

CARDIO-VASCULAR SYSTEM

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Microbiology

Writer: Fahed Zakout

S.corrector: Khaled alzoubi

F.corrector: Dana Alnasra

Doctor: Nader Alaridah



Infective Endocarditis:-

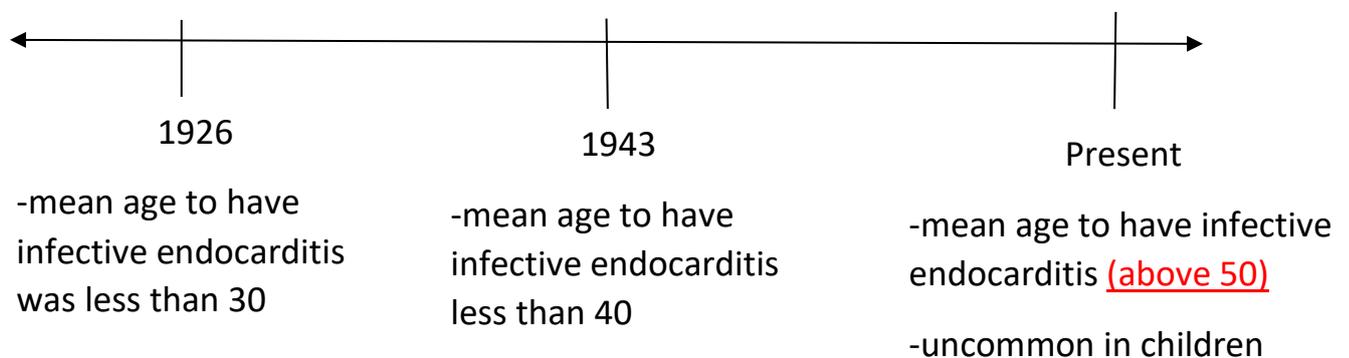
(before we start, anything between brackets [] and written in blue color is JUST EXTRA INFORMATION and anything underlined and written in RED means it's very important).

What is infective endocarditis?

It is an inflammation of the endocardium (inner surface of the heart + the epithelial lining of heart valves).

infective endocarditis is a rare disease but it's fatal with a mortality rate of >25%. Once established, IE can involve almost any organ system

Epidemiology:-



Predisposing factors:

Before we talk about the predisposing factors, we need to know three things:

- 1- They differ according to time (which means that predisposing factors before 50 years are not the same as now).
- 2- Causes differ in developed and developing countries.
- 3- We have two types of predisposing factors:
 - A- Cardiac (which means that we have an underlying cardiac disease that causes infective endocarditis).
 - B- Non-cardiac (which means that we have other things that can cause infective endocarditis).

Some notes on the predisposing factors:

- a. Rheumatic heart disease is a major risk factor, as it's caused by group A streptococci
- b. degenerative valve diseases , diabetes , cancer , intravenous drugs , and congenital heart disease have replaced rheumatic fever as the major risk factors for IE.
- c. Any procedure that can cause introducing flora to blood can cause IE. e.g. dental procedures, colonoscopy, tonsillectomy, urethral dilation, etc.
Thus, antibiotic prophylaxis is recommended.

[1938-1967 predisposing factors]:

Cardiac causes:

1- valvular heart disease

2- Rheumatic disease **40%**

non cardiac causes:

1- IV drug users

2- diabetes

3- urological diseases

Predisposing factors since 2000- until now:

Cardiac causes:

1- valvular heart disease.

2- degenerative valve disease.

3- rheumatic fever; 3% in developed countries but it's still one

Of the most common causes in developing countries.

4- prosthetic valves; 20%.

Non cardiac causes:

IV drug users

Some important notes: -

- 90% of cases (of infective endocarditis) are caused by Gram-positive cocci.
- The most common cause of infective endocarditis in developing countries is viridans streptococci; they are a large group of streptococcus Gram-positive species that are alpha-hemolytic, and they include:
 - a. *sanguinis* (most common)
 - b. *anginosus*
 - c. *mitis*
- The most common cause of infective endocarditis in developed countries (staph. Aureus).

Now before going to the pathophysiology of infective endocarditis we have to know that we have two types of infective endocarditis:-

1- Acute; it's quickly progressing and it's caused mostly by (staphylococcus aureus). a febrile illness that rapidly damages cardiac structures, seeds extracardiac sites, and if untreated, progresses to death within weeks.

