"He who studies medicine without books sails an uncharted sea, but he who studies medicine without patients does not go to sea at all"
William Osler

Medicine

430

Infective Endocarditis

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Infective Endocarditis

Definition:

Infection of endothelium surface of heart either of

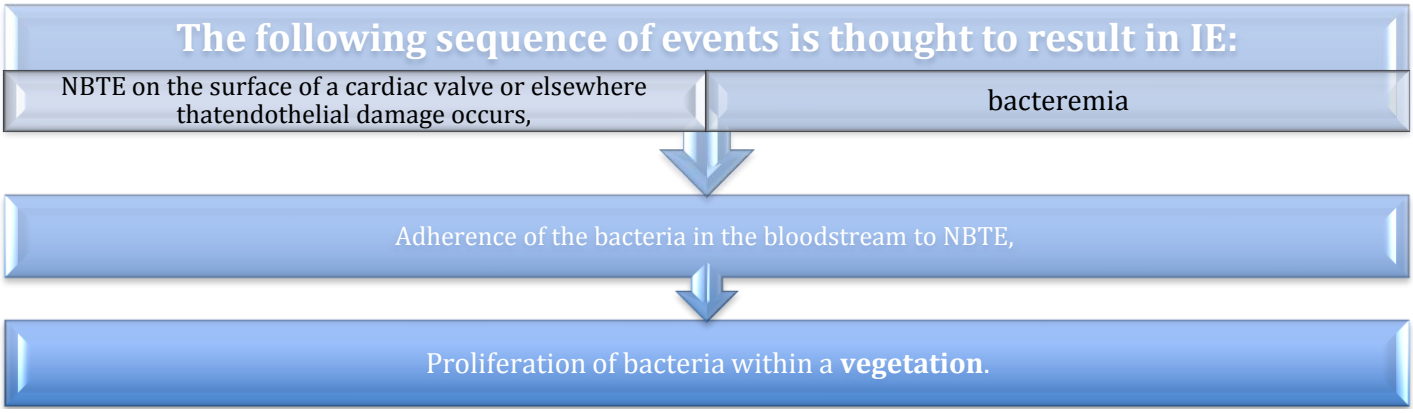
- **Heart valves .**
- **Septal defects.**
- **Chordae tendinea .**
- **A.V shunt.**

Remember:
heart condition + bacteria in the blood = vegetation

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

Pathogenesis of IE (Infective endocarditis):

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.



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 secondary to regurgitation of mitral valve) or across a narrowed orifice, traumatizes the endothelium (endocardium (any part of the valve) 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.

