Pathology of Rheumatic heart disease, Infective endocarditis and Valvular heart disease

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.

Black: original content. Red: Important. Light Purple:From Robbin's. Blue:only found in boys slides. Green: Boy's doctor notes . Dark orange: Girl's Doctor notes. Grey: Explanation. Pink: Only found in girls slides.



Rheumatic heart disease (RHD)

Helpful video

Definition

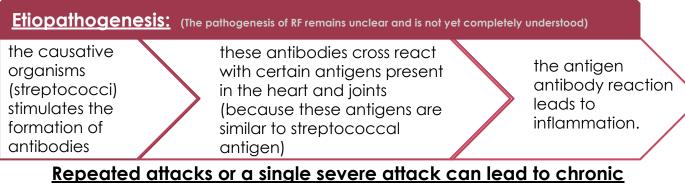
It is a heart disease caused by **rheumatic fever (RF)** which is a condition that can result from inadequately treated streptococcal throat infection.

It has two types:

- A- Acute
- B- Chronic

Rheumatic fever

Definition	An acute, immune mediated, multi-system, non-suppurative inflammatory disease that occurs a few weeks(1-5 weeks) after, group A-beta hemolytic streptococcal infection with cardiac and extracardiac manifestations
Site	Mainly in the heart, joints, central nervous system and skin.
Epidemiology	 Occurs in only <u>3%</u> 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).



rheumatic heart disease leading to cardiac failure.

Acute rheumatic heart disease (RHD)

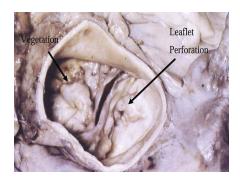
Cardiac manifestations of Rheumatic FEVER

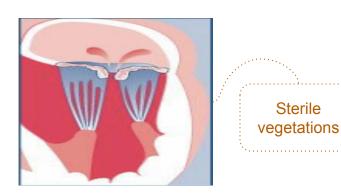
- Also called acute rheumatic heart disease or acute rheumatic carditis/ pancarditis.
- What is pancarditis? It's the inflammation of all heart layers (Endocarditis, myocarditis, pericarditis)

Pericarditis	Endocarditis			
 Inflammation of pericardium Lead to accumulation of secretions (fibrinous or serofibrinous) between the visceral & parietal layers Like butter between two slices of bread therefore also called "bread & butter" pericarditis 	 Inflammation of endocardium, the valves (valvulitis) & chordae tendineae Results in fibrin deposition on valve leaflets forming tiny thrombi along lines of closure called rheumatic vegetations Mitral & aortic valves are mainly involved Aschoff bodies/nodules are uncommon in the valves May either resolve completely or progress to scarring with development of chronic fibrotic deformities of the heart valves and chordae tendineae leading to CHD many years later. 			
Myocarditis	Subendocardial nodules			
 Inflammation of myocardium Many aschoff bodies seen Might cause sudden death 	 Commonly seen in left atrium Called as MacCallum plaques 			

What are Rheumatic vegetations?

- A mass of platelets, fibrin, microcolonies of microorganisms, and scant inflammatory cells.
- Tiny(size of pin's head), sessile arranged in a row and firmly with the underlying tissue.
- These are situated in the valve cusp, a few millimeters away from the free margin(this is the traumatized area)





Acute rheumatic heart disease (RHD)

	Aschoff bodies (characteristic lesion of rheumatic fever)
Definition	They are multiple tiny granulomatous lesions of the heart, situated next to small arteries and are characteristically seen in the myocardium (rheumatic myocarditis).
Components	 An Aschoff body, consists of: Focus of eosinophilic collagen necrosis (representing the site of antibody-antigen reaction), Plump activated macrophages/ histiocytes called Anitschkow/caterpillar cells. Some of the macrophages become multinucleated to form Aschoff giant cells. Chronic inflammation.
	Aschoff nodule
Site	 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.

Extra cardiac (outside the heart) manifestations of Rheumatic FEVER			
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 nodules and erythema marginatum.	 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. 		
 Rheumatic nodules: mainly seen over the bony prominences e.g. knuckle, elbow, patella etc. 	 chronic interstitial inflammation and fibrinous pleuritis. In lungs. it's uncommon. 		

