CVS

PATHOLOGY

Modified NO: 8

كتابة: ليث الخزاعلة و ميس قشّوع

تدقيق: Done

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Valvular Heart Disease

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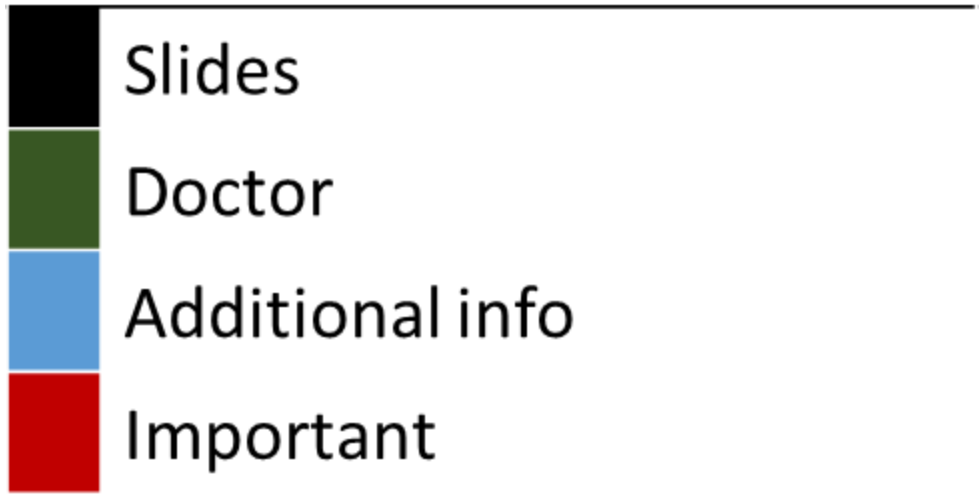
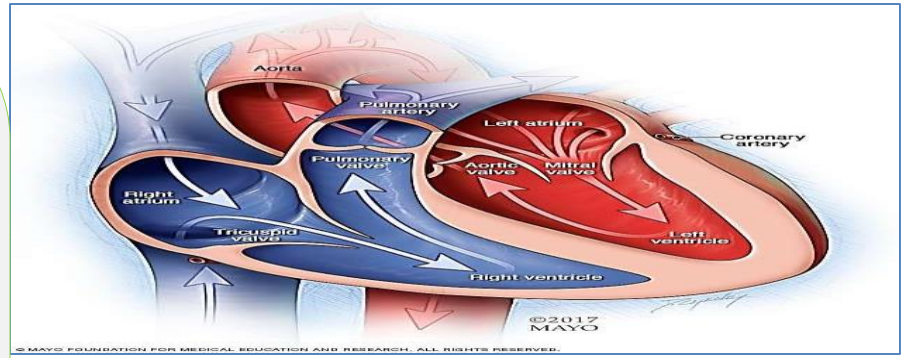


Normal Heart Valves

The heart contains four valves that play a crucial role in ensuring proper blood flow. These valves are:

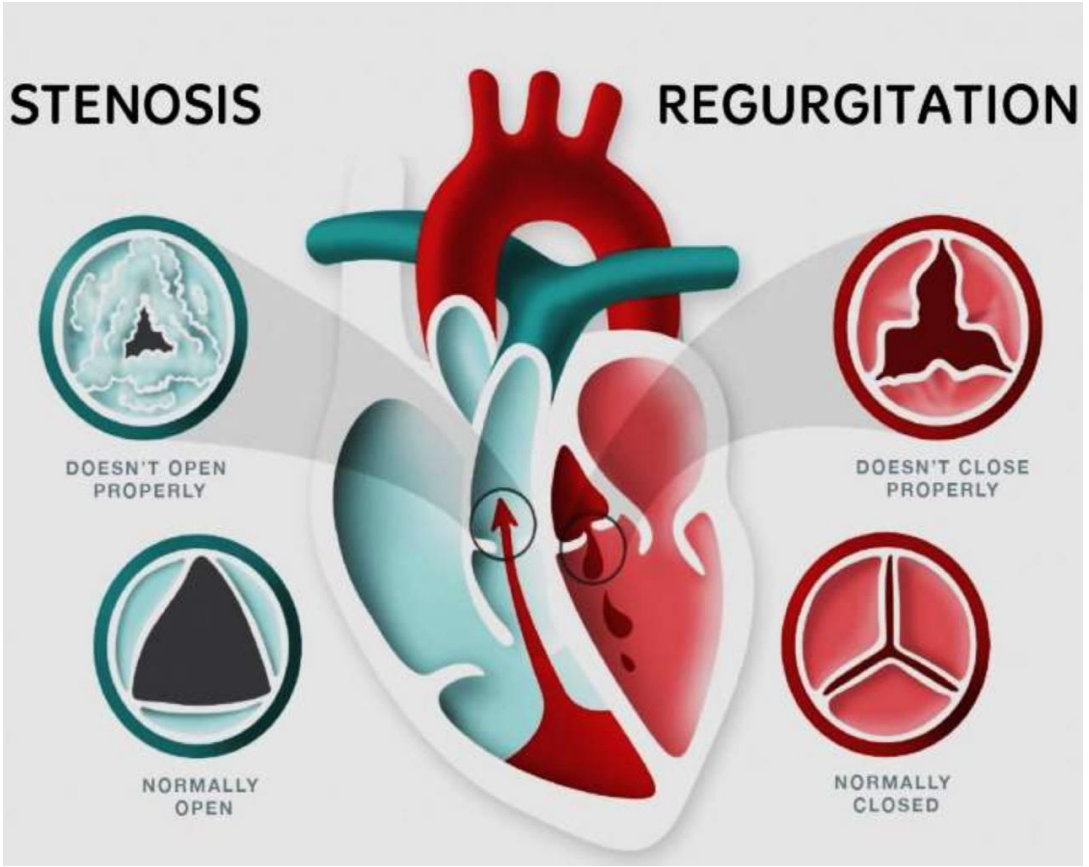
1. **Tricuspid Valve**: Located between the right atrium and right ventricle, it regulates blood flow from the atrium to the ventricle.
2. **Pulmonary Valve**: Positioned between the right ventricle and the pulmonary artery, it allows blood to flow from the heart to the lungs for oxygenation.
3. **Mitral Valve**: Found between the left atrium and left ventricle, it directs oxygenated blood from the atrium to the ventricle.
4. **Aortic Valve**: Located between the left ventricle and the aorta, it controls the flow of oxygen-rich blood from the heart to the rest of the body



VALVULAR HEART DISEASE

Due to a chronic process (e.g calcification or scarring)

Scarring can cause stenosis and regurgitation but most important in stenosis



Regurgitation is also known as leaky valve

Abnormality:
1 valve cusps
2 supporting structures (e.g. mitral annulus, tendinous cords, papillary muscles)

It can be either acute (e.g. chordal rupture) or chronic (e.g. scarring)

Functional abnormalities , when we think about any disease (acquired or congenital) we need to think about the functional consequences of that problem

Valvular heart disease typically leads to one of two main functional problems: **stenosis** or **regurgitation**.

1) Stenosis (doesn't open probably)

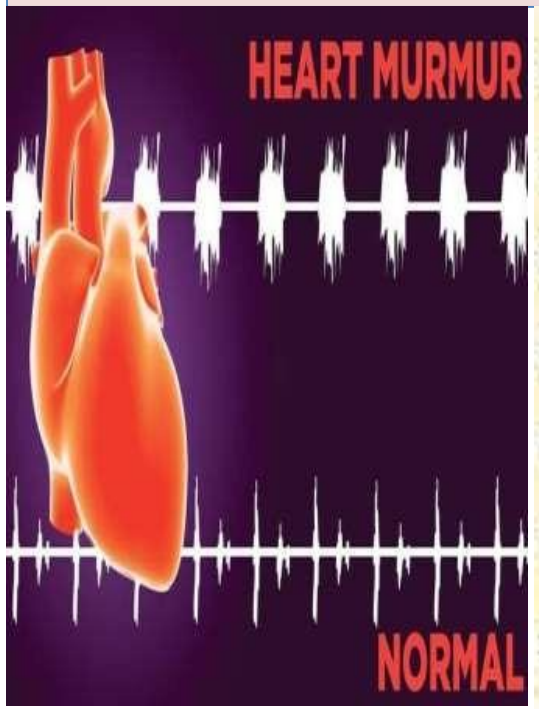
Stenosis refers to the narrowing of a heart valve, which restricts the flow of blood through it. A common example is **aortic stenosis**, where the aortic valve becomes narrowed. This obstruction increases the workload on the left ventricle, causing it to pump harder to maintain blood flow. Over time, this leads to **left ventricular hypertrophy** (thickening of the ventricular wall). The causes of stenosis are usually related to a **chronic process**, such as calcification ,scars ,chronic inflammation with consequence fibrosis of the valve or long-standing rheumatic heart disease.

