PATHOLOGY TEAM
439

جامعة الملك سعود
King Saud University
1957

Rheumatic fever, endocarditis and heart valves

Rheumatic fever (cardiac lesions)
(recommended before you start studying)

Click here for Pathoma's video lecture part 1

Click here for Pathoma's video lecture part 2

Index:
Important
NOTES
Extra Information

introduction:

Anatomy of the heart:

The heart has three layers

- Pericardial cavity: serous cavity made of two layers parietal and visceral lined by mesothelial cells contain a small amount of fluid between 1 to 2 ml, when the fluid increases that causes pericardial effusion (due to metastatic cancer, TB, inflammation, myocardial infarction), and the aspiration of pericardial fluid can enable us to microbiological culture (Microbiology) and enable us to study the cells (Cytology).

pericardial effusion can cause cardiac tamponade (means pressure on the heart) then cause shortness of breath and pain that increase when the patient lays down.

- Myocardial fibers (Muscles) that covered inside by endocardium which also cover the valves.

- There are papillary muscles and chordae tendineae that hold the valves (Mitral valves and tricuspid valves).

The most common cause of valvular diseases is rheumatic fever.

Anatomy of coronary arteries:

- Left anterior descending coronary artery (Most common artery closed).
- Right coronary artery
- Circumflex coronary artery

some histological features of pathological heart:

- myocardial fibers with enlarged, boxed like nuclei are marks of heart failure
- lipofuscin pigments do not cause any diseases and are a sign of wear-and-tear aging process

Acute Rheumatic fever

Definition

Rheumatic fever is an **ACUTE,** immunologically mediated, multisystem inflammatory disease that occurs after Group A **β-hemolytic streptococcal infectious.**
Or It is an acute post-streptococcal non-suppurative inflammatory disease with cardiac and extracardiac manifestations.

- The inflammation is mainly in the heart (Heart Valves), joints, central nervous system (Brain) and skin.**Note From Prof rikabi (The valves involved in rheumatic cardiac diseases are aortic and mitral valves, can affect tricuspid but is rare. Pulmonary valves are affected Congenitally but not in rheumatic fever).
- It is the most common cause of valve diseases.
- 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.
- It is more common in children.

Etiopathogenesis:

it is not yet clear and not completely understood.

Group A β-hemolytic streptococcal bacteria (found in tonsils and pharynx) stimulate antibodies, by antigenic m-protein

The antibodies cross react with antigens in heart and joints.

Antigen-antibody reaction leads to inflammation.

GAS does not migrate to the heart in rheumatic fever itself.

RHEUMATIC HEART DISEASES

It is known as the heart disease that is caused by Rheumatic fever.

Classification:

ACUTE

CHRONIC

CARDIAC MANIFESTATIONS OF RHEUMATIC FEVER

Acute rheumatic heart disease

in this case patient comes with a **pancarditis.**
Pancarditis:
is an inflammation of all the 3 layers of the heart
-Pericardium ,Myocardium , Endocardium (the endocardium covers the valves)

Cardiac manifestations

Pericarditis

inflammation of Pericardium.
fibrinous or serofibrinous secretion in the pericardium between visceral and parietal layer
- **bread-butter** appearance

Myocarditis

inflammation of Myocardium
- many Aschoff bodies.
- can cause **sudden** death

Endocarditis

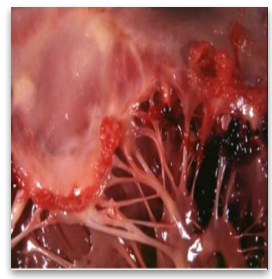
inflammation of Endocardium
- results in fibrin deposition on valve leaflets forming tiny thrombi along lines of closure called rheumatic vegetations.
- **Mitral and aortic** valve are mainly involved.
- may either resolve completely or or progress to scarring with development of chronic fibrotic deformities of the heart valves and chordae tendineae
- **Thus leading to chronic rheumatic heart disease many years later.**

Subendocardial lesions

may be seen commonly in left atrium
Called **MacCallum plaques.**

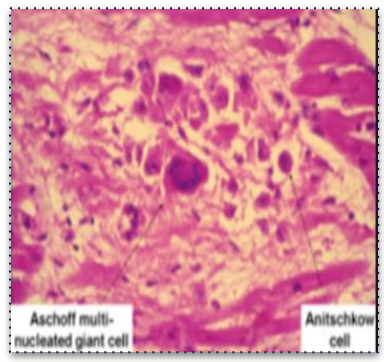
Rheumatic Vegetations

Definition	Tiny (size of pin's head), sessile arranged in a row and firmly with the underlying tissue.
Site	These are situated in the valve cusp, a few millimeters away from the free margin(this is the traumatized area).
From robbins	Valve involvement results in fibrinoid necrosis and fibrin deposition along lines of closure that cause disturbance in cardiac function.



Aschoff bodies
(characteristic lesion of acute rheumatic fever)

Definition	multiple tiny granulomatous lesions of the heart.
Components	1. A focus of **eosinophilic collagen necrosis** (site of antibody-antigen reaction) 2. **Anitschkow/ caterpillar cells** which is Plump activated macrophages/ histiocytes.(Some of the macrophages become multinucleated to form Aschoff giant cells). 3. chronic inflammation.
Site	- found mainly in the myocardium and pericardium. - situated next to small arteries - characteristically seen in the myocardium (rheumatic myocarditis).
The result	They ultimately "heal" by fibrosis resulting in a nodule of scar tissue.



Extracardiac manifestations of Rheumatic Fever:

Joints

- Arthralgia

- **Migratory polyarthritis** which is "fleeting arthritis" in the large joints

Skin

- Skin nodules
- Erythema marginatum

Subcutaneous tissue

- Rheumatic nodules mainly seen over the bony prominences

Neurological disorder

- **Sydenham'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.

Peak incidence: 5-15 years (4-14 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/ pharyngeal cultures are usually negative.

Clinical Features

Acute symptoms usually subside within 3 months

-High serum antistreptolysin O (ASO titer/ antibodies to group A streptococcal antigens)
-High serum Anti-DNAse B
-High serum Antihyaluronidase

The mortality from acute rheumatic carditis is low.

It is best to use throat swab to diagnose ASO

- may also affect adults more than one major criterion shows
- mostly affects Africa, middle east and southeast Asian parts
- may also be genetic (genes in chromosome No.6 makes them more susceptible to be affected)

JONES CRITERIA

Definition: when clinical features / criteria are met.
There is no specific test for rheumatic fever.

The diagnosis is made based on the clinical findings when either:
two major or one major and two minor

MAJOR	MINOR
Carditis (murmurs, pericardial friction rubs, weak heart sounds, tachycardia and arrhythmias cardiomegaly, pericarditis, and congestive heart failure)	**Lab tests indicative of inflammation** - high ESR (erythrocyte sedimentation rate) - CRP (C-Reactive protein) - leukocytosis
Migratory polyarthritis of large joints	**Arthralgia**
Erythema marginatum of skin (not in the face, irregular red margin)	**Previous** rheumatic fever
Subcutaneous nodules	**Fever** with malaise
Sydenham's chorea (St. Vitus' dance) (It is involuntary movement and grimaces, and is not common in chronic cases)	**ECG changes (PR interval prolonged,might be because heart block)**

Chronic Rheumatic Heart Disease

is the result of valvular damage caused by an abnormal immune response to Streptococcus pyogenes infection

Rheumatic fever can affect

Endocarditis

Cause

- **acute valvulitis**
- **chordae tendinitis**

-They heal by **fibrosis(scarring)**,and result in irreversible deformity of the involved cardiac valve and chordae tendineae.