Acute rheumatic heart disease (RHD)

Clinical features

Acute symptoms usually subside within 3 months.
The mortality from acute rheumatic carditis is low

Peak incidence: 5-15 years

History of sore throat (Symptoms start 10 days to 6 weeks after group A streptococcal pharyngitis)

Throat/ pharyngeal cultures are usually negative. (When the symptoms start) High serum antistreptolysin O (ASO titer/ antibodies to group A streptococcal antigens)

High serum Anti-DNAase B

High serum Antihyaluronidase

Mnemonic: "JONES CAFE PAL" Major Criteria

J Joint Involvement

E Erythema marginatum

S Sydenham chorea

0 0 looks like a heart = myocarditis N Nodules, subcutaneous **Minor Criteria**

CRP Increased Arthralgia

Elevated ESR

Leukocytosis

Prolonged PR Interval

Anamnesis of Rheumatism

Fever

P

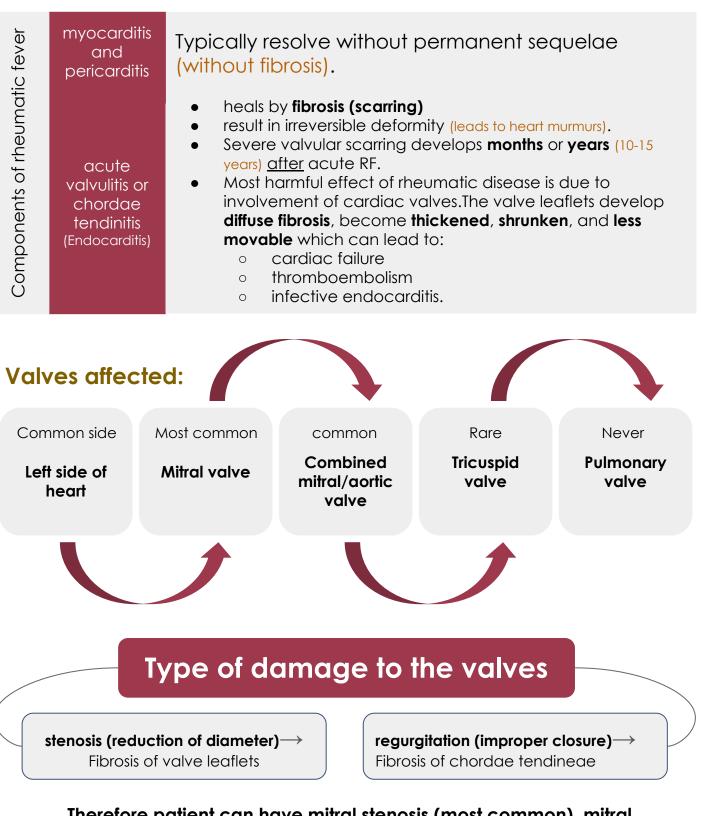
nes	Cri	eria

- There is no specific test for rheumatic fever.
- The diagnosis is made based on the clinical findings when either:
- <u>two major</u> or <u>one major and two minor</u> criterias are met.

<u>Major</u>	<u>Minor</u>		
Carditis: Murmurs, pericardial friction rubs, weak heart sounds, tachycardia and arrhythmias cardiomegaly, pericarditis, and congestive heart failure.	 Elevated acute phase reactants: Elevated ESR (erythrocyte sedimentation rate). Increased CRP (C-Reactive protein). Ieukocytosis 		
Migratory polyarthritis of the large joints	Arthralgia ¹		
Erythema marginatum of the skin	Fever		
Subcutaneous nodules	ECG changes Prolonged PR interval		
Sydenhem's chorea (St. Vitus' dance)	Previous rheumatic fever		

1: Pain of the joint with no infection . If there's an infection it's called arthritis