In 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

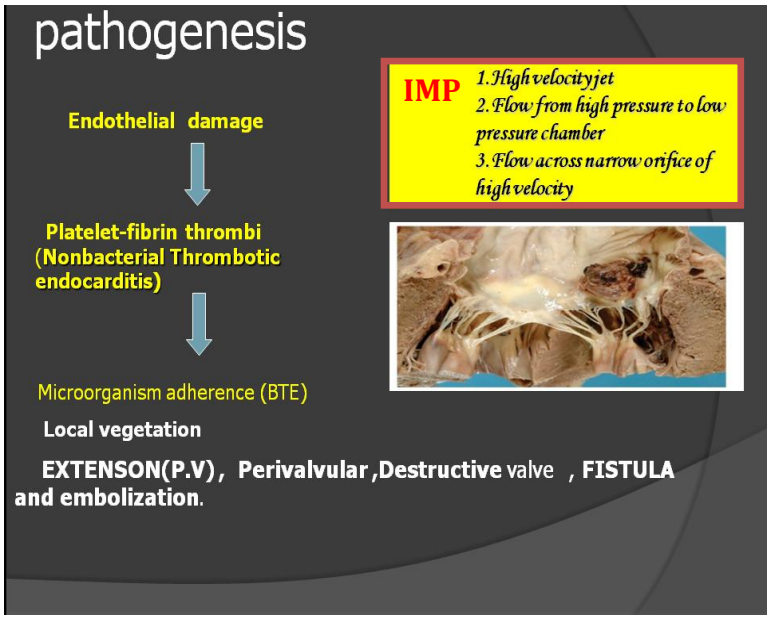
Gingiva around teeth,

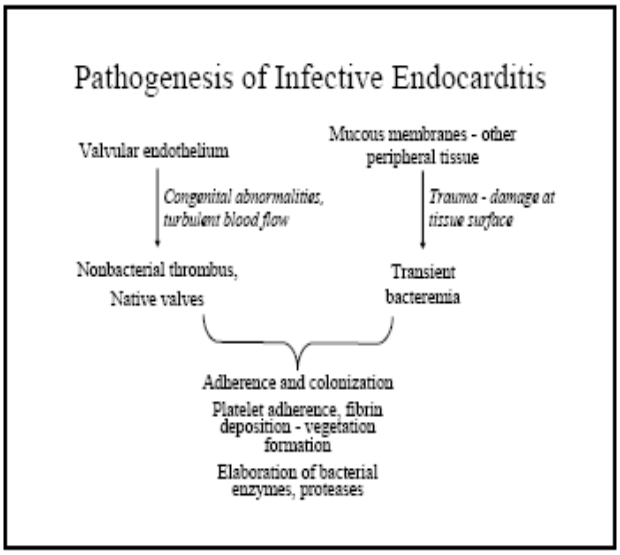
- Oropharynx

Remember:
Highest risk: oropharyngeal procedures
Intermediate risk: GU
Lowest risk: GI

- GI tract
- urethra
- Vagina,

This will release many different microbial species **transiently** into the bloodstream which will leads to Transient **bacteremia** caused by the organism. e,g **streptococci viridans**





Structural cardiac conditions that make adults and children at risk

- 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

- Type of Procedure
- Cardiac Condition.

Example: Cardiac pt. having a dental procedure = High Risk

Cardiac conditions which predisposition for IE

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

HIGH risk	prophylaxis
MODERATE risk	prophylaxis
NEGLIGIBLE risk	no prophylaxis

1. Cardiac Conditions – **High** Risk "IMPORTANT"

- **Prosthetic Valves (400x risk2)** "MCQ"
- Previous endocarditis
- Congenital
  - Complex cyanotic dz (Tetralogy of Fallot, Transposition, Single Vent)
  - Patent Ductus Arteriosus (PDA)
  - VSD (ventricular septal defect)
  - Coarctation of the Aorta

Mitral Regurgitation Alone = High Risk
Mitral Stenosis + Mitral Regurgitation = High Risk
Mitral Stenosis Alone = Moderate Risk

- Valvular:

– Aortic Stenosis/ Aortic Regurg.
– Mitral Regurgitation
– Mitral Stenosis with Regurg

- Surgically constructed systemic pulmonary shunts or conduits

2. Cardiac Conditions - **Moderate** Risk

- Valvular
  - **MVP** (mitral valve prolapsed) **+ regurg and/or thickened leaflets** "MCQ"
  - **Pure** Mitral Stenosis
  - TR/TS (Tricupid regurg. and stenosis)
  - Pulmonic Stenosis
  - Bicuspid AV/ Aortic Sclerosis
  - degenerative valve dz in eldery
- Asymmetric Septal Hypertrophy (HOCM)
- surgically repaired intracardiac lesions w/o hemodynamic abnormality**, < 6 months after surgery.** "MCQ"

3. Negligible Risk (no prophylaxis)

- **MVP** 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** "MCQ" (implanted cardiovascular defibrillator)
- **Isolated Secundum ASD** "MCQ" (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 contains a lot of bacteria (The brain doesn't have organisms that's why Brain procedures are sterile and it's away from any source of bactermia)
- Intermediate risk GU(genitourinary) and pulmonary.
- Low risk GI.

CLASSIFICATION					
Type of lesion		Onset & progress		Acquire of infection	
Native.	Prosthetic	Acute	Sub acute	Nosocomial	Community

ORIGINAL CLASSIFICATION (Prior to Antibiotic era)

Infective Endocarditis

Acute	Subacute
Virulent Organisms	Relatively avirulent organisms
Normal Valve	Abnormal valve
Death < 6 weeks	Indolent course

Clinical Features:

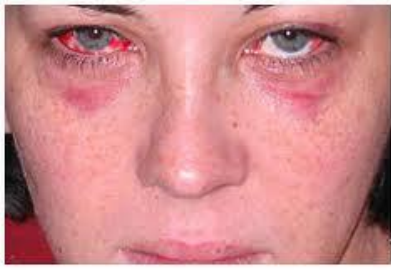
Onset usually **within 2 weeks** of infection

- Indolent course
  - **fever**
  - Malaise
  - Fatigue
  - Night sweats
  - Anorexia
  - Weight loss
- Explosive course
  - CCF ,**New Onset murmer** or changing characters,
  - S/o severe systemic sepsis

Remember:
Unexplained fever + New murmur onset >> IE

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)



Pronounced petechiae in the whites of the eyes and on the cheeks/face.