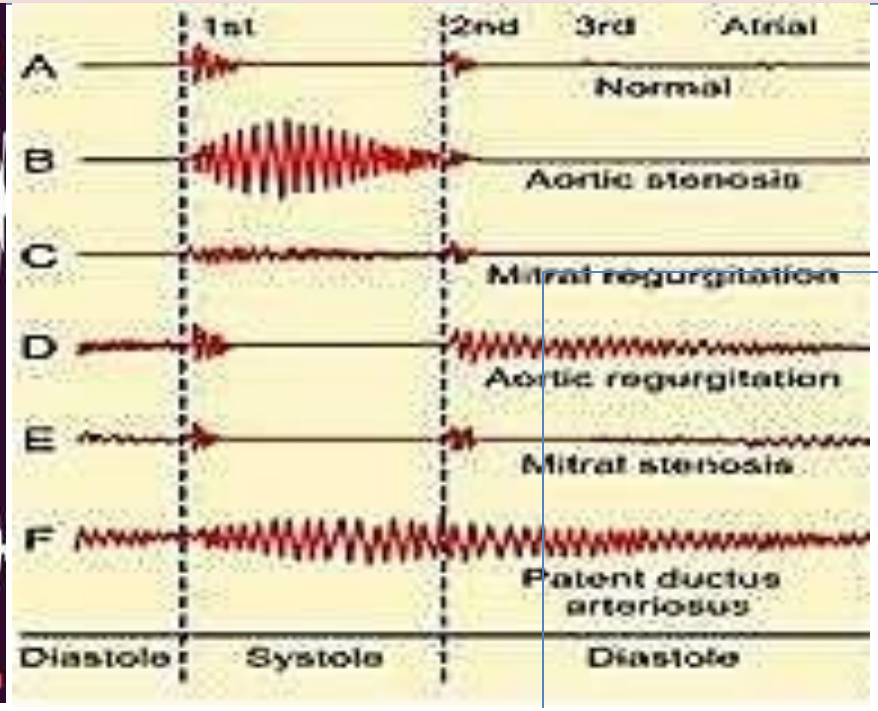
2) Regurgitation

Regurgitation, also called **incompetence** or **insufficiency**, occurs when a valve does not close properly, allowing blood to flow backward. A common example is **mitral valve regurgitation**, where blood flows back into the left atrium during ventricular contraction. This backward flow leads to **dilation of the left atrium** and can cause blood stasis ,increase risk of thrombus and embolus. Moreover , conductive abnormalities because part of the conduction system was affected leading to arrhythmias, such as **atrial fibrillation**. Also, this will decrease the stroke volume. The regurgitation can happen because of a problem in the valve cusps or a problem on the supporting structures of the valves , including the uvula or chordae tendineae and the Papillary muscles. Unlike stenosis, regurgitation can be associated with either an **acute** (e.g., due to a sudden valve rupture , and papillary muscle rupture) or **chronic** process.

Clinical Signs of Valve Disease

- Abnormal heart sounds (**murmurs)**
- Palpated heart sounds (**thrills**)
- Specific clinical signs according to involved valve





Clinical signs of valvular heart disease often include the presence of **murmurs**, which are abnormal heart sounds caused by turbulent blood flow through the valves. Murmurs are detected using a **stethoscope**.

In a normal heart, two distinct heart sounds can be heard:

- **S1**: Corresponds to the closure of the mitral and tricuspid valves at the beginning of systole.
- **S2**: Represents the closure of the aortic and pulmonary valves at the beginning of diastole.

- Might have sometimes physiological **S3**

Heart murmurs vary based on the affected valve, the type of abnormality (**stenosis** or **regurgitation**), and the timing within the cardiac cycle (**systolic** or **diastolic**) the onset considering S1 & S2 . Other characteristics, such as the **duration** and the specific nature of the abnormality, help in diagnosing the underlying condition

Thrills are palpable vibrations (loud) felt on the chest wall during a physical examination. They are caused by turbulent blood flow through the heart or great vessels, often associated with significant heart murmurs.

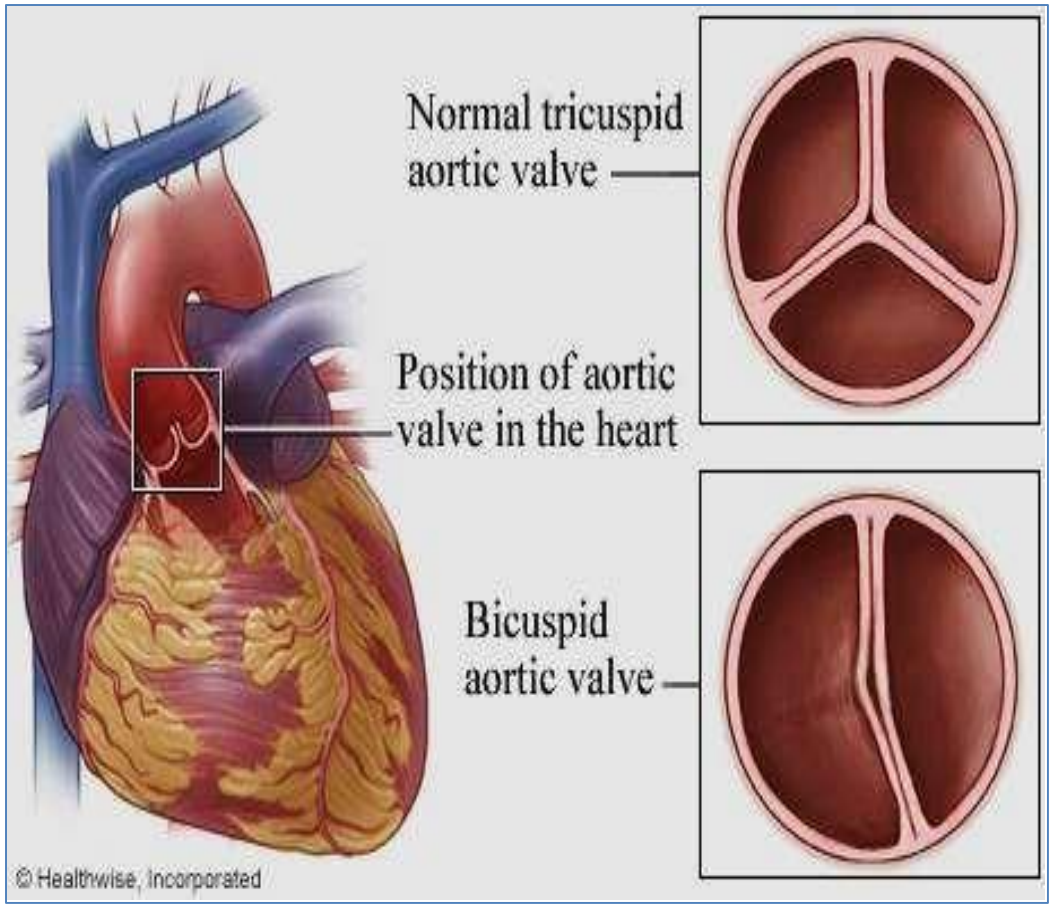
Thrills can be detected by placing the palm or fingertips gently on specific areas of the chest, corresponding to the location of the heart valves. Their presence usually indicates a severe valvular abnormality, such as advanced **stenosis** or **regurgitation**.

