Pathophysiology

Dr. Yasser Mufeed

Lecture 11

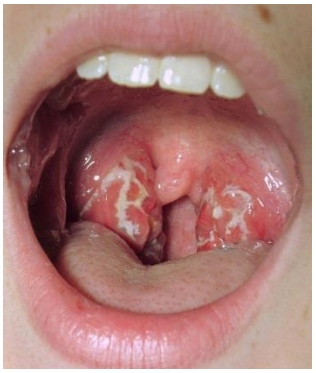
III. Disorders of cardiovascular system

VIII. Rheumatic heart disease

The chronic heart valve damage that can occur after a person has had an episode of acute rheumatic fever. This valve damage can eventually lead to heart failure. Rheumatic fever is caused by a preceding group A streptococcal (strep) infection.

Pathophysiology

Group A Streptococcus is a gram-positive coccus that frequently colonizes the skin and oropharynx. This organism may cause **suppurative disease**, such as pharyngitis, impetigo, cellulitis, myositis, pneumonia, and puerperal sepsis.



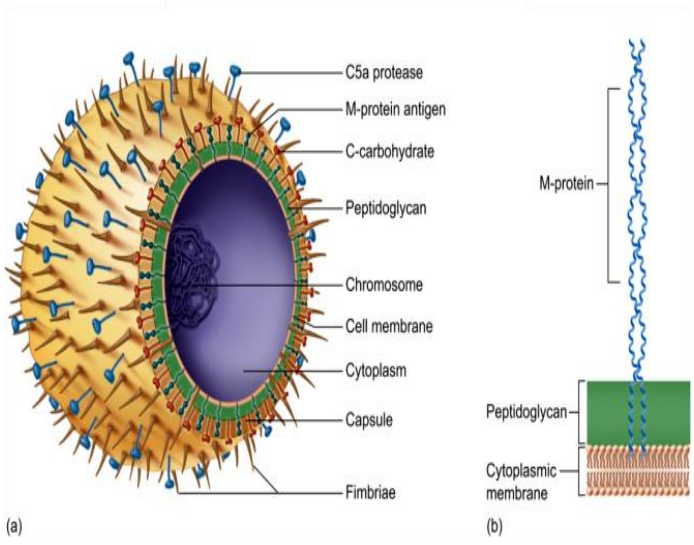
It also may be associated with non suppurative disease, such as rheumatic fever and acute post-streptococcal glomerulonephritis.

Pharyngitis produced by group A streptococcal (strep) infection (GABHS) can lead to:

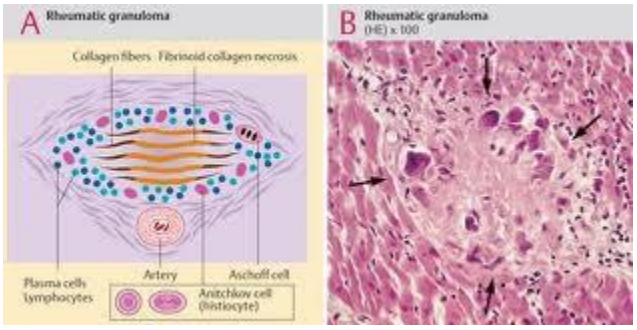
- acute rheumatic fever, rheumatic heart disease & post streptococcal Glomerulonephritis

Skin infection- produced by GABHS leads to post streptococcal glomerulonephritis only. It will not result in Rh. Fever or carditis as skin lipid cholesterol inhibit antigenicity

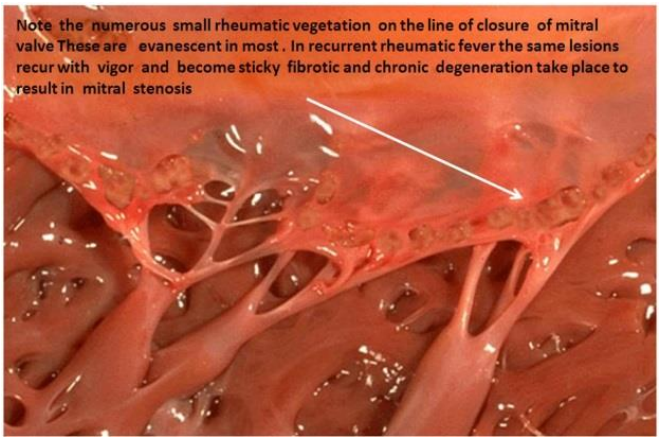
Rheumatic fever develops in some children and adolescents mostly having a **genotype of HLA-DR$_4$** following



pharyngitis with group A beta-hemolytic Streptococcus.
Group A Streptococcus, as identified using the Lancefield classification, has a group A carbohydrate antigen in the cell wall that is composed of a branched polymer of L- rhamnose and N- Acetyl-D-glucosamine in a 2:1 ratio.
The presence of the M protein of the sero-types such as 1, 3, 5, 6, 14, 18, 19 and 24 have been linked with the development of Rheumatic heart disease in, as part of the bodies defense the immune system will react to these antigens and other streptococcal superantigens by activation of T-cell (helper & cytotoxic) and B-cell lymphocytes, the later will respond by producing IgM and IgG which will cross react with the valve myosin.
A break in the endothelial continuity of a heart valve would expose subendothelial structures and lead to a “chain reaction” of valvular destruction.
A Characteristic feature of this chronic immune response is the development of granulomatous inflammation specified by the presence of Aschoff bodies these nodules are spheroidal or fusiform distinct tiny structures, 1-2mm in size, occurring in the interstitium of the heart. It may be visible to the naked eye.



Once valve leaflets are inflamed through the valvular surface endothelium and new vascularization occurs, the newly formed microvasculature allows T-cells to infiltrate and perpetuate the cycle of valvular thickening and damage.
Acute rheumatic heart disease often produces a pericarditis (endocarditis, myocarditis, and pericarditis).



Endocarditis is manifested as valve insufficiency.
The mitral valve is most commonly and severely affected (65-70% of patients), and the aortic valve is second in frequency (25%).
Fusion and shortening of the chordae tendineae (valve apparatus) resulting in

stenosis or a combination of stenosis and insufficiency develops 2-10 years after an episode of acute rheumatic fever, and recurrent episodes may cause progressive damage to the valves which might end up in heart failure.

IX. Heart failure

Heart failure is a condition in which a defect in the pumping action of the heart being insufficient to meet the circulatory demands of the body. With too little blood being delivered, the organs and other tissues do not receive enough oxygen and nutrients to function properly.

Types of Heart Failure

Heart failure can be classified in several ways

1) **Low-Output Heart Failure**
   - **A. Systolic Heart Failure:**
     - Decreased cardiac output.
     - Decreased Left ventricular ejection fraction. (*pumped blood <50%*)
   - **B. Diastolic Heart Failure:**
     - Elevated Left and Right ventricular end-diastolic pressures.
     - May have normal LVEF.
2) **High-Output Heart Failure**
   - Seen with peripheral shunting, low-systemic vascular resistance, hyperthyroidism, beriberi (deficit in Vitamin B_1), carcinoid, anemia
   - Often have normal cardiac output
3) **Right-Ventricular Failure**

Cardiac output is *the amount of blood pumped out of the heart each minute.*

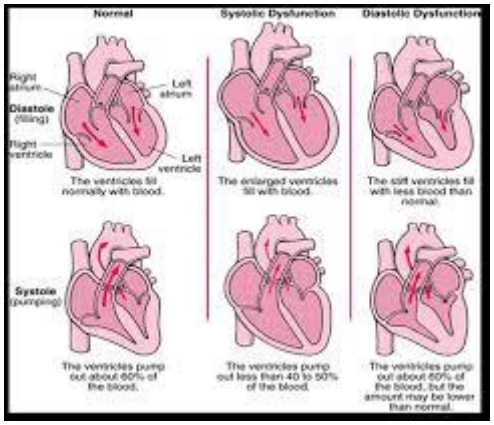
CO= Stroke volume x the heart rate (beats/min).

4800= 60ml x 80

End diastolic volume (EDV)= stroke volume (ejection fraction) + end systolic volume (ESV)

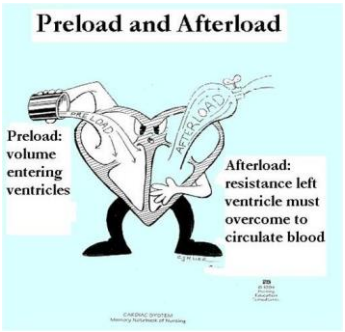
stroke volume Depends on:

