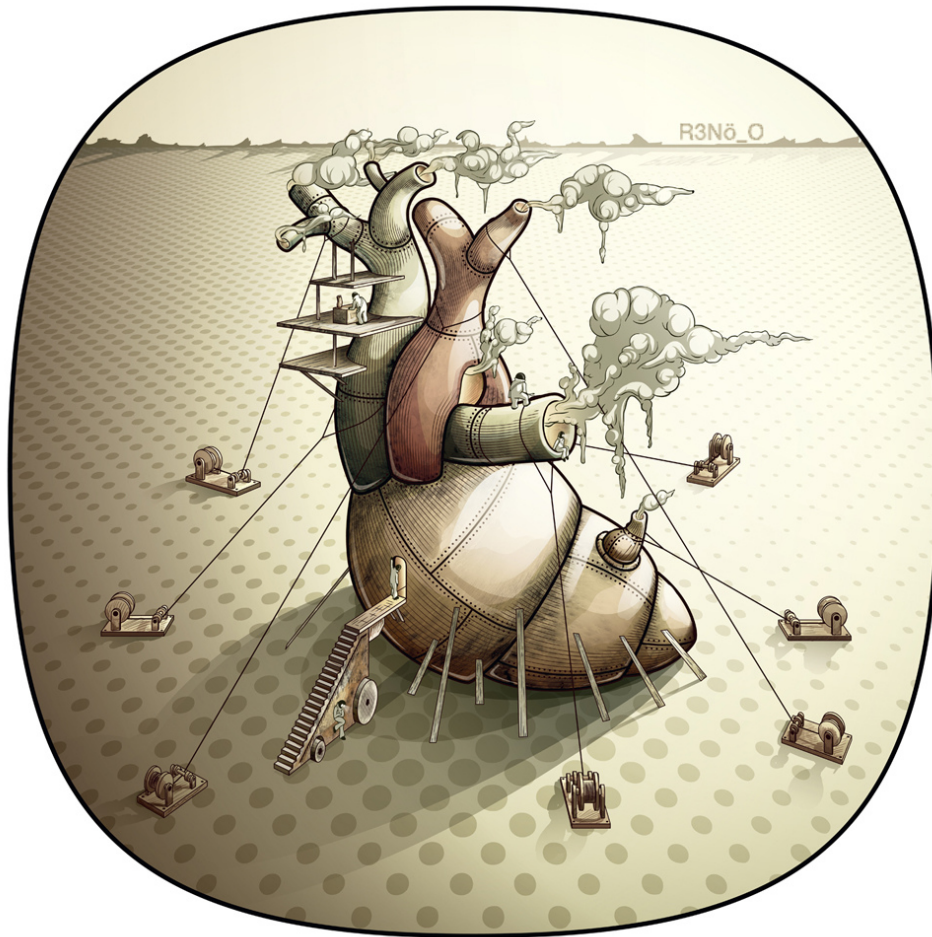


“Rheumatic fever, endocarditis & heart valves”

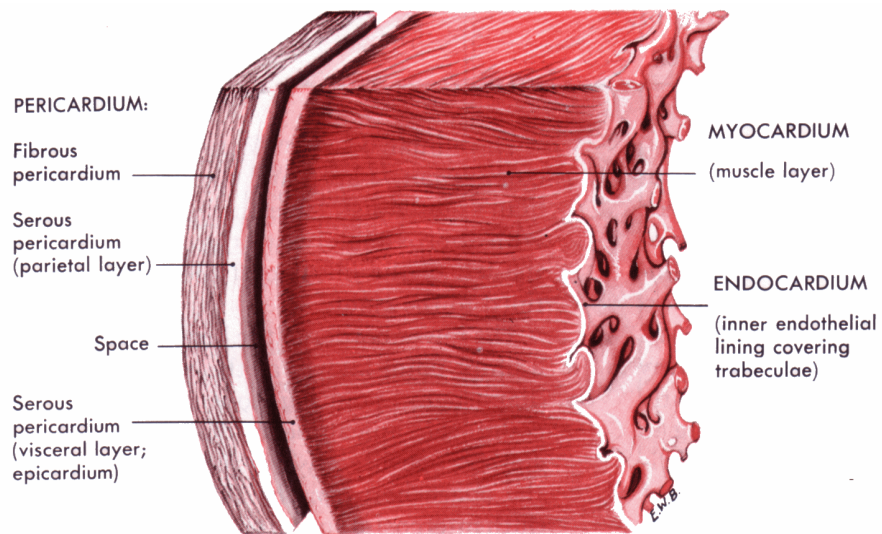
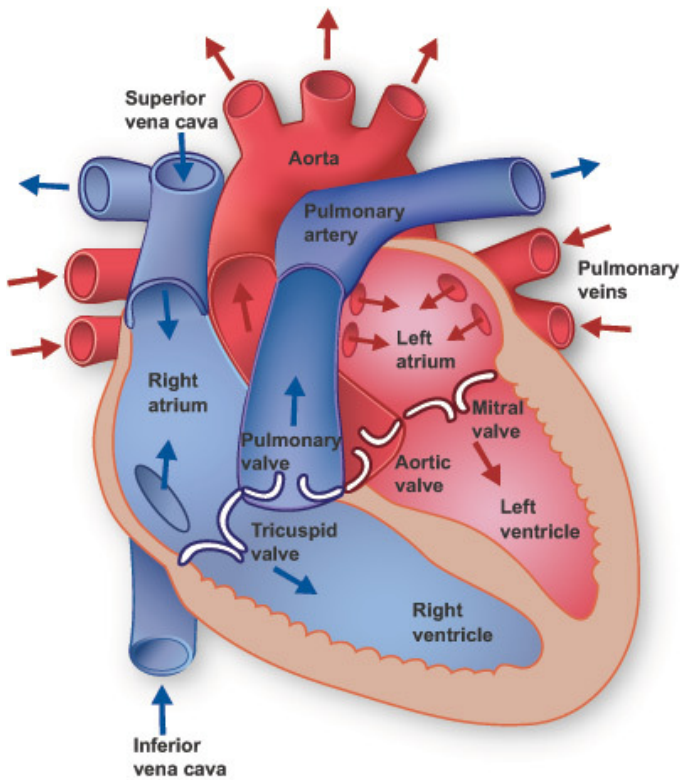


