PATHOLOGY OF RHEUMATIC HEART DISEASE, INFECTIVE ENDOCARDITIS AND VALVULAR HEART DISEASE

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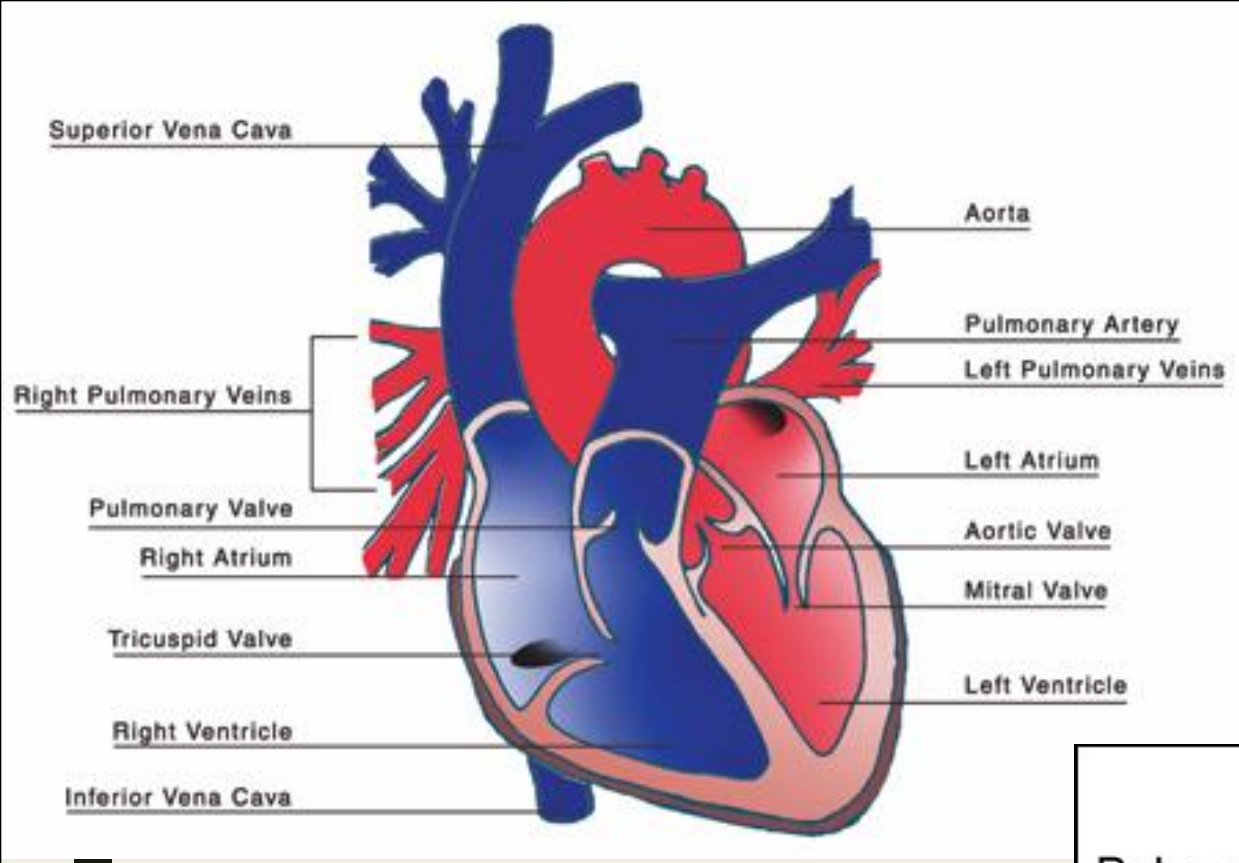
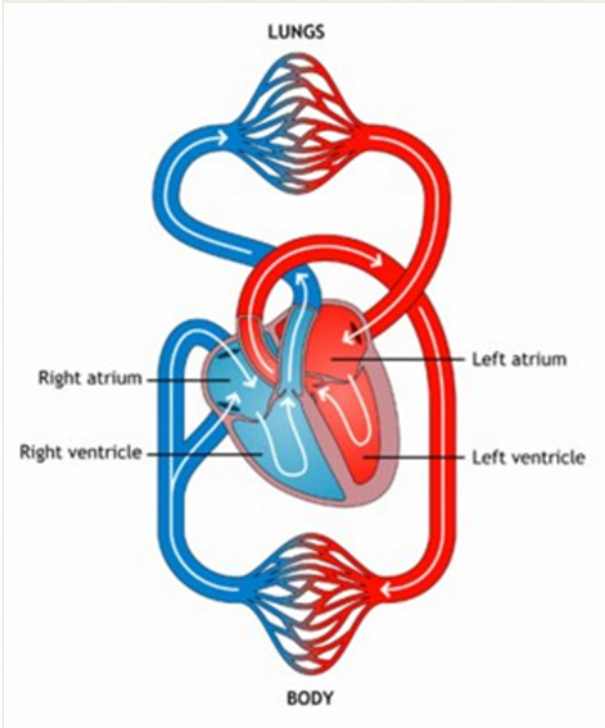
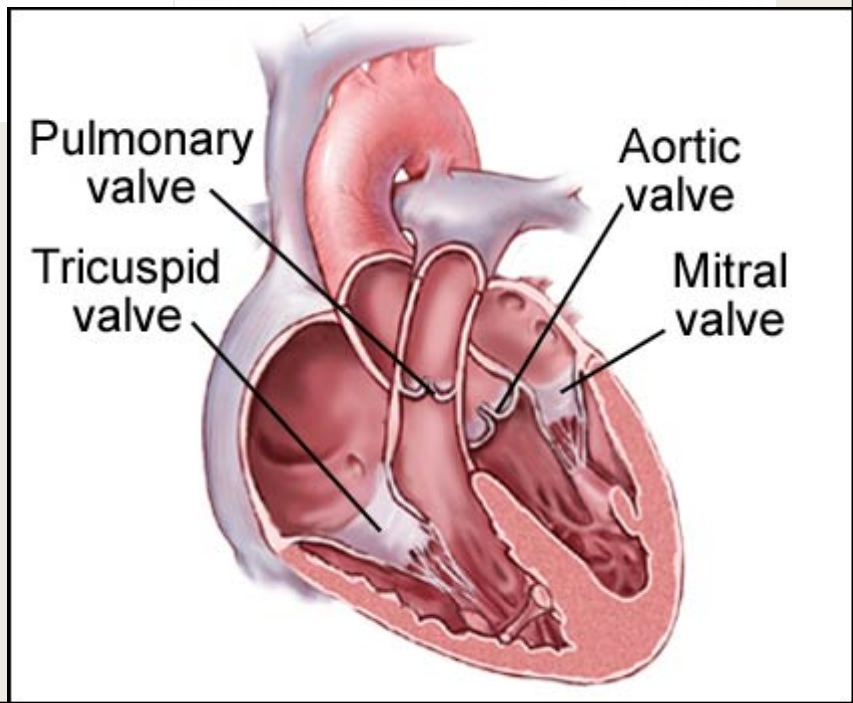
Reference: Robbins & Cotran Pathology and Rubin's Pathology


Superior Vena Cava
Aorta
Pulmonary Artery
Left Pulmonary Veins
Right Pulmonary Veins
Left Atrium
Pulmonary Valve
Aortic Valve
Right Atrium
Mitral Valve
Tricuspid Valve
Left Ventricle
Right Ventricle
Inferior Vena Cava


LUNGS
Right atrium
Left atrium
Right ventricle
Left ventricle
BODY


Pulmonary valve
Aortic valve
Tricuspid valve
Mitral valve

Objectives:

At the end of this lecture, the students should be able to:

(1) 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.

(2) Know the pathological causes and pathophysiological consequences of stenosis and incompetence of all the cardiac valves but particularly the mitral and aortic valves.

