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Infective Endocarditis

★ Objectives:

1. Understand the Endocarditis definition
2. Patho-physiology of endocarditis
3. Presentation of patients with endocarditis
4. Treatment of endocarditis
5. Prevention of endocarditis

★ Resources Used in This lecture:

Davidson, Master The Boards, Step Up, Kaplan video, Class Notes.

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Definition

It is infection of endothelial surface of heart . Either of:

1. Heart valves (native or prosthetic). Most common
2. Congenital anomaly (Septal defects).
3. The lining of a cardiac chamber or blood vessel (Chordae Tendinea).
4. A.V shunt[1].

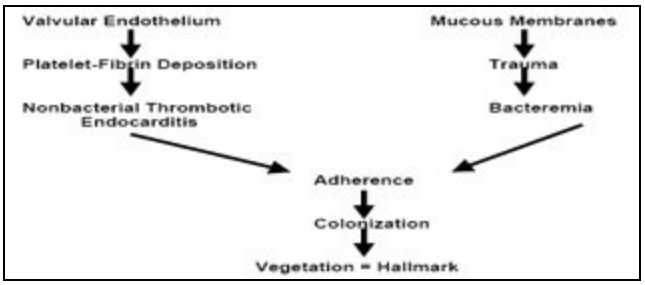
Pathogenesis

1- Endothelial damage: Causing Turbulent blood flow produced by certain types of *congenital* or *acquired* heart disease.(e.g ventricular septal defect, mitral regurgitation and aortic regurgitation.)

2- Abnormal cardiac endothelium facilitates → The deposition of **platelets** and **fibrin** on the surface of the endothelium→ Thus formation of **nonbacterial thrombotic endocarditis.**
Note: *Platelets and fibrin are vulnerable to colonisation by blood-borne organisms.*

3- Trauma to a mucosal surface like: *Gingiva around teeth*, *Oro-pharynx*, *GI tract, Urethra, Vagina*, will release many different microbial species.
Note: *Mucosal surfaces are populated by a* ***dense endogenous microflora.***
(e.g **viridans group streptococci**[2])

4- Bacteremia: Invasion of the bloodstream with a microbial species that has the pathogenic potential to colonize this site ,then result in Proliferation of bacteria within a **vegetation** and form IE.



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

★ Infective endocarditis typically occurs at sites of **preexisting endocardial damage**, but severe bacteremia or infection with particularly virulent or aggressive organisms (e.g. **Staphylococcus aureus**) can cause endocarditis in a previously normal heart.

Simply: (Dr. Mostafa explanation)
1- Abnormal structure → abnormal blood flow → 1-Fibrin 2- platelet 3-clot formation → combine forming Nonbacterial thrombotic Endocarditis. (NBTE)
2- Bacteria from mouth ,GI, vagina or urethra travel to NBTE→ forming vegetations → causing further destruction, erosion or dislodge into circulation to infect any other organ (e.g coronary → MI).
3- Destruction mainly by the immunological response .

[1] An **arteriovenous fistula** is an abnormal connection or passageway between an artery and a vein. It may be congenital, surgically created for hemodialysis treatments, or acquired due to pathologic process, such as trauma.
[2] Are abundant in the mouth, so after dental procedure *e.g tooth extraction* they may travel to the bloodstream & infect the heart in people with heart valves defect; that's why dentists should ask the patient about any cardiac diseases before doing any procedure.

Classification Based on:

- **Acuteness:** This classification reflects the virulence of the causative organism.
  - **Acute bacterial endocarditis (ABE):**
    - ➔ Most commonly caused by S. aureus.(Occurs in normal valves)
    - ➔ IF not treated fatal in less than 6 weeks.
  - **Subacute bacterial endocarditis (SBE):**
    - ➔ low virulence organism like viridans streptococci(from mouth)or Enterococcus (from GI).
    - ➔ If not treated takes more than 6 weeks to cause death. (occurs in normal Valves)