Objectives:

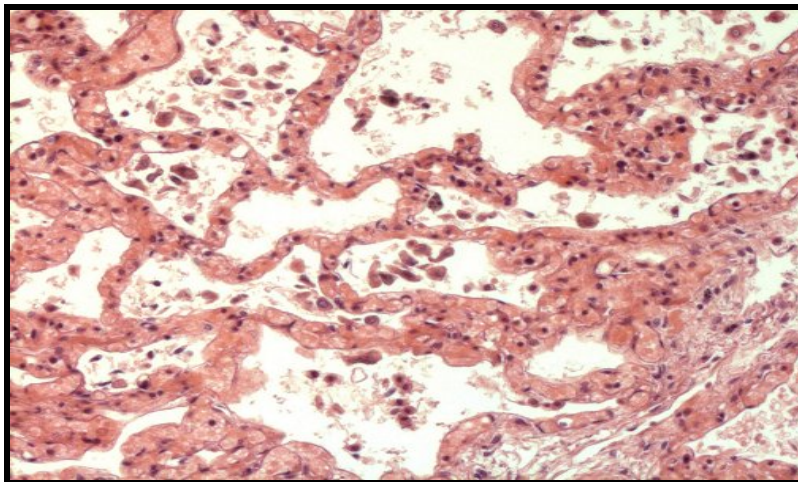
- Understands the clinicopathological features of rheumatic heart disease which is a major cause of acquired mitral and aortic valve diseases in the Kingdom of Saudi Arabia.
- Know the pathological causes and pathophysiological consequences of stenosis and incompetence of all the cardiac valves but particularly the mitral and aortic valves.
- Understands the pathology of infective endocarditis so as to be able to identify patients at risk and when appropriate ensure prophylactic treatment is given.

Important note: During the previous blocks, we noticed some mistakes just before the exam and we didn't have the time to edit the files. To make sure that all students are aware of any changes, please check out this link before viewing the file to know if there are any additions or changes. The same link will be used for all of our work: [Pathology Edit](#)

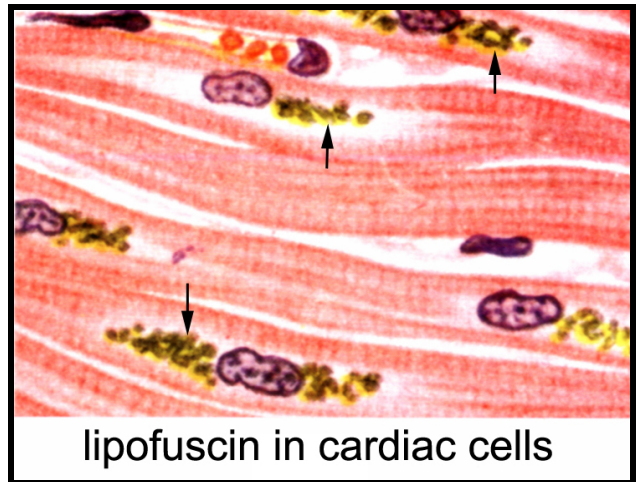
Introduction [Anatomy & Histology of the Heart].



Section of the heart wall showing the components of the outer pericardium (heart sac), muscle layer (myocardium), and inner lining (endocardium).



Big nuclei → indicates heart failure.



lipofuscin in cardiac cells

Yellowish brown pigmentation → lipofuscin.

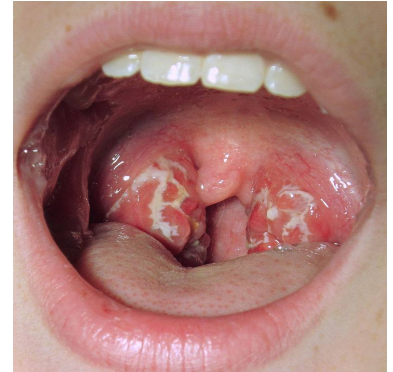
Rheumatic fever & its effect on the heart & valves.

Rheumatic fever (3 minutes documentary).

It's the most important cause of valvular diseases in KSA, Asia and Africa.

Rheumatic fever: An immunologically mediated inflammatory condition caused by abnormal reaction to an infection usually caused by **Group A Beta Hemolytic Streptococci**. They cause sore throat: (pharyngitis, tonsillitis) especially in children (5-15 years old).

Following this after 2 - 5 weeks 3% of them may show the signs and symptoms of rheumatic fever.



The **Jone's criteria** is divided into major and minor criteria. It is used for the diagnosis of rheumatic fever. If the patient got **One major & Two minor** **OR** **Two Major and Zero minor** then he has the disease.