(3) Understands the pathology of infective endocarditis so as to be able to identify patients at risk and when appropriate ensure prophylactic treatment is given.

Key principles to be discussed:

(1) Pathology and manifestations of rheumatic heart disease as a major cause of valvular diseases in the Middle East and Saudi Arabia.
(2) Complications of rheumatic heart disease including atrial fibrillation, valvular and atrial thrombus formation with systemic embolism, cardiac failure and infective endocarditis.
(3) Infective endocarditis: predisposing factors, clinical acute and subacute forms, common pathogenic bacteria in IE and complications including valve perforation, thrombosis and septic embolization of the vegetations.
(4) Causes and consequences of valvular heart disease with special emphasis on aortic and mitral valve including "floppy or prolapsed" mitral valve.

RHEUMATIC HEART DISEASE

- Rheumatic heart disease is a heart disease caused by **rheumatic fever**.
- Rheumatic heart disease can be
  - acute or
  - chronic

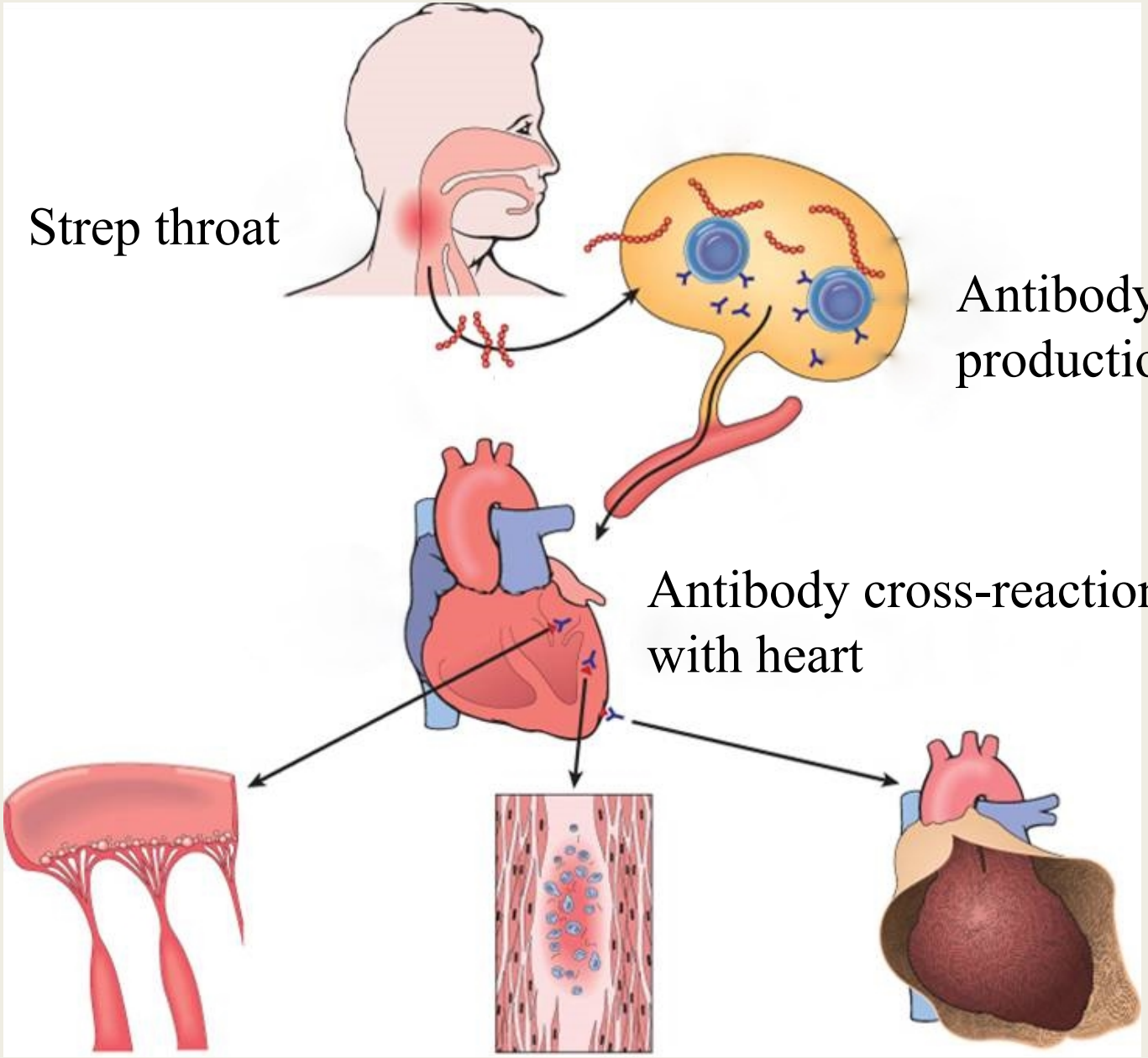
ACUTE RHEUMATIC FEVER

ACUTE Rheumatic Fever

- Definition: Rheumatic fever (RF) is
  - an acute, immune mediated, multi-system inflammatory disease that occurs a few weeks after, group A-beta hemolytic streptococcal infection.
  - It is an acute post-streptococcal non-suppurative inflammatory disease with cardiac and extracardiac manifestations.
  - The inflammation is mainly in the heart, joints, central nervous system and skin.
  - Occurs in only 3% of patients with group A streptococcal pharyngitis.
  - It is seen mainly in children, 5 to 15 years of age.
  - Rheumatic fever is a major health problem in 3rd world countries and in crowded, low socioeconomic urban areas.
  - The incidence and mortality of rheumatic fever has declined over the past 30 years (due to improved socioeconomic condition and rapid diagnosis and treatment of strep. pharyngitis).

Etiopathogenesis:

- The pathogenesis of RF remains unclear and is not yet completely understood.
- It is linked to streptococcal infection. Disease occurs 1 to 5 weeks after pharyngeal infection by Group A beta -Hemolytic Streptococcus.
- It is most likely an immune mediated process in which → the causative organisms (streptococci) stimulates in the formation of antibodies → these antibodies cross react with certain antigens present in the heart and joints → the antigen antibody reaction leads to inflammation.
- Repeated attacks or a single severe attack can lead to → chronic rheumatic heart disease leading to → cardiac failure.


Strep throat
Antibody production
Antibody cross-reaction with heart
vegetations
Aschoff body
pericarditis

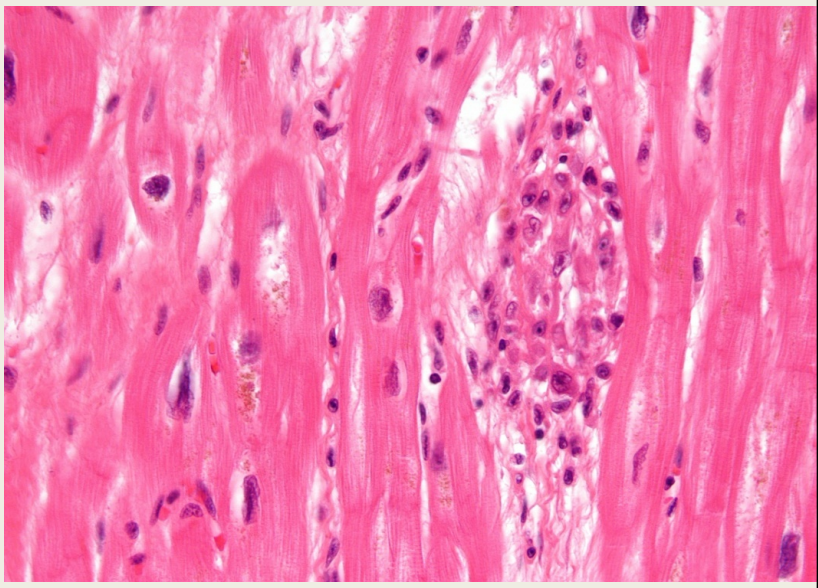
CARDIAC MANIFESTATIONS OF RHEUMATIC FEVER (also called "acute rheumatic heart disease" or "acute rheumatic carditis")

