



PATHOLOGY TEAM 430

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Note

The important notes with

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1st Lecture:

Pathology of Rheumatic Fever, Infective Endocarditis and Heart Valves

RHEUMATIC FEVER

❖ Definition

Rheumatic fever is a multisystem inflammatory disorder causing major cardiac manifestations and sequelae, most often affecting children between 5 and 15 years of age.

- ✚ It usually occurs 1-4 weeks after an episode of tonsillitis or other throat infections caused group A-beta hemolytic streptococci.
- ✚ The main diagnosis: An elevated titer of antistreptolysin a (ASO) is evidence of a recent streptococcal infection.
- ✚ It is characterized by inflammatory reaction involving heart, joints, central nervous system and skin.

❖ Etiology

- ✚ It is postulated to occur as a result of streptococcal antigens that elicit (causes) an antibody response reactive to streptococcal organisms as well as to human antigens in the heart and other tissues.

Just to understand:

When bacteria "Group A-beta hemolytic streptococci" attack the body (recurrently), this will lead to formation of antibodies against it. Later on bacteria will go, but the body has memory cell against specific protein in the bacteria, so the body will direct antibodies against the heart because it has which called "molecular mimicry" which is similar to specific molecule in the bacteria. Because of this mechanism, Rheumatic fever is considered as an autoimmune disease.

✚ Aschoff body "small granuloma"

- (1) This is the classic lesion of rheumatic fever.
- (2) This is an area of focal interstitial myocardial inflammation that is characterized by fragmented collagen and fibrinoid material (necrosis) surrounded, by large

cells (Anitschkow myocytes) and by occasional multinucleated giant cells (Aschoff cells).

❖ It affects all the 3 layers of the heart:

Characteristics include **pancarditis, inflammation of the pericardium, myocardium and endocardium.**

- (1) **Pericarditis** may result in **pericardial, pleural or other serous effusions.**
- (2) **Myocarditis** may lead to **cardiac failure** and is the cause of most deaths.
- (3) **Endocarditis** leads to **valvular damage.**

- ✚ Rheumatic endocarditis usually occurs in valve closure and the posterior wall of the left atrium, resulting in the formation of the so-called MacCallum plaque.
- ✚ The mitral and aortic valves, which are subjected to much greater pressure and turbulence, are more likely to be affected than are the tricuspid and pulmonary valves.

- ❖ In the early stage, the valve leaflets are red and swollen, and tiny, warty, bead-like, rubbery vegetations (verrucae) form along the lines of closure of the valve leaflet.
- ❖ As a consequence of fibrotic healing, the valves become thickened, fibrotic and deformed, often with fusion of valve cups as well as thickening of the chordate tendineae. Calcification is often prominent.

❖ **The mitral valve is the valve that is most frequently involved in rheumatic heart disease.**

- ✚ It can be affected by stenosis with fish-mouth buttonhole deformity, insufficiency or a combination of both.
- ✚ Mitral stenosis is marked by diastolic pressure higher in the left atrium than in the left ventricle.
- ✚ The aortic valve is affected most often along with the mitral valve. It can be affected by stenosis or insufficiency.
- ✚ The tricuspid valve is affected with the mitral valve and aortic valves (trivascular involvement) in approximately 5% of cases of rheumatic heart disease.
- ✚ The pulmonary valve is rarely involved.

Rheumatic Fever: Involvement of Other Organs

- ✓ **Migratory polyarthritis:** It causes "fleeting arthritis" in the large joints, self limited, no chronic deformities.
- ✓ **Arthralgia: joint pain without clinically evident inflammation.**
- ✓ **Skin: subcutaneous nodules, erythema marginatum.**
- ✓ Central nervous system involvement, including **Sydenham chorea,**

characterized by involuntary, purposeless muscular movements, and bizarre grimaces, as well as emotional disturbances.

Clinical Presentation

"need 2 major or 1 major and 2 minor criteria to make a diagnosis"

<u>Major criteria</u>	<u>Minor criteria</u>
Carditis	Previous rheumatic fever
Polyarthrititis	Arthralgia
Sydenhem's chorea	Fever
Erythema margination	Elevated ESR, elevated CRP, leukocytosis
Subcutaneous nodules	EKG changes

Infective endocarditis.

This bacterial or sometimes fungal, **infection of the endocardium is marked by prominent involvement of the valvular surfaces.**

1. General considerations

- (a) Characteristics include **large, soft, friable, easily detached vegetations, consisting of fibrin and intermeshed inflammatory cells and bacteria.**
- (b) Complications may include ulceration, often with perforation of the valve cups or rupture of one of the chordate tendinae.

2. Classification

(a) Acute endocarditis

- ✚ It is caused by pathogens such as **Staphylococcus aureus** **"high virulence"**
- ✚ This type of endocarditis is **often secondary to infection occurring elsewhere in the body.**
- ✚ **Infect even normal valves**
- ✚ **Progress rapidly, little local host reaction.**

(b) Subacute (bacterial) endocarditis

- ✚ It is caused by organisms such as **Streptococcus viridians**.
"less virulent"
- ✚ Infection of previously abnormal valves
- ✚ Progress slowly, induce local inflammatory reaction.
- ✚ Source of bacteremia: I.V drug abusers, elsewhere infection, previous dental, surgical or interventional procedure (catheterization). In some cases the source of bacteremia is occult.

Infective Endocarditis "subacute type": People at Risk

- ✓ Cardiac abnormalities: e.g. chronic valvular diseases, congenital heart disease and septal defects.
- ✓ Prosthetic heart valves.
- ✓ Intravenous drug abusers.
- ✓ Rheumatic fever

3. Clinical features

(a) Valvular involvement

- Valvular regurgitation and congestive heart failure due to progressive valvular destruction.
- ✓ The mitral valve is most frequently involved.
- ✓ The mitral valve along with the aortic valve is involved in about 40% of cases.
- ✓ The tricuspid valve is involved in more than 50% of cases of endocarditis of intravenous drug users, in whom endocarditis is most often caused by staphylococcal infection.

(b) Complications

- ✓ Distal embolization occurs when vegetations fragment.
- ✓ Embolization can occur almost anywhere in the body and can result in septic infarcts in the brain or in other organs.
- ✓ Glomerulonephritis caused by immune complex disease

Non-bacterial thrombotic endocarditis (marantic endocarditis)

1. This form of endocarditis associated **with debilitating disorders, such as metastatic cancer and other wasting conditions.**
2. Characterized by **the deposition of small masses of fibrin, platelets, and other blood components on the leaflets of the cardiac valves (sterile).** There is no infective organism. **It is aseptic.**
3. The disease can result **in peripheral embolization but unlike infective endocarditis, the emboli are sterile.**
4. Pathogenesis/ association:
 - ✓ **Subtle endothelial abnormalities.**
 - ✓ **Hypercoagulability.**
 - ✓ **Association with malignancy (50%).**

Examples:

❖ Endocarditis of the carcinoid syndrome

1. **The cause is the secretory products of carcinoid tumors** (vacoactive peptides and amines, **especially serotonin (5-hydroxytrptamine).**
2. **The valves on the left side of the heart are rarely involved, because serotonin and other carcinoid secretory products are detoxified in the lung.**
3. This form of endocarditis results in thickened endocardial plaques characteristically involving the mural endocardium or the valvular cusps of the right side of the heart.

❖ Libman-Sacks endocarditis

Less common, noninfective, **verrucous (Libman-Sacks) endocarditis** attributable to elevated levels of circulating immune complexes may occur in patients with systemic lupus erythematosus.

Valvular Heart Disease

✚ General considerations

1. **Valvular heart disease occurs often as a late result of rheumatic fever.** It may be secondary to various other inflammatory processes.
2. **This disease may be congenital (like the Bicuspid aortic valve).**
3. In addition, valvular heart disease can occur even with prosthetic cardiac valves, which are subject to physical deterioration or can be the site of thrombus formation or infectious endocarditis.

Types:

1. Mitral valve

- Prolapse is the most frequent valvular lesion in Western countries, **most often in young women.**

Characteristics: Include myxoid degeneration of the ground substance of the valve **(it can be a component of Marfan syndrome).**

- ✚ Results include **stretching of the posterior mitral valve leaflet, producing a "floppy" cusp (parachute deformity)** with prolapsed into the atrium during systole. **These changes produce a characteristic systolic murmur with a mid systolic click.**
- ✚ The lesion is usually **benign and asymptomatic.**
- ✚ Stenosis is almost always due to **rheumatic heart disease.**
- ✚ Insufficiency can also result from **mitral valve prolapsed, infective endocarditis or damage to a papillary muscle from myocardial infarction.**

2. Aortic valve

- **This valve, along with the mitral valve, is frequently involved in rheumatic heart disease and in infective endocarditis.**
- ✚ **Stenosis:** often presents a **calcific aortic stenosis** caused by calcification of:
 - (a) An otherwise normal aortic valve as an age-related degenerative change.
 - (b) A congenital bicuspid aortic valve.
 - (c) **A valve affected by rheumatic heart disease. In this case, scarring may be evidenced by fusion of the valve commissures.**
- ✚ **Insufficiency** 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.

3. Tricuspid valve.

- **This valve is rarely involved along in rheumatic heart disease but may be involved together with the mitral and aortic valves.**

4. 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, **it may be in the carcinoid syndrome.**



Good Luck