Minor criteria:

- History fever and arthralgia¹.
- Leukocytosis. (increase neutrophils count).
- laboratory finding increase in (ESR , CRP).
- ECG changes. (prolongation of PR segment).
- previous rheumatic fever or rheumatic heart diseases.

Major criteria:

- **Pancarditis** which means (Pericarditis, Myocarditis, Endocarditis).

The valves are affected because they are covered by endocardium, so they are part of endocarditis.

- Migratory polyarthritis². (wrist, knee, ankle, elbow).
- **Sydenham chorea**³: The CNS is affected by the immunological reaction - especially the basal ganglion - → causes involuntary movements of the musculoskeletal system, behavioral and personality changes.
- Erythema marginatum⁴.
- Subcutaneous Nodules (Rheumatic nodules).



Don't be confused between Rheumatic Fever and Rheumatoid Arthritis. There's a big difference between them.

¹ arthralgia = ألم مفاصلي

² a temporary form of arthritis caused by rheumatic fever. Migratory means منتقل يعني الألم غير ثابت في مكان واحد. For example the patient can sleep with a pain in his shoulder then wake up and find his shoulder okay but his knee joint suddenly in pain.

³ Sydenham chorea = داء الرقص

⁴ Redness of skin that got very distinct margin.

Pathogenesis.

Why do those people (who were infected in throat by Group A Beta Hemolytic Streptococci) develop these symptoms ?

Rheumatic fever is immunological (hypersensitivity) reaction. It is developed from antibody reaction against a protein that is found in the streptococci which is called **M Protein**.

There are similar proteins found in the (*joints, skin, synovium, endocardium, myocardium*), because of that the antibodies will get confused & start attacking those organs.

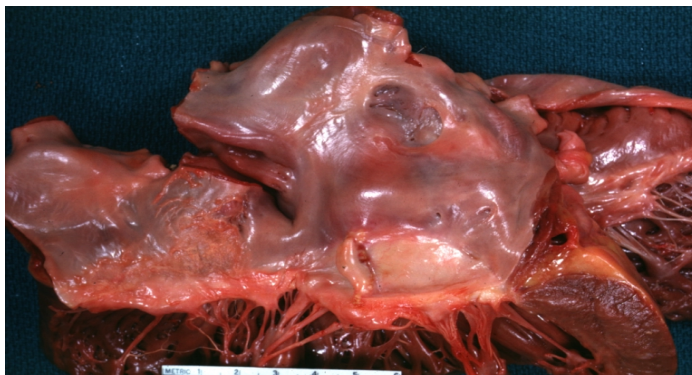
Antibodies will binds to these protein that is found in myocardium and the cardiac valves → stimulation of **T-cells (CD4 Cell)** & activation of **complement** and **Fc Receptor-bearing including macrophages** → **Pancarditis** (inflammation in all layers of heart).

- So, it's a pure immunological disease (**Blood culture isn't effective for diagnosis**).

Biopsy Findings:

There is Pancarditis (Inflammation in all layers): Pericarditis, Myocarditis, Endocarditis and valvulitis.

- **Pericardium:** exhibit a fibrinous exudate (*resolve without sequelae*⁵).
- **Myocardium:** scattered Aschoff bodies.
- Valve involvement result in *fibrinoid necrosis* and *fibrin deposition* along the lines of the closure and Rheumatic vegetations are seen too. (which will cause disturbance in cardiac function)
- Subendocardial lesions can also be seen, commonly in left atrium called as **Maccallum plaques**.



MacCallum plaques

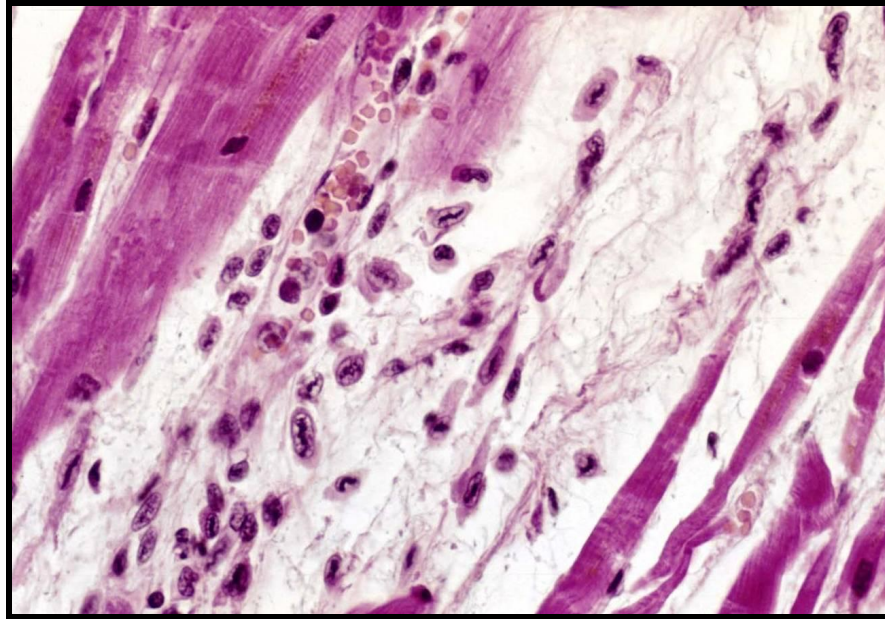
Aschoff nodules.