-**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.
- Infective endocarditis.

myocarditis
pericarditis

are components of RF
typically
resolve without permanent sequelae

Valvular heart disease

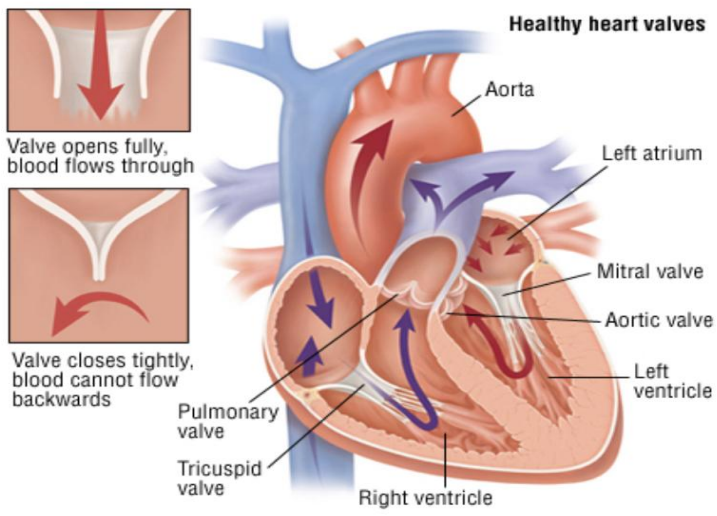
- Left side of heart is more commonly involved than the right.
-Therefore patient can have mitral stenosis (most common), mitral regurgitation, aortic stenosis and aortic regurgitation

- **Mitral valve** alone is **most commonly** affected
- followed by combined **mitral/aortic valve**
- Tricuspid valve is rarely affected
- Pulmonary valve is practically never affected (only congenital abnormalities)

Type of damage

stenosis
fibrosis of valve leaflets
(Reduction of diameter)

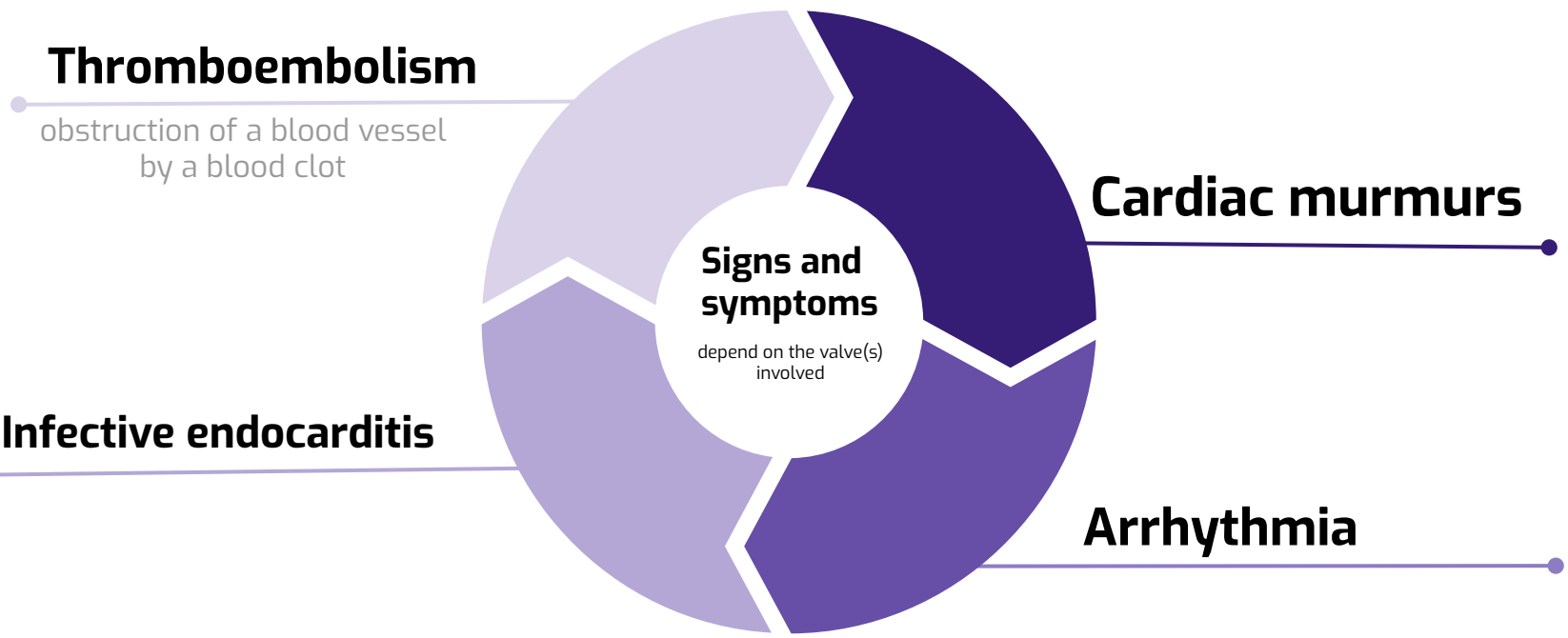
regurgitation
fibrosis of chordae tendineae
(improper closure)