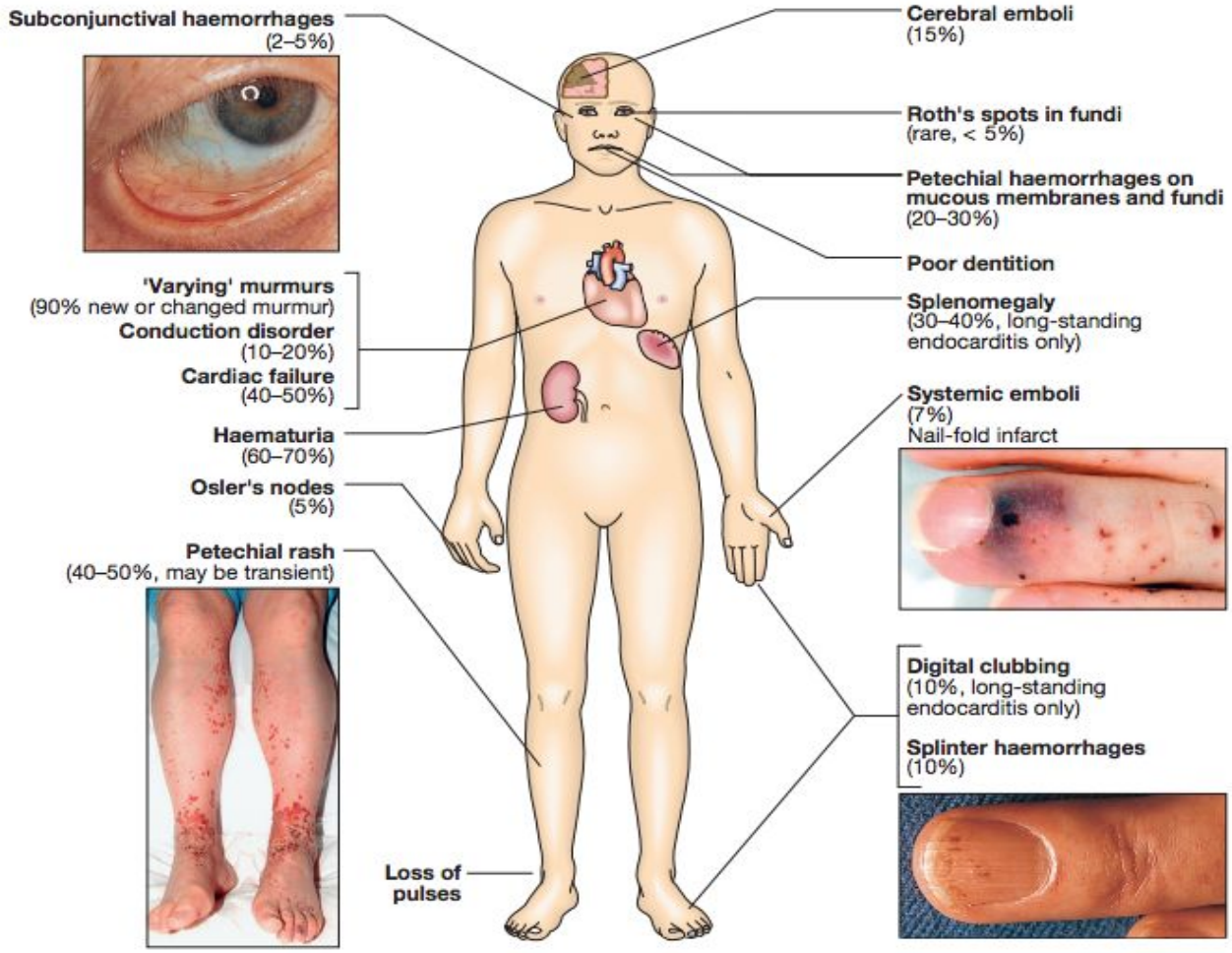
- **The nature of involved valve:**
  - ➢ Native valve endocarditis (NVE).
  - ➢ Prosthetic valve endocarditis (PVE).*More serious .

- **Acquire of Infection:**
  - ➢ Health-care related IE.
  - ➢ Nosocomial IE.

> Note: These categories are often combined (e.g. S.aureus tricuspid valve nosocomial ABE).

Clinical Feature

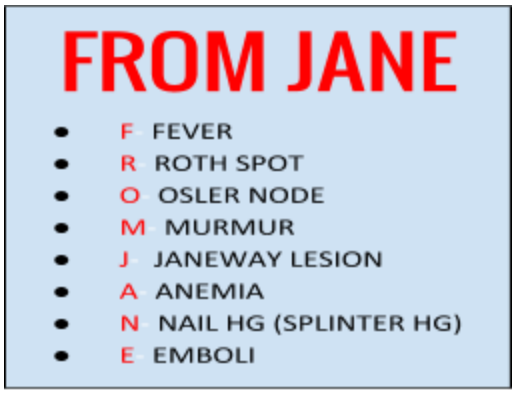
Due to infection or **dislodge of vegetations** into the system causing **immune response** in site it rely.