A collection of chronic inflammatory cells (especially macrophages -histiocytes-). They are large, have a lot of cytoplasm & central wavy nucleus. They are surrounded by lymphocytes, plasma cells, giant cells (not real granuloma) & collagen necrosis.

- Appear in a late stage of the disease.

Aschoff nodules Mostly found in hemodynamic areas where blood is always flowing:

1. can found in all layer of the heart (pericardium, myocardium and endocardium).
2. The cusps of the valves.
3. Posterior wall of the left atrium (**Maccallum Plaque**).



Aschoff Bodies

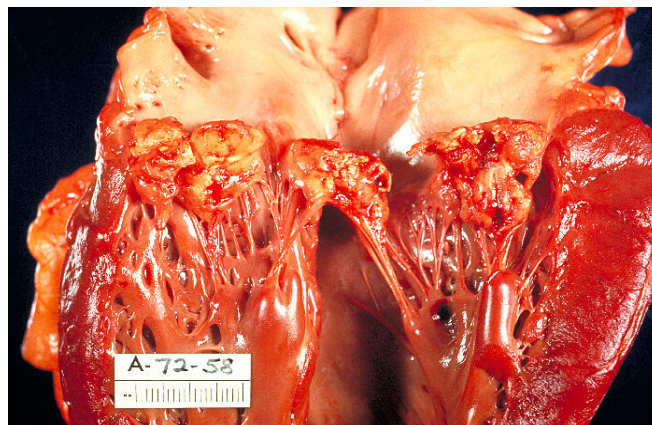
Rheumatic fever likes to affect **mitral valve** (bicuspid) mainly, then the aortic valve, very rare tricuspid valve and never affects pulmonary valve. It could be found in other areas also.

Chronic valvulitis.

Phases of this chronic inflammation are: Chronic exudate (fibrin & inflammatory cells) → vegetations⁶ that sets in the wall of the cusps (it's the proof that tell as that there's endocarditis) → forming vascular granulation tissue like areas → *fibrosis*.

Those vegetation are sterile (don't include bacteria). Why?

Because they are inflammatory mediated. It includes fibrin, exudate, necrosis, inflammatory cells.

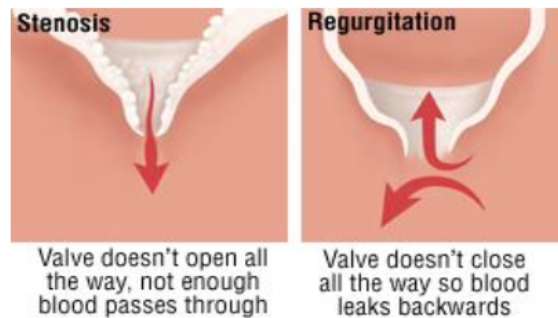


vegetation

⁶ In medicine, a **vegetation** is an abnormal growth named for its similarity to natural vegetation. Vegetations are often associated with endocarditis. It can be made of fibrin and platelets



What the difference between stenosis and Regurgitation

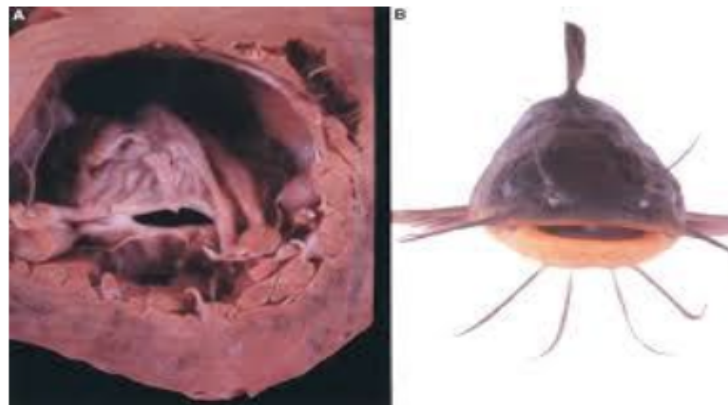


As a result of fibrosis the cusps fuse together → deformity in the valves causes two conditions:

1. **Stenosis** of the valves.
2. **Regurgitation**:
 - a. **Mitral valve** → Blood will flow back from ventricle to atrium during contraction.
 - b. **Aortic valve** → Aortic regurgitation towards the left ventricle.

How to diagnose?

- Stethoscope → Murmur caused by stenotic valve (*fish mouth orifice*).
- Echocardiogram.
- X-ray or CT-scan → Hypertrophy in left atrium & ventricle.
- Neurologically → might find thrombus caused by atrial fibrillation.
- Serum titers show elevation in **streptolysin O**.



fish mouth orifice

Complication:

- Left atrium hypertrophy causes atrial fibrillation → stagnation of blood → forming blood clot (thrombus) → could cause brain stroke or heart failure.
- **Rheumatic fever can cause senile calcific aortic stenosis.**

Endocarditis.

It can be caused by any **high** virulent organism. it's divided into two major groups: Acute & Subacute.

Acute endocarditis.

It is a very rare disease and it is caused by **Staphylococcus aureus** which is a very virulent organism. this type of endocarditis is often secondary to infection occurring elsewhere in the body like bronchiectasis and brain abscess. It's very severe disease and found mainly in people who are **drug addicted** that inject drugs under non-sterile environments. It could also causes **septicemia**.

Complications:

- Large, soft, friable, easily detached vegetations consisting of fibrin and intermeshed inflammatory cells and bacteria (non-sterile vegetation).
- Proliferation and ulceration and often perforation of the valve cusps.
- Rapture of one or more of the chordae tendinae.