- Valvular abnormalities can be congenital or acquired

- The most common **congenital** valve lesion is **bicuspid aortic valve**
- Most important cause of **acquired** valve disease is **rheumatic fever**

Bicuspid aortic valve and rheumatic fever will be discussed this lecture

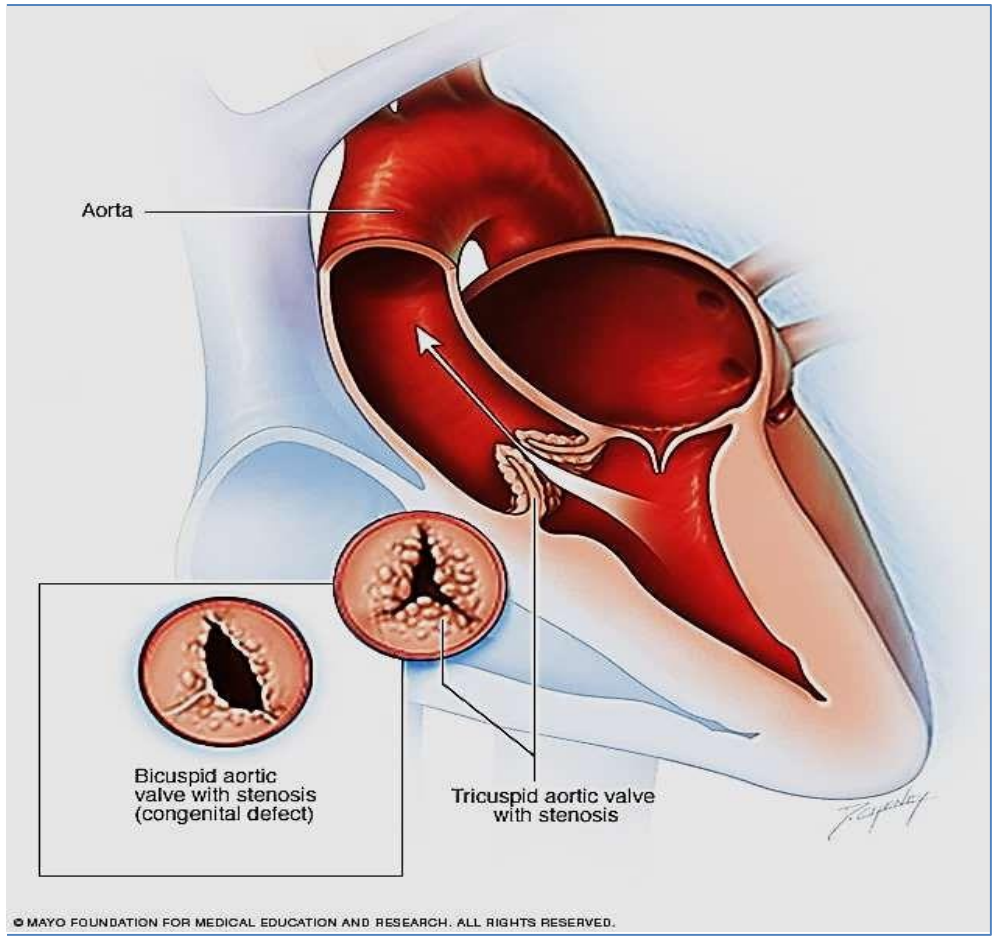
Bicuspid Aortic Valve

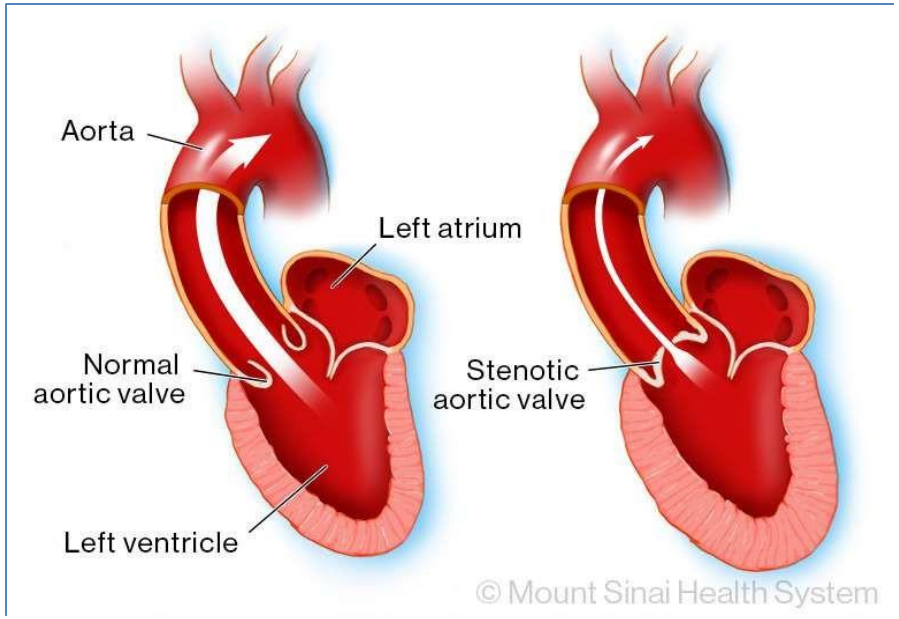


-only 2 functional cusps instead of 3
-1% - 2% of live births
-Isolated or associated with genetic mutations
-early life □Asymptomatic
-Later □ early (earlier than aged matched people)& progressive degenerative calcification of aortic valve

The absence of a cusp will increase the load on the valve which leads to degenerative calcification & associated fibrosis of aortic valve which eventually will lead to aortic valve Stenosis. Normally there are 3 cusps, in this situation only 2 are precent only.

Aortic Valve Stenosis





Consequences of this is heart inability to eject enough blood to the aorta which will lead to increased load on left ventricle, resulting in **left ventricular hypertrophy** and reduced cardiac output **decreased stroke volume**.
Tip: remember the place of the valve to know to possible Consequences

- **Acquired Valve Diseases**

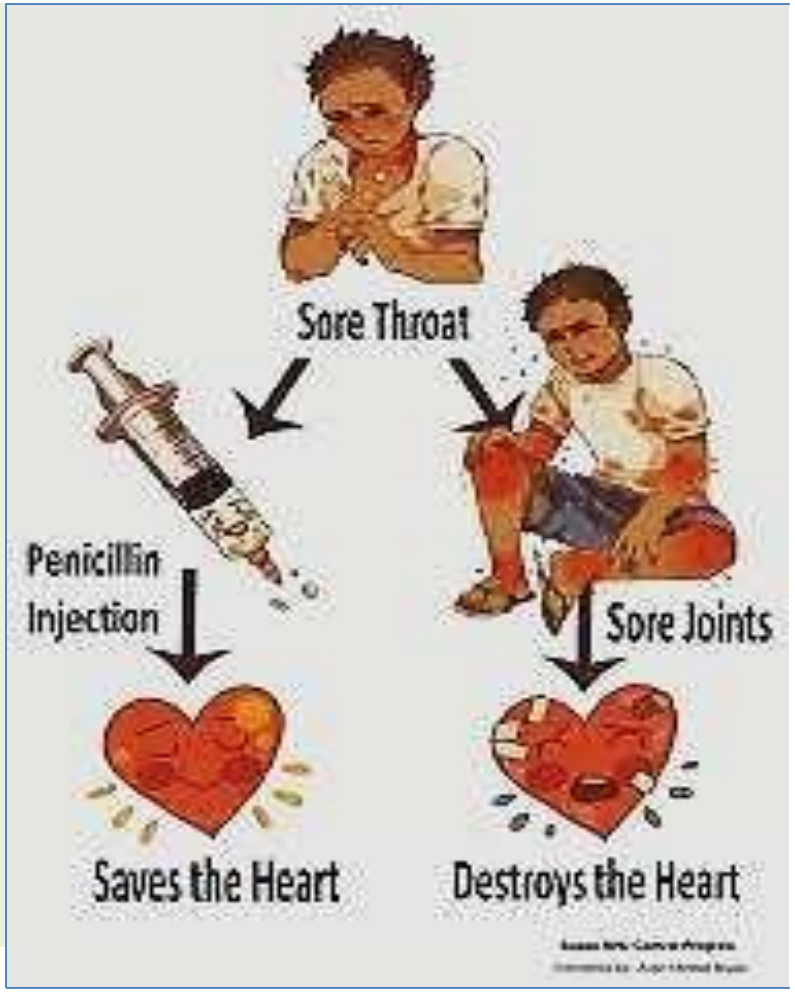
- Mitral valve most common target of acquired valve diseases

- Most common cause of **acquired** valvular diseases is **post- inflammatory scarring** due to rheumatic fever (2/3)

Mitral valve most common target of acquired
valve diseases but why? One of the reasons is Because the pressure in left ventricle .

