing empyema is pyothorax, pneumothorax with empyema is pyopneumothorax)
- Lt. Sided vegetations ((coming from the Rt side b/c of shunt for ex. Or something else happened to the Lt side ))
  - Pyogenic Meningitis
  - Splenic Abscesses
  - Pyelonephritis
  - Osteomyelitis

### ➤ **Renal impairment d/t Glomerulonephritis** (it's an indication for surgery & a complication)

## **Prevention**

### **Cardiac Conditions Associated with the Highest Risk of Adverse Outcome from Endocarditis for Which Prophylaxis with Dental Procedures is Recommended**

- Prosthetic cardiac valve
- Previous infective endocarditis
- Congenital heart disease (CHD)\*
  - Unrepaired cyanotic CHD, including those with palliative shunts and conduits
  - Completely repaired CHD with prosthetic material or device either by surgery or 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

\*Except for the conditions listed above, antibiotic prophylaxis is no longer recommended for any other form of congenital heart disease.

\*\*Prophylaxis is recommended because endothelialization of prosthetic material occurs within 6 months after the procedure.

## Endocarditis Prophylaxis for Dental Procedures

Highest-risk patients require endocarditis prophylaxis for all dental procedures that involve manipulation of gingival tissue or the periapical region of teeth or perforation of the oral mucosa.

Exceptions that do not require prophylaxis:

- 
- Routine anesthetic injections through noninfected tissue
  - Taking of dental radiographs
  - Placement of removable prosthodontic or orthodontic appliances
  - Adjustment of orthodontic appliances
  - Placement of orthodontic brackets
  - Shedding of deciduous teeth and bleeding from trauma to the lips or oral mucosa

## Regimens for a Dental Procedure

Situation	Agent	Regimen – Single Dose (30-60 Minutes Before Procedure)	
		Adults	Children
Oral	amoxicillin	2 gm	50 mg/kg
Unable to take oral medication	ampicillin or cefazolin or ceftriaxone	2 g IM or IV 1 g IM or IV	50 mg/kg IM or IV 50 mg/kg IM or IV
Allergic to penicillins or ampicillin (oral)	cephalexin*† or clindamycin or azithromycin or clarithromycin	2 g 600 mg 500 mg	50 mg/kg 20 mg/kg 15 mg/kg
Allergic to penicillins or ampicillin (unable to take oral meds)	cefazolin or ceftriaxone† or or clindamycin	1 g IM or IV 600 mg IM or IV	50 mg/kg IM or IV 20 mg/kg IM or IV

\*Or other first or second generation oral cephalosporin in equivalent adult or pediatric dosage.

†Cephalosporins should not be used in an individual with a history of anaphylaxis, angioedema, or urticaria with penicillins or ampicillin. IM = intramuscular; IV = intravenous.

## Treatment

NB: most important that should be given initially are :

**ceftriaxone alone** or **(ampicillin + gentamycin)** until culture results are known.

- Pre-antibiotic era - a death sentence
- Antibiotic era
- microbiologic cure in majority of patient
- Highly penicillin-susceptible *Streptococcus viridans* or *bovis*
  - Once-daily ceftriaxone for 4 wks
    - cure rate > 98%
  - Once-daily ceftriaxone 2 g for 2wks followed by oral amoxicillin qid for 2 wks

\*\*\*\*\*

Simple Notes from the Summary:

- Subsequent reemboilization of the vegetation causes complication
- Drug interaction b/w the risk of cardiac condition and the risk of surgery
- a) Highest risk: oropharyngeal procedures
- b) Intermediate risk: GU
- c) Lowest risk: GI

## MCQs!!! :

- ◆ Complications? Choose the right complication
- ◆ Which grp of pt I should give Prophylaxis before dental procedure
- ◆ Major criteria? He gives all minor except one major and we should choose it
- ◆ Manifestations (S/S) "وحدة من الأسماء الفظيعة":  
Osler's Nodes, Roth spots, ...
- ◆ Or something related to the organisms
- ◆ Which is the slow growing organism in IE pt:
- ◆ Choices would include all possible organisms then he'll name one of the "HACEK"  
so we should memorize all the names of the "HACEK" organisms