Treatment: IV line of Penicillin or Vancomycin or Erythromycin.

Prognosis: Very bad it could lead to **death**.

Subacute.

infections by organisms of **low** virulence involving a previously abnormal heart, caused mostly by (***Streptococcus viridans* or *streptococcus bovis***).

Mitral valves are most common sites to be infected followed by aortic valves. It affects people with underlying cause which makes the heart weak and more susceptible to be infected.

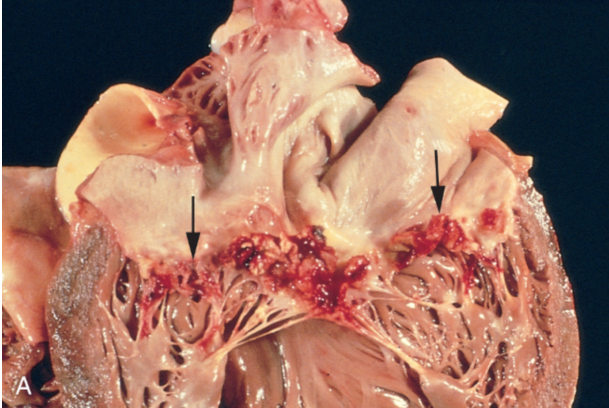
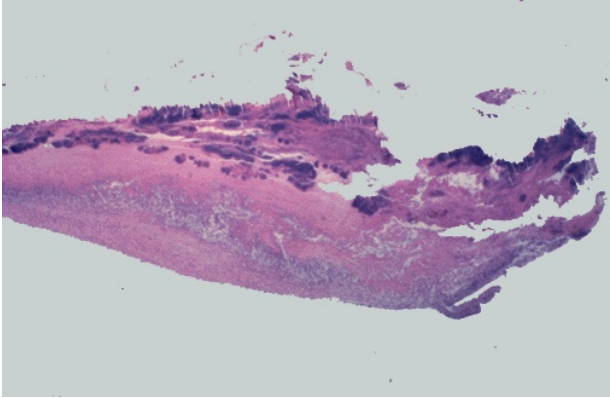
Those conditions are:

- Congenital heart disease (malformation of the heart): atrial-septal defect, ventricular-septal defect, persistent foramen ovale, deformity in the aortic artery, transposition of great vessels, tetralogy of fallot.
- Rheumatic valve disease.
- Drug addicts → right heart is more affected (tricuspid valve).
- Septicemia → rare cause.
- People with artificial valves.

How to protect people with these conditions?

If they are going to have a procedure (e.g. *tooth extraction*) the doctor should give them a course of **antibiotic** before the procedure.

prognosis: most patients recover after appropriate antibiotic therapy.

Gross subacute	Microscopic
 <p>Proliferation ulceration & destruction of the cusps, wholes, vegetation, hemorrhage, dystrophic calcification.</p>	 <p>Microscopically, the valve in infective endocarditis demonstrates friable vegetations of fibrin and platelets (pink) mixed with inflammatory cells and bacterial colonies (blue).</p>

Dystrophic calcification: is calcification of necrotic tissue associated with normal calcium level and caused by local inflammation.

Complications:

- Fibrosis causes retraction⁷ of chordae tendineae → causes incompetence → uncontrolled blood flow → heart failure.
- Because these vegetation are very friable, they shoot septic emboli → could cause brain abscess.

Rheumatic fever	Endocarditis
sterile (immune reaction)	non-sterile (septicemia)
vegetation near the lines of closure (سطحي)	vegetation is deep & involving the whole cusp (إلى الداخل)

The patient comes to you because he has palpitation. You do the following investigations:

- ECG → atrial fibrillation.
- X-ray → hypertrophy of left side of the heart.
- Echocardiography⁸ → mitral valve disease.
- ESR → very high.
- Antistreptolysin O → high due to previous infection with streptococci.

Treatment: Antibiotic & treating the heart condition (antiarrhythmic). Covering the patient with antibiotics if going to have a minor surgery (tonsillitis, tooth extraction, cleaning abscess).

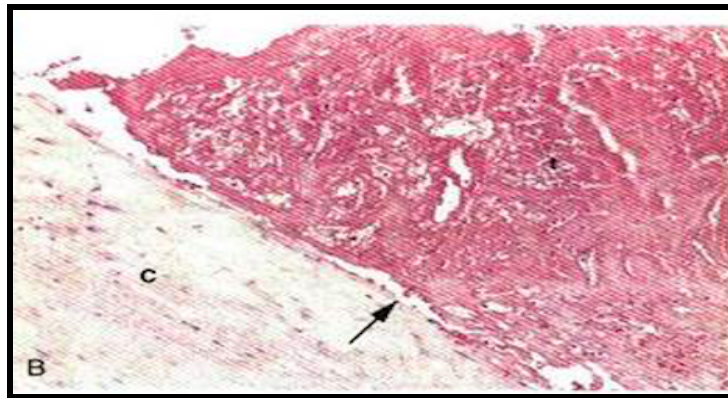
⁸ Echocardiography = تخطيط صدى القلب

Marantic endocarditis.

It's also called **Non-Bacterial Thrombotic Endocarditis (NBTE)**. It is sterile, happens in people who are terminally ill (cancer, immunocompromised, advanced chronic diseases).

Characterized by the deposition of small masses of fibrin, platelets, and other blood components on the leaflets of the cardiac valves (sterile) and non-destructive. There is no infective organism. It is aseptic. Aortic valve most common site. The fibrin deposits are randomly arranged. May embolize to different parts of the body including brain, but the emboli are sterile

How do they develop it? There's some sort of hemostatic abnormality so they develop this fibrin-like vegetations of the cusps.



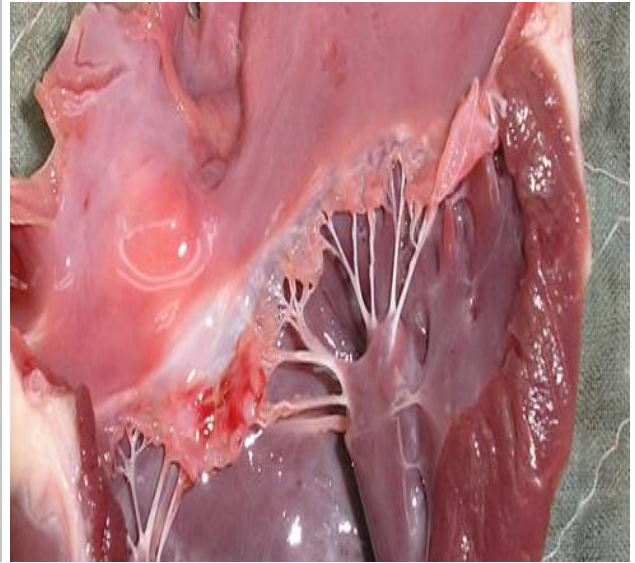
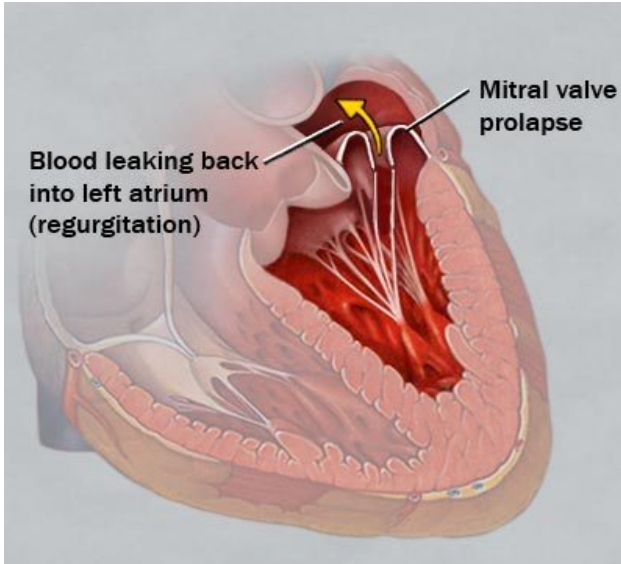
Blood, fibrin, little inflammatory cells (sterile).

Myxomatous Mitral Valve (Floppy⁹ mitral valve).

it is very common in the west, Caused by accumulation of mucin (material within the collagen of the valve). This will cause insufficiency (regurgitation) & special sound during systole called (mid-systolic click). It is characterized by accumulation of mucopolysaccharidosis. During contraction "Parachuting"¹⁰ happens. **No vegetation, no fibrosis.**

- Pathogenesis is unknown, can be a component of Marfan syndrome. Most patients asymptomatic but can result in mitral insufficiency and arrhythmias. Patients are predisposed to infective endocarditis.

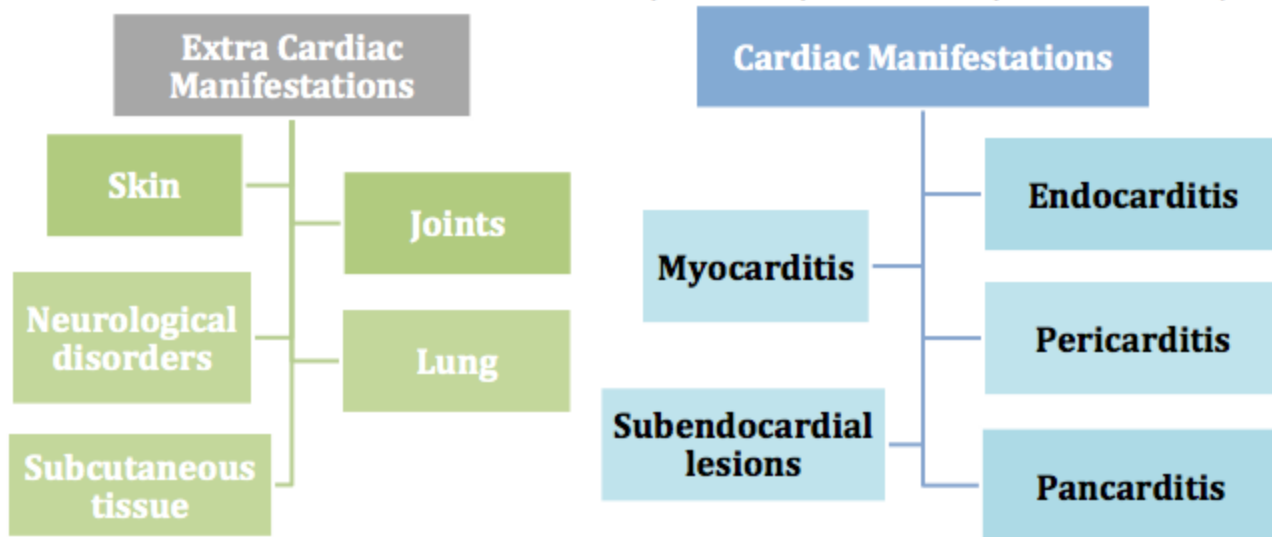
¹⁰ Parachuting = النزول بالمظلة



Parachuting in myxomatous mitral valve

Summary.