Rheumatic fever
(Rheumatic Valve Disease)

- Immune- mediated inflammatory disease that follows infection by **group A streptococci**
- Incidence↓ in Western world (improved socioeconomics, rapid diagnosis, and Rx of strept. pharyngitis
- Still, important public health problem in developing countries



Rheumatic Fever is an **immune-mediated disease**, meaning the problem arises from an overreaction of the immune system. It typically occurs after an infection with **Group A Streptococci** bacteria. Most of these infections cause **pharyngitis** (throat infection), while a minority result in **skin infections**.

In some individuals, the immune system overreacts to the bacterial infection and produces **antibodies** against the bacterial antigens. However, these antibodies can also mistakenly target the body's own tissues due to **cross-reaction** with **host antigens**. These host antigens are found in four main organs: the **brain**, **heart**, **skin**, and **joints**.

The antibodies attack the host antigens in these organs, leading to inflammation. This immune response recruits additional inflammatory components, such as **T lymphocytes**, **activated macrophages**, and **plasma cells**. These cells accumulate to form **Aschoff bodies**, which are collections of inflammatory cells causing damage and symptoms in the affected organs.

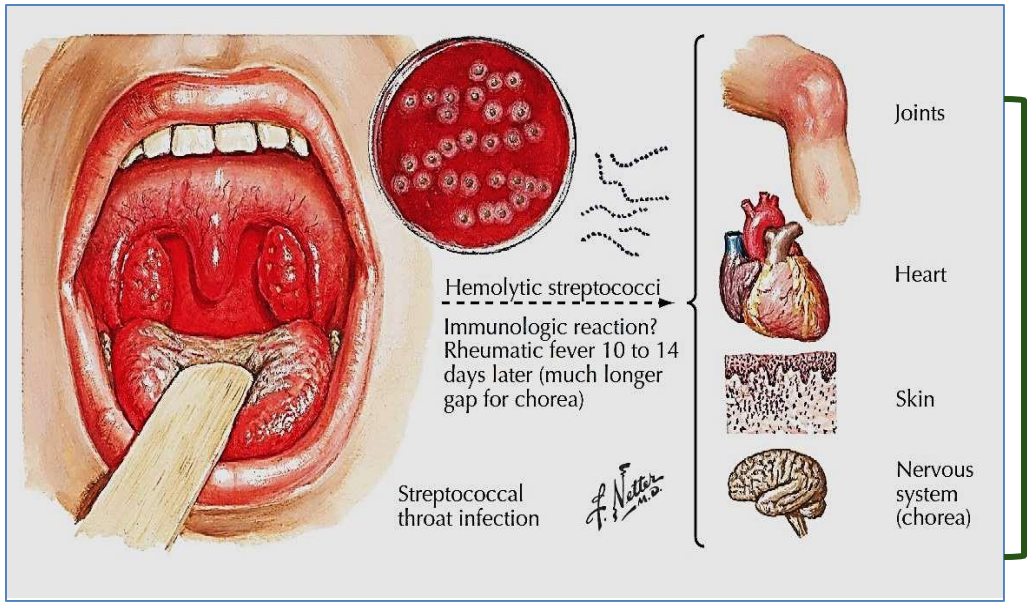
- In the **brain**, this can lead to abnormal involuntary movements known as **chorea**.
- In the **heart**, if the antibodies target the **valves**, they can cause **cardiac vegetations**.
- If the **myocardium** (heart muscle) is affected, it results in **myocarditis**.

Skin: Development of skin lesions such as **erythema marginatum** (a characteristic rash) or **subcutaneous nodules**.

- **Joints**: Swelling, pain, and tenderness in the joints, referred to as **arthritis**.

Rheumatic Fever

Why Antibiotics Reduce the Incidence of Rheumatic Fever:
Antibiotics, when used appropriately, eliminate the Group A Streptococci bacteria responsible for the initial infection. By clearing the bacteria, antibiotics prevent the immune system from mounting an exaggerated response and producing the cross-reactive antibodies. This significantly reduces the risk of developing Rheumatic Fever and its complications. Early treatment of streptococcal infections, particularly pharyngitis, is crucial in preventing this immune-mediated disease.



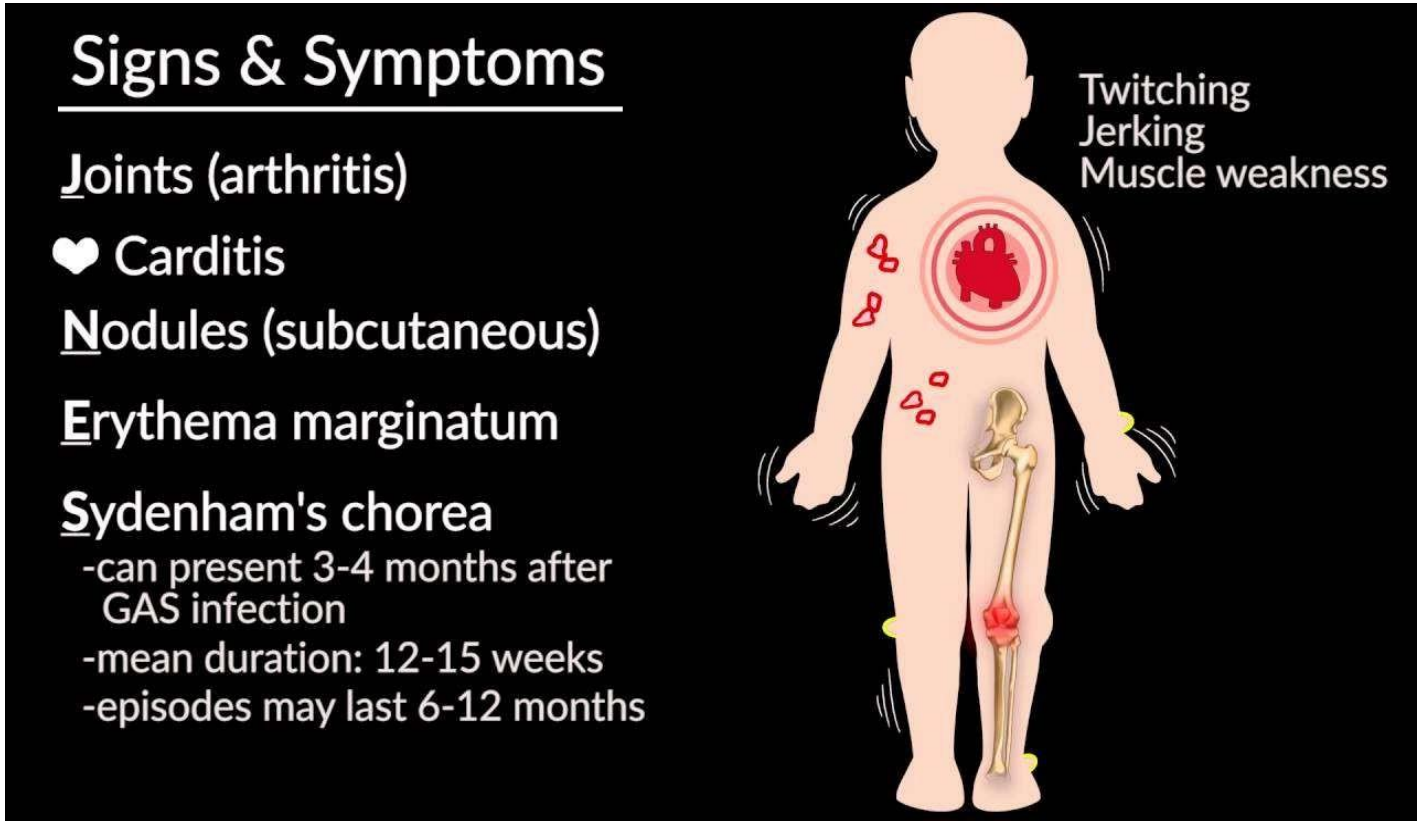
These are the target organs for Rheumatic Fever

