

Lecture One

Rheumatic Fever, Endocarditis and Valvular disease



Done By:

Main editor: Wael Al-Saleh

*With: Mohammed AlSari,
Abdulmajeed Aljasser*

Reviewed by:

Fahad S Aldhahri

Samma Albukhayyet

Cardio vascular Block



NOTE: (robbin's) means that the info is taken from Robbin's basic pathology

Rheumatic fever

Rheumatic fever → systemic disease

Definition: Rheumatic fever (RF) is an acute, immunologically mediated, multisystem inflammatory disease that occurs a few weeks after an episode of group A β -hemolytic streptococcal pharyngitis; it can also rarely occur with streptococcal infections at other sites.

It is an important disease in Saudi Arabia and the Middle East. That because the most of the valvular diseases occur due to rheumatic heart disease.

NOTE: Acute rheumatic heart disease (RHD) is the cardiac manifestation of RF and is associated with inflammation of the valves, myocardium, or pericardium. (robbin's)

Epidemiology:

Community:

-It's usually found in low socioeconomic condition which are associated with poor sanitation, and areas where the infectious diseases are predominant.

-Most often affecting children between 5 and 15 years of age, but about 20% of first attacks occur in adults.

- It occurs in both male and female. Also, the complication of the disease can run to the late adult life.

Cause:

Rheumatic fever is not a result of direct bacterial involvement, instead it is thought to be of an immunological origin ; however, the precise nature of the immune mechanisms of injury remains unclear. It is thought to occur as a result of streptococcal antigens that elicit (causes) an antibody response reactive to streptococcal organisms as well as to human antigens in the heart and other tissues (cross reaction auto immune disease or antigen mimicry)

NOTE: The incidence has been remarkably reduced in the Western world in recent years but the disease is still very common in the Middle East and Saudi Arabia.

The pathology and pathogenesis of Rheumatic fever:

Recurrent infection → M protein production → antibodies production → cross reaction auto immunity → Inflammation → Aschoff bodies → Manifestations

Always remember that rheumatic fever is a systemic disease, and that **it is not caused directly by the infectious agent (strept.A)**.

Recurrent infection → M protein production → antibodies production → cross reaction auto immunity → Inflammation → Aschoff bodies → Manifestations

A recurrent throat infection pharyngitis or recurrent tonsillitis (**usually caused by Group A β -Hemolytic Streptococci**) affects the child (It's very rare to be infected by other organisms)

Recurrent infection → M protein production → antibodies production → cross reaction auto immunity → Inflammation → Aschoff bodies → Manifestations

The bacteria produces a protein called "M protein" on its surface. **The M protein shares its structure with other body antigens** in the heart valves, pericardium, endocardium, synovium, basal ganglia and motor neurons. This is due to the similarity in the biochemical structure between M protein and collagen which form these organs.

Recurrent infection → M protein production → antibodies production → cross reaction auto immunity → Inflammation → Aschoff bodies → Manifestations

The body produces antibodies specific for M protein → Those antibodies attack the M protein in the throat infection.

Recurrent infection → M protein production → antibodies production → cross reaction auto immunity → Inflammation → Aschoff bodies → Manifestations

The antibodies mistakenly attack structures similar to M protein in other places, ex: heart, synovium, basal ganglia...etc. and this is why you get the manifestations

Recurrent infection → M protein production → antibodies production → cross reaction auto immunity → Inflammation → Aschoff bodies → Manifestations

The immunological reaction triggers an inflammatory reaction → chemotaxis which will activate the complement system (C3a and C5a) + secretion of interleukins and chemical mediators → accumulation of inflammatory cells at the site.

The inflammation will result in fibrosis & calcification of the affected areas.

Fibrosis and calcification of the aortic valve or tricuspid valve will result in either stenosis or regurgitation.

REMEMBER: Valvular calcification due to fibrosis is **DYSTROPHIC**

Recurrent infection → M protein production → antibodies production → cross reaction auto immunity → Inflammation → Aschoff bodies → Manifestations

Aschoff bodies: are **the main pathological lesion occurring in the heart.**

This is an area of focal interstitial myocardial inflammation that is characterized by :

- fragmented collagen and fibrinoid material
- surrounded by large cells (Anitschkow myocytes)
- occasional multinucleated giant cells (Aschoff cells)

The Aschoff bodies will accumulate in the wall of the left atrium or near the left ventricle and make this place thickened. These thickened places are called "**MacCallum plaques**".