Acute Rheumatic fever: Immune mediated, inflammatory disease, caused by *group A-beta hemolytic streptococcal* infection with cardiac and extracardiac manifestations. The inflammatory reaction mainly involves the heart, joints, central nervous system and skin.



Chronic rheumatic heart diseases.

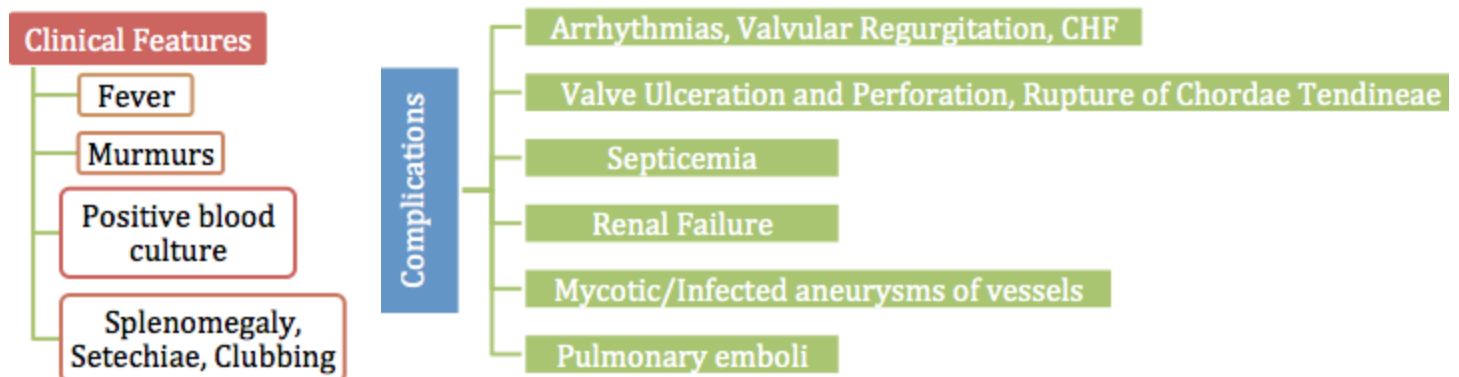
- **Clinical features:** cardiac murmurs, hypertrophy, dilation, congestive heart failure, arrhythmia, thromboembolism and infective endocarditis.
- **Complications:** Bacterial infective endocarditis - Mural thrombi - Congestive heart failure - Adhesive pericarditis - Atrial fibrillation.

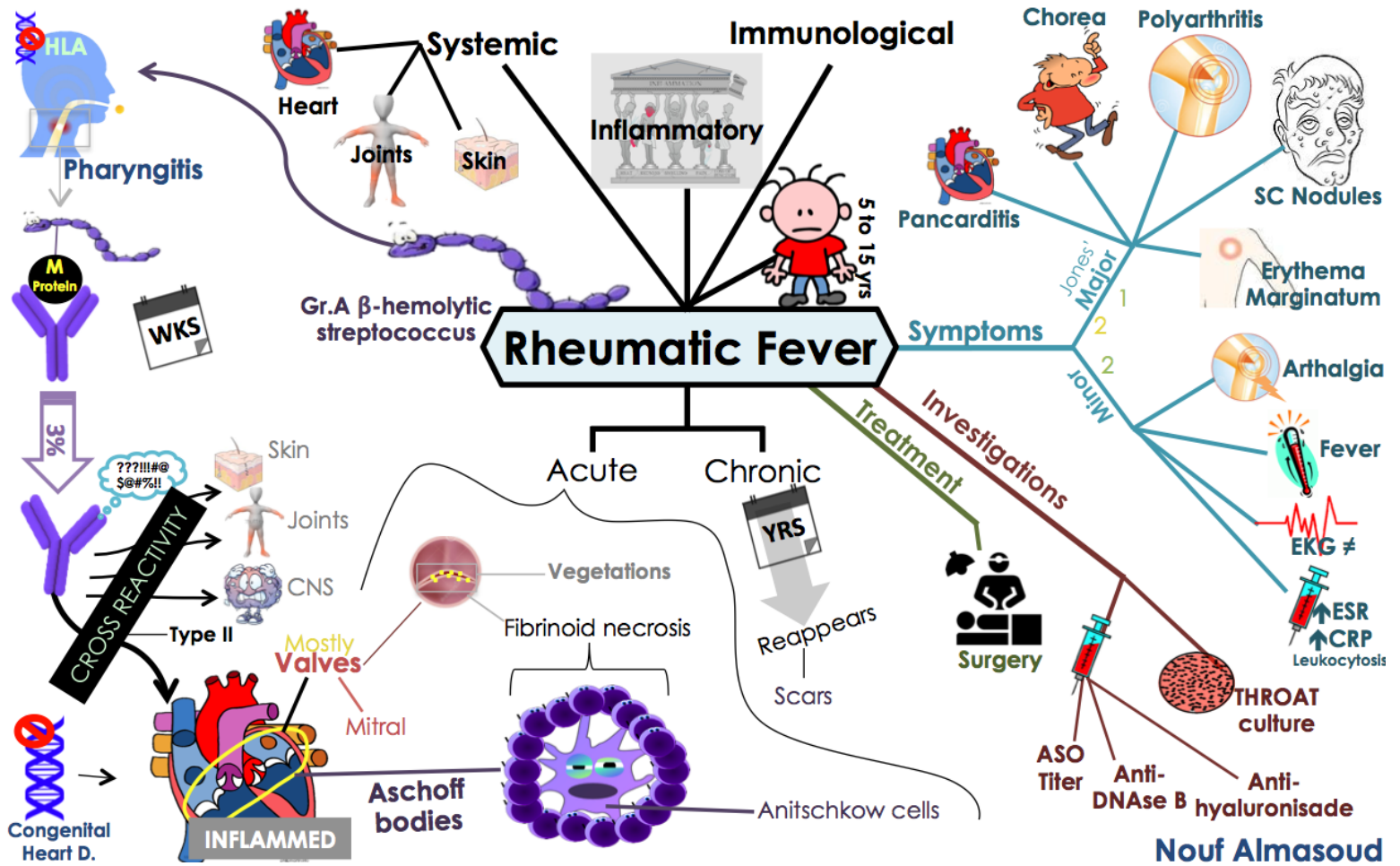
Infective Endocarditis (IE).