Chronic Rheumatic heart disease

Clinical features

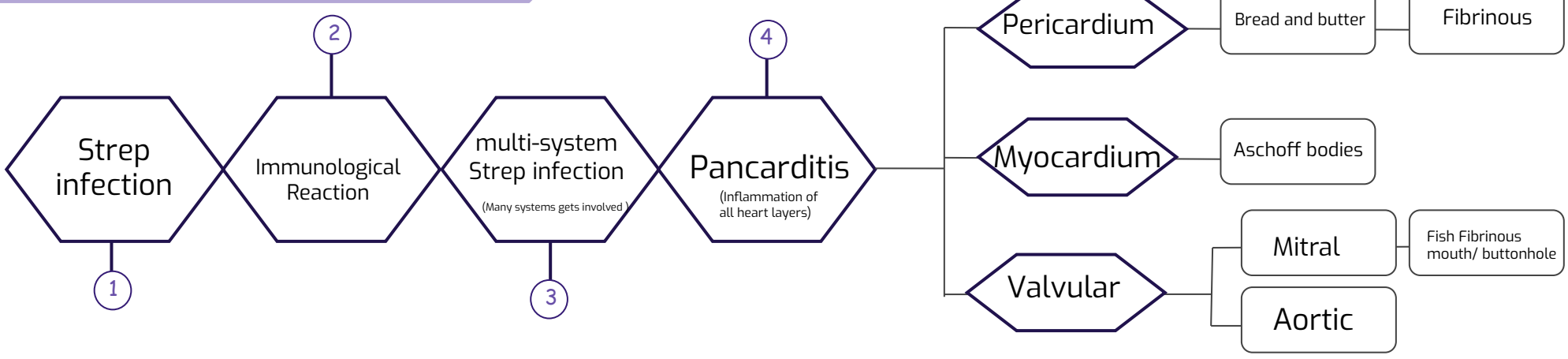
-Occurs many years after the initial episode of rheumatic fever.
- Treatment may require valve surgery.



Complications

1. **Bacterial infective endocarditis :** the scarred valves of rheumatic heart disease provide an attractive environment for bacteria to grow
2. **Mural thrombi :** form in cardiac chambers. They give rise to thromboemboli, which can produce infarcts in various organs.
3. **Congestive heart failure**
4. **Adhesive pericarditis** adhesions between the two pericardial layers
5. **Atrial fibrillation** a condition in which the heart beats with an irregular or abnormal rhythm