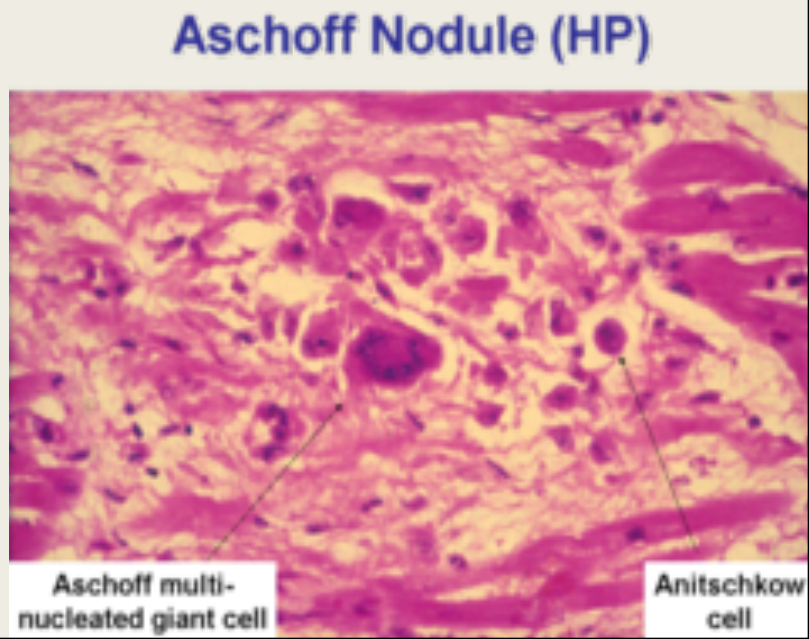
Patients present with pancarditis. Pancarditis is inflammation in all 3 layers of the heart →endocardium, myocardium and pericardium.

1. **Pericarditis**: inflammation of pericardium → fibrinous or serofibrinous secretion in the pericardium. These secretion collect between the visceral and parietal pericardium like butter between two slices bread and therefore also called "bread and butter" pericarditis.
2. **Myocarditis**: inflammation of myocardium → many Aschoff bodies. Can cause sudden death.
3. **Endocarditis**: inflammation of the endocardium including the heart valves (valvulitis) and chordae tendineae → results in fibrin deposition on valve leaflets forming tiny thrombi along lines of closure called rheumatic vegetations. Mitral and aortic valve are mainly involved. This acute inflammation may either resolve completely or progress to scarring with development of chronic fibrotic deformities of the heart valves and chordae tendineae leading to chronic rheumatic heart disease many years later.
4. **Subendocardial lesions** can also be seen, commonly in the left atrium called as **MacCallum plaques**.

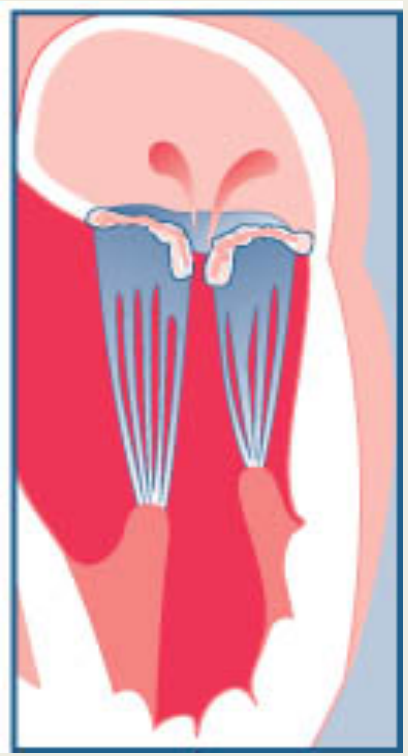
Aschoff bodies

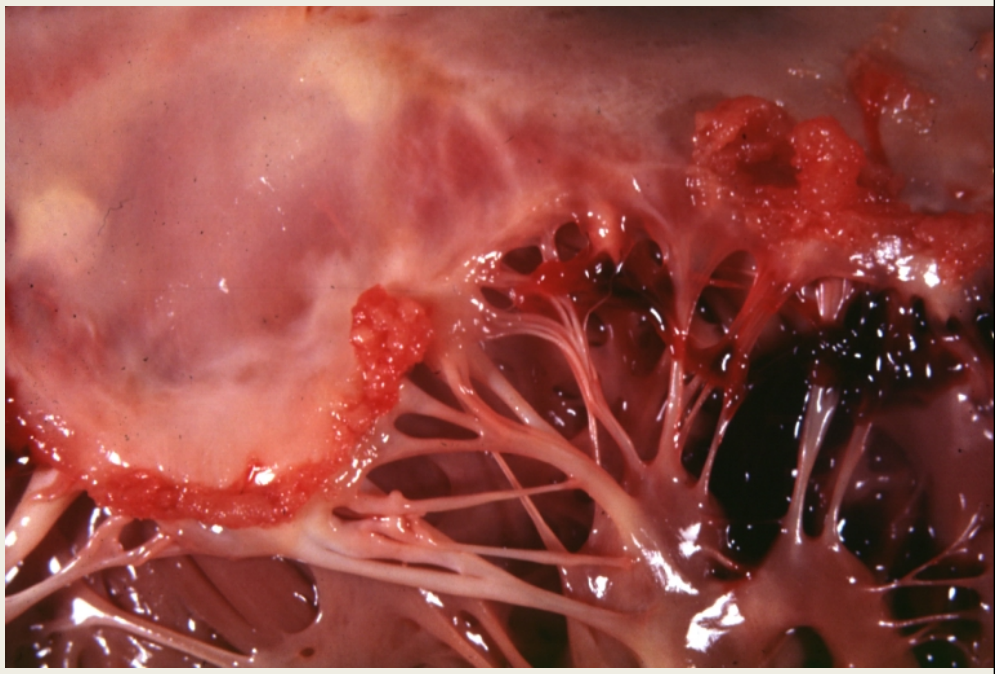
- The characteristic lesion of acute rheumatic fever is the **Aschoff body.**
- **Aschoff bodies** are multiple tiny granulomatous lesions of the heart. They are situated next to small arteries and are characteristically seen in the myocardium (rheumatic myocarditis).
- **An Aschoff body,** consists of:
  1. a focus of eosinophilic collagen necrosis (representing the site of antibody-antigen reaction),
  2. plump activated macrophages/ histiocytes called **Anitschkow/ caterpillar cells.** Some of the macrophages become multinucleated to form Aschoff giant cells.
  3. chronic inflammation.
- **Aschoff bodies** are found mainly in the myocardium and pericardium. Uncommon in the endocardium and heart valves.
- They ultimately "heal" by fibrosis resulting in a nodule of scar tissue.





Rheumatic Vegetations:





1. Tiny (size of a pin's head), sessile arranged in a row and firmly fixed with the underlying tissue.
2. These are situated in the valve cusp, a few millimeters away from the free margin (this is the most traumatized area).

tatic.wikidoc.org/1/1e/Rheumatic_fever_003.jpg

Extra cardiac manifestations of Rheumatic Fever:

Involvement of Other Organs

- **Joints:**
  - Arthralgia
  - Migratory polyarthritis which is "fleeting arthritis" in the large joints e.g. knee, ankle, elbow wrist etc. It is self limiting with no chronic deformities. Aschoff bodies may be present in the synovial membrane, joint capsule, ligament etc. with joint effusion.
- **Skin:** skin nodules → erythema marginatum.
- **Subcutaneous tissue:** Rheumatic nodules mainly seen over the bony prominences e.g. knuckle, elbow, patella etc.
- **Neurologiocal disorder**: Sydenhem's chorea (St. Vitus' dance) characteristized by series of rapid involuntary purposeless movements of the face and arms. This occurs late in the disease.
- **Lung**: uncommon, chronic interstitial inflammation and fibrinous pleuritis.