2- Subacute; slowly progressing, indolent and it's mostly caused by (viridans streptococci) causes structural cardiac damage only slowly, if at all. Rarely metastasizes, and is gradually progressive unless complicated by a major embolic event or a ruptured mycotic aneurysm.

Pathophysiology of infective endocarditis:

Three factors contribute to the development of infective endocarditis:

1. Bloodstream infection (bacteremia from skin or mucous membrane flora)
2. A problem with blood flow across cardiac valves (congenital or acquired)
3. Colonization and establishment of infection and inflammation on the valves (vegetation)

What will happen is that we have an abnormal valve, this abnormal valve will cause turbulent blood flow, and if the endothelium becomes damaged by the turbulent blood flow, platelets and fibrin will go to the damaged area and try to heal it and as a consequence, they will stick together forming **(NON-bacterial thrombotic vegetation)**. But if we have also circulating bacteria in the bloodstream we will have **(INFECTIVE ENDOCARDITIS)**.

Important concept: **BIOFILM** is an accumulation of bacteria, platelets, fibrin that occurs in (infective endocarditis).

MICROBIAL CAUSES:

1. **Gram-positive cocci:** facultative anaerobes, diplococci, chains/clusters or pairs cocci, e.g. Catalase +ve Staphylococci group, catalase-ve Streptococci & Enterococci groups.
 - a. **Streptococci:** are also subdivided into groups according to their hemolytic reaction on blood agar in vitro and by serotypes according to surface cell wall specific carbohydrate antigens.

i. Viridans streptococci group (VGS)

-they are part of the oral normal flora and are common causes of dental carries. What happens is that after dental surgical procedures (or due to a gingival abscess), they might travel to the bloodstream and cause infective endocarditis, so it's better to give antibiotics before the surgery.

-they have dextran on their surface, which can bind to fibrin and platelets in damaged areas preventing the thrombus from detaching and this leads to vegetations.

St.mutants, St.mitis (accounted for many cases and tend to be less susceptible to penicillins).

ii. Group A streptococci (S.pyogenes) :

With repeated sore throat infection, they can cause rheumatic heart disease in children. And observed later in young adults.

[Streptococcus bovis :

-normal in the gut, associated with colon cancer

-but in colon cancer, they migrate to bloodstream and cause endocarditis

so, if you have infective endocarditis that's caused by S.bovis, don't forget to do colonoscopy to check if this patient has colon cancer or not]

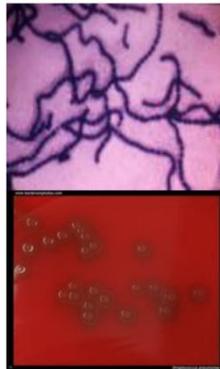
b. S.AUREUS

-most common cause of acute endocarditis as we have mentioned on page 2.

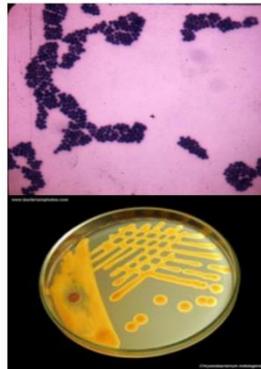
- it's introduced to the body after surgical procedures or intravenous drug use. Also, it can infect vascular catheters.

c. **S.epidermidis:** mostly infects prosthetic valves

d. **Enterococcus :** (E.fecalis, E.faecium) are responsible for 5-10% of cases and some strains may be resistant to penicillin and vancomycin.



Streptococci



staphylococci

2. Gram-negative bacteria:

Not only Gram-positive bacteria can cause infective endocarditis, but also Gram-negative can cause it, but it's rare. Clinically, these bacteria spp. cause subacute or chronic course, and often present with embolic lesions from large biofilm vegetations in heart valves.

I. HACEK group:

- Gram-negative bacteria, they are part of the normal flora in the mouth and throat.

H = Haemophilus , A= Aggregatibacter , C= cardinobacterium , E= Eiknella , K= Kingella

II. **Pseudomonas species:** gram-negative, they can enter the body through IV drugs

III. **Bartonella:** gram-negative, it is associated with cats

3. Yeast and filamentous fungi :

- very rare to cause infective endocarditis
- occurs in immune-compromised patients.
- occurs in patients who are receiving prolonged antibiotics, or IV drugs
- high mortality rate
- the most common species to cause endocarditis are Candida albicans, followed by less common candida species. Infection follows using catheters or respiratory intubation. Histoplasma capsulatum and aspergillus can also cause infection.