Summary



Infective Endocarditis

Definition	infection of the cardiac valves or mural/ inner surface of the endocardium, resulting in the formation of an adherent mass of thrombotic debris mixed with microorganisms.		
Valves	- **Mitral valves** are the most common sites of IE followed by **aortic valve**. - **Vegetations** may be single or multiple, involve one or more valve(s), differ in appearance according to the causative agent.		
Divided into		Acute IE	Subacute IE
	Microorganism	highly virulent organisms (staphylococcus aureus)	low virulence (hemolytic streptococci viridans),
	Valves involved	normal/healthy valves, (mainly tricuspid valves)	previously abnormal/ damaged valves
	Prognosis	rapidly	slowly
	host reaction	Has little local host reaction	It induces a local inflammatory reaction.
	causes	(risk factors mentioned next)	- rheumatic valvular diseases (like from previous rheumatic fever) - congenital heart disease - people that have artificial valve
	prophylaxis	------	long acting antibiotics before dental treatment or other surgical procedure (even if it is minor) especially if artificial valve is present.
Prognosis	Prognosis: depends to some extent on the offending organism and the stage at which the infection is treated. About 1/3rd of cases of Staph. aureus endocarditis are still fatal.		

Risk Factors

1

Children
an underlying cardiac lesion (congenital heart disease is most common).

2

Adults
More than half of adults with bacterial endocarditis have no predisposing cardiac lesion. Mitral valve prolapse and congenital heart disease are the most frequent cause for bacterial endocarditis in adults.

3

Rheumatic Heart Disease
Also The elderly (due to degeneration of heart valves e.g. calcific aortic stenosis) can be of risk ,
diabetics and pregnant women are at increased risk.

4

Intravenous drug abusers
end up injecting micro organisms intravenously
when taking intravenous drugs, leading to IE. The tricuspid valve is infected in half of cases. About 50 % of the IE in IV drug abusers are caused by S. aureus.

5

Prosthetic valves
Prosthetic valve endocarditis is caused commonly by coagulase negative staphylococci (e.g. S. epidermidis).

6

Transient bacteremia
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.

Clinical Features

- fever , fatigue, weight loss and chills.
- Cardiac murmurs
- after 6 weeks: splenomegaly, petechiae , and clubbing of the fingers.
- Positive blood culture for the organisms (only minority of cases remain negative).
- Olser's node (painful)
  Roth spots (eye hemorrhage)

Complications

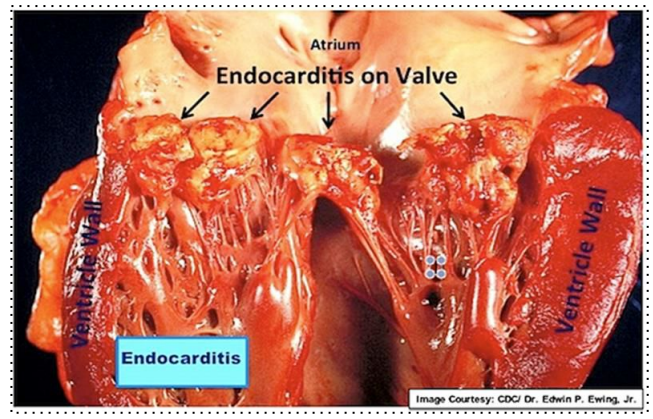
Septicemia or septic systemic embolization of infected vegetations which travel to multiple sites, causing infarcts or abscesses in many organs (e.g. neurologic deficits due to embolization to the brain or infarcts of the myocardium due to embolization to the coronary artery)

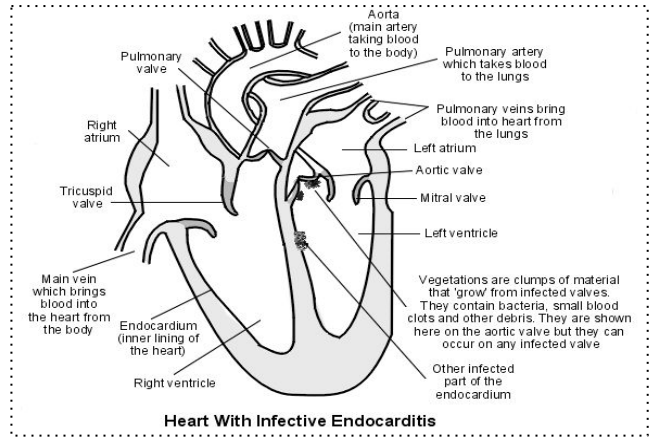
Pulmonary emboli is seen in tricuspid valve/ right sided endocarditis e.g. IV drug addicts.

Arrhythmias, valvular regurgitation and congestive heart failure (due to destruction of a valve).

Valve ulceration & perforation, rupture of chordae tendineae.

Mycotic/infected **aneurysms** of vessels & **renal failure**

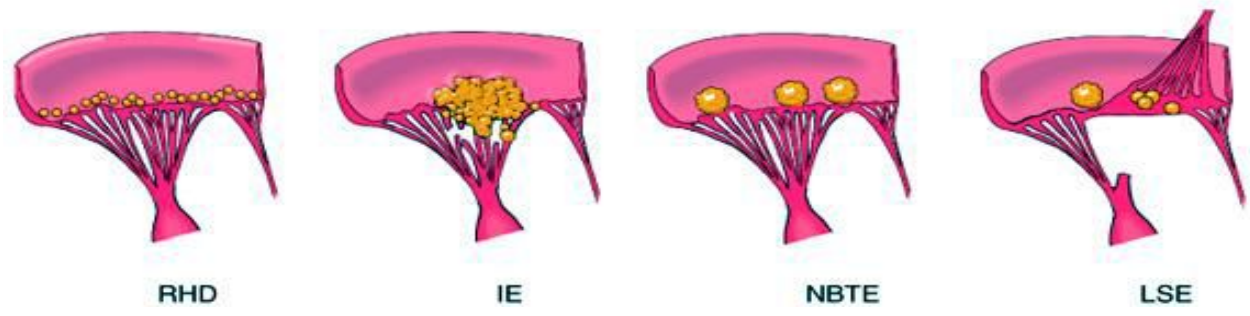




Heart With Infective Endocarditis

Other Types

Libman Sacks endocarditis	Endocarditis of carcinoid syndrome	Nonbacterial thrombotic endocarditis (marantic endocarditis)
Less common, non infective, verrucous endocarditis associated with elevated levels of circulating immune complexes. Seen in patients with **systemic lupus erythematosus**.	Secretory products of carcinoid syndrome,especially **5 hydroxytryptamine** can cause endocarditis. The endocardial plaques are seen in the right side of heart.	Characterized by **sterile (no infection) vegetations** (small masses of fibrin, platelets, and other blood components) 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. The fibrin deposits are randomly arranged. • May embolize to different parts of the body including brain, but the emboli are sterile.



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.

Types of

Valvular Heart Diseases

1 Stenosis (Failure to open)

2 Regurgitation (Insufficiency or failure to close leading to backflow of blood)

Causes

Acquired

Acq

post inflammatory scarring e.g. as a late complication of **rheumatic fever (most common)** or secondary to various other inflammatory processes.

Acq

can occur even with **prosthetic cardiac valves**.

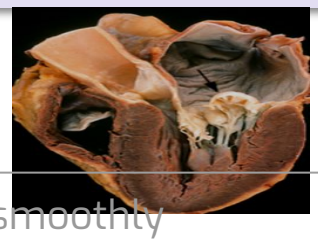
Acq

can be secondary to thrombus formation or **infectious endocarditis**.