PATHOGENESIS:
- **Hypersensitivity reaction due to antibodies against group A streptococcal antigens.**
- **These antibodies are cross-reactive with host antigens (heart; brain; joints; skin).**

Rheumatic Fever

- Manifestations seen a few weeks after pharyngitis or skin infection
- Major organs involved: heart; joints; skin; and brain
- 2 phases:
- Acute: fever; arthritis; CNS symptoms; carditis, skin rash and subcutaneous nodules.
- Chronic: it doesn't develop in all cases but when it happens it can cause significant cardiac valve disease
- ……
- **Acute phase:**
- 80% children
- fever; migratory polyarthritis; **carditis** and skin Manifestations.
- Symptoms of Carditis (arrhythmias; myocarditis; cardiac dilation; functional mitral insufficiency and CHF).
- How to prove that this a case of acute Rheumatic Fever ? We need an evidence of previous streptococcal infection so we use serum titers of antibody against streptococcal antigens (anti-streptolysin O; DNA-ase), you will find this serum titer is high.
- I can't depend on the **culture for streptococci because is usually (negative) at time of symptom onset**

Acute Rheumatic Fever- JONES criteria (These are the major clinical criteria for diagnosing acute rheumatic fever)



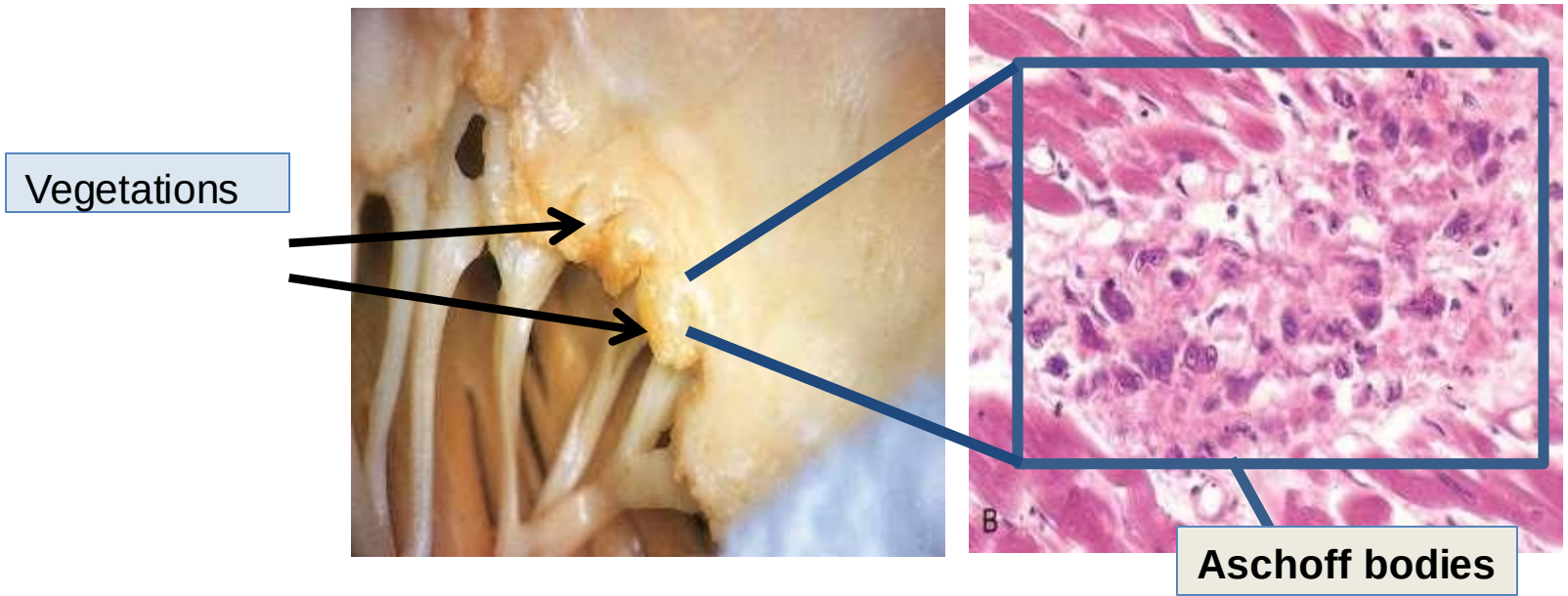
- Erythema marginatum: are the unique skin rash (skin rash has a red margin).
- Chorea: is involuntary or jerky movements caused by the presence of inflammatory collections in the brain.

Carditis Morphology- Acute Phase

- The affected heart tissue may show Valve vegetations and inside the inflammatory lesions we can find Aschoff bodies.
- **Aschoff bodies : (collections of inflammatory cells in an affected tissues)**

- Are inflammatory lesions in affected tissues (in the brain, joints and skin lesions) and in the heart I can see them inside a valve vegetation or in inflamed myocardium.

- pathognomonic (diagnostic) for RF
- collections of T lymphocytes+ plasma cells+ activated macrophages



Diagnosis of Acute Rheumatic Fever

- They might use the minor criteria if they don't find enough number of major criteria.

Major Criteria

J	Joint Involvement
O	**O** looks like a heart = myocarditis
N	Nodules, subcutaneous
E	Erythema marginatum
S	Sydenham chorea

Minor Criteria

C	CRP Increased
A	Arthralgia
F	Fever
E	Elevated ESR
P	Prolonged PR Interval
A	Anamnesis of Rheumatism
L	Leukocytosis

- YOU DON'T HAVE TO MEMORIZE MINOR CRITERIA.