Recurrent infection → M protein production → antibodies production → cross reaction auto immunity → Inflammation → Aschoff bodies → Manifestations

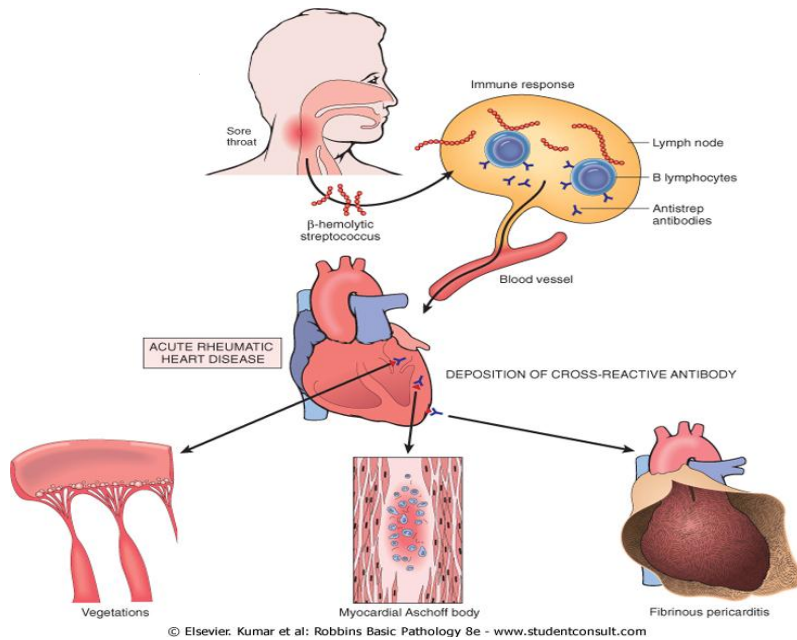
The patient develops many manifestations due to the cross reaction:

- Heart Diseases: Those antigens found in pericardium, myocardium, endocardium and mitral valve.
- Polyarthrititis
- Valvular diseases: The rheumatic fever loves to attack the mitral valve. 60% of the cases occur in the mitral valve and 25% of cases occur in aortic valve and almost never in the pulmonary valve.

In addition, Many patients with valvular disease have to change their valves by replacement surgery because they have chronic rheumatic fever which has been existing in there body for years.

- Erythema marginatum ... etc.

NOTE: Physicians noticed that some patients who get recurrent throat infection (similar to those who develop RF) don't develop the disease!! **Thus, it seems that affected people are predisposed for this antigen-antibody reaction.**



Pathogenesis and key morphologic changes of acute rheumatic heart disease. Acute rheumatic fever causes changes in the endocardium, myocardium, and epicardium. Chronic rheumatic heart disease is almost always caused by deformity of the heart valves, particularly the mitral and aortic valves.

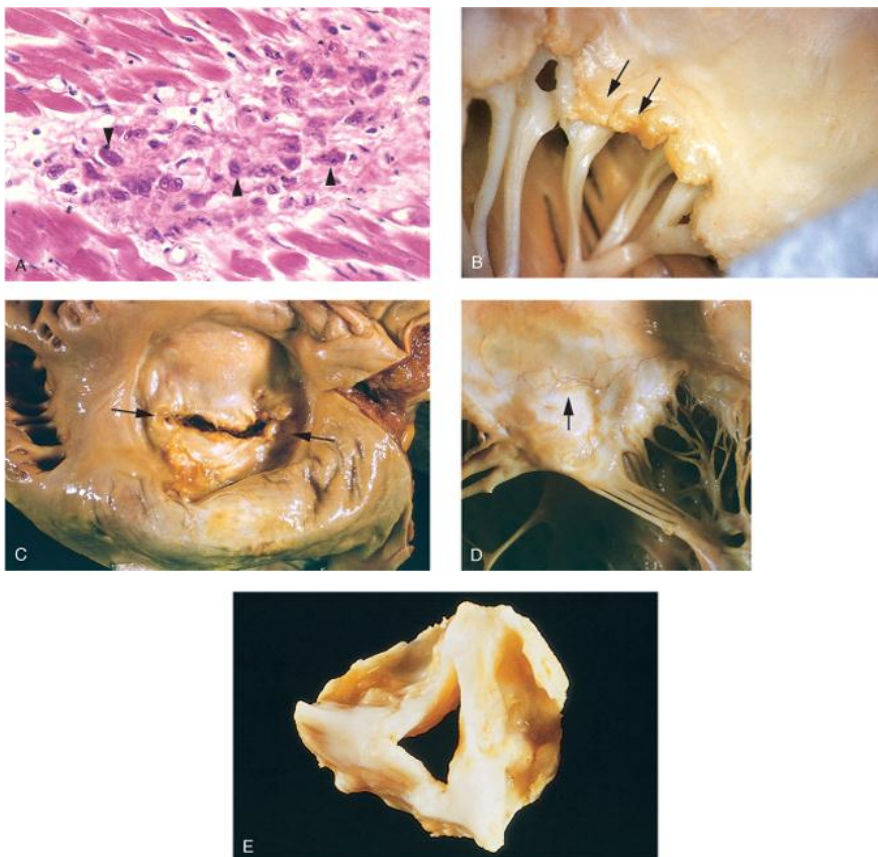
A, Microscopic appearance of an Aschoff body in a patient with acute rheumatic carditis; there is central necrosis with a circumscribed collection of mononuclear inflammatory cells, with some activated macrophages (Anitschkow cells)(arrows).

