# Cardiovascular System

Sheet 1

Subject | Micro

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## Infective Endocarditis (IE):

It is an inflammation in the inner most layer of the heart muscle, the endocardium. The real danger is when the epithelial layer of the heart valves becomes inflamed, as we have a loss of function. Although this disease is rare, it has a very high mortality of more than **30%**, which is worse than most cancers. Usually the infective agent of IE is bacterial which colonizes the endocardium. This results in cardiac and extra-cardiac manifestations (extra-cardiac manifestations are immune mediated). This disease is difficult to diagnose, and there are some major and minor criteria that must be met for a diagnosis.

Regarding the pathogenesis of IE three things must occur; there must be an infective agent in the blood (**bacteremia**), there must be a congenital or acquired defect in the heart (mechanical or endothelial injury causing **turbulent blood flow**), and the infective agent must **colonize** the leaflet of a heart valve (vegetation or biofilm formation). If these three things occur, there will be IE.

There are 2 types of IE we will discuss; **acute** (days-weeks) and **sub-acute** (longer and has more complications later).

## Epidemiology:

1-10 / 100,000 cases per year (developed world). In the developing world **rheumatic heart disease is the major risk factor** (2/3 of cases linked), while in the developed world the major risk factors are:

- Degenerative heart disease
- Diabetes
- Cancer
- IV drug use
- Congenital heart disease

Rheumatic heart disease is an **immune mediated** disease that proceeds a Group-A Streptococcus infection of the pharynx. During the infection, antibodies against the virulence factor M-protein are produced which cross react with human tissues (heart valves, joints). This only happens in untreated infections, and is rare.

The mean age of people infected with IE **used to be below 30**, but has **now become greater than 50**. This is due to improvements in diagnosing and treating Group-A Streptococcus (GAS) infections (the first step in developing rheumatic heart disease). There has also been a change in the microbiology of IE, with GAS and Viridans Group Streptococci (VGS) being the main culprits, currently in the developed world Staph Aureus is the #1 cause, and in the developing world it is VGS (sanguinis, anginosus, and mitis). In either case, **90% of IE is caused by Gram+ Cocci.** Other groups that have the ability to cause IE are enterococci (also gram+ cocci), gram- bacteria, and fungi (candida albicans and asprigillus flavus). The last 2 are for immunocompromised patients or patients undergoing heart surgery).

The main controversy with this disease is the use of prophylactic antibiotic for any minor surgery (which only prevented 10% of IE cases), and that normal activities such as chewing gum and brushing your teeth introduce bacteria to the blood without causing infections (transient bacteremia). The predisposing factors that we haven't mentioned so far are large in number, but mainly include minor dental operations, skin infections, or anything that could introduce mucosal flora into the blood.

## Microbiology:

As we mentioned, **90% of IE cases are caused by gram+ cocci**, S. aureus for high income countries (30% overall), VGS in low income countries (no figure because of a lack of studies), while enterococci cause 10% overall, and HACEK group cause 3% (Haemophilus, Aggregatibacter, Cardiobacterium, Eikenellacorrodens, Kingella). Fungal IE is rare but fatal.

If a patient presents with a fever that does not have an obvious center and has heart murmurs, you must be afraid of IE. The first thing you do with this patient is take at least 3 blood samples at 3 different times (30 minutes, 1 hour, 8 hours). This is so we can culture the patient's blood sample and use it to figure out the microbial cause of his fever.

| | Catalase | Hemolysis |
|---|---|---|
| S. Aureus | + | β |
| VGS | - | α |
| Enterococci | - | α, β, γ |

The streptococcus groups are subdivided based on carbohydrates specific to each bacteria's cell wall.

### Streptococcus:

VGS:

Normal oral flora, common cause of dental carries (cavities) and oral abscess gingivitis. They deposit dextran, adhesins, and fibronectin binding protein.

St. mitis is less susceptible to pencillins.

GAS:

St. pyogenes is common cause of strep throat in children, cause of rheumatic heart disease.

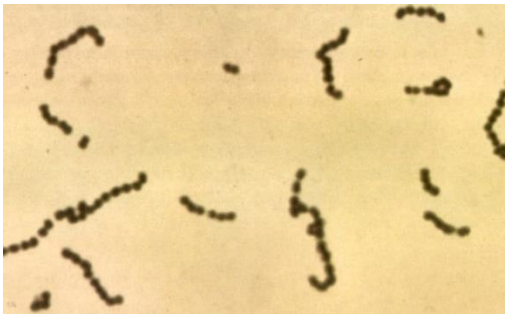
**Staphylococcus/Enterococcus:**

S. Aureus:

Common cause of **acute endocarditis** 2 months to 1-year after usage of vascular catheters, surgeries, skin injury, and invasive dental procedures among others.