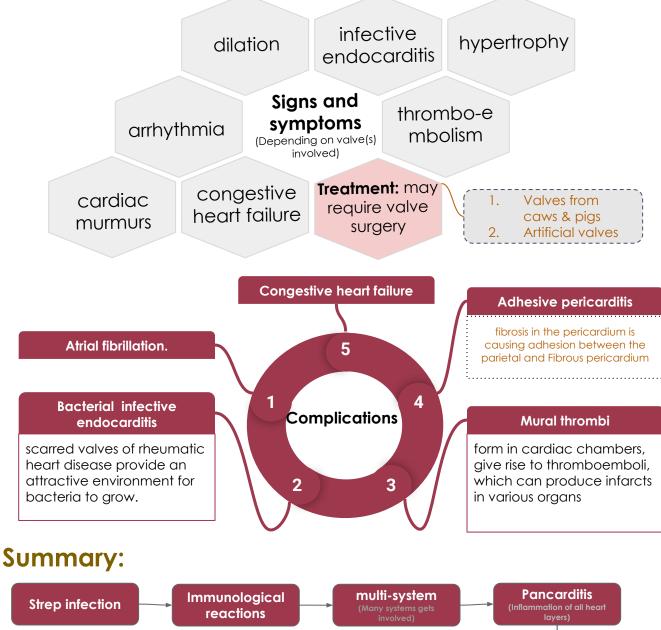
Chronic rheumatic heart disease

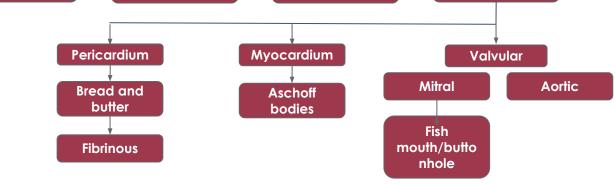


<u>Therefore patient can have mitral stenosis (most common), mitral</u> <u>regurgitation, aortic stenosis and aortic regurgitation.</u>

Chronic rheumatic heart disease

Manifestations can continue for years or decades after the initial episode of rheumatic fever





Infective Endocarditis (IE)¹

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.

Helpful video

- 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.

	Acute IE	Subacute IE			
Infected valves	Normal/healthy	Previously abnormal/damaged			
Causative organisms	Highly virulent organisms (staphylococcus aureus)	Low virulence (a-hemolytic streptococci viridans) ²			
Progress	Rapidly	Slowly			
Host reaction	Little local host reaction ³	Induces local inflammatory reaction			
✤ 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 Staphylococcus aureus endocarditis are still fatal. 				
Why it's difficult to treat? Infective endocarditis is a particularly difficult infection to eradicate because of the avascular nature of the heart valves. Endocardium gets most of the oxygen from the chambers of the heart by the flow of blood not capillaries so antibiotics won't be effective.					
Cardiac murmurs fever					
Positive blood culture for the organisms (only minority of cases remain negative) Clinical features Grant features					
weight loss and chills					
1: The difference between IE & the endocarditis rheumatic fever: The endocarditis rheumatic fever is non infectious (sterile) and aseptic. It's also a complication from a sore throat/pharyngitis. IE though is infectious (contains microorganisms) 2: because the valve is already damaged it doesn't need to be highly virulent to cause infection :) 3: due to the fast progression, the body does not get enough time to react 4: lesions in the skin					

Infective Endocarditis (IE)

Risk factors

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

In adults: <u>More than half</u> of adults with bacterial endocarditis have no predisposing cardiac lesion. The rest: <u>Mitral valve prolapse</u> and <u>congenital heart disease</u> are the most frequent cause for bacterial endocarditis in adults.

Rheumatic heart disease

Intravenous drug abusers¹:

- end up injecting microorganisms intravenously when taking IV drugs, leading to IE.
- The tricuspid valve: most common site (half of the cases)
- S. aureus: in 50% of cases
- Elderly (due to degeneration of heart valves e.g. calcific aortic stenosis)
- diabetics
- pregnant women

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

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.

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

1: Intravenous blood abusers share the same needles which cause infections \rightarrow vein \rightarrow inferior vena cava \rightarrow right side of the heart \rightarrow pumped to the body

2: The infected thrombus will break \rightarrow descending aorta \rightarrow throughout the body \rightarrow blocks the area it lands in.