Infection of the cardiac valves or mural surface of the endocardium, resulting in the formation of an adherent mass of thrombotic debris and microorganisms. Infective endocarditis is a particularly difficult infection to eradicate because of the avascular nature of the heart valves. Mitral valves are the most common sites of IE followed by aortic valve. In IV drug users right side valves like the tricuspid are more commonly involved.

Acute IE: by highly virulent (**staphylococcus aureus**).

Sub acute IE: by low virulence (**a-hemolytic streptococci viridans**).





Nouf Almasoud

Additional treatment for the infection: Penicillin. (It's effective against Streptococcus group A infections).

While surgery is applied in the case of vasculitis.

MCQs.

A 10-year-old girl develops subcutaneous nodules over the skin of her arms and torso 3 weeks after a bout of acute pharyngitis. She manifests choreiform movements and begins to complain of pain in her knees and hips, particularly with movement. A friction rub is heard on auscultation of the chest. Which of the following serum laboratory findings is most characteristic of the disease affecting this patient?

- A. Elevated cardiac troponin I level
- B. Positive ANA test
- C. Raise ESR
- D. Elevated antistreptolysin O level

Ans: (D) The findings suggest acute rheumatic fever, which can involve any or all layers of the heart. Because rheumatic fever follows streptococcal infections, the antistreptolysin O titer is elevated. Raise ESR isn't specific.

During the past year, a 34-year-old woman has had palpitations, fatigue, and worsening chest pain. On physical examination, she is afebrile. Auscultation of the chest indicates a midsystolic click with late systolic murmur. A review of systems indicates that the patient has one or two anxiety attacks per month. An echocardiogram is most likely to show which of the following?

- A. Mitral valve prolapse
- B. Aortic valvular vegetations
- C. Pulmonic stenosis
- D. Patent ductus arteriosus

Ans:A , the most frequent valvular lesion. Which is Ballooning of mitral valves (floppy cusp), parachute deformity with prolapse of the cusp into the atrium with systolic murmur.

Two weeks after having a mild upper respiratory tract infection, a 14-year-old girl has fever and chest pain. A friction rub is audible on auscultation of the chest. A chest radiograph shows pulmonary edema. An echocardiogram shows small vegetations at the closure line of the mitral and aortic valves. An endocardial biopsy showed focal interstitial inflammation with Aschoff nodules. Her condition improves over the next month. The representative gross appearance of the disease process 20 years later is shown in the figure. Which of the following additional complications of this illness is most likely to be seen in the patient?



- A. Aortic stenosis
- B. Constrictive pericarditis
- C. congenital malformations
- D. Mitral valve prolapse

Ans:A, Caused by calcification and is caused by calcification and is called Calcific Aortic stenosis

One of the tests that is done to confirm diagnosis of R.F:

- A. Alpha 1 antitrypsin
- B. Rheumatoid factor
- C. Anti-streptolysin O
- D. Creatine kinase

Ans:C

Sub-Acute endocarditis usually follows an infection with:

- A. Streptococcus group A
- B. Staphylococcus aureus
- C. H. influenzae
- D. Streptococcus viridans

Ans:D

13- What is the main pathological lesion occurs in the heart in acute R.F ??

- A. Osler nodes
- B. Aschoff body
- C. Buttonhole stenosis
- D. Ring abscess

Ans:B

Direct Qs.

In Rheumatic Fever Subendocardial lesions appear as irregular thick patches commonly in the left atrium ?

Ans:Maccallum patch=plaques .

what is the most common site for infective endocarditis ??

Ans:Mitral followed by aortic valve. except IV drugs users right sided like tricuspid valve is the most common

where can we see fish mouth (Buttonhole) deformity ?

Ans:In mitral valve stenosis (leaflet is thickened and fibrotic).

The cause of aortic valve stenosis is:

Ans:Dystrophic calcification.

Contact us on: Pathology434@gmail.com

Twitter: @Pathology434

Good Luck!

مها الربيعة
ملاك الختلان
ريما الرشيد
ريم لبني
ريما الناصر
مشاعل حسين
نوف المسعود

عمر الرهيني
حسين الكاف
أحمد الصالح