Petechiae: a minute reddish or purplish spot containing blood that appears in skin or mucous membrane as a result of localized hemorrhage.

Diagnosis tests:

- C.B.C : Leukocytosis , thrombocytopenia or thrombocytosis may occur
- ESR :
- **Blood cultures:** 1. At least **3 samples** of blood cultures 2. Taken at different times (**30 minute**) 3. Taken from different locations (**different 3 veins**)
- RFT: (renal function test)
- URINE: microscopic haematuria, proteinurea
- 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 investigations: ECHO & Blood culture

A. Native Valve Endocarditis Microbiology:

1. ›› Streptococci 50 - 70%
   - Viridans Streptococci "MCQ" (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 involves 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
  - Staph aureus "MCQ" ~60%
  - Streptococci and Enterococci ~20%
  - Gram -ve bacilli ~10%
  - Fungi (Candida and Aspergillus) *** ~5%

C. Prosthetic Valve Endocarditis: MCQ

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 patent immediately for surgery

CLASSIFICATION	
Early (< 60 days)	**Late (> 60 days)**

• 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%)**
	• After **endothelialization**
	• Incidence 0.2 -0.5 % / pt. year
	• Transient bacteraemia from dental, GI or GU
	• Microbiology
	  ○ **resembles native valve endocarditis (strept.)** "MCQ"

Diagnostic (Duke) Criteria: (Duke Criteria: 2 major OR 1 major and 3 minor , 5 minor)

- **Major Criteria**
  - positive ***blood*** cultures
    - Typical organisms for 2 separated blood cultures
    - Persist positive blood cultures
    - Positive blood culture for **coxella burniti** (this organism effects heart only)
  - Evidence of Endocardial involvement
    Positive ***Echo***cardiogram
    - Oscillating **intra cardiac mass**
    - **Abscess**
    - **Dehiscence** of **prosthetic valve**
    - **New Valvular regurgitation**
- **Minor criteria**
  - predisposition (heart condition or IV drug use)
  - fever of 100.40F 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:

- **pathologic criteria** (one of these indicate IE) microorganisms or pathologic lesions: demonstrated by culture or histology in a vegetation, or in a vegetation that has embolized, or in an intracardiac abscess
- **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 **< or = 4 days**
(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 < or = 4 days

Treatment

- Medical: antibiotics
- 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.* (We don't wait for the results of the culture, we start treatment immediately)
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 an infected embolism from the vegetation.. if it ruptures it causes septicemia then death.

Complications:

- *Congestive Cardiac Failure (Commonest complication) 2ry to:*
  - Valve Destruction
  - Myocarditis
  - Coronary artery embolism and MI
  - Myocardial Abscesses

- *Neurological Manifestations (1/3 cases)*
    - Major embolism to MCA territory ~25%
    - Mycotic Aneurysms (infected embolism) 2 - 10%
- *Metastatic infections*
    - Rt. Sided vegetations
        - Lung abscesses vegetation metastesize & 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 pyopneamothorax)
    - Lt. Sided vegetations (coming from the Rt side b/c of shunt for example)
        - 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.

Regimens for dental procedure:

	NOT Allergic to penicillin	Allergic to penicillin
Oral	**Amoxicillin** "MCQ"	**Cephalexin, clindamycin, azithromycin or clarithomycin.**
Unable to take oral drugs	**Ampicillin, cefazolin or ceftriaxone**	**Cefazolin, ceftriaxone or clindamycin**

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	2 g IM or IV	50 mg/kg IM or IV
	cefazolin or ceftriaxone	1 g IM or IV	50 mg/kg IM or IV
Allergic to penicillins or ampicillin (oral)	cephalexin*† or	2 g	50 mg/kg
	clindamycin or	600 mg	20 mg/kg
	azithromycin or clarithromycin	500 mg	15 mg/kg
Allergic to penicillins or ampicillin (unable to take oral meds)	cefazolin or ceftriaxone† or	1 g IM or IV	50 mg/kg IM or IV
	or clindamycin	600 mg 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.

Simple Notes from the Summary:
 Subsequent reembolization 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

Treatment

NB: most important that should be given initially are: **ceftriaxone alone** or (**ampicillin + gentamycin**) until culture results are known.

- Pre-antibiotic era (before antibiotic discovered) - a death sentence
- Antibiotic era (after antibiotic discovered)- 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**