Endocarditis

Libman-Sacks endocarditis

Less common, non-infective, verrucous endocarditis associated with: elevated levels of circulating immune complexes. Seen in patients with systemic lupus erythematosus

Endocarditis of carcinoid syndrome

Secretory products of carcinoid syndrome, especially **5-hydroxytryptamine** can cause endocarditis. The endocardial plaques are seen in the right side of heart

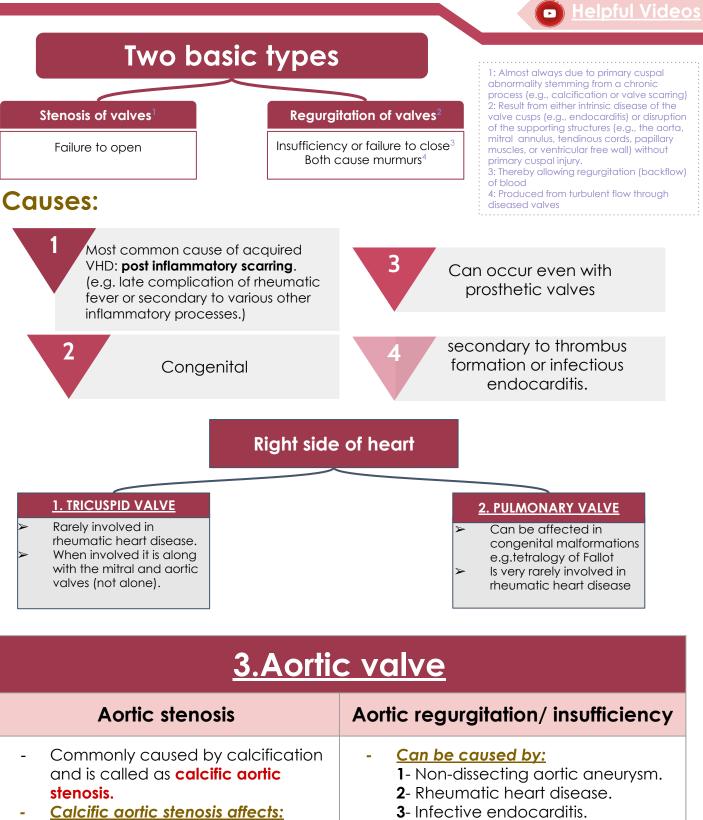
Nonbacterial thrombotic endocarditis (marantic endocarditis)

- 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.
- 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.
- Pathogenesis/association:
 - a. Subtle endothelial abnormality
 - b. Hypercoagulability.
 - c. Association with malignancy (50%) and other debilitating diseases

Diagrammatic comparison of the lesions in the four major forms of vegetative endocarditis

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

Valvular heart diseases (VHD)



1-Normal aortic valve as part of the

aging degenerative process in > 60

2- Congenital bicuspid aortic valve. 3- Valves scarred by rheumatic

yrs old.

heart disease.

- 3-Infective endocarditis.
 - 4- Syphilitic (luetic) aortitis(rare).





Stenotic Valve

Valvular heart diseases (VHD)

4. Mitral valve



Mitral valve prolapse (MVP)

- 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.
- most frequent valvular lesion in developed countries.
- Seen in young women.
- Pathogenesis is unknown
- There is myxoid/mucoid degeneration¹ 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 a characteristic **systolic murmur** (mid-systolic click).
- Most patients asymptomatic but can occasionally lead to mitral insufficiency and arrhythmias.
- Can be a component of Marfan syndrome².
- Patients are predisposed to infective endocarditis.
- No vegetations, no fibrosis.

T: On histologic examination, the essential change is thinning of the valve layer known as the fibrosa layer of the valve, on which the structural integrity of the leaflet depends, accompanied by expansion of the middle spongiosa layer owing to increased deposition of myxomatous (muccid) material.

2: a disorder of connective tissue that is caused by a defect in the gene controlling the production of fibrillin, and is characterized by abnormal elongation of the long bones and often by ocular and circulatory defects.

