

Cardiovascular system block

Pathology team 431



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Pink color : notes from girls slides .

Green color : notes from boys slides & Dr. Al-Rikabi hand out.

Blue color box : for extra notes from doctors or students .

1st lecture

Pathology of rheumatic fever, endocarditis and heart valves

Objectives:

At the end of these two lectures, the student should:

- (1) Understand the pathogenesis and clinical consequences of atherosclerosis.
- (2) Be able to discuss pathology and complications of ischaemic heart diseases with special emphasis on myocardial infarction.
- (3) Know how lifestyle modifications can reduce the risk of ischaemic heart disease.

Key principles to be discussed:

- (1) Risk factors of atherosclerosis.
- (2) Pathogenesis of the fibrolipid atherosclerotic plaque.
- (3) Clinical complications of atherosclerosis.
- (4) Commonest sites for the clinically significant coronary atherosclerosis.
- (5) Macroscopic and microscopic changes in myocardial infarction.
- (6) Biochemical markers of myocardial infarction.
- (7) Complications of myocardial infarction: immediate and late.

Rheumatic fever

is a multisystem, **immune** and **inflammatory** disorder representing a reaction to **group A streptococci** (which causes throat infections) that effects all layers of the heart. Most often in **children** between ages 5 and 15.

Rheumatic fever usually acquired after 1-4 weeks from an attack of sore throat

Complication of rheumatic fever:-

valvular problem in endocarditis (Deforming fibrotic valvular abnormalities (esp MS(mitral stenosis)) are important cardiac complications), **myocarditis and pericarditis**

Rheumatic fever also Involves heart, blood vessels, joints, subcutaneous tissue and CNS. (Multisystem)

Two ways to prevent rheumatic fever in patients with sore throat:

1- Tonsillectomy (removing tonsils)

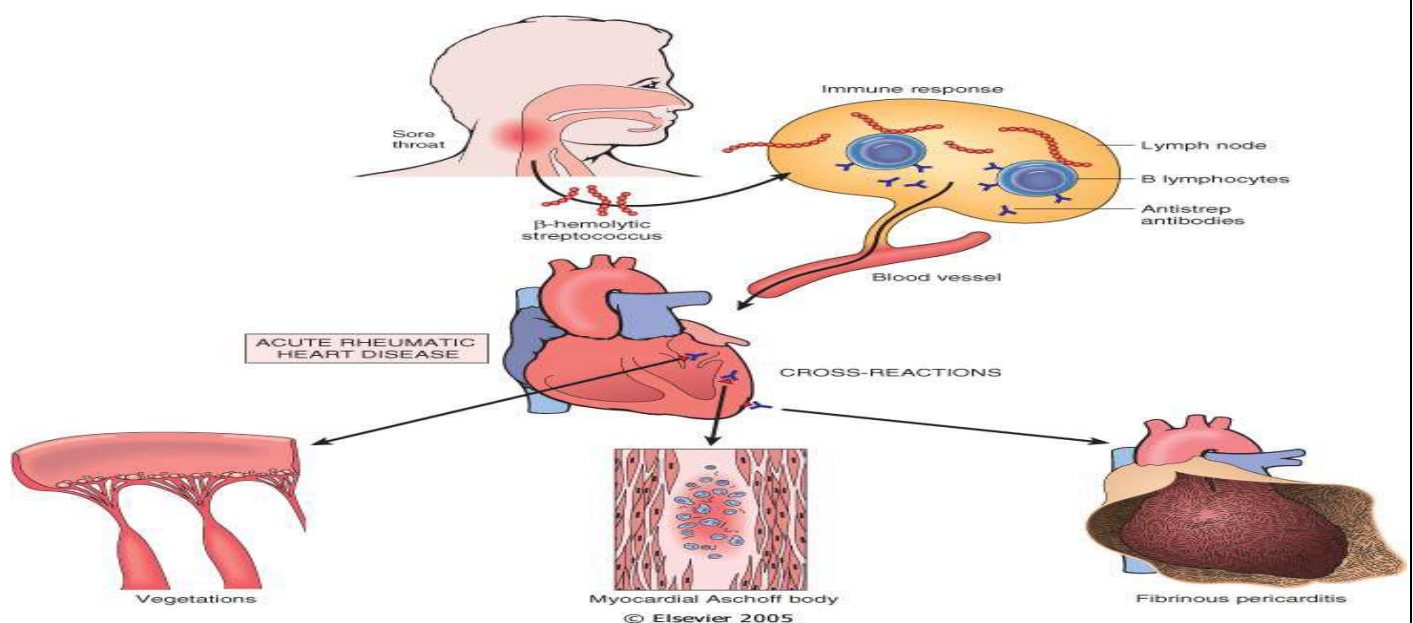
2- long-acting penicillin (if he doesn't response do tonsillectomy)