Congenital

Mitral valve

Prolapse (MVP)



Definition	A condition in which the two valve flaps of the mitral valve do not close smoothly or evenly, but instead bulge (prolapse) upward into the left atrium.
Epidemiology	• most frequent valvular lesion in **developed countries**. • Seen in **young women**.
Pathogenesis	**unknown**
	There is myxoid/mucoid degeneration of the valve which causes **ballooning** of mitral valves **(floppy cusp)** → 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 characteristic **systolic murmur with a click**.
Clinical features	Most patients **asymptomatic** but can occasionally lead to mitral insufficiency and arrhythmias.
Complications	Patients are predisposed to infective endocarditis (subacute).
	Can be associated with Marfan syndrome*.

Stenosis

Caused by	**Rheumatic heart disease**.
Epidemiology	Mitral stenosis is more common than mitral regurgitation.
Pathogenesis	Valve closed → **blood can't flow** to left ventricle which will **increase the pressure in the left atrium leading to hypertrophy and dilatation** → Due to high pressure in left atrium the blood coming from the pulmonary veins won't be able to fill in the left atrium → The blood will return to the lungs which will lead to pulmonary hypertension and lungs are firm and heavy (chronic passive congestion). → Right side of the heart may be affected later (right ventricular hypertrophy).
Picture 	Leaflets are thickened, fibrotic and fused leading to fish mouth/buttonhole deformity (**stenosed valve looks like fish's mouth or buttonhole**). • secondary deposition of Ca++ (any deformity will show deposition of calcium leading to heart failure).

Regurgitation

Caused by	**- Rheumatic heart disease**, mitral valve prolapse, infective endocarditis, papillary muscle injury in myocardial infarction etc.
Complication	left vent. hypertrophy and dilatation.

Aortic valve

Right side of heart

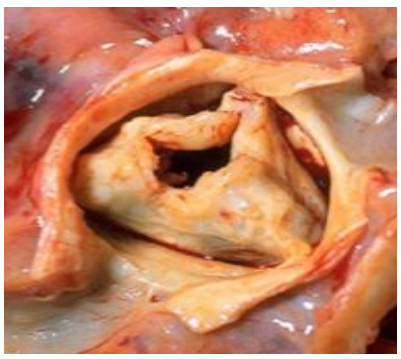
Valvular heart disease of the right side of heart is very uncommon.

Stenosis

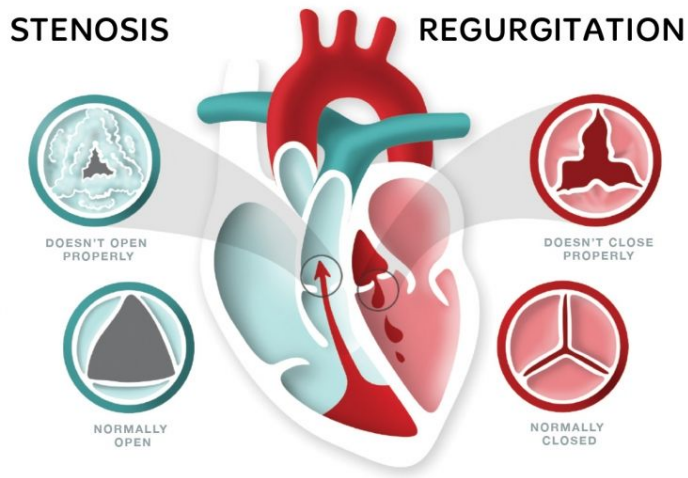
Epidemiology	**Usually seen in old people over 60 years old.**
Caused by	**calcification** and is called as calcific aortic stenosis. Also caused by Rheumatic heart disease.
Calcific aortic stenosis affects	a) Normal aortic valve as part of the aging degenerative process in > 60 yrs old. b) Congenital bicuspid aortic valve c) Valves scarred by rheumatic heart disease

Normal Valve

Stenotic Valve



regurgitating valve



Regurgitation

Caused by	1- Non-dissecting aortic aneurysm. 2- Rheumatic heart disease. 3- Infective endocarditis. 4- Syphilitic (luetic) aortitis(rare).