Mitral stenosis

- More common than regurgitation.
- Most commonly due to rheumatic heart disease.
- Pathogenesis:

Valve closed \rightarrow blood can't flow to left ventricle which will increase the pressure in the left atrium leading to hypertrophy and dilatation \rightarrow Due to high pressure in left atrium the blood coming from the pulmonary veins won't be able to fill in the left atrium \rightarrow The blood will return to the lungs which will lead to pulmonary congestion and pulmonary hypertension \rightarrow Right side of the heart may get affected later (leading to congestive heart failure)

- Leaflets are thickened, fibrotic and fused leading to fish mouth buttonhole deformity (stenosed valve looks like fish's mouth or buttonhole)
- secondary Ca++ deposition.

No symptoms picked up when doing an investigation for something else.

Mitral regurgitation

- Usually due to rheumatic heart disease.
- Can also be due to MVP, IE, papillary muscle injury in MI.
- Leads to left ventricular hypertrophy and dilatation.





Summary

Rheumatic Fever							
Types	Acute				Chronic		
Cause	Post group /	A Strep	ptococcus infect	ion		repeated attacks of eumatic fever	
Characteristic	A	schof	ff bodies			arring ickened valvular cusps	
	Pericarditis		Fibrinous or ser "Bread and	butter"		ide of the heart	
0 11	Myocarditis		Aschoff b	odies			
Site	Endocarditis		Rheumatic ve	getations	• M	itral valve alone	
	Subendocardia lesions	I	MacCallum	olaques		combination of itral/aortic valve	
Clinical features	 Elevated Antistreptolysin O Jones criteria: Two major One major and two minor 			• Th	ardiac murmurs Iromboembolism fective endocarditis		
Infective Endocarditis							
Site of infection	Mitral valve fo	ollowe	d by aortic valv	e, Tricusp	id valve is see	n in IV drug users	
Types	Acute			Su	ubacute		
Cause	Streptococcus Aureus			α hemolytic S	lpha hemolytic Streptococcus Viridans		
Affect	No	Normal valves			Damo	Damaged valves	
Progress	Rapid and	⅓ of	cases are fat	al		Slow	
Clinical features	 Fever Cardiac murmur Petechiae Clubbing of the fingers +ve blood culture for the organisms Splenomegaly 			S			
Complications	Septicemia Renal failure Valve ulceration and perforation						
Valvular Heart Disease							
Cause	Post inflamme	atory :	scarring as a l	ate com	olication of R	heumatic Fever	
Types	Ster	Stenosis			Regurgitation		
Types	Mitral	Aortic		١	Mitral	Aortic	
Cause	RHD	Calcification			RHD	RHD	

Dr.AlRakabi notes

Rheumatic fever

Definition

A multi-system immune mediated disease, it's also considered to be the most common cause for valvular diseases.

Pathogenesis

Pharynx infection by Group A streptococcus \rightarrow Immune system recognize the M protein on Group A strept (has similar molecular structure to certain parts in the body, e.g. Heart) \rightarrow produces M protein antibodies(will attack all sites that have similar structure to M protein \rightarrow Antigen-antibody complex deposition \rightarrow Complement cascade (C3a, C5a) which will recruit inflammatory cells \rightarrow inflammation and CD4+ cells activation.

Diagnosis

- 1- Throat swab culture.
- 2- Serological tests: Anti-streptolysin O , Anti-hyaluronidase.
- 3- Jones criteria (2 major or 1 major and 2 minor).

Valvular diseases

Valvular diseases are either stenosis or regurgitation, both causes murmurs of the heart, Mitral valve is the most common valve involved followed by Aortic > tricuspid > pulmonary.

Mitral stenosis (Due to rheumatic fever)	Calcific aortic stenosis	Myxomatous degenerative (floppy) mitral valve
 Will cause Fish mouth deformity to the valve. Treated with antibiotics and anticoagulants before surgery to prevent endocarditis. 	 Due to old age. Dystrophic calcification leading to Bicuspid aortic valve. 	 Mitral regurgitation. Systolic click is heard by stethoscope. Chordae tendineae is relaxed.

Dr.AlRakabi notes

Full Notes? Click here

Infective endocarditis

Definition

Inflammation of the endocardium most commonly caused by bacteria.