E. Fecalis / Faecium:

Responsible for 5-10% of IE and can be resistant to penicillins and vancomycin.



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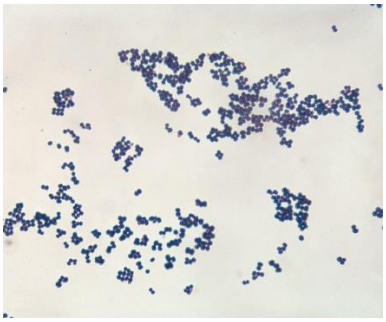
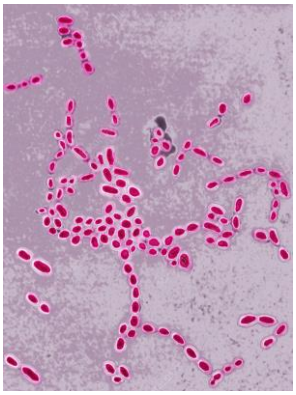


Staph



Enterococci

Also, we use mannitol agar in order to selectively culture S. aureus.

**Fungal:**

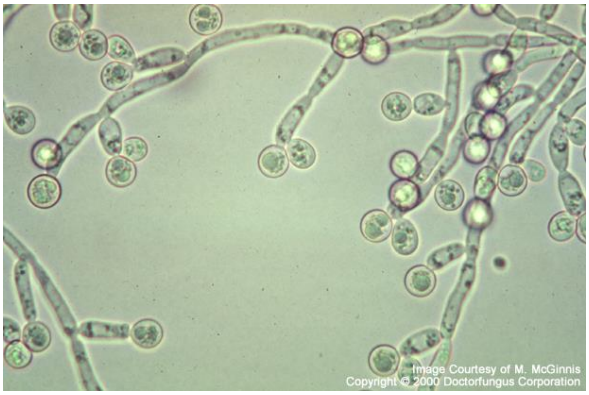
Most commonly occur in patients receiving long course antibiotics, are receiving intravenous nutrition through central vascular catheters, or are immunocompromised.

Candida Albicans:

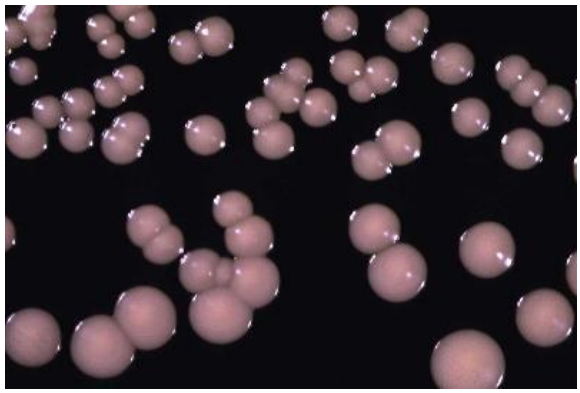
Part of normal oral, intestinal, and urinary flora. Infection after use of catheters or intubation.

Aspergillus/Histoplasma Capsulatum:

Rare, in immunocompromised patients.