Note: **The cardinal clinical feature of EI are fever (90% of cases) and heart murmur (85%).**

Other clinical features:

- Splenomegaly
- Petechiae
  - Conjunctivae
  - Buccal mucosa
  - Palate
  - Skin in supraclavicular regions
- Osler's Nodes
- Splinter Haemorrhages
- Roth Spots
- Musculoskeletal (arthritis)



Onset usually within 2 weeks of infection:
› **Indolent course:** fever, Malaise, Fatigue, Night sweats, Anorexia and Weight loss.
› **Explosive course:** congestive heart failure, murmur new onset or changing characters, with severe systemic sepsis.

Janeway lesion, Osler's Nodes, Roth spots and splinter hemorrhage → are painless and usually in long term untreated EI as a complication,"It's Irrelevant".

The causative organisms of IE

The causative pathogen of infective endocarditis depends on the *patient condition*→ (native valve IE, prosthetic valve IE, drug abuser IE)

Native valve endocarditis	IE in IV Drug Abusers	Prosthetic Valve Endocarditis (postoperative)

• **Streptococci** (most common) specially Viridans Streptococci (50% of all Strep)
• **Staphylococci** (Staph. Aureus) Coagulase +ve more common than (Staph. Epidermidis) Coagulase -ve
• **Enterococci**
• **HACEK** (Rare)
  • Haemophilus species,
  • Actinobacillus Actinomycetemcomitans,
  • Cardiobacterium hominis,
  • Eikenella,
  • Kingella
	• **Staph aureus** (most common)
	• **Streptococci and Enterococci**
	• **Gram -ve bacilli** (mostly pseudomonas)
	• **Fungi (Candida and Aspergillus 5%**
	
	Note: The patient frequently presents with right-sided endocarditis.
		1. **Early-onset:** occurs in (less than 60 days after the surgery)
		• **Staph** (most common) Staph. Epiderm *more common than Staph. Aureus.*
		• **Gram -ve aerobes**
		• **Fungi**
		• **Strep and Entero**
		
		2. **Late-onset:** occurs in (more than 60 days after the surgery)
		• **Streptococci** (most common)

High Risk factors → Need for Prophylaxis

Significant cardiac defect	Risk of bacteremia
1- Prosthetic Valve, Including transcatheter valve or any prosthetic procedure for valve repair 2-Patients with previous IE. 3- Patients Congenital Heart defect[3].	1-Dental procedure

Low Risk → No need for Prophylaxis

- Acquired Valvular heart disease with stenosis or regurgitation.
- Hypertrophic cardiomyopathy.
- I.V drug abuser.
- Respiratory tract procedure.
- GI or Urogenital procedure.
- Skin and soft tissue procedure.

Investigations

1-Initial test:

- Blood cultures:3 times, 3 different sites and 3 different needle→**to identify the organism**
- ECHO mostly TTE[4] (vegetation , abnormality of the valves).

2- Further test:

- C.B.C : Shows leukocytosis + anemia
- ESR : Will be elevated
- RFT : Shows Glomerulonephritis
- URINE : Shows hematuria
- ECG: shows first degree block
- Chest X-Ray: Shows cardiomegaly, pulmonary embolism.

Note: These investigations will **help** in the diagnosis but the definitive diagnosis is based on Duke criteria.

[3] tetralogy of fallot has the highest IE potential.
[4] Transthoracic echocardiogram

Diagnosis of IE

Based on Duke criteria 2015 by either Two major criteria , one major and 3 minor criteria or 5 minor criteria.

Major criteria

1. Positive blood culture : → by common organism that cause IE
- Typical organism from two cultures
- Persistent positive blood cultures taken > 12 hrs apart
- Three or more positive cultures taken over > 1 hr
- Single positive blood culture for Coxiella burnetii.