The child comes to you with:- 1-recurrent infection 2-jone's criteria

Investigations:- 1- Throat swab culture. >> Patient grows Group A Beta-Hemolytic Streptococci.

2- Anti-streptolysin O Test >> ASO is elevated in the serum of the patient.

Pathologic sequence and key morphologic features of acute RHD



The diagnosis is established by **Jones criteria**:- evidence of a preceding group A streptococcal infection, with the presence of two of the major manifestations listed below with high ASO (antistreptolysin o) or one major and two minor manifestations with the high ASO

Major criteria	Minor criteria
migratory polyarthritis of the large joints	fever
pancarditis	arthralgia
subcutaneous nodules	elevated blood levels of acute-phase reactants
erythema marginatum of the skin	leukocytosis
Sydenham chorea	heart (valve) problem

- *Sydenham chorea: (a neurologic disorder with involuntary rapid, purposeless movements. The infect the basal ganglia of the brain by the immune reaction induced by streptococci (the child comes and makes funny movement - rare and a serious manifestation)
- *Migratory Polyarthritis: A temporary form of arthritis that progressively affects a number of large joints and finally settles in one or more
- *Pancarditis: inflammation of all the three layers of the heart, causing pericarditis, myocarditis, or endocarditis
- *Subcutaneous Nodules: Painless, firm collections of collagen fibers over bones or tendons
- *Erythema marginatum of the skin: It's a rash that begins on the trunk or arms. This rash never starts on the face and it is made worse with heat.

Pathogenesis:-

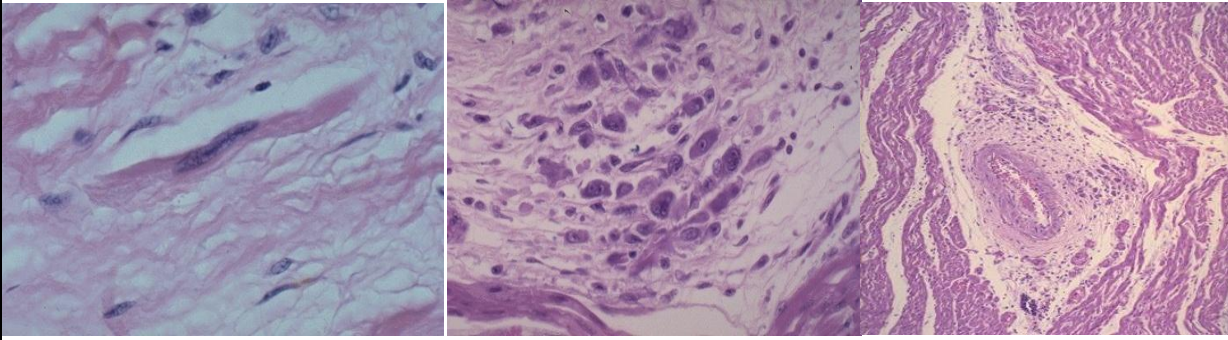
Group A Streptococci has a proteinaceous material, which is similar in its structure to certain proteins in the heart. Therefore, when they get infected, the antibodies which are formed against the bacteria's proteins will attack the bacteria and attack the organ which has a similar biochemical structure with them; in this case, the heart. After that inflammation occurs which leads to fibrosis, calcification and deformities of the valves (stenosis or regurgitation (insufficiency)).

Inflammation > Fibrosis > Calcification > Valve deformities.