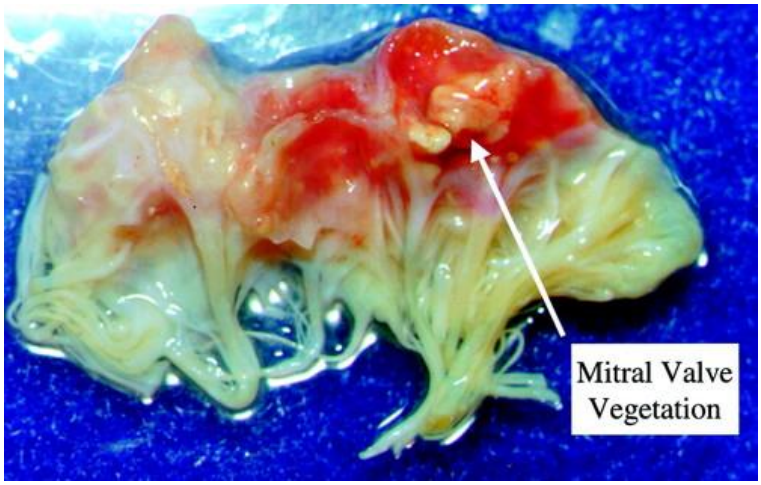

C. Albicans Pseudohyphae



C. Albicans Yeast

## Pathophysiology:

As we said, there must be three factors occurring simultaneously: **bacteremia, turbulent blood flow, and colonization of infective agent.** After this a biofilm must form, which is the accumulation of **bacteria, fibrin, platelets, and leukocytes** around the area of colonization; this is what we call a vegetation. Vegetations mostly form on heart valves and have the ability to break off and form an embolus, which is can cause many problems such as pulmonary embolism, stroke, myocardial infarction, and so on.



## Clinical Manifestations:

Remember, there are cardiac and extra-cardiac symptoms, and that there is acute and sub-acute endocarditis. Acute is always paired with S. aureus.

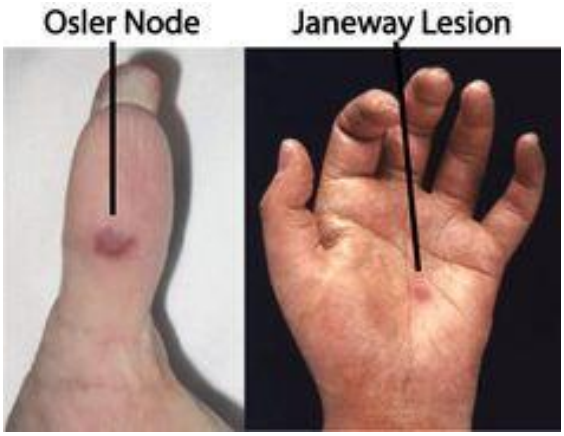
Usually the patient will present with non-specific symptoms, such as fever and chills. Acute patients have aggravated febrile illness that will rapidly damage the heart, as well as infect other tissues, and lead to death if left untreated.

Sub-acute patients have a slow course that damages the heart slowly, if at all, and will rarely metastasize. These patients have symptoms develop over time, unless compounded by a major event (ruptured mycotic aneurysm, or large embolus). These patients will develop the extra-cardiac, immune mediated manifestations we spoke of earlier.

In either case, **a patient with a fever of unknown origin and heart murmurs is IE until proven otherwise.**

Cardiac symptoms are murmurs, and sometimes regurgitation (results in heart failure in 30-40% of patients).

Extra-cardiac symptoms (immune mediated; sub-acute IE) are usually peripheral, such as Janeway lesions, Osler nodes, Roth spots, and subungual hematoma/hemorrhage. These are known as minor manifestations.




Janeway lesions are simply discolorations that the patient will not complain of, while Osler nodes are raised lesions that are painful/tender.

Subungual hematoma

## Diagnosis:

Diagnosis is difficult, and we need multiple pieces of evidence to rule everything else out. We need **microbiological evidence** (cultures), or **evidence of structural changes in the heart** (echocardiography). These 2 are the major criterion of diagnosis. **You need at least 1 major criterion to diagnose.** Diagnosis can be achieved through 2 majors, or 1 major and 2 minors (eg. Positive blood cultures and Osler nodes with subungual hematoma). In the case of gram- infection, serology can help, but always think of the most common cause first. This system of diagnosis is called the **modified Duke criteria.**

## Treatment:

**Always start empirical treatment after obtaining blood samples.** If you suspect IE, never start antimicrobial before you take blood samples because this will give you a negative culture, and eliminate one of your methods of diagnosis. After you take blood samples immediately begin treatment with **gentamycin** and **vancomycin,** which will cover the most common causes of IE (gram+ cocci, but not fungi). Then you will wait for your lab results which will tell you the causative agent, what antimicrobials it is sensitive to and what it is resistant to. After receiving your lab results alter your treatment according to the sensitivity and resistance tests to achieve the best results. You may require a cardiac surgeon in order to repair the structural damage to the heart after you treat the infection.

### Prevention:

In the past, doctors have recommended giving prophylactic antimicrobials before any minor procedure, but that has fallen in controversy recently due to rising antimicrobial resistance, and its lack of a substantial benefit on patient outcome. Currently, prophylaxis is only recommended for high risk patients, or those undergoing major surgeries (see risk factors under epidemiology).