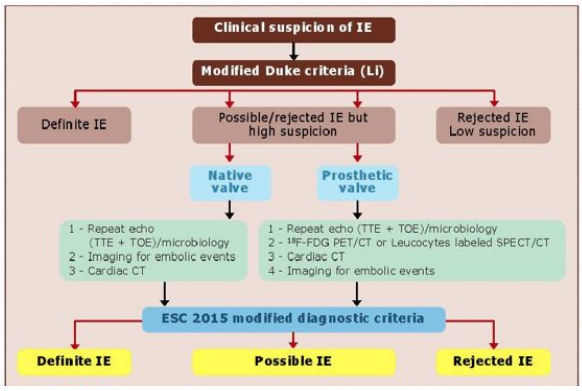
2. Positive imaging for IE :
- **Positive echocardiogram** : vegetations , abscess, valve perforation ,prosthetic dehiscence
- **Abnormal activity around prosthetic valve by CT , PET or F-FDG**
- **Paravalvular lesion by CT**

Minor criteria

1. **Predisposing condition :** such as cardiac abnormality , drug injection
2. **Fever**
3. **Vascular phenomenon :** janeway lesion . intracranial hemorrhage , major emboli . Mycotic aneurysm , septic pulmonary infarct , conjunctival hemorrhage
4. **Immunological phenomenon :** Osler's nodes , roth spot , rheumatoid factor , glomerulonephritis
5. **Positive blood culture:** organism not achieving major criteria.

Management of IE

1. **Initial therapy (before culture result)**
- Vancomycin and gentamicin
2. **After culture result**
- Streptococcus viridans → ceftriaxone for 4 weeks or ceftriaxone 2 weeks followed amoxicillin 2 weeks
- Staphylococcus Aureus → oxacillin , nafcillin or cefazolin
- Staphylococcus epidermidis or Resistant Staphylococcus → Vancomycin
- Enterococci → ampicillin and gentamicin
- Fungal → amphotericin and valve replacement
3. **Surgery**:Indicated in CHF, Uncontrolled infection and Prevention of embolism.



- The antibiotic should be bactericidal.
- In case of prosthetic valve endocarditis the treatment should be more than 4 weeks .
- In Acute IE : do blood culture and start treatment within three hours.
- In Subacute IE: do Blood culture then antibiotic can be started within three days.
- If culture is positive for → S.Bovis or clostridium you should perform endoscopy , it's usually associated with Colon pathology (e.g. colon cancer).

Prevention

- Strict dental and cutaneous hygiene.
- Disinfection of wounds.
- Eradication or decrease of Chronic bacterial carriage.
- Curative antibiotics for bacterial infection.
- No self medication with antibiotic.
- Discourage piercing and tattooing.
- Strict infection control.
- Limit the use of infusion catheters and invasive procedure.

Prophylaxis

Should be only for High risk people

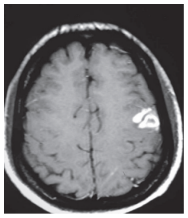
- amoxicillin or ampicillin

If the patient has allergy to amoxicillin or ampicillin use the clindamycin , azithromycin or clarithromycin.

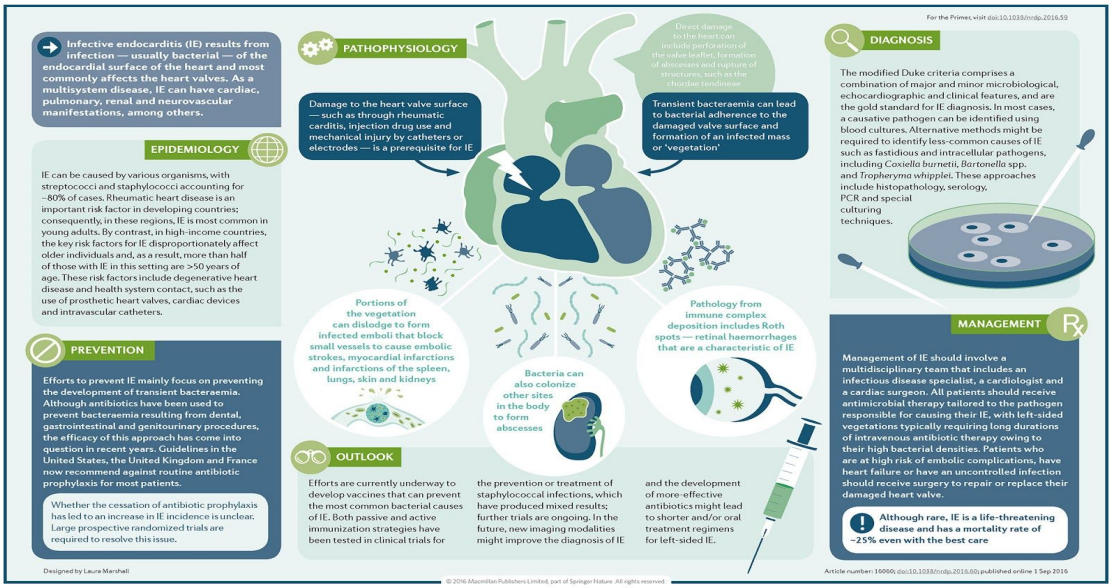
Complications of IE

Congestive Cardiac Failure (Commonest complication)	**Metastatic infections** (various solid organ damage from showered emboli)