Acute Rheumatic Fever: Clinical features

- Peak incidence: 5-15 years.
- History of sore throat: symptoms start 10 days to 6 weeks after by group A Streptococcal pharyngitis
- By that time the symptoms start the throat/ pharangeal cultures are usually negative.
- Serum **antistreptolysin O** (**ASO titer/** antibodies to group A streptococcal antigens), anti-DNAase B, and antihyaluronidase are raised and provide evidence of a recent infection with group A Streptococcus.
- Acute symptoms usually subside within 3 months
- The mortality from acute rheumatic carditis is low.

There is no specific test for rheumatic fever. The diagnosis is made based on the clinical findings when either:

1. **two major or**
2. **one major and two minor**

clinical features / criteria are met. This is called as the Jones criteria.

Acute Rheumatic Fever: Clinical Features continued....

JONES CRITERIA:

Major criteria/ clinical features

- Carditis (murmurs, pericardial friction rubs, weak heart sounds, tachycardia and arrhythmias cardiomegaly, pericarditis, and congestive heart failure)
- Migratory polyarthritis of the large joints
- Erythema marginatum of the skin
- Subcutaneous nodules
- Sydenhem's chorea (St. Vitus' dance)

Minor criteria / clinical features

- Previous rheumatic fever
- Arthralgia
- Fever
- Lab tests indicative of inflammation — ESR (erythrocyte sedimentation rate), CRP (C-Reactive protein), leukocytosis
- EKG changes

CHRONIC RHEUMATIC HEART DISEASE

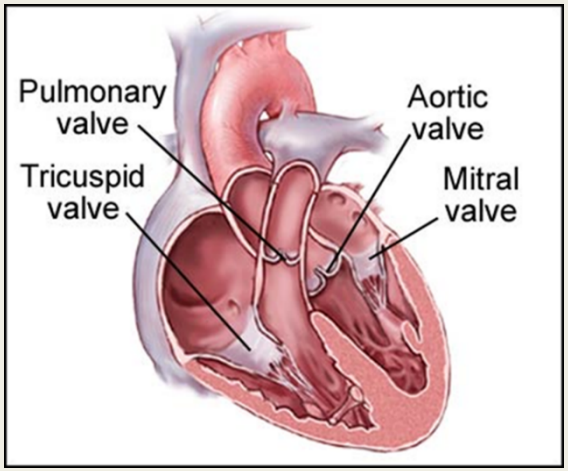
CHRONIC RHEUMATIC HEART DISEASE

- The myocarditis and pericarditis components of RF typically resolve without permanent sequelae.
- In contrast, the acute valvulitis or chordae tendinitis of rheumatic fever heals by fibrosis (scarring) and result in irreversible deformity of the involved cardiac valve and chordae tendineae. Severe valvular scarring develops months or years after acute RF.
- Most harmful effect of rheumatic disease is due to involvement of cardiac valves. The valve leaflets develop diffuse fibrosis, become thickened, shrunken and less movable which can lead to cardiac failure, thromboembolism and infective endocarditis.

CHRONIC RHEUMATIC HEART DISEASE

Valves affected in chronic rheumatic heart disease: left side of heart is more commonly involved than the right.

- Mitral valve alone is most commonly affected
- followed by combined mitral/aortic valve
- Tricuspid valve is rarely affected.
- Pulmonary valve is practically never affected.



Type of damage

- fibrosis of valve leaflets → stenosis (Reduction of diameter)
- fibrosis of chordae tendineae → regurgitation (improper closure)

Therefore patient can have mitral stenosis (most common), mitral regurgitation, aortic stenosis and aortic regurgitation

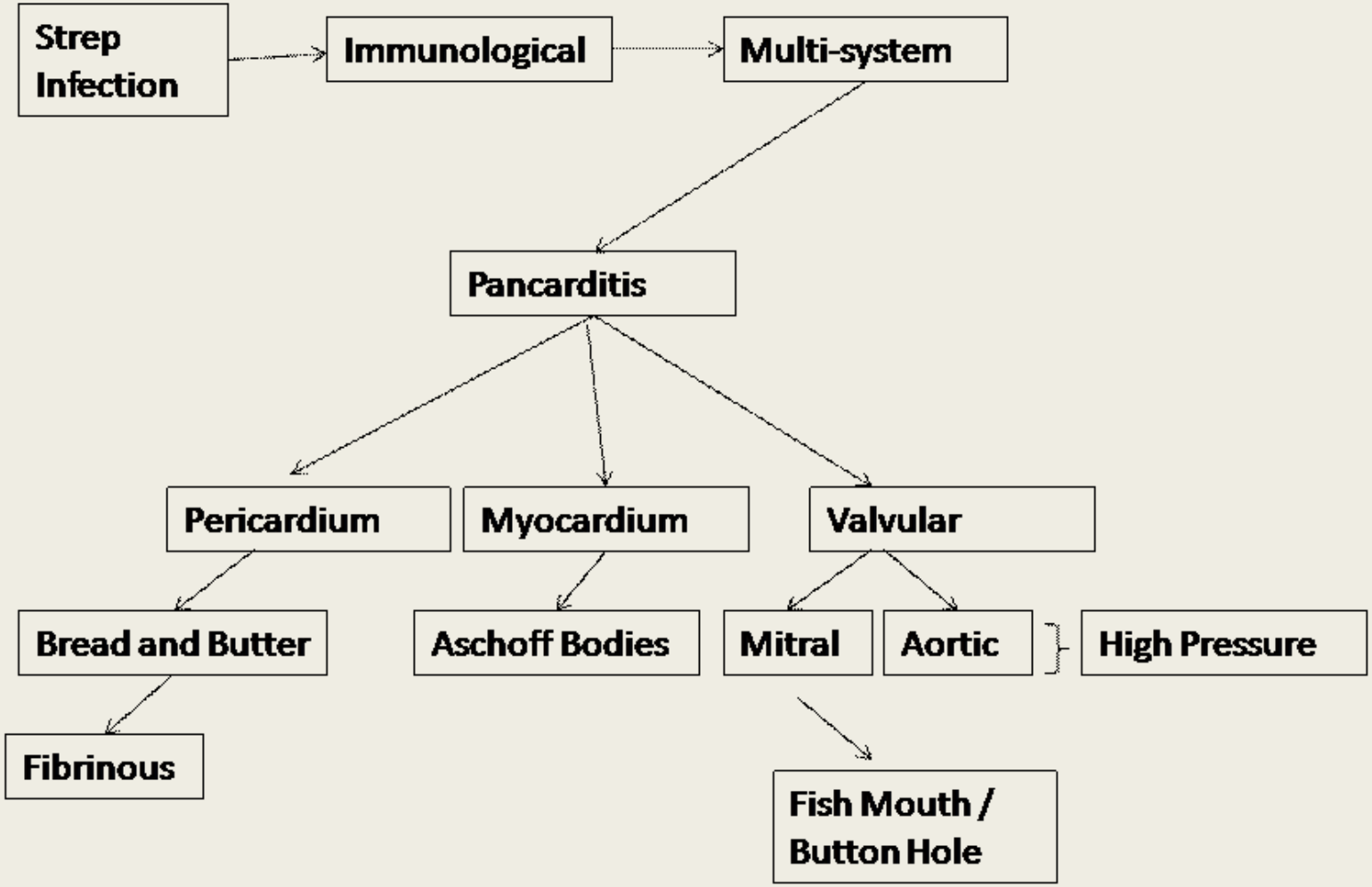
Chronic Rheumatic heart disease: Clinical features

Clinical features

- Occurs many years after the initial episode of rheumatic fever.
- Signs and symptoms depend on the valve(s) involved: cardiac murmurs, arrhythmia, thromboembolism, infective endocarditis etc.
- Treatment may require valve surgery.