Types

- 1- Acute: More severe and caused by staphylococcus aureus.
- 2- Subacute: Less severe and caused by Streptococcus viridans.

Risk factors

- 1- Congenital heart disease e.g. ASD, VSD.
- 2- Prosthetic (artificial) valve.
- 3- Rheumatic heart disease.
- 4- Drug addict (most common cause is S.aureus).
- 1- Fever.

ymptoms

- 2- Roth spots.(Eye hemorrhage)
- 3- Olser's node (Painful).
- 4- Peteachiae.

Other types of endocarditis

Nonbacterial thrombotic endocarditis	Libman-Sacks endocarditis			
 Marantic(due to wasting over time). Usually diagnosed at autopsies. Occurs in people with chronic disease, Doesn't show colonies of bacteria under microscope, only fibrin. 	 Presence of sterile vegetations in people with Systemic Lupus Erythematosus. Vegetations will be on the surface of the cusps (inner/outer), not the lines of closure. 			

Quiz

1) A 30-year-old woman presents with a heart murmur and SLE There is a history of recurrent episodes of arthritis, skin rash, and glomerulonephritis. Blood cultures are negative. Laboratory tests for antinuclear antibodies (ANA) and anti-double-stranded DNA are positive. Which of the following is the most likely cause of heart murmur in this patient?		2) A 16-year-old girl, who arrived in the United States from Africa, comes to the hospital with chest pain and respiratory distress. On physical examination, the patient is short of breath, wheezing, and gasping for air. A prominent pansystolic heart murmur and a prominent third heart sound are heard on cardiac auscultation. An X-ray study of the chest shows marked enlargement of the heart. The patient expires despite intense supportive measures. At autopsy, microscopic examination of the myocardium discloses aggregates of mononuclear cells arranged around centrally located deposits of eosinophilic collagen. What is the appropriate diagnosis?		
A) Libman-Sacks endocarditis	B) Mitral valve prolapse	A)Acute bacterial endocarditis	B) Rheumatic heart disease	
C) Myocardial infarct	D) Angina pectoris	C) Subacute bacterial endocarditis	D) Systemic lupus erythematosus	
E) Rheumatic fever		E) Viral myocarditis		
3) A 40-year-old woman with a history of rheumatic fever presents with shortness of breath, weight loss, fatigue, and abdominal distension. Physical examination shows rales in the lungs, hepatosplenomegaly, and 2+ pitting edema of the legs. A chest X-ray reveals only left atrial enlargement and pulmonary edema. What is the most likely cause of pulmonary edema in this patient?		4) A 53-year-old woman presents with a 6-week history of fever, fatigue, and weight loss. Her temperature is 38.7°C (103°F), pulse rate 110 per minute, and blood pressure 140/80 mm Hg.Physical examination reveals petechiae and clubbing of the fingers. The patient develops mental status changes, suffers a massive stroke, and expires. The mitral valve is examined at autopsy (shown in the image). Which of the following is the appropriate pathologic diagnosis?		
A) Aortic insufficiency.	B) Aortic stenosis.	A) Bacterial endocarditis.	B) Carcinoid heart disease	
C) Mitral stenosis.	D) Pulmonic stenosis.	C) Libman-Sacks endocarditis	D) Marantic endocarditis	
E) Tricuspid insufficiency.		E) Marantic endocarditis		
5) A 10-year-old boy with a 2-week history of an upper respiratory infection was admitted to the hospital with malaise, fever, joint swelling, and diffuse rash. The patient is treated and discharged. However, the patient suffers from recurrent pharyngitis and, a few years later, develops a heart murmur. This patient's heart murmur is most likely caused by exposure to which of the following pathogens?		6) For the patient described in Question 5, which of the following is the most common life-threatening complication of his valvular heart disease?		
A) Beta-hemolytic streptococcus	B) Candida albicans.	A) Congestive heart failure	B) Dissecting aneurysm.	
C) Epstein-Barr virus D) Staphylococcus aureus		C) Hemolytic anemia	D) Myocardial infarction	
E) Streptococcus viridans		E) Pulmonary thromboembolism		

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