B, Acute rheumatic mitral valvulitis superimposed on chronic rheumatic heart disease. Small vegetations are visible along the line of closure of the mitral valve leaflet (arrows). Previous episodes of rheumatic valvulitis have caused fibrous thickening and fusion of the chordae tendineae.

C-D, Mitral stenosis with diffuse fibrous thickening and distortion of the valve leaflets, commissural fusion (arrows), and thickening and shortening of the chordae tendineae.

D, Opened valve. Note neovascularization of anterior mitral leaflet (arrow).

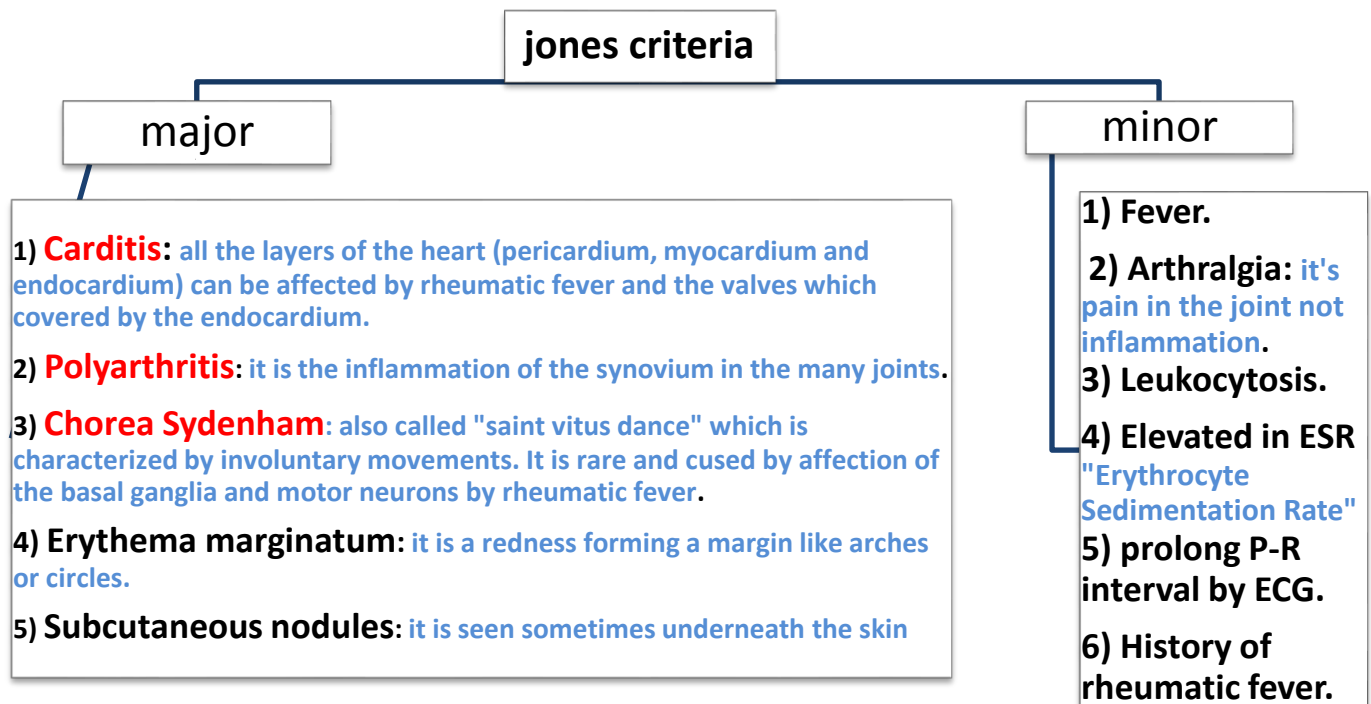
E, Surgically removed specimen of rheumatic aortic stenosis, demonstrating thickening and distortion of the cusps with commissural fusion