Complications

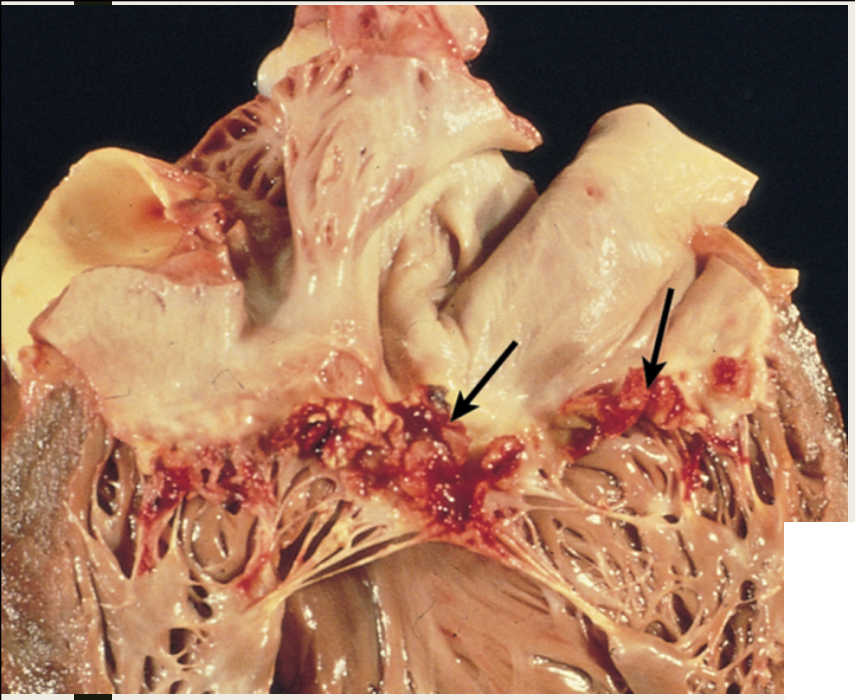
- **Bacterial infective endocarditis:** the scarred valves of rheumatic heart disease provide an attractive environment for bacteria to grow.
- **Mural thrombi** form in cardiac chambers. They give rise to **thromboemboli**, which can produce infarcts in various organs.
- **Congestive heart failure**
- **Adhesive pericarditis**
- **Atrial fibrillation.**

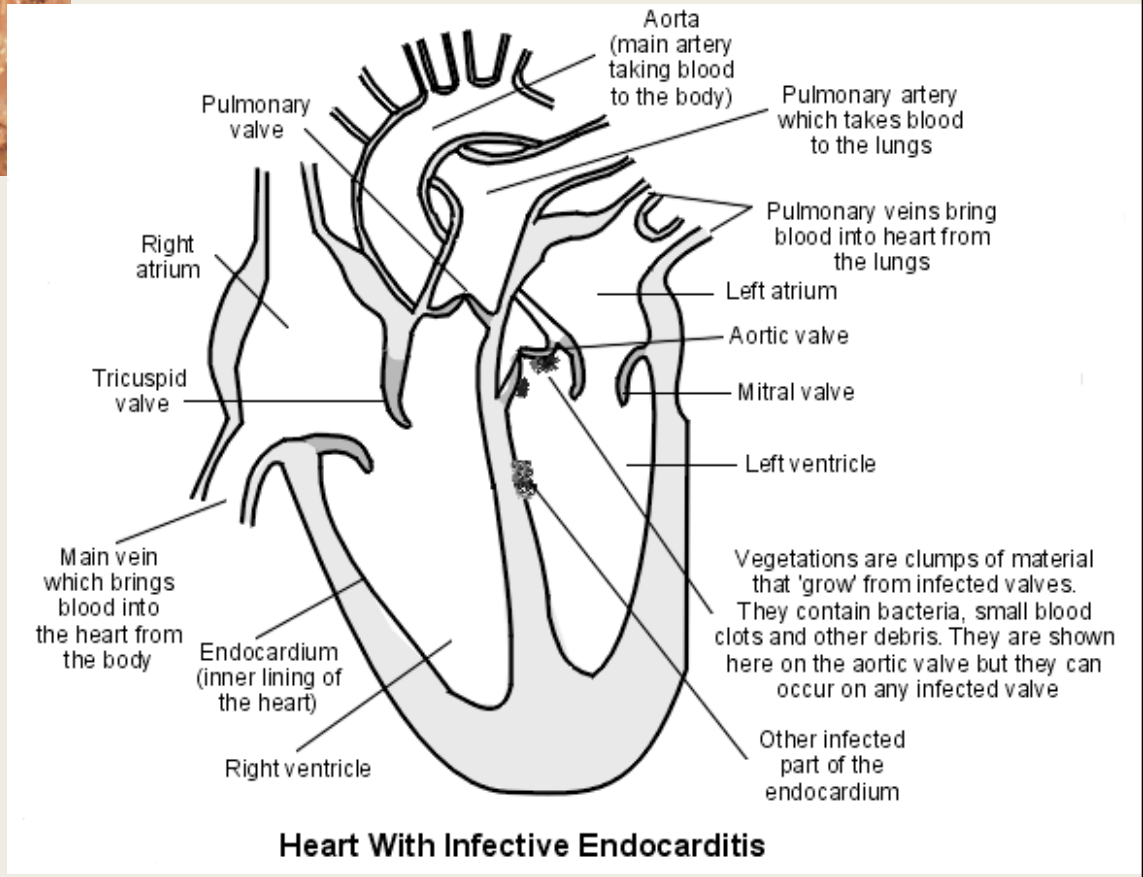


INFECTIVE ENDOCARDITIS

Infective Endocarditis (IE)

- **Definition**: infection of the cardiac valves or inner (mural) surface of the endocardium, resulting in the formation of an adherent mass of thrombotic debris that contains micro-organisms.
- Infective endocarditis is a particularly difficult infection to eradicate because of the avascular nature of the heart valves.
- **IE is Divided into:**
  - ***Acute IE:***
    - ☑ Is caused by highly virulent organisms (**staphylococcus aureus**)
    - ☑ infects even normal/healthy valves,
    - ☑ progresses rapidly,
    - ☑ Has little local host reaction.
  - ***Subacute IE:***
    - ☑ It is an infection in a previously abnormal/ damaged valves by organisms of low virulence (**α-hemolytic streptococci viridans**),
    - ☑ progresses slowly,
    - ☑ It induces a local inflammatory reaction.
- Prognosis: depends to some extent on the infecting organism and the stage at which the infection is treated. About 1/3rd of cases of Staph. aureus endocarditis are still fatal.





Heart With Infective Endocarditis

http://m.patient.media/images/127.gif

Risk factors of Infective Endocarditis:

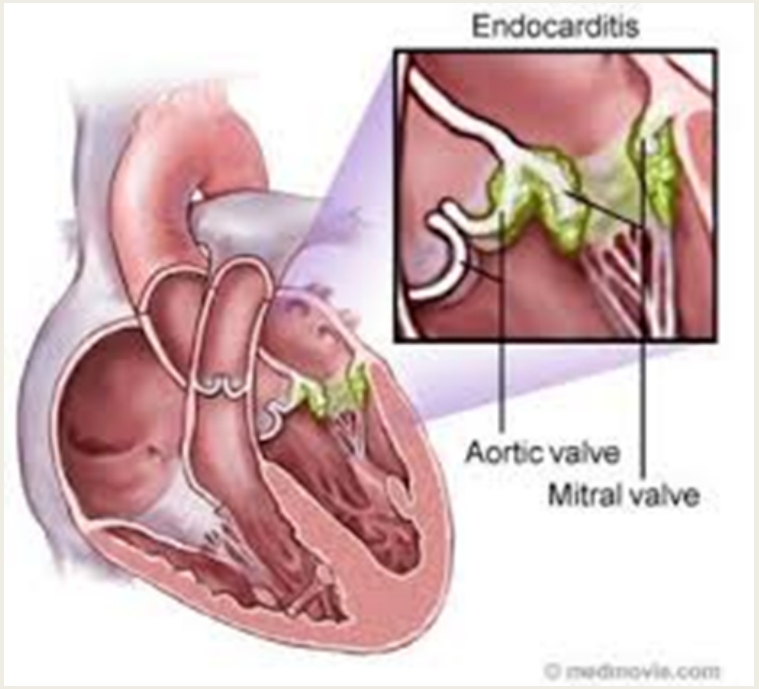
In children: an underlying cardiac lesion (congenital heart disease is most common).