Diagnosis

In serum
OR
Elevated anti-streptolysin O titers

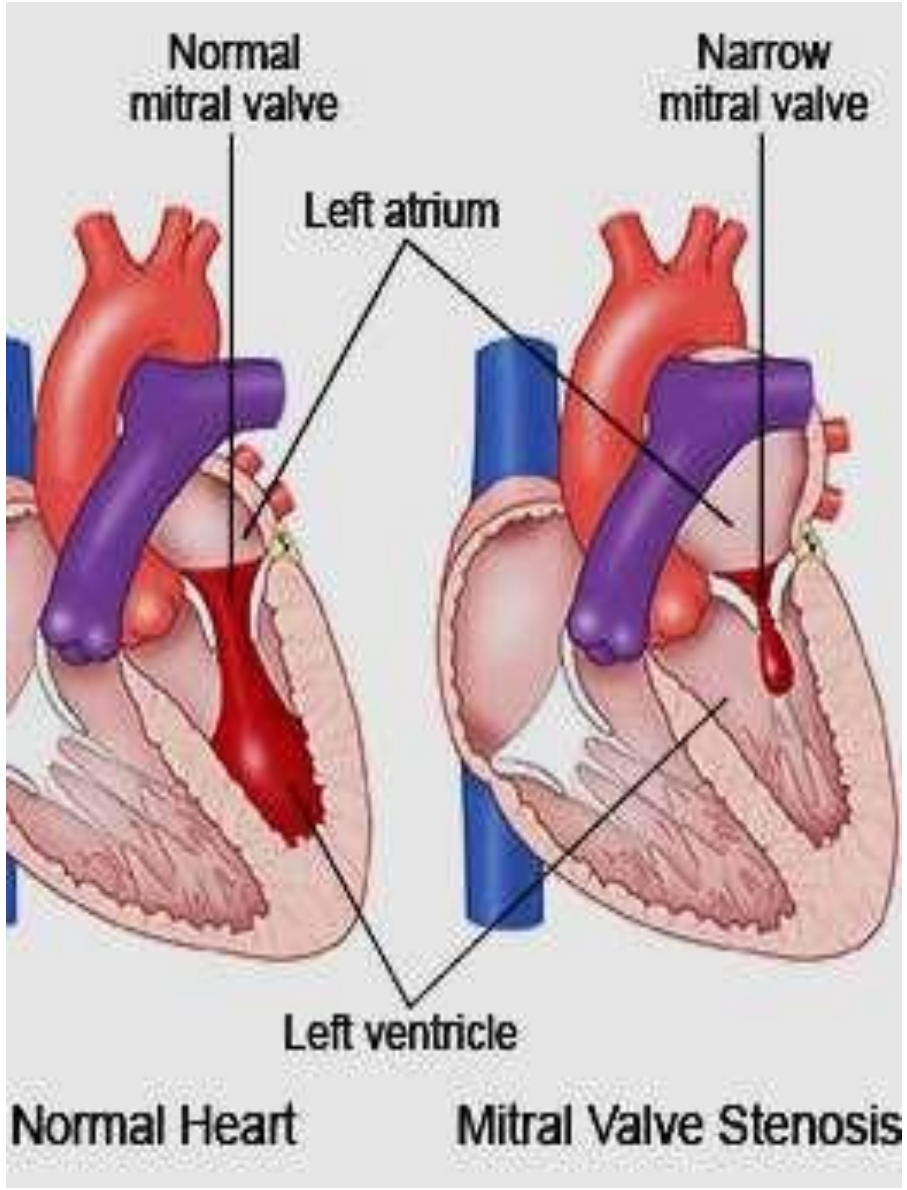
+

2 Major criteria

OR

1 Major criterion and 2 Minor criteria

Chronic Rheumatic Carditis- Clinical Picture



- As we said it doesn't develop in all cases, but when it does it can produce significant cardiac valve problem.

- **Onset: years/ decades** after initial acute episode
- During these years what will happen? Chronic inflammation scarring fibrosis and valve stenosis.
- This will manifest as murmurs – CHF (Congestive heart failure) - arrhythmias- mural thrombi.
- Prognosis: variable.
- Management: Surgical (repair or replacement of diseased valve).

- All valves can be affected but the mitral valve is the most common target.

Chronic Phase - Morphology

- Inflammation is followed by **scarring**
- Aschoff bodies **rarely** seen now

- **Valve stenosis** (most imp. functional consequence)

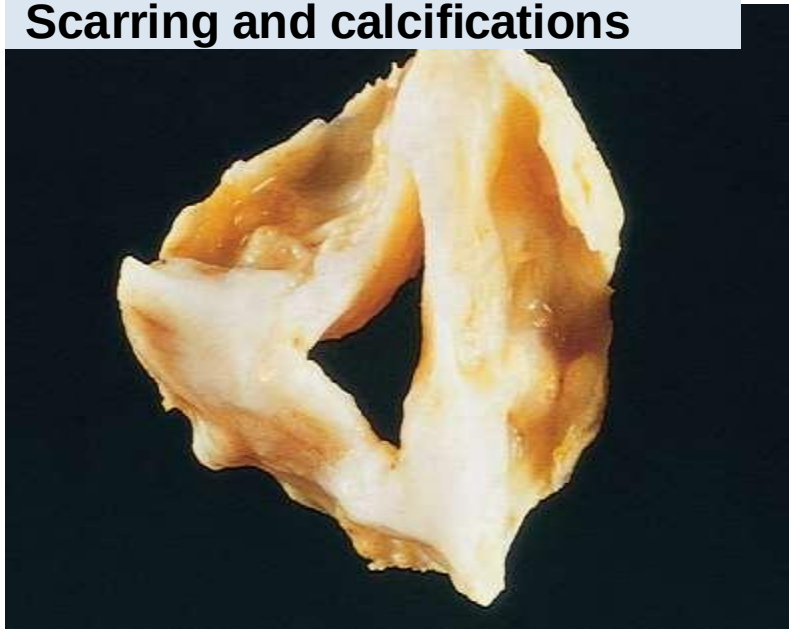
mitral valve (m/c) aortic disease

tricuspid valve

pulmonary valve (rare)

→

Scarring and calcifications



- If I asked you RF is an infection of the heart, am I correct?
No (rheumatic fever is an autoimmune inflammatory reaction, not a direct infection of the heart).

Infective Endocarditis

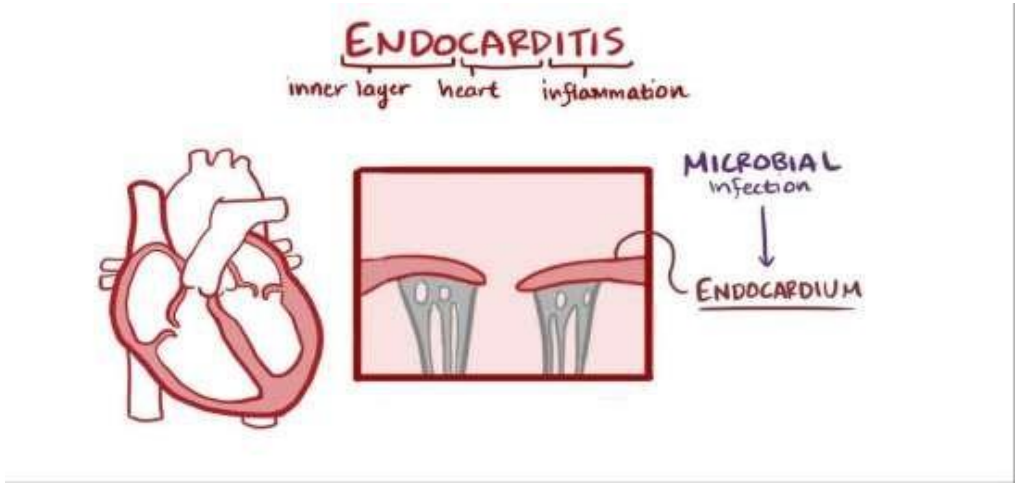
- It is an infection of the endocardium layer of the heart that leads to inflammation.
- Endocardium layer is the innermost layer of the heart which covers inside of the heart and the heart valves

Infective Endocarditis (IE)

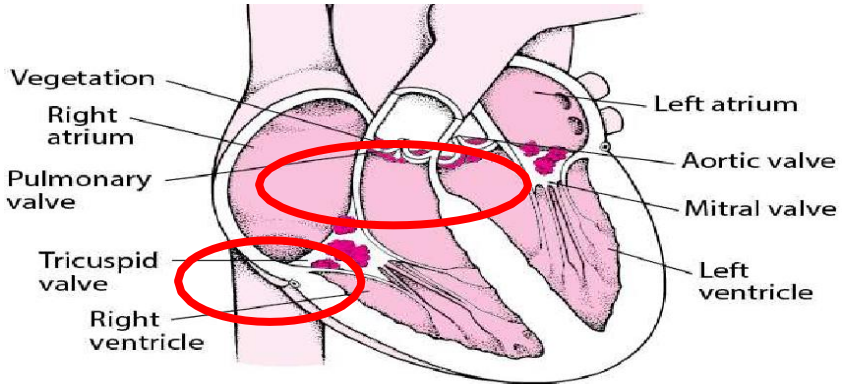
- Microbial (mostly bacterial) invasion of heart valves and endocardium.

- Formation of bulky, friable [fragile] vegetations (necrotic debris+ thrombus+ organisms).
- The fragile nature of this vegetation makes it highly susceptible to embolization. Since it contains microorganisms, any emboli that break off will transport these microorganisms to other parts of the body.

:) What kind of microorganisms that cause IE?
- Mainly Staphylococcus and Streptococcus and Others include fungi, rickettsiae; and chlamydia , HACEK & other gram-positive bacteria.