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Clinical presentation:

The patient will present with several manifestations classified according to what is called "**JOHN'S CRITERIA**"



The patient to be pointed as an RF, he/she has to have at least:

- ❖ two major criteria
- ❖ or two minor criteria with one major criteria.

Diagnosis:

- 1) Throat swap: to look for beta hemolytic streptococci.
- 2) Serological test: **in the serum you will find raised antistreptolysin o**
- 4) Examination of the joints: will be swelled.
- 5) Auscultation of the heart: Both stenosis and regurgitation, can be detected by auscultation, the examiner will notice an abnormal heart sound (murmur).
- 6) Body temperature measurement: you will find fever

Treatment:

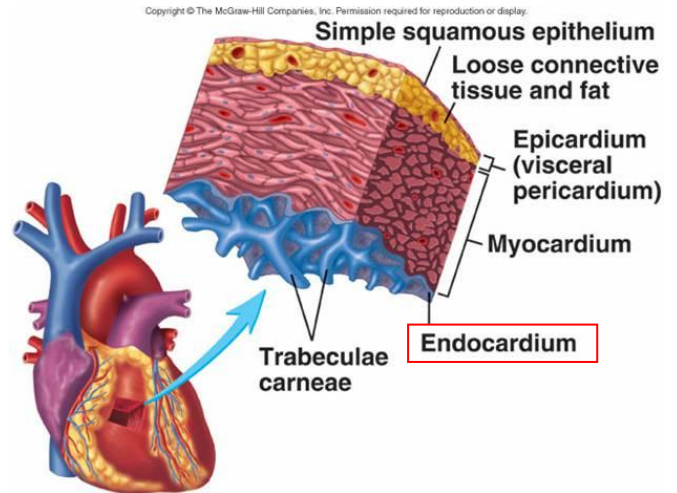
The treatment of valvular stenosis an regurgitation is by replacement of the valve by an animal's valve (from a cows usually) or an artificial valve.

The treatment of RF is antibiotics

Infective Endocarditis (IE)

Definition : Endocarditis is the inflammation of the endocardium.

Infective endocarditis : It is a serious infection characterized by **colonization or invasion** of the heart valves or the mural endocardium by a microbe most commonly caused by **streptococcus viridians**



The endocardium is the layer covering the inner aspect of the heart (ventricles or valves).

Classification:

acute	subacute
Highly virulent organism Staphylococcus aureus (50% of cases)	Low virulent organism Streptococcus viridians (>50% of cases)
Attacking a previously normal valve secondary to infection occurring elsewhere in the body.	Colonize a previously abnormal heart occur in patients with congenital heart disease or presenting valvular heart disease, often of rheumatic origin
Cause substantial morbidity and mortality even with appropriate antibiotic therapy	Follows a protracted course of weeks to months and most patient recover after appropriate antibiotic therapy

Etiology:

The most common bacteria which causes endocarditis is **streptococcus viridians**, in addition sometimes **staphylococcus aurues** which can cause acute endocarditis in right side of heart. And sometimes you may find candida or fungus in drug abusers (**but the main cause in drug abusers is staph aureus**).

Characteristics:

The main characteristics are

- 1- **large, soft, friable, easily detached VEGETATIONS**, consisting of:
 - fibrin
 - intermeshed inflammatory cells
 - Bacteria (**Remember: In endocarditis (unlike RF) the bacteria itself will attack the valves.**)

If you open the heart you will find the vegetations and they are destructive to the cusps. They will cause acute incompetence or perforation in the valves.