This table summarizes what we were talking about:

	Catalase	Coagulase	Hemolysis†	Distinguishing Features	Disease Presentations
<i>Staphylococcus</i> Species					
<i>S. aureus</i>	+	+	β	Ferments mannitol Salt tolerant	Infective endocarditis (acute) Abscesses Toxic shock syndrome Gastroenteritis Suppurative lesions, pyoderma, impetigo Osteomyelitis
<i>S. epidermidis</i>	+	-	γ	Novobiocin ^S Biofilm producer	Endocarditis in IV drug users Catheter and prosthetic device infections
Viridans group (not groupable)	-	-	α	Optochin ^R	Infective endocarditis Dental caries
<i>Enterococcus</i> sp. (Group D)	-	-	α, β, or γ	PYR [†] Esculin agar	Infective endocarditis Urinary and biliary infections
<i>S. bovis</i>	-	-	γ	Bile esculin [†]	Endocarditis, especially in patients with colon cancer

Symptoms :

Cardiac:

- 1- New heart murmur (results from turbulent blood flow)
- 2- unexplained congestive heart failure develops in 30-40% of cases.

Non-cardiac:

- 1- fever in 80% of cases
- 2- septic emboli (it happens when a fragment of vegetation detaches and goes to the bloodstream).

This detached embolus can go to several places:

Where can septic emboli go

It can go to fingernails and stick there causing (subungual haemorrhage).
Associated with acute *S.aureus* IE



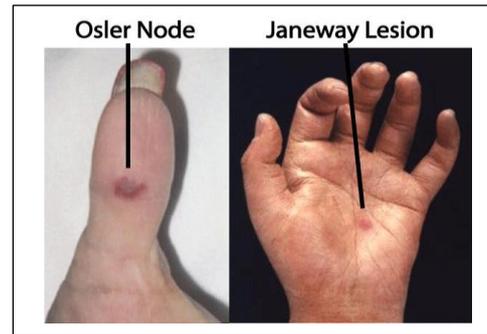
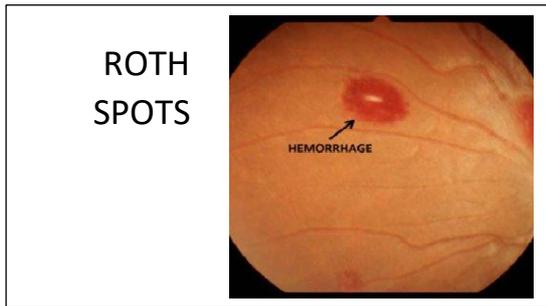
It can go to palms or soles causing what's known as (Janeway lesions) characterized by:

- A- Flat, nonsuppurative hemorrhage
- B- painless
- C- associated with subacute IE

The pathogen (detached emboli) can also trigger IMMUNE REACTION where antigen-antibody complex form deposits in different parts of the body:

- 1) in acute IE, deposits in fingers and toes forming (Osler node), that's characterized by a painful, raised, nodule, in contrast to Janeway lesion.

- 2) EXTRA: in the eye forming (Roth spot) which is retinal hemorrhage with a white center, this Roth spot can also be found in other diseases.
- 3) EXTRA: they can rarely deposit in the kidney causing glomerulonephritis.



Diagnosis :

Is based on DUKE criteria -the doctor didn't explain this very well but what you have to know is that it includes all the following :

A- clinical presentation, what you see on the patient like fever, etc...

B- blood cultures

C- Echocardiography; looking for any vegetations.

Management:

1. antimicrobial therapy

-Vancomycin + gentamicin initiated after blood samples are taken for cultures

- extended course of parenteral therapy with bactericidal or fungicidal agents is typically required.

2. Surgical treatment

Prevention:

You have to give prophylactic antibiotics to people with high-risk factors before any surgical procedure e.g. :

- A- people with a history of endocarditis or rheumatic heart disease
- B- people with prosthetic heart valves

EXTRA: In DUKE diagnosis, findings are classified to major and minor criteria:

For a definite diagnosis we have to meet 2 major, 1 major and 3 minor, or 5 minors

Major criteria:

1. Positive blood cultures for bacteria known to cause IE
2. Echocardiographic evidence for endocardial involvement

Minor criteria:

1. Predisposing heart condition or IV drug use
2. Temperature $>38^{\circ}\text{C}$
3. Vascular phenomena
4. Immunologic phenomena
5. Microbiologic evidence (not meeting major criterion)