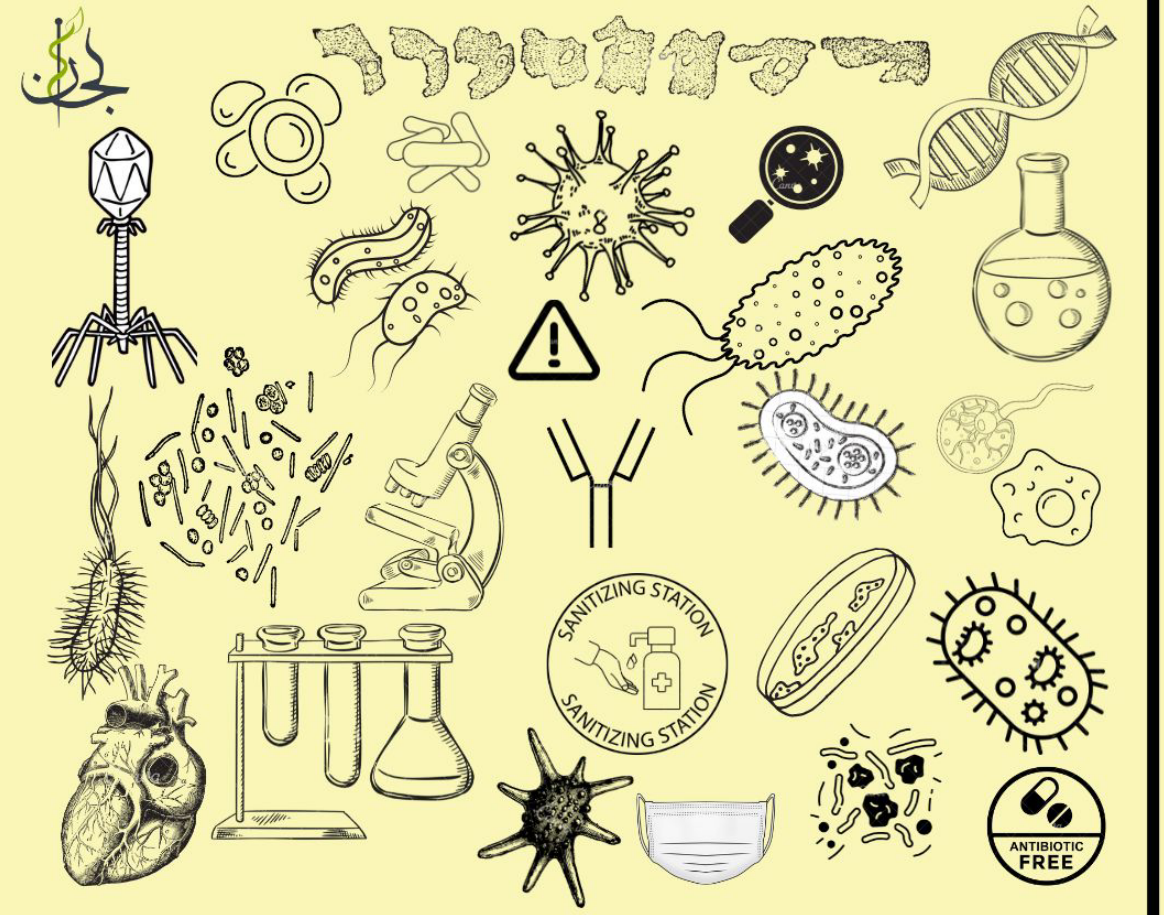


CVS MICROBIOLOGY

Writer: Rahaf Turab

Corrected by: Alaa BanyAmer

Doctor: Nader Al-aridah

modified no. :

Infective endocarditis (IE)

No only caused by bacteria so called infective endocarditis instead of bacterial endocarditis.