Rheumatic fever: this disease likes the heart especially the endocardium and will affect **the mitral valve(50% of the patient)** and **aortic valve** (45% of the patient). The disease also effect the tricuspid valve (5% of the patient)

The Mitral valve can be affected by stenosis with Fish-mouth buttonhole deformity, insufficiency, or both.

Aschoff nodule and anitschkow cell



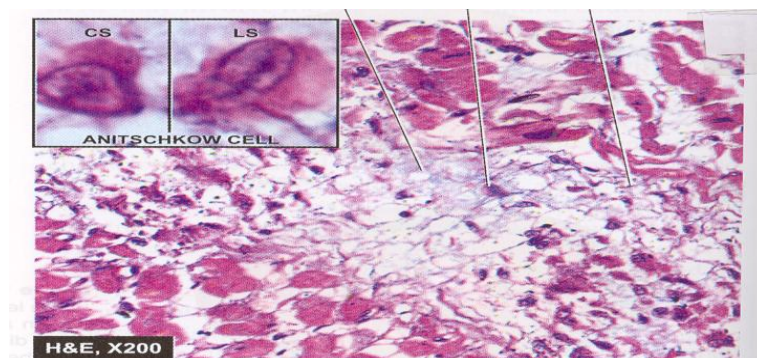
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Pathological hallmark : **Aschoff bodies**.

Aschoff bodies consist of foci of fibrinoid degeneration surrounded by lymphocytes (primarily T cells), occasional plasma cells, and plump activated macrophages called **Anitschkow cells**.

Anitschkow cells : have abundant cytoplasm and central round-to-ovoid nuclei in which the chromatin is disposed in a central, slender, **wavy ribbon ("caterpillar cells")**

Rheumatic endocarditis



Inflammation results in fibrinoid necrosis within the cusps or along the tendinous cords.

Overlying these necrotic foci are small (1- to 2-mm) vegetations, called verrucae, along the lines of closure.

Subendocardial lesions, exacerbated by regurgitant jets, may induce irregular thickenings called MacCallum plaques, usually in the left atrium.

In chronic disease the mitral valve is virtually always involved.

Mitral valve in chronic RHD are leaflet thickening, commissural fusion and shortening, and thickening and fusion of the tendinous cords

MacCallum patch (plaque) is an area that is commonly effected by the Aschoff nodule and its situated in the posterior aspect of the left atrial wall (because of increase turbulence **of blood in this area** Aschoff bodies may be found in any of the three layers of the heart, causing (**pancarditis**)

Infective endocarditis:- has two type:-

Acute endocarditis (rare, Acute can lead to abscess and have high mortality , may be caused by **Staphylococcus aureus** or other bacteria, secondary to infection, the patient may (be drug addict or immuneocompromise) and

sub acute endocarditis (we see it a lot in rheumatic fever as a complication, Subacute less destructive and have low mortility). Most cases are caused by bacterial infections (*bacterial endocarditis*). Occur in patients with congenital heart disease or presenting valvular heart disease.

There are four causes of endocarditis:-

- 1-rheumatic fever affecting the valves (you will see areas of inflammation and necrosis we call it verrucous)
- 2-congenital heart disease (you must cover it with antibiotics)
- 3-patients who have artificial (prostheses) valves (you should give him anticoagulant, antibiotic (every time he got an infection and before minor surgery)
- 4-general infection in the body (septicemia)

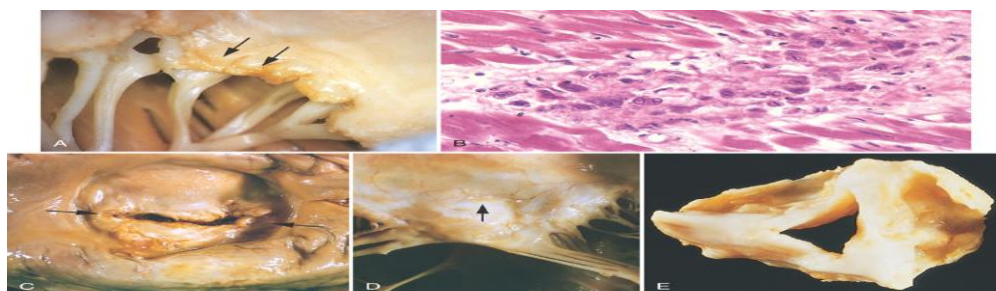
Histopathology:

An areas of necrosis, bluish (bacteria and (fungal if the patient is immunocompromised) The hallmark of IE is the presence of friable, bulky, potentially destructive vegetations

Vegetations containing fibrin, inflammatory cells, and bacteria on the heart valves

Vegetation sometimes erode into the underlying myocardium and produce an abscess (ring abscess).The vegetation may be single or multiple and may involve more than one valve.(There's a different vegetation between IE)

Vegetations are composed of thrombotic debris and organisms, often associated with destruction of the underlying cardiac tissues Although fungi and other classes of microorganisms can be responsible, *Staph aureus* is most common bacteria involved



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, Acute rheumatic mitral valvulitis superimposed on chronic rheumatic heart disease. Small vegetations (verrucae) 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. **B**, Microscopic appearance of Aschoff body in a patient with acute rheumatic carditis. The myocardial interstitium has a circumscribed collection of mononuclear inflammatory cells, including some large macrophages with prominent nucleoli and a binuclear macrophage, associated with necrosis. **C** and **D**, Mitral stenosis with diffuse fibrous thickening and distortion of the valve leaflets

Complication of infective endocarditis in GENERAL:-

1- septic emboli

2- they may develop glomerulonephritis because the patient may have Type III immune reaction (antigen-antibody complex)(you have bacteria and the body will react against it by forming antibodies

,so these bacterial proteins with the antibody will form a molecule with very high molecular Weight and therefore it get deposits in area that have large blood supply (like kidney) and inflammation occurs)

3- septicemia

Clinical presentation and complications

Acute: Fever, rigor, malaise Large vegetation => emboli:

Infarction

Metastatic infection

Distant organs like spleen, brain or heart

Kidney: Ag-Ab complex -> GN-> nephrotic syndrome or Renal failure

Congestive heart failure due to valve disease

Can lead to ring abscess and perforation of the aorta and myocardium

Death up to 60%

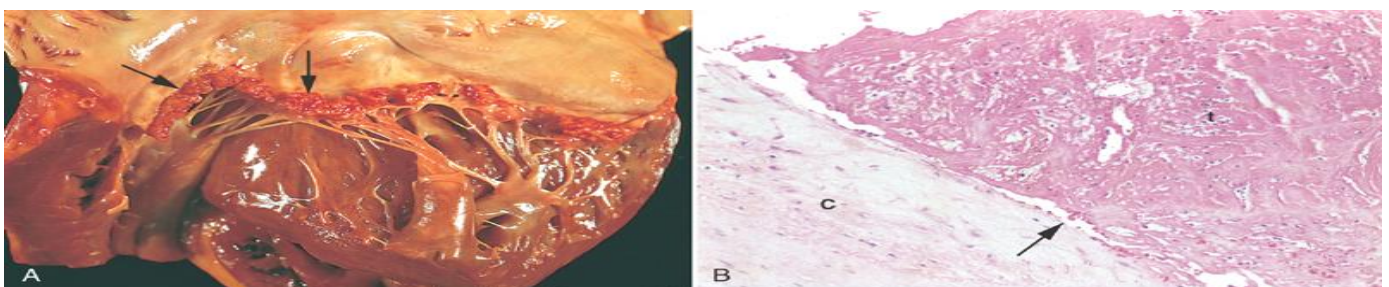
Subacute: Insidious ,Splenomegaly, Non specific : fever, weight loss

1-the embolis goes and sets in the brain and it will make brain abscess secondary to septic embolis (which came from the heart)) it go to the brain ,liver, spleen....