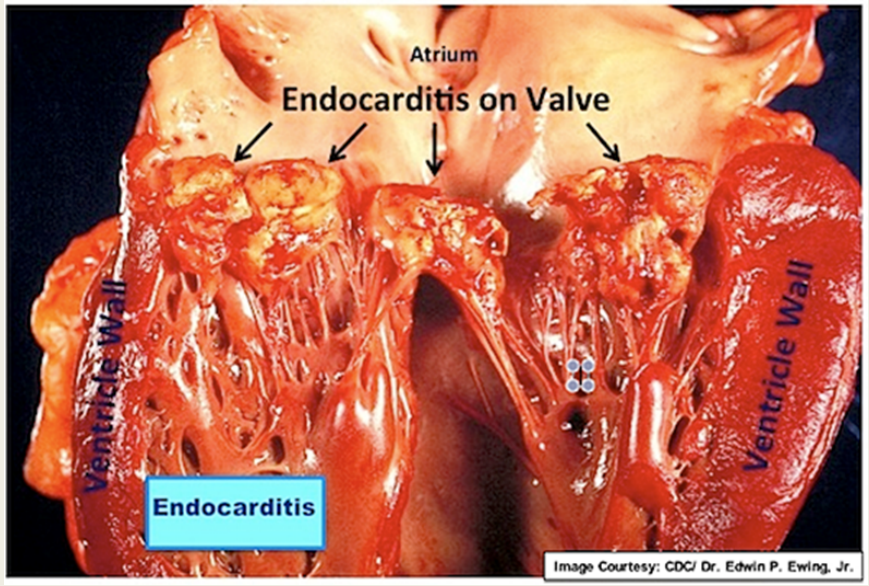
In adults: More than half of adults with bacterial endocarditis have no predisposing cardiac lesion. Others are:

1. **Mitral valve prolapse and congenital heart disease** are the common risk factors for bacterial endocarditis in adults.
2. **Rheumatic heart disease**.
3. **Intravenous drug abusers** can inject micro-organisms intravenously when taking intravenous drugs, leading to IE. The **tricuspid valve** is most commonly infected. About 50% of the IE in IV drug abusers are caused by **S. aureus.**
4. **People with prosthetic valves** are at high risk of developing IE . Prosthetic valve endocarditis is caused commonly by **coagulase-negative staphylococci** (e.g. S. epidermidis).
5. **Transient bacteremia from any procedure** may lead to infective endocarditis e.g. dental procedures, urinary catheterization, infected indwelling vascular catheters gastrointestinal endoscopy, and obstetric procedures.
6. **The elderly** (they have degenerated of heart valves e.g. calcific aortic stenosis), **diabetics and pregnant women** are at increased risk.

Infective Endocarditis:

- Mitral valves are the most common sites of IE followed by aortic valve.
- In IV drug users, the right side valves (tricuspids) are commonly involved.
- Vegetations can be single or multiple, involve one or more valve(s), differ in appearance according to the causative agent.





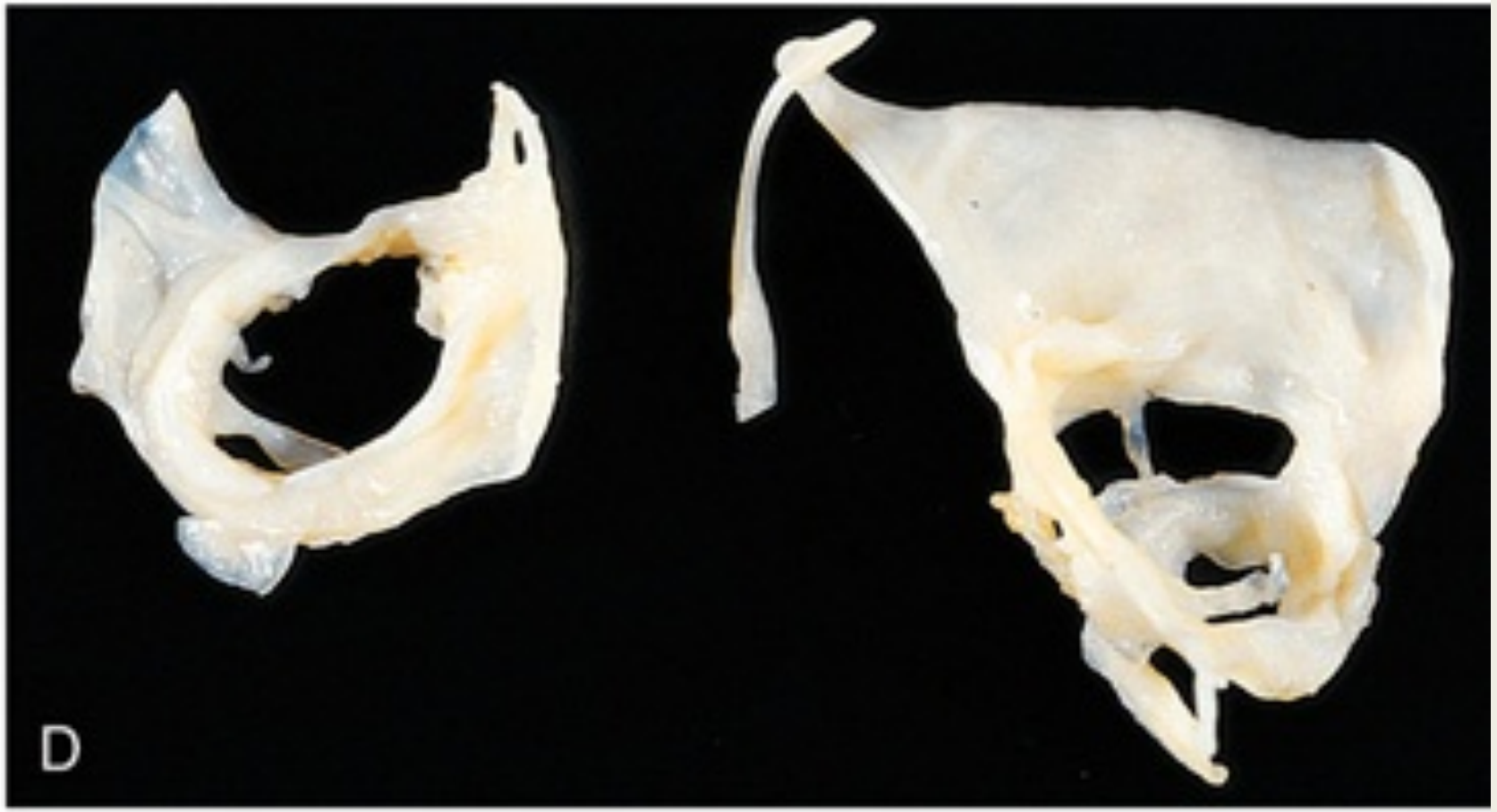
Infective Endocarditis:

Common clinical features

- **fever**, fatigue, weight loss and chills.
- Cardiac **murmurs**.
- **Splenomegaly, petechiae, and clubbing** of the fingers.
- **Positive blood culture** for the organisms (only minority of cases remain negative).