Summary

from team 438
(thank you team 438)

Rheumatic Fever

Types	Acute		Chronic
Cause	Post group A Streptococcus infection		Severe/repeated attacks of rheumatic fever
Characteristic	Aschoff bodies		• Scarring • Thickened valvular cusps
Site	**Pericarditis**	Fibrinous or serofibrinous "Bread and butter"	Left side of the heart
	Myocarditis	Aschoff bodies	
	Endocarditis	Rheumatic vegetations	• Mitral valve alone • or combination of mitral/aortic valve
	Subendocardial lesions	MacCallum plaques	

Clinical features	• Elevated Antistreptolysin O
	• Jones criteria:
	  ○ Two major
	  ○ One major and two minor
			• Cardiac murmurs
			• Thromboembolism
			• Infective endocarditis

Infective Endocarditis

Site of infection	Mitral valve followed by aortic valve, Tricuspid valve is seen in IV drug users	
Types	Acute	Subacute
Cause	Streptococcus Aureus	α hemolytic Streptococcus Viridans
Affect	Normal valves	Damaged valves
Progress	Rapid and ⅓ of cases are fatal	Slow
Clinical features	• Fever • Cardiac murmur • Petechiae	• Clubbing of the fingers • +ve blood culture for the organisms • Splenomegaly
Complications	• Septicemia • Renal failure	• Valve ulceration and perforation

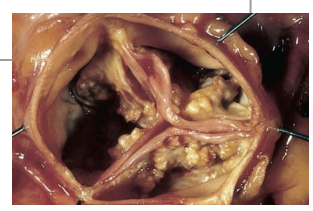
Valvular Heart Disease

Cause	Post inflammatory scarring as a late complication of Rheumatic Fever			
Types	Stenosis		Regurgitation	
	Mitral	Aortic	Mitral	Aortic
Cause	RHD	Calcification	RHD	RHD

Lecture’s notes

Quiz

1-a patient with bronchogenic tumor develops symptoms like fever and abdominal pain and and Clubbing of fingers later on doctors discovered non bacterial IE and gave him antibiotics to treat him , what is the most valve is affected?			
a- aortic valve	b- mitral valve	c- tricuspid valve	d- pulmonary valve
2- Sarah had a rheumatic fever 5 years ago and 2 weeks a go she diagnosed with RHD what is the most common affected valve?			
a- Pulmonary valve	b- Mitral valve	c- aortic valve	d- Tricuspid valve
3- Ahmad used to take drugs intravenously but in the last episode he suffered from high grade of fever and chills what is the most common valve that is prone to infection ?			
a- mitral	b-aortic	c- tricuspid	d- pulmonary
4-:what kind of deformity will you see in mitral valve stenosis?			
a- fish's mouth or button hole	b- ballooning deformity	c- breed and butter □	d- nothing
5-20 years old girl comes with systolic murmur it's an incidental finding, she has no symptoms and suffering from Marfan syndrome, what kind of valvular heart disease she might suffering from?			
a- mitral valve stenosis	B-aortic stenosis	C- Mitral valve prolapse	d-mitral regurgitation
6- 78-year-old man with a history of recurrent syncope undergoes surgery for aortic valve disease. A hard, markedly deformed valve is observed, but the patient expires during surgery. The aortic valve at autopsy is shown in the image. What is the appropriate diagnosis?			
a- Calcific aortic stenosis	b- IE	C- mitral valve prolapse	d- RF



SAQ :

1/Mention two type of damage that can affect the valve after endocarditis?
2/pancarditis is inflammation of ?

1-stenosis: fibrosis of valve leaflets(Reduction of diameter)
regurgitation: fibrosis of chordae tendineae (improper closure)
2-pancarditis is inflammation of entire heart : myocardium , endocardium , and pericardium

1-a
2-b
3-c
4-a
5-c
6-a

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