- Valve Destruction
- Myocarditis
- Coronary artery embolism and MI
- Myocardial Abscesses
	- **Rt. Sided vegetations**
	  ○ Lung abscesses
	  ○ Pyothorax/ Pyo-pneumothorax
	- **Lt. Sided vegetations**
	  ○ Pyogenic Meningitis
	  ○ Splenic Abscesses
	  ○ Pyelonephritis
	  ○ Osteomyelitis

Neurological Manifestations (1/3 cases)	**Renal impairment (Glomerulonephritis)**
- Major embolism to MCA territory ~25% - Mycotic Aneurysms 2 - 10% 	-As a result of immunological phenomena.

Summary



Recommended video: https://www.youtube.com/watch?v=kW-85yk0ErQ

MCQ's

1-The condition associated with the *highest risk* of developing infective endocarditis (IE) is:

A. Mitral valve prolapse with regurgitation.
B. The presence of prosthetic heart valve.
C. rheumatic fever without valvular defects.
D. intravenous drug abuse.

2- Which of the following organisms is *not* commonly implicated in infective endocarditis?

A. *Streptococcus* species.
B. *Staphylococcus* species.
C. *Enterococcus* species.
D. *Candida* species.

3- 64-year-old man presents to the emergency department with chest pain, fever, fatigue, and arthralgias. His past medical history is significant for rheumatic heart disease and a dental procedure a few weeks before admission. He currently shows no "stigmata" of endocarditis on physical examination, although endocarditis is suspected. The most likely organism is:

A. *viridans* streptococci.
B. *Staphylococcus aureus*.
C. *Enterococcus fecalis*.
D. *Pseudomonas*.

4-A patient that recently had mitral valve replacement (38 days ago) was admitted to the clinic with persistent fever and malaise. Endocarditis is suspected, and the most likely etiology is:

A. group A streptococci.
B. *viridans* streptococci.
C. *Staphylococcus epidermitis*.
D. *Enterococcus fecalis*.

5- A 74-year-old man with a history of endocarditis underwent prostate surgery 3 weeks ago. For the past week he has had persistent fever and weakness. Blood cultures are pending, but an echocardiogram suggests a potential change consistent with new endocarditis. If the patient is subsequently diagnosed with this infection, the most likely organism is:

A. group A streptococci.
B. *viridans* streptococci.
C. *Staphylococcus epidermitis*.
D. *Enterococcus fecalis*.

6-Based on the recent IE diagnostic criteria, the two most important parameters for the diagnosis of this infection are

A. laboratory abnormalities and positive blood cultures.
B. positive blood cultures and echocardiographic changes.
C. ECG changes and positive physical findings.
D. positive physical findings and positive blood cultures.

7-TH is a 65-year-old woman who has developed endocarditis with *viridans* streptococci (MIC ≤ 0.1 ug/mL) on a native heart valve. The patient has no known drug allergies and normal renal function. Which of the following intravenous regimens is *most appropriate*?

A. Ceftriaxone 2 g once daily for 2 weeks
B. Penicillin G 12-18 million units every 24 hours for 4 weeks
C. Cefazolin 2 g every 8 hours for 2 weeks plus gentamicin 1 mg/kg every 8 hours for 2 weeks
D. Penicillin G 12-18 million units every 24 hours for 4 weeks plus gentamicin 1 mg/kg every 8 hours for 2 weeks

8-45-year-old woman is scheduled for a major dental extraction in 3 days. She has a history of prosthetic valve replacement. She is allergic to penicillin. Her physician asks whether she should receive antibiotic prophylaxis before her procedure. The most appropriate response is:

A. yes, ampicillin 2 g orally 1 hour before the procedure.
B. yes, clindamycin 600 mg orally 1 hour before the procedure.
C. yes, cephalexin 500 mg orally 2 hours before the procedure.
D. no, the most recent guidelines do not recommend prophylaxis in this situation.

Answers: 1.B 2.D 3.A 4.C 5.D 6.B 7.B 8.B