Complications:

- Ulceration and perforation of valves
- Rupture of chordae tendineae
- Arrhythmias, valvular regurgitation and congestive heart failure (due to destruction of a valve).
- Septicemia
- Septic systemic embolization of infected vegetations which travel to multiple sites, causing infarcts or abscesses in many organs (e.g. neurologic deficits due to embolization to the brain or infarcts of the myocardium due to embolization to the coronary artery),
- In IV drug addicts (tricuspid valve/ right sided endocarditis) → pulmonary emboli.
- Mycotic/ infected aneurysms of vessels.
- Renal failure



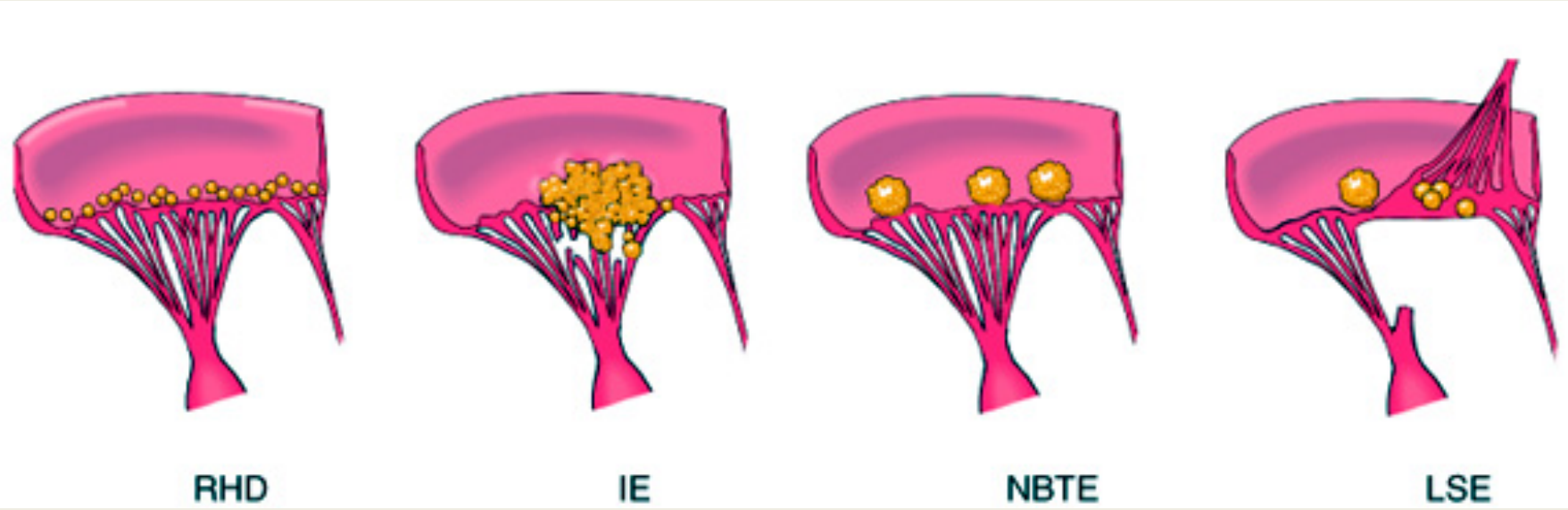
D. Gross photograph illustrating healed endocarditis with perforations on bicuspid aortic valve

Other types of endocarditis

1. **Libman-Sacks endocarditis:** Less common, non-infective, verrucous endocarditis associated with elevated levels of circulating immune complexes. **Seen in patients with systemic lupus erythematosus**
2. **Endocarditis seen in carcinoid syndrome:** Secretory products of carcinoid syndrome, especially 5-hydroxytryptamine can cause endocarditis. The endocardial plaques are seen in the right side of heart
3. **Nonbacterial thrombotic endocarditis (marantic endocarditis)**
   - ❖ Characterized by sterile vegetations on the leaflets of the cardiac valves. There is no infective organism. It is aseptic.
   - ❖ **Pathogenesis/ association:**
     - Subtle endothelial abnormalities.
     - Hypercoagulability.
     - Association with malignancy (50%) and other debilitating diseases.
   - Aortic valve most common site.
   - May embolize to different parts of the body including brain, but the emboli are sterile.

(Note: sterile = no infection,

vegetations = small masses of fibrin, platelets and other blood components)



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

Robbin and Cotran Pathology

VALVULAR HEART DISEASE

Valvular Heart Disease

Two basic types:

1. Stenosis of valves: failure to open
2. Regurgitation of valves: Insufficiency or failure to close

Both cause murmurs

Causes

- Congenital
- Acquired
  - post inflammatory scarring e.g. as a late complication of rheumatic fever (most common) or secondary to various other inflammatory processes.
  - can occur even with prosthetic cardiac valves
  - can be secondary to thrombus formation or infectious endocarditis.

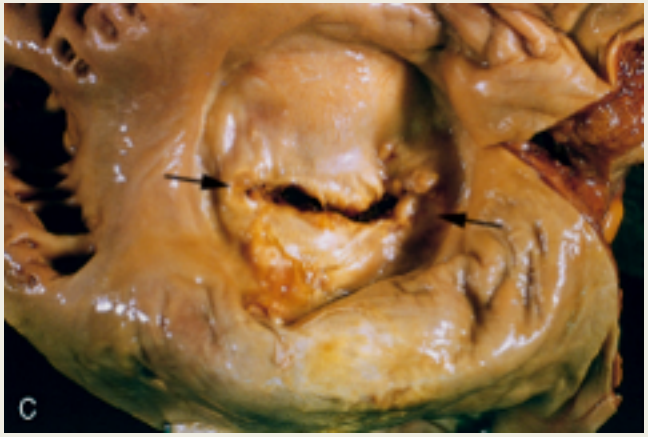
MITRAL VALVE

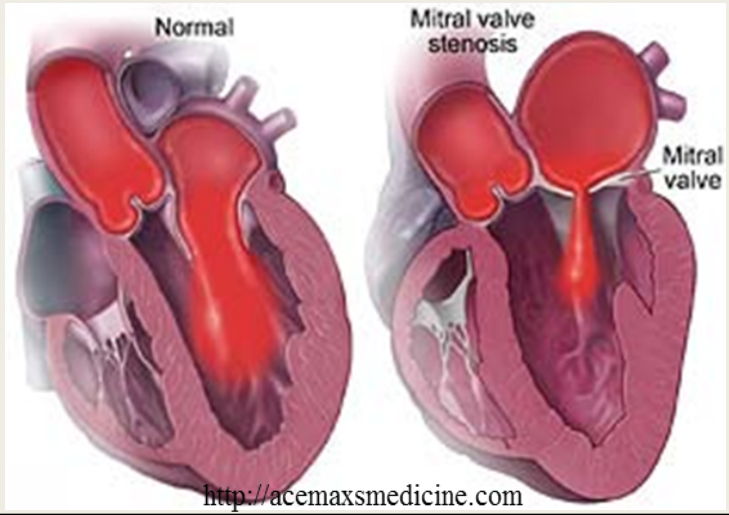
Mitral valve Prolapse

- It is the most frequent valvular lesion in developed countries
- Seen in young women.
- There is myxoid/mucoid degeneration of the valve which causes ballooning of mitral valves (floppy cusp).
- It results in stretching of the mitral valve, producing a parachute deformity of the cusp with prolapse of the cusp into the atrium during systole. These changes produce a characteristic systolic murmur.
- Pathogenesis unknown
- Can be associated with Marfan syndrome
- Most patients asymptomatic but can occasionally lead to mitral insufficiency and arrhythmias.
- Patients are predisposed to infective endocarditis.