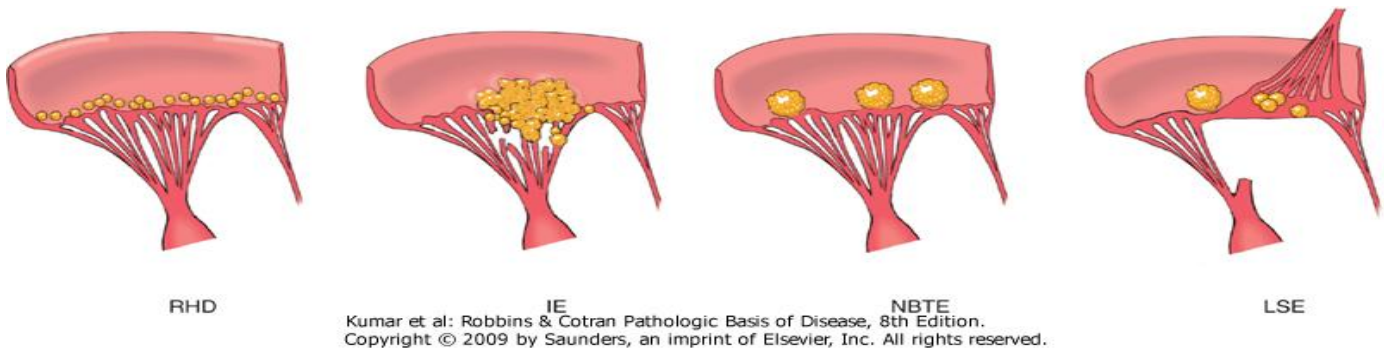
2- Why the deposit (immune complex) doesn't go to the brain ? because the brain isn't rich in blood vessels

Non-bacterial thrombotic endocarditis (**marantic** endocarditis):-develop in people who have **chronic debilitating disease** Its make vegetation which is Hemorrhagic but not as much necrotic and destructive as bacterial endocarditis (**not invasive and do not elicit any inflammatory reaction**) .**no bacteria only fibrin and thrombus sitting on the vessels, cusps and valves** .The disease can result in peripheral embolization but unlike infective endocarditis, the emboli are sterile. Nonbacterial thrombotic endocarditis and the endocarditis of SLE, called Libman-Sacks endocarditis.

Histologically they are composed of bland thrombi that are loosely attached to the underlying valve.



Nonbacterial thrombotic endocarditis (NBTE). A, Nearly complete row of thrombotic vegetations along the line of closure of the mitral valve leaflets (*arrows*). B, Photomicrograph of NBTE, 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*).



Comparison of the four major forms of vegetative endocarditis. The rheumatic fever phase of rheumatic heart disease (RHD) is marked by small, warty vegetations along the lines of closure of the valve leaflets. Infective endocarditis (IE) is characterized by large, irregular masses on the valve cusps that can extend onto the chordae. Nonbacterial thrombotic endocarditis (NBTE) typically exhibits small, bland vegetations, usually attached at the line of closure. One or many may be present. Libman-Sacks endocarditis (LSE) has small or medium-sized vegetations on either or both sides of the valve leaflets.

Valvular Heart Disease

Can come to clinical attention due to stenosis, insufficiency (regurgitation or incompetence), or both.

Stenosis is the failure of a valve to open completely, which impedes forward flow

Insufficiency, in contrast, results from failure of a valve to close completely, thereby allowing reversed flow

The most frequent causes of the major functional valvular lesions are:

Aortic stenosis: calcification of anatomically normal and congenitally bicuspid aortic valves.

Aortic insufficiency: dilation of the ascending aorta, usually related to hypertension and aging

Insufficiency of aortic valve can be caused by:

- (a) Nondissecting aortic aneurysm resulting from cystic medial necrosis.
- (b) Rheumatic heart disease usually in association with mitral valve disease.
- (c) Syphilitic (luetic) aortitis (now rare) with dilation of the aortic valve ring.

Pulmonary valve. This valve is most commonly affected by congenital malformations occurring either alone or along with other congenital defects, such as in the tetralogy of Fallot. It is rarely involved in rheumatic heart disease, although it may be involved in the carcinoid syndrome

Mitral stenosis: rheumatic heart disease

Mitral insufficiency: myxomatous degeneration (mitral valve prolapse)

(it can be a component of Marfan syndrome).