- 2- **Immune complex formation:**

It will occur in the heart. These immunocomplexes will accumulate in the heart and cause inflammation. **They may migrate and accumulate in places that are rich in blood vessels like the eye.**

The predisposing factors are the following:

- 1) **Rheumatic fever**: It is very common that RF is associated with endocarditis.
- 2) Having **congenital heart disease**. E.g: VSD & Bicuspid valve instead of tricuspid.
- 3) **Replacement of a diseased valve with artificial valve.**
- 4) Having **infective focus**: such as in mouth due to poor oral hygiene.
- 5) **Intravenous drug abusers**

Clinical presentation:

- 1- The patient usually has a history of one of the predisposing factors.
- 2- Fever
- 3- Fatigue
- 4- When you examine the fundus of the eye you will find a **roth spot**, which is a **hemorrhagic area**, caused by deposition of



immunocomplexes

- 5- He may have anemia
- 6- Obviously he "looks sick".
- 7- When you examine his hand you will find "**osler's nodes**" in his fingers and spider hemorrhages in the nails which are also caused by deposition of immunocomplexes.



Clinical features:

1- Valvular involvement

- a. **The mitral valve is most frequently involved.**
- b. The mitral valve along with the aortic valve is involved in about 40% of cases.
- c. **The tricuspid valve is involved in more than 50% of cases of endocarditis in intravenous drug users**, in whom endocarditis is most often caused by staphylococcal infection.

2- Complications

- a. Distal embolization occurs when fragments of the vegetation leaves the heart and enters the blood stream.
- b. **Embolization can occur almost anywhere in the body and can result in septic infarcts in the brain or in other organs.**
- c. The renal glomeruli may be site of focal glomerulonephritis (focal necrotizing glomerulitis) caused by immune complex disease or by septic emboli.

Other signs in acute IE:

Rapidly developing Fever, rigor and malaise.

Large vegetation , death up to 60%

Other signs in subacute IE:

fever maybe absent specially in elderly, fatigue, weight loss and flulike syndrome.

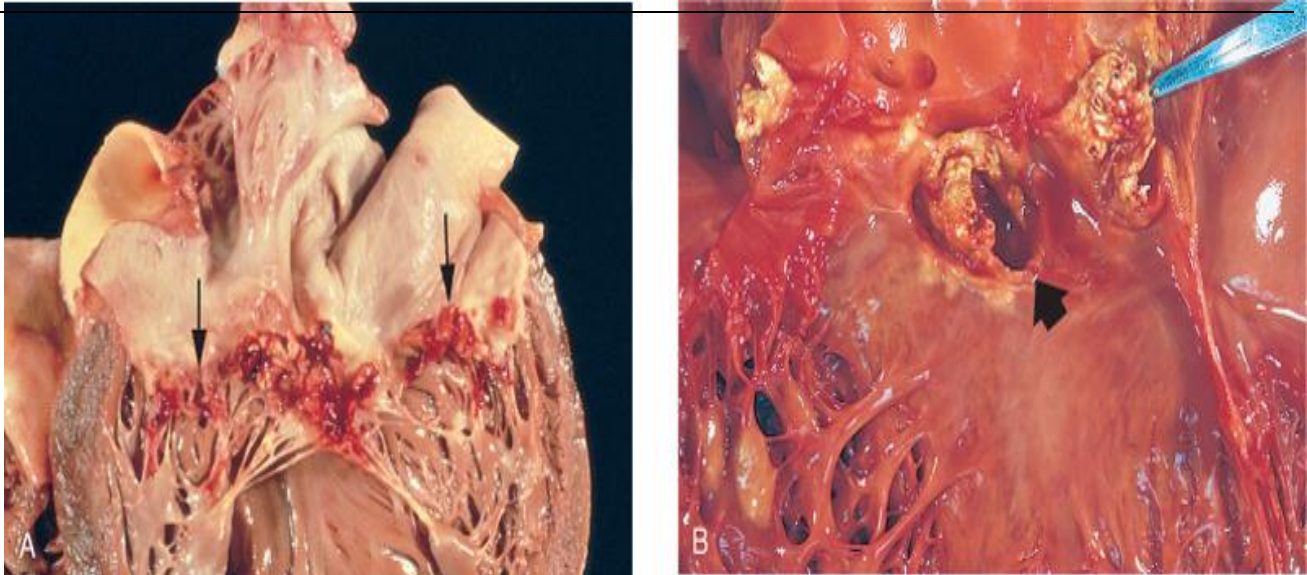
Small vegetation

Diagnosis:

Usually, the diagnosis is achieved by isolating the bacteria from the blood culture.