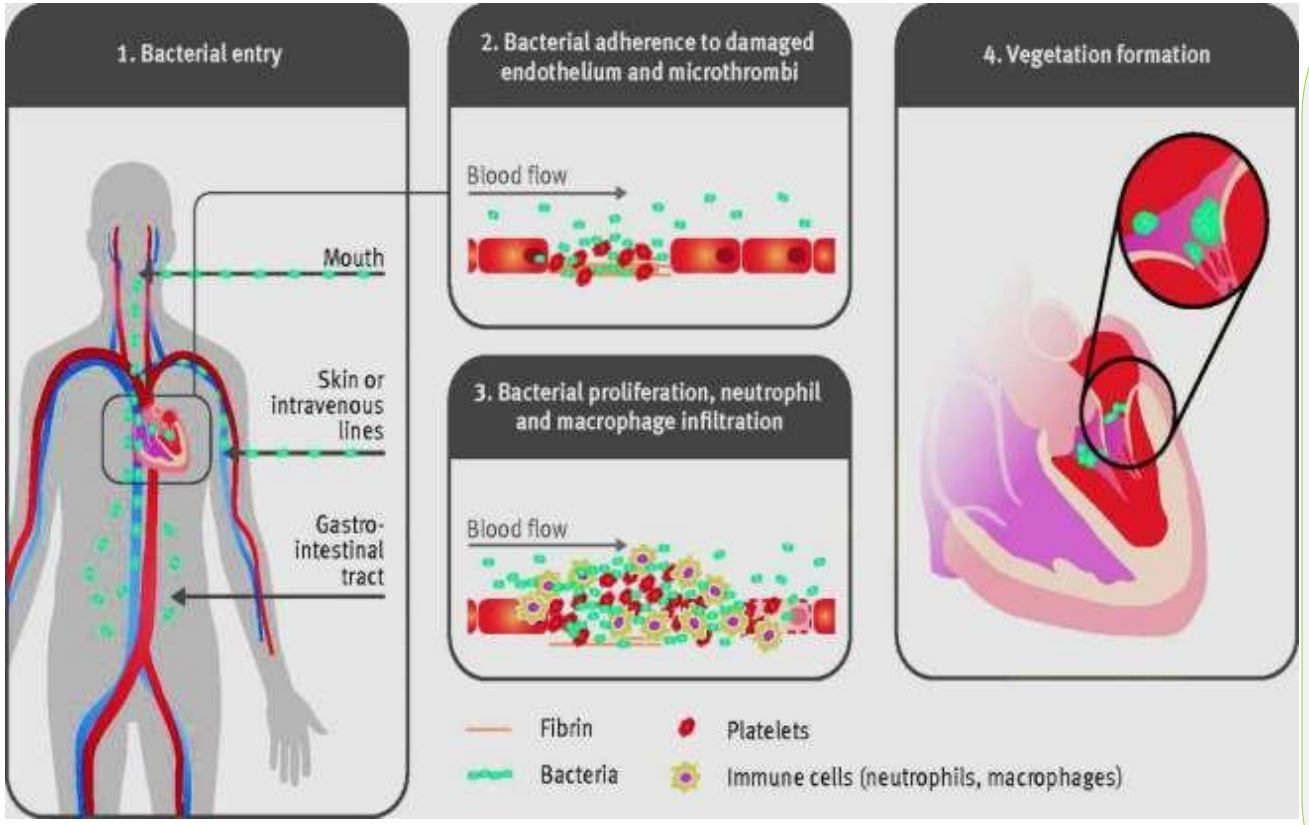


Infection of heart valves and endocardium



Infective Endocarditis

(Infection of heart valves and endocardium)

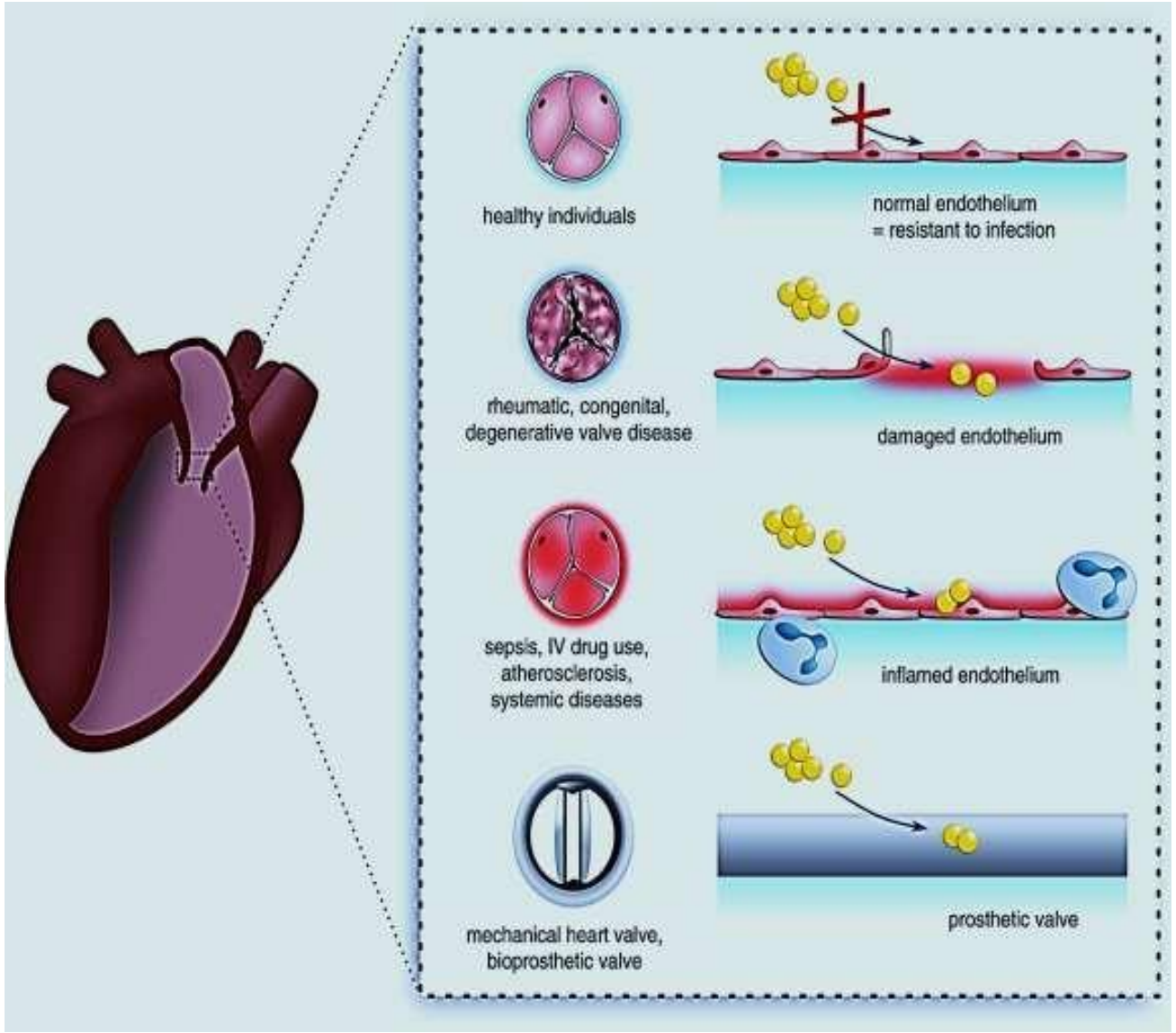


- **How does this thing happen?**
- Microorganisms can gain access to the bloodstream (bacteremia) and travel to the endocardium, where they cause injury to the endothelial cells. This injury triggers the activation of platelets, leading to their aggregation and the formation of a thrombus. This thrombus consists of fibrin, platelets, various types of cells, and microorganisms, forming what is known as a septic or infectious vegetation. These vegetations are typically large, haemorrhagic, and have the potential to cause embolization.

Infective Endocarditis- Risk Factors

- Congenital heart disease
- Acquired heart disease (including rheumatic fever)
- Indwelling vascular catheters (such as ICU residents)
- Intra-cardiac devices & prostheses
- Immunodeficiency
- I.V. drug use/ abuse
- Septicemia

- Dental procedures (in patients with risk factors)

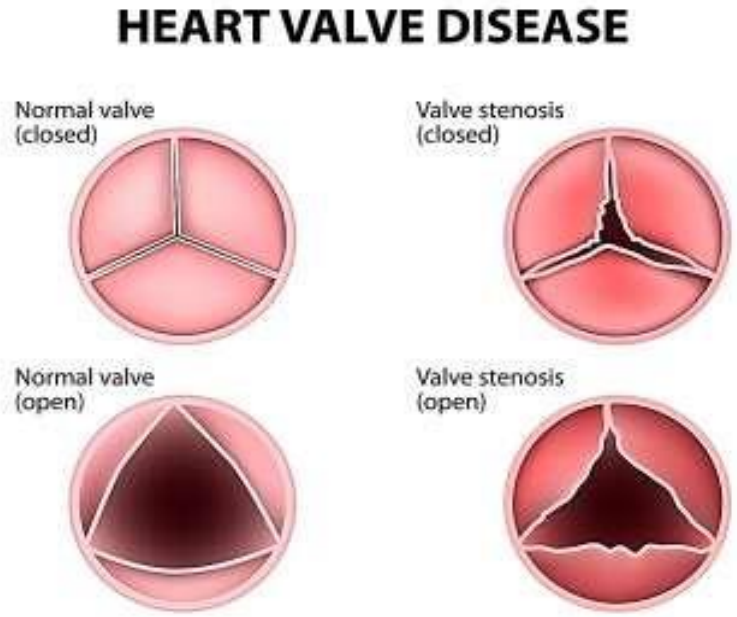


Infective Endocarditis (IE)

Classified into **acute** and **subacute** based on:

1. The virulence of microorganism (refers to its level of aggression, meaning how much is this microorganism capable of causing disease).