The floppy mitral valve disease:- is because of myxoid degeneration inside the collagen:-the valve shape change to parachute that's why the floppy mitral disease is called the parachuting of the mitral valve, effect only the mitral valve, one of the most important reason of regurgitation of mitral valve

A child is infected by endocarditis or rheumatic fever with bicuspid valve you should replace his valve

If the patient is Saudi and he have regurgitation of mitral valve :- you say he has rheumatic fever (we don't consider The floppy mitral valve disease unless we investigate the Johns criteria)

The tricuspid valve can be affected in endocarditis specially in drug addicted

Fish-mouth (buttonhole) valve:-the 3 cusps has been fused (because of inflammation , fibrosis (the chordae tendineae get pulled because of fibrosis) and dystrophic calcification)

carcinoid syndrome :rare Valvular disease that like to effect the right side of the heart.

carcinoid syndrome is commonly seen in tricuspid (regurgitation) and sometimes in pulmonary valves .so it is one of the rare causes of in tricuspid regurgitation

The carcinoid tumor secrete vasoactive amine and from it 5 hydroxytryptamine (serotonin)

The vasoactive amine when it goes to the lung it gets inactivated that's why you don't get infection of the left side of the heart in the case of carcinoid syndrome in the case of carcinoid syndrome

Calcific Aortic Stenosis:-

The most common of all valvular abnormalities,

The consequence of age-associated "wear and tear.

heaped-up calcified masses within the aortic cusps.

It ultimately protrude preventing the opening of the cusps.

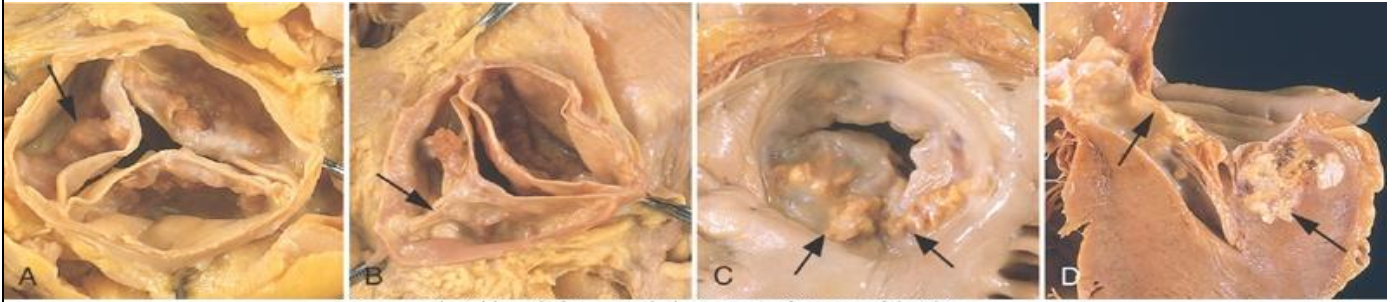
Microscopically, the layered architecture of the valve is largely preserved.

Valve becomes stiff and fibrotic, impeding blood flow with LV contraction

Results in LV hypertrophy, increased O2 demands, and pulmonary congestion.

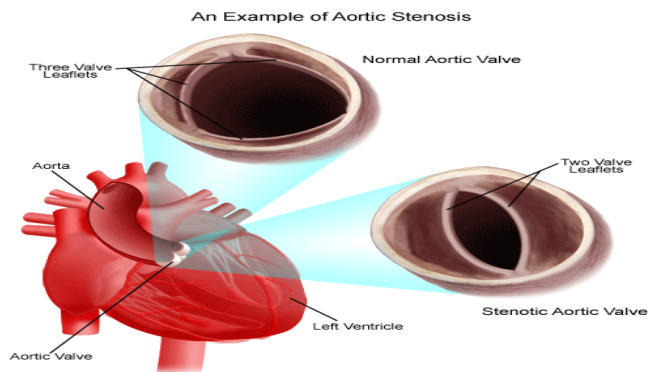
Causes – rheumatic fever, congenital, atherosclerosis

Atherosclerosis and calcification is primary cause in the elderly



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Bicuspid Aortic Valve Stenosis



Calcific valvular degeneration. **A**, Calcific aortic stenosis of a previously normal valve (viewed from aortic aspect). Nodular masses of calcium are heaped up within the sinuses of Valsalva (*arrow*). Note that the commissures are not fused, as in post-rheumatic aortic valve stenosis. **B**, Calcific aortic stenosis of a congenitally bicuspid valve. One cusp has a partial fusion at its center, called a *raphe* (*arrow*). **C** and **D**, Mitral annular calcification, with calcific nodules at the base (attachment margin) of the anterior mitral leaflet (*arrows*). **C**, Left atrial view. **D**, Cut section of myocardium