Mitral stenosis

- Mitral stenosis is more common than mitral regurgitation.
- Most common cause → rheumatic heart disease.
- In mitral stenosis (picture):
  - Leaflets are thickened, fibrotic and fused leading to fish mouth/button hole deformity (stenosed valve looks like fish's mouth or button hole)
  - Increased pressure, dilatation and hypertrophy of left atrium.
  - secondary deposition of Ca++
  - Pulmonary hypertension and lungs are firm and heavy (chronic passive congestion).
  - Right heart may be affected later (right ventricular hypertrophy).





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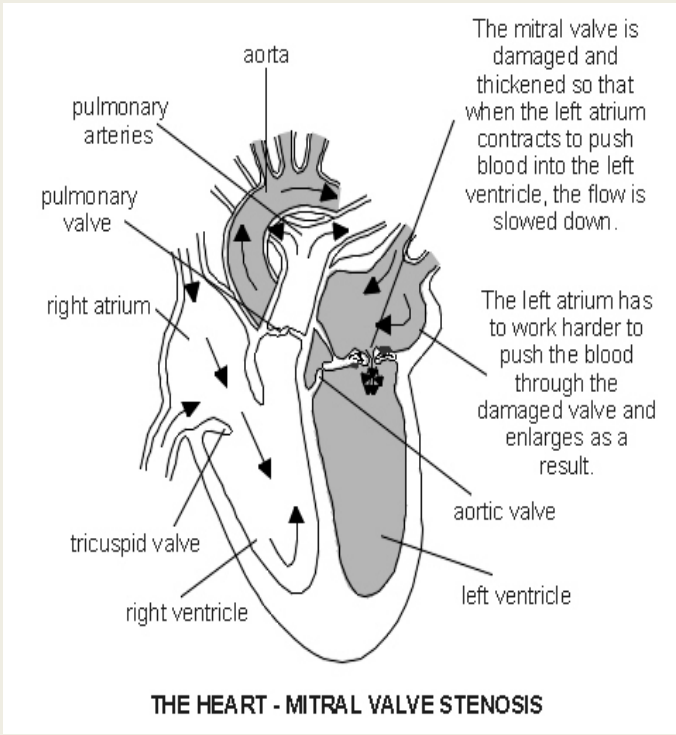


http://medical.cdn.patient.co.uk/images

Mitral regurgitation

- Is usually due to rheumatic heart disease.
- can also be due to mitral valve prolapse, infective endocarditis, papillary muscle injury in myocardial infarction etc.
- Leads to left vent. hypertrophy and dilatation.

AORTIC VALVE

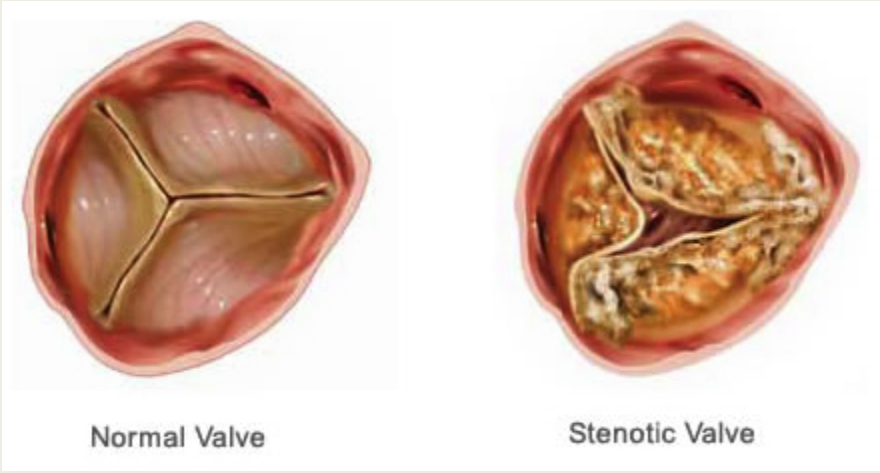
Aortic stenosis

Commonly caused by calcification and is called as calcific aortic stenosis. Calcific aortic stenosis affects:

a) Normal aortic valve as part of the aging degenerative process in > 60 yrs old.

b) Congenital bicuspid aortic valve

c) Valves scarred by rheumatic heart disease



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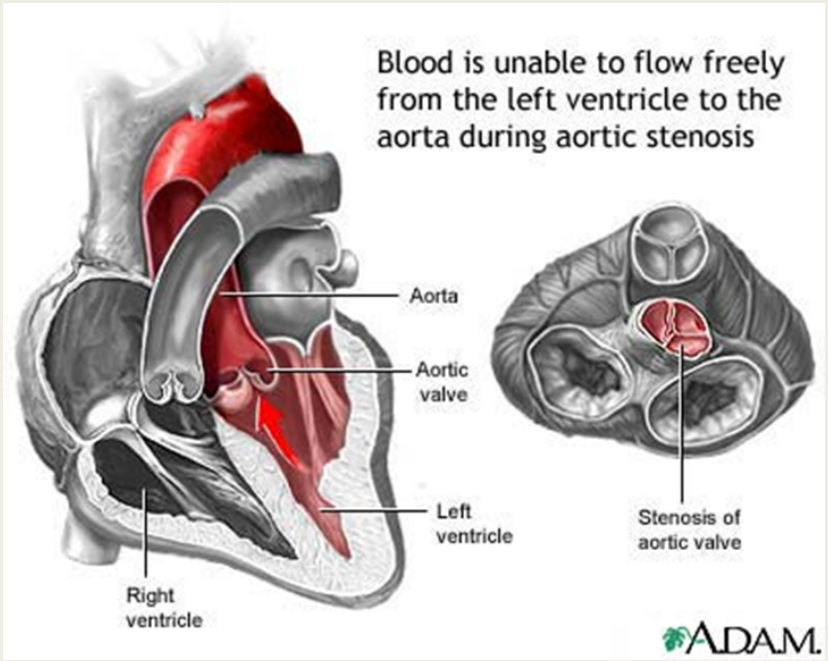

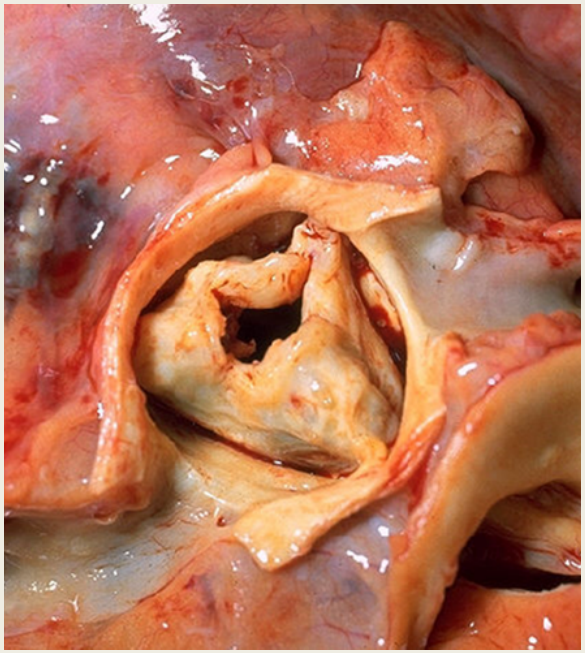

http://www.totalhealth.co.uk/clinical-experts/dr-michael-mullen-and-mr-john-yap/aortic-stenosis-and-transcatheter-aortic-valve-implantation

Aortic regurgitation/ insufficiency

can be caused by:

a) Non-dissecting aortic aneurysm.
b) Rheumatic heart disease
c) Infective endocarditis
d) Syphilitic (luetic) aortitis (rare)

Right side of heart

Valvular heart disease of the right side of heart is very uncommon.