2. presence of underlying cardiac disease.



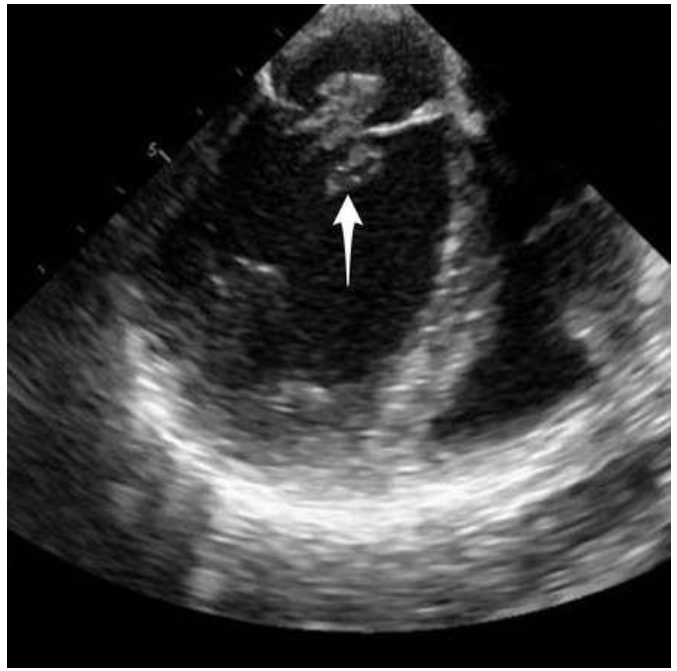
Feature	Acute endocarditis (aggressive)	Subacute endocarditis
Virulence	highly virulent organism (which can infect even normal heart valves)	low virulent organism
Most common organism	Staph. aureus	Streptococcus viridans
Underlying cardiac disease	previously normal valve	previously abnormal valve (scarred or deformed)
Clinical course	rapidly developing	Insidious disease
Outcome	High morbidity and mortality	most patients recover after appropriate antibiotic therapy with low morbidity and mortality , patients respond better to antibiotic therapy

Streptococcus viridans is a part of normal flora of the oral cavity and it can cause dental caries.

- So, the key factors that determine whether patient A has acute endocarditis (IE) and patient B has subacute IE are the: 1. Virulence of the microorganism and 2. The underlying valve condition (the presence of underlying valvular heart disease).

Infective Endocarditis- Clinical Features

- Patients present with Fever, chills, weakness, and murmurs Requires cardiac evaluation
- **Valve vegetations can cause emboli** in different target tissues
- **Diagnosis = positive blood cultures + echocardiographic (echo) findings**

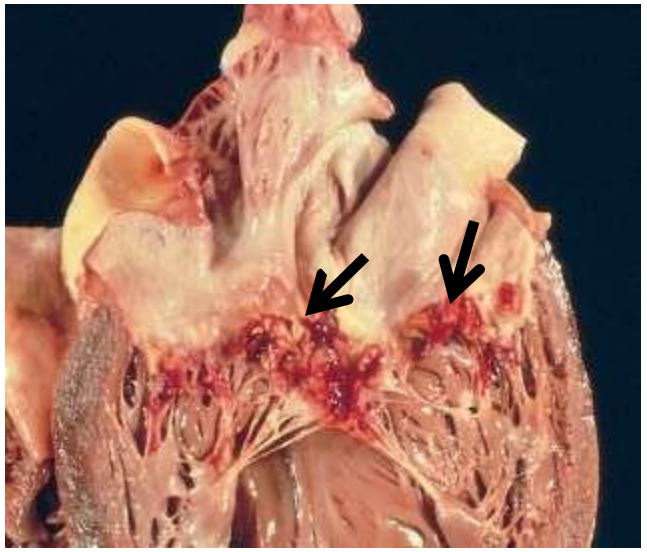


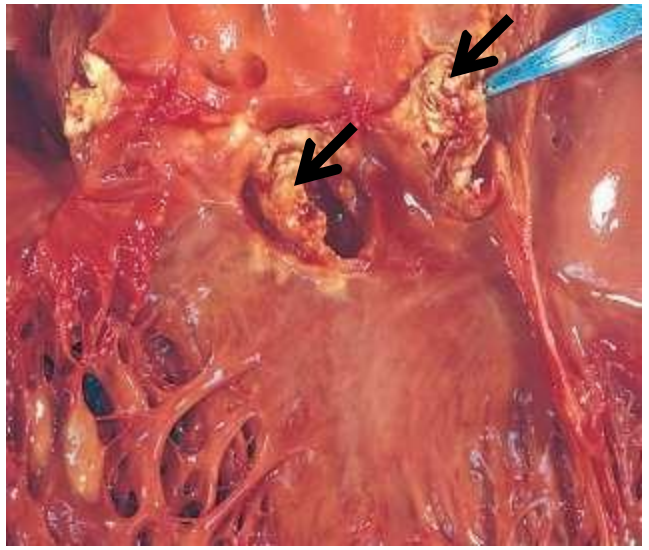
- * depends on certain criteria….

- The diagnosis of IE depends on clinical signs and symptoms, positive blood cultures, and echocardiographic (echo) findings, which together are known as the Duke criteria or modified Duke criteria.

Infective Endocarditis- Morphology

- **Friable, bulky, and destructive vegetations** on heart valves (can produce embolus)
- Most common: aortic and mitral valves
- Tricuspid valve common in I.V. drug abusers





Clinical Features

The vegetation is created & infected with microorganism , it is fragile thus can form emboli easily , these septic embolies can travel with the blood stream and goes everywhere and produce complications

- **<u>Complications of IE vegetations:</u>**

1 emboli

2 abscesses

3 septic infarcts (infection)

4 mycotic aneurysms

- **Treatment**: long-term (≥ 6 weeks) I.V. antibiotic therapy (might require admitting to the hospital)
- and/or valve replacement (surgical intervention).

NOT REQUIRED

Infective Endocarditis: Diagnosis

Duke Criteria

- 1994 a group at Duke University standardised criteria for assessing patients with suspected endocarditis
- **Definite**
  - 2 major criteria
  - 1 major and 3 minor criteria
  - 5 minor criteria
  - pathology/histology findings
- **Possible**
  - 1 major and 1 minor criteria
  - 3 minor criteria
- **Rejected**
  - firm alternate diagnosis
  - resolution of manifestations of IE with 4 days antimicrobial therapy or less

Modified Dukes' criteria

Major-

- 2 positive blood cultures, for an organism known to cause IE
  or
  persistent bacteremia- 2 +ve 12 hours apart or 3 of 4 +ve drawn over 1 hour
- ECHO evidence- oscillating mass on valve or supporting structures
  or abscess
  or new valvular regurgitation or partial dehiscence of prosthetic valve

Minor-

- Predisposing factor- cardiac lesion, IVDU
- Fever >38 °C
- Vascular phenomenon
- Immunologic phenomenon
- +ve blood culture
- +ve ECHO

Let’s find out?

- Are all people with streptococcal pharyngitis exposed to risk of rheumatic fever?
- In what ways are rheumatic fever and infective endocarditis similar?
- What is different between rheumatic fever and infective endocarditis ?

(اللَّهمَّ لا سَهْلَ إلَّا ما جعَلْتَه سَهلًا وأنتَ تجعَلُ الحَزْنَ سَهلًا إذا شِئْتَ)

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V1→ V2			
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