Symptoms Angina, Syncope, Congestive Heart Failure (CHF)

- Complications – right sided heart failure, pulmonary edema, and A-fib

Aortic Regurgitation

- **Etiologies**
 - Abnormalities of the Leaflets
 - Rheumatic, Bicuspid, Degenerative
 - Endocarditis
 - Dilation of the Aortic Annulus
 - Aortic Aneurysm / Dissection
 - Inflammatory
 - Inheritable (Marfans, Osteogenesis Imperfecta)

Mitral Stenosis

Etiologies

Rheumatic – almost all cases in adults

Mitral Annular Ca⁺ - massive (rare)

Congenital – rare

Symptoms of Mitral Stenosis

- **Dyspnea**
 - Pulmonary venous congestion
- **Fatigue**
 - Diminished cardiac output
- **Inability to tolerate increased volume**
- **Inability to tolerate increased HR**
 - Decreased filling
 - Increased LA pressure/PV congestion
- **Hemoptysis**

Mitral Regurgitation

Symptoms:- Fatigue and weakness, Dyspnea and orthopnea, Right sided HF

summary

-Rheumatic fever:-

* is an **immune** and **inflammatory** disorder caused by **group A streptococci**

* Most often in **children**.

rheumatic fever

: effect **the mitral valve (50% of the patient) and aortic valve (45%)**

infective endocarditis:-

* has two type:-acute endocarditis, may be caused by Staphylococcus aureus or other bacteria and sub acute endocarditis, Subacute less destructive and have low mortality).

Non-bacterial thrombotic endocarditis (marantic endocarditis):

*-develop in people who have **chronic debilitating disease**

Aortic stenosis:

calcification of anatomically normal and congenitally bicuspid aortic valves

Questions

Q1:-Which valve that isn't effected by rheumatic fever from the choices:-

A-Mitral valve

B-Pulmonary valve

C-tricuspid valve

D-aortic valve

Q2:- dilation of the ascending aorta, usually related to hypertension and aging is called

A-Aortic stenosis

B-Aortic insufficiency

C-Mitral stenosis

D-Mitral insufficiency

Q3- an adult that has been diagnosed by endocarditis affecting The tricuspid valve

And you see bruises in his arms What do you consider from those symptoms

about the cause of the disease :

A-drug addiction

B- alcohol abuse

C- Congenital disease

D-not from the above

Q4:-which one of the following isn't from Jones major criteria:-

A- pancarditis

B-subcutaneous nodules

C- arthralgia

D- Sydenham chorea

Answers:-

1- B

2- B

3- A

4- C

Q5:. Which of the following types of infection , precedes by several weeks, the development of acute rheumatic fever?

- A. Group A Beta hemolytic streptococcal infection of the pharynx.
- B. Group D Alpha hemolytic streptococcal infection of the heart.
- C. *streptococcus aureus* infection of the lung
- D. *Streptococcus pyogenes* infection of the skin.

Q6:. A 6-year-old boy develops fever, joint pain, and a diffuse skin rash approximately 3 weeks after recovering from a sore throat. Physical examination finds several small skin nodules, and laboratory examination finds an elevated erythrocyte sedimentation rate(ESR) along with an elevated antistreptolysin O titer. Which of the following abnormalities is most characteristic of this boy's disease?

- A. Anitschkow cells within the epidermis.
- B. Aschoff bodies within the myocardium.
- C. Langhans giant cells within the dermis.
- D. Virchow cells within the nasopharynx.

Q7:. A 44-year-old women presents with worsening fatigue and dyspnea. The pertinent medical history is that she had rheumatic fever during childhood. Physical examination finds an early diastolic opening snap with rumbling late diastolic murmur. A chest radiograph shows an enlarged left atrium. Which of the following is the most likely diagnosis?

- A. Aortic regurgitation.
- B. Aortic stenosis.
- C. Mitral regurgitation.
- D. Mitral stenosis.

Answers:

- 5- A
- 6- B
- 7- D