Blood culture is the most important to diagnosis and the only way to confirm it.

Treatment: intravenous antibiotics.



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A, Endocarditis of mitral valve (subacute, caused by *Streptococcus viridans*). The large, friable vegetations are denoted by arrows.

B, Acute endocarditis of congenitally bicuspid aortic valve (caused by *Staphylococcus aureus*) with extensive cuspal destruction and ring abscess (*arrow*).

Marantic Endocarditis or Non-Bacterial Thrombotic Endocarditis (NBTE) :

Usually occurs in elderly people and diagnosed during the autopsy.

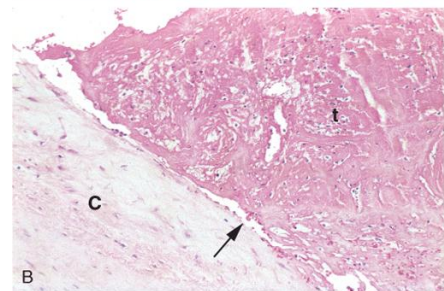
It is usually associated with debilitating disorders, such as metastatic cancer and other wasting condition such as adenocarcinoma, autoimmune disease, TB, Diabetes...etc.

It is characterized by non destructive hemorrhagic vegetation in one side of the cusps called **(Libman-sacks endocarditis)**

The blood culture is –ve.

The disease can result in peripheral embolization but unlike infective endocarditis, **the emboli are sterile**. Thus, when you look at the histology of this non-bacterial thrombotic endocarditis you'll find **only fibrin and blood**. (no inflammation and no bacteria)

Picture: Nonbacterial thrombotic endocarditis. **A**, Nearly complete row of thrombotic vegetations along the line of closure of the mitral valve leaflets (*arrows*). **B**, Photomicrograph of nonbacterial thrombotic endocarditis, showing bland thrombus, with virtually no inflammation in the valve cusp (c) or the thrombotic deposit (t). The thrombus is only loosely attached to the cusp (*arrow*).



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Endocarditis of the carcinoid syndrome

1. The cause is the **secretory products of carcinoid tumors** (vacoactive peptides and amines, especially serotonin (5-hydroxytrptamine)).
2. **The valves on the left side of the heart are rarely involved**, because serotonin and other carcinoid secretory products are detoxified in the lung.
3. This form of endocarditis results in thickened endocardial plaques characteristically involving the mural endocardium or the valvular cusps of **the right side of the heart**.

Valvular Diseases

د. الركابي تكلم عنها بطريقة محيوسة جددددددا... بالإضافة إلى إنه كثير من الأشياء ما تكلم عنها... ننصحكم بالرجوع للهاتداوت ووضعنا جدول يلخصها لكم... كما ذكرنا العلاج اللي ذكره الدكتور.

Mitral stenosis:	Mitral regurgitation:	Aortic stenosis:	Aortic regurgitation
<u>Caused by</u> rheumatic heart disease	<u>Caused by</u> Infective endocarditis, mitral valve prolapse.	<u>Caused by</u> calcification of anatomically normal and congenitally bicuspid aortic valves	<u>Caused by</u> infective endocarditis, degenerative aortic dilation
Symptoms: <ul style="list-style-type: none"> • Dyspnea • Fatigue • hemoptysis 	Symptoms <ul style="list-style-type: none"> • Fatigue and weakness • Dyspnea and orthopnea • Right sided Heart failure 	Symptoms <ul style="list-style-type: none"> • Angina • Syncope • Congestive Heart Failure (CHF) 	Symptoms <ul style="list-style-type: none"> • Angina • Fatigue • palpitation

Floppy mitral valve disease

The most important cause of the mitral valve incompetence in west countries. It is floppy because the accumulation of mucopolysaccharides within the valve. Only happen in mitral valve.

Treatment

We treat advanced cases of rheumatic valve disease by valve replacement. Before we do valve replacement, we have to make sure he has no subacute bacterial or infective endocarditis. You must kill any infective focus in his body by antibiotics.



432 Pathology Team

Good Luck ^_^