By Assis. Prof. Nader Alaridah MD , PhD

The prerequisites for it:
1- bacteria or fungi found in the systemic circulation (normally it must be sterile)
This makes colonization, vegetation on the valve causing embolism that may reach the lung causing pulmonary embolism or, brain causing stroke or even the heart causing congestive heart failure.
2- damage to the inner most layer of the heart or in the epithelial lining, This damage can be acquired during surgical procedures (prosthetic valve) or on a native valve with inflammation especially with rheumatic fever

- Infective endocarditis (IE) is an inflammation of the endocardium.. inner of the heart muscle & the epithelial lining of heart valves.

- Infective endocarditis is a rare, life-threatening disease that has long-lasting effects even among patients who survive and are cured

Healthcare associated contact

- Infective endocarditis is caused by damage to the endocardium of the heart followed by microbial, usually bacterial, colonization.

- Once established, IE can involve almost any organ system in the body and can be fatal if left untreated.

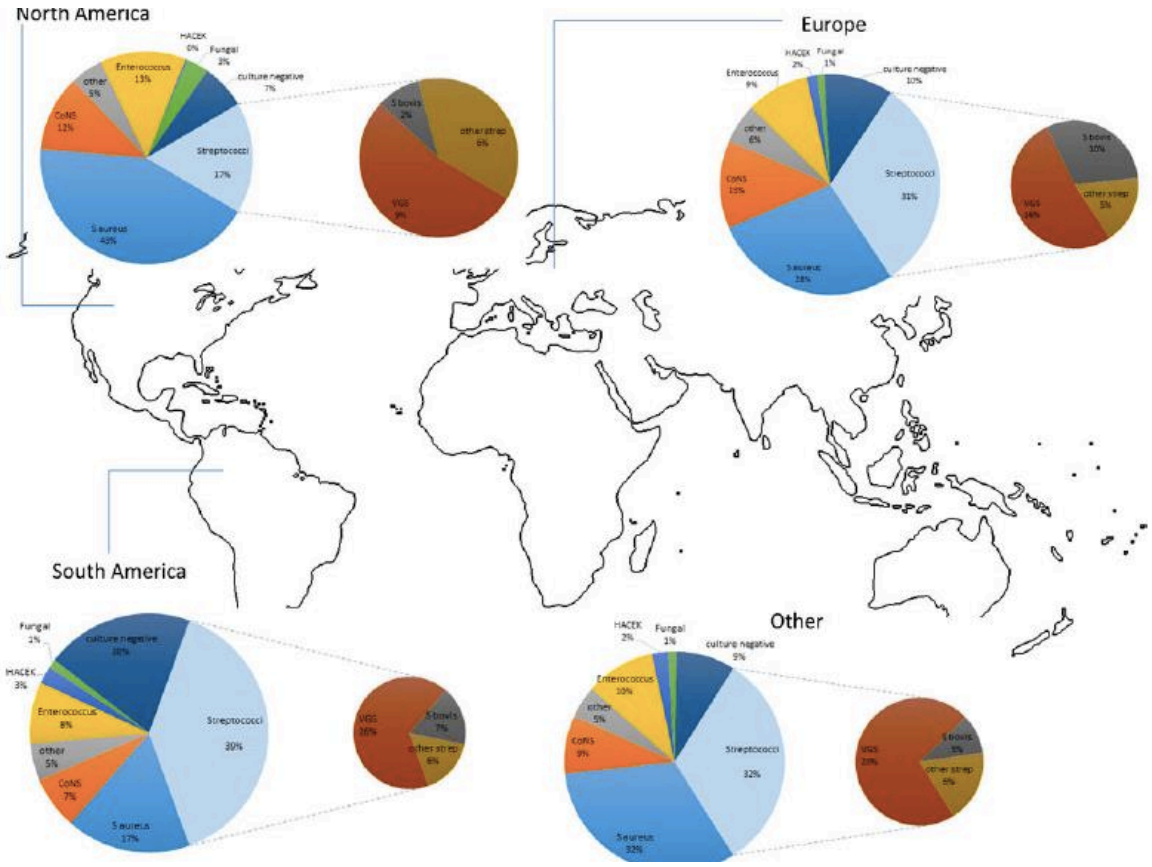
One year Mortality rate reaches 30% which is worse than the worst cancer fatality

Epidemiology

IE epidemiology shifted in 2 things during the years:
1- rheumatic fever was the most common predisposing factor worldwide (in developed, and developing countries), but now degenerative valve disease is more common in developed countries.
2- the mean age was <30 years, but now >50 years (people seen in ICU)

- The crude incidence ranged from 1 to 10 cases per 100,000 person-years .
- Rheumatic heart disease remains the key risk factor for infective endocarditis in low-income countries and underlies up to two-thirds of cases.
- In high income countries, However, degenerative valve disease, diabetes, cancer, intravenous drug use, and congenital heart disease have replaced rheumatic heart disease as the major risk factors for infective endocarditis.
- The mean age of patients with IE has increased significantly (past <30 Now >50 years old).
- Untreated, mortality from IE is uniform. Even with best available therapy, contemporary mortality rates from IE are approximately 25%

The causative agents



Causative agent varies geographically, but about 90% of the cases are associated with G+ve cocci (80% strept & staph, 10% enterococci).5% caused by G-ve (HACEK), 5-10% fungal causes.
In developed countries; staph. Aureus is the most common cause
In our region: viridian group strept.

Predisposing Factors for Endocarditis

High risk group

- Historically, **Rheumatic Disease ..caused by** Group A Streptococci was considered a frequent pre-disposing factor for endocarditis.
- Congenital heart disorders, Prosthetic heart valves

  Pacemaker, following pneumonia and meningitis
- Periodontal procedures/disease, Damaged gingival tissue due to plaque accumulation on teeth →

So they give prophylactic antibiotics, because strept. viridian is considered an oral flora causing dental caries

- Dental extractions, Dental implants
- Hemodialysis Tonsillectomy , Esophageal dilation
- Skin infections.. Intravenous drug users
- Cystoscopy. Colonoscopy, Urethral dilation,

All these procedures introduce skin comennsal bacteria to the systemic circulation

- All these procedures.. associated with mucosal commensal flora.. May cause endogenous infections. Thus Antibiotic Prophylaxis is recommended.

Microbiology Overview

Most common native valve affected by IE is the mitral valve. but it might be different as in IV drug users, the most common is the right sided valve.

- The microbiology of the disease has also changed, and staphylococci, most often associated with health-care contact and invasive procedures, have overtaken streptococci as the most common cause of the disease.

- streptococci and staphylococci have collectively accounted for approximately 80% of IE cases, the proportion of these two organisms varies by region.

Microbiology outline

- The Gram-positive cocci of the staphylococcus, streptococcus, and enterococcus species account for 80–90% of infective endocarditis.
- S aureus is the most frequently isolated microorganism associated with infective endocarditis in high-income countries and is reported in up to 30% of cases.
- Streptococcal infective endocarditis caused by the oral viridans group remains most common in low-income countries.
- Enterococci account for 10% of cases overall.
- The HACEK bacteria (Haemophilus, Aggregatibacter, Cardiobacterium, Eikenella corrodens, kingella), which cause about 3% of cases.
- Fungal endocarditis, usually Candida or Aspergillus, is rare but often fatal, arising in patients who are immunosuppressed or after cardiac surgery, mostly on prosthetic valves.

So we give these patients: vancomycin + gentamicin

If the patient is not responding to the antibiotic you give, you must think about non-bacterial causes, espiecally in ICU patients (immunocompromised patients) who are given broad spectrum antibiotics because they are more susceptible to fungal IE.

	Catalase	Coagulase	Hemolysis†	Distinguishing Features	Disease Presentations
			***Staphylococcus* Species**		
S. aureus	+	+	β	Ferments mannitol Salt tolerant	Infective endocarditis (acute) Abscesses Toxic shock syndrome Gastroenteritis Suppurative lesions, pyoderma, impetigo Osteomyelitis
S. epidermidis	+	–	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
Enterococcus sp. (Group D)	–	–	α, β, or γ	PYR† Esculin agar	Infective endocarditis Urinary and biliary infections
S. bovis	–	–	γ	Bile esculin†	Endocarditis, especially in patients with colon cancer

Staph.

Strep.

↳ resistant to vancomycin

We can differentiate between strep. Species by the hemolysis pattern

Microbial Causes-1

- Gram-positive cocci.. facultative anaerobes, diplococci chains/clusters or pairs cocci.. Catalase +ve /Staphylococci group.. catalase-ve/ Streptococci & Enterococci groups.

- Streptococci subdivided into groups according their hemolytic reaction on blood agar in vitro & by serotypes according to surface cell wall specific carbohydrate antigens.

Microbial Causes-1A

❖**Viridans streptococci Group (VGS)**

- Normal oral-intestinal flora.. Common causes of dental caries.. Oral abscesses Gingivitis Deposit dextran, adhesins, Fibronectin-binding protein.

To have the suitable condition to make colonization on the endocardium or the heart valves.

- *St. mutans, St. mitis* accounted for many cases, and tend to be less susceptible to penicillins.

❖**Group A Streptococci** (*S. pyogenes*).. Repeat Sore throat infection.. Less skin infection.. Develop Pos-streptococcal Diseases ..Rheumatic heart disease.. Children. Observed later in young adults

The immune system makes anti-bodies against the M protein (that is considered a virulence factor), this complex cross react the myosin in the heart causing damage to the native valve.

Microbial Causes-1B

Acute IE:
S. Aureus, group A beta haemolytic strep., strep. Pneumonia
Subacute (indolent) IE:
Any other causative agent
Acute and subacute differs in: 1-level of toxicity 2-their onset 3-progression of the disease

❖ ***S. aureus*** is a common cause of acute endocarditis, may result in a severe sepsis syndrome with a fatal outcome.

- Most endocarditis cases occurred within 2-month-1 year following vascular catheters & surgical wounds, skin injury/ invasive dental procedures and others.

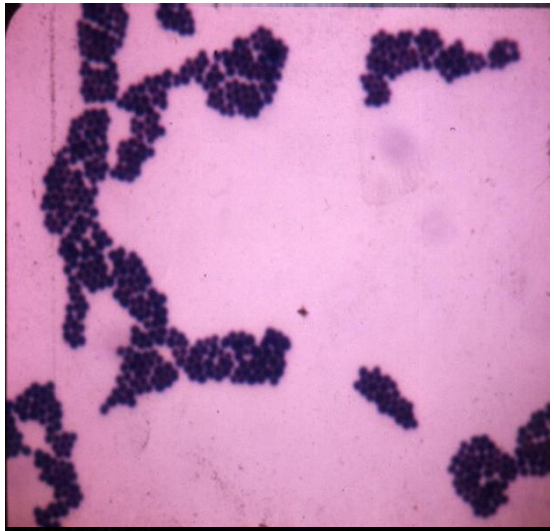
❖ *Enterococcus species* (*E. fecalis, E. faecium*) are responsible for up to 5-10% of cases; some strains may be resistant to penicillin,vancomycin.

10% of 90%

Streptococci-Staphyloccoci

Strep. are usually forming chains

Blood agar
To know the the pattern of hemolysis
This image Shows partial hemolysis (alpha) so it is strep. Viridians



Staph. are usually diplococci or grape like

Mannitol salt agar (Differential and selective for staph. Aureus).

Deep yellow Color

Microbial Causes-2

Some types have association with the environment or the occupation of the patient
In our area brucella was known to cause IE, burtonella causes IE in people taking care of cats

- A group of fastidious gram-negative bacteria can cause rarely endocarditis : Gram-ve *bacteria: Brucella, Salmonella, Haemophilus, Cardiobacterium, Eikenella, Gram+ve Actinobacillus* part of Normal oral flora .

- Clinically, these bacteria spp. causing subacute or chronic course, and often present with embolic lesions from large biofilm vegetations in heart valves .

- Most cases of fungal endocarditis occur in patients who are receiving prolonged antibiotics or intravenous nutrition through central vascular catheters.. Immuno-compromised patients.

Yeast & Filamentous Fungi

- The most common species is *Candida albicans*, followed by other less common *Candida spp.* (C. glabrata, C. krusei, C. tropicals).
- Candida part of human normal flora.. Oral-intestinal-Urinary tract (Vagina).. Infection often followed often using catheters or respiratory intubation.
- Endocarditis due to *Histoplasma capsulatum* / *Aspergillus* species is very rare.. Immuno-suppressed patients.

Candida albicans Pseudohyphae

On dextrose agar candida albican appear as yellow creamy feathery colonies.
In corn meal agar they form chlamydospore.

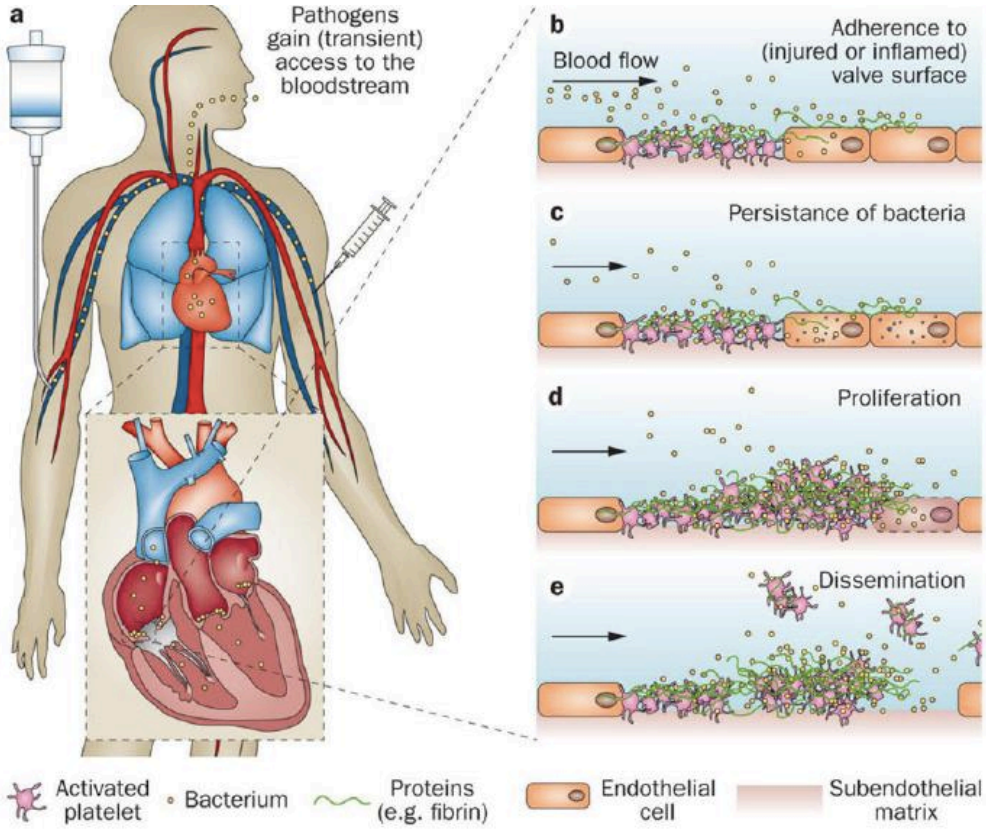
(germ tube test to differentiate candida albican)
We can put these colonies in a tube with human serum, then we incubate them in 37 degree for half an hour, so each pseudohyphae form a germ tube.

Pathophysiology

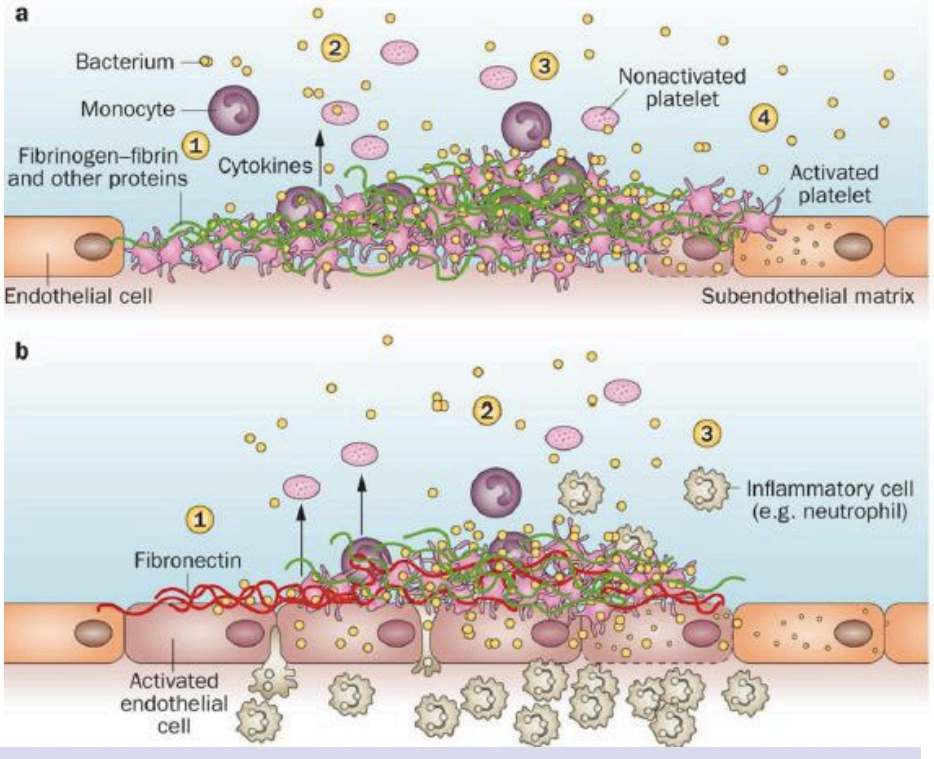
- The healthy cardiac endothelium is resistant to frequent bacteremia caused by daily activities such as chewing and tooth brushing.

- Bloodstream infection is a prerequisite for development.

- The development of IE requires the simultaneous occurrence of several independent factors: alteration of the cardiac valve surface to produce a suitable site for bacterial attachment and colonization; bacteraemia with an organism capable of attaching to and colonizing valve tissue; and creation of the infected mass or ‘vegetation’ by ‘burying’ of the proliferating organism within a protective matrix of serum molecules (for example, fibrin) and platelet A **Biofilm ..** Accumulation Bacteria, platelets, fibrin and few leucocytes.



Pathogen or normal flora found in different site than their original place, enter the systemic circulation reaching the inner most layer of the heart, colonize on a previously injured endothelium, then persist and proliferate and get buried by platelet, fibrinoclot, neutrophils causing dissemination process.

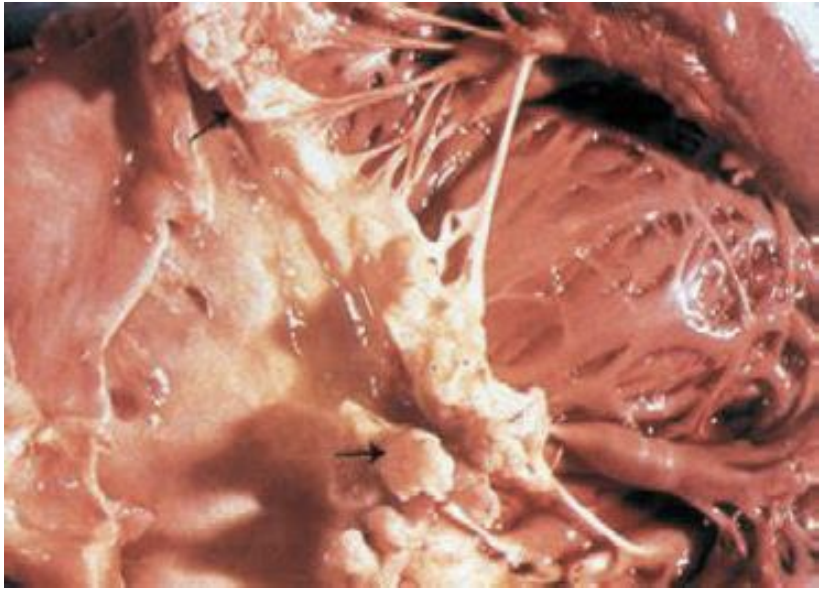


This picture shows discontinuous endothelial layer (like in surgical interventions ,prosthetic valve)

This shows continuous (native) endothelium but inflamed (like in rheumatic fever)

Both have appropriate conditions for systemic bacteria to make colonization...

This pic shows vegetation in the heart that might dislodge



Clinical features

- The clinical presentation of infective endocarditis is particularly diverse and non-specific.

- Acute endocarditis is a hectically febrile illness that rapidly damages cardiac structures, seeds extracardiac sites, and, if untreated, progresses to death within weeks. Especially in staph. Aureus

- Subacute endocarditis follows an indolent course; 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 And lower toxicity

Cardiac Manifestations

If inpatient developed fever of unknown origin (FUO) + newly heart murmur –- he is considered IE until proving otherwise

- Although heart murmurs are usually indicative of the predisposing cardiac pathology rather than of endocarditis, valvular damage and ruptured chordae may result in new regurgitant murmurs.

- Congestive heart failure (CHF) develops in 30–40% of patients as a consequence of valvular dysfunction.

Modified DUKE criteria, have major and minor criteria
Major criteria:
1- +ve blood culture for any of the microbes causing IE 2- transthoracic echocardiography (can show if there is any structural damage in the heart)
Minor criteria: (non-specific)
1- fever. 2- vascular phenomena (Janeway lesions, subungual hemorrhage). 3- immunological phenomena (osler's nodes -usually on tip of the finger in hand-)

👉According this criteria the diagnosis might be definite, possible, reject

Noncardiac Manifestations

- The classic nonsuppurative peripheral manifestations of subacute endocarditis (e.g., Janeway lesions are related to prolonged infection).

- In contrast, septic embolization mimicking some of these lesions (subungual hemorrhage, Osler's nodes) is common in patients with acute S. aureus endocarditis.

DIAGNOSIS

- The diagnosis of IE typically requires a combination of clinical, microbiological and echocardiography results .

- Blood culture is the most important initial laboratory test in the workup of IE. Bacteremia is usually continuous and the majority of patients with IE have positive blood cultures.

- Echocardiography is the second cornerstone of diagnostic efforts and should be performed in all patients in whom IE is suspected.

- A highly sensitive and specific diagnostic schema—known as the modified Duke criteria—is based on clinical, laboratory, and echocardiographic findings commonly encountered in patients with endocarditis

Some causative agents shows negative blood culture test, so we use serological tests, stains… to confirm IE case.

- Non-Blood-Culture Tests : Serologic tests culture, microscopic examination with special stains, (i.e., the periodic acid–Schiff stain for T. whipplei), direct fluorescence antibody techniques and by the use of polymerase chain reaction to recover unique microbial DNA or DNA encoding the 16S or 28S ribosomal unit.

- Echocardiography

Management

❖ANTIMICROBIAL THERAPY

- Vancomycin plus Gentamicin initiated immediately after blood samples are taken for cultures.

- Extended courses of parenteral therapy with bactericidal (or fungicidal) agents are typically required.

❖Surgical Treatment.

PREVENTION

The recommendation now is:
If the patient is from a high risk group and you need to make any of the procedures mentioned in slide no.6, give him a prophylactic antibiotic to stay in the safe side 👨‍⚕️

- To prevent endocarditis (long a goal in clinical practice), past expert committees have supported systemic antibiotic administration prior to many bacteremia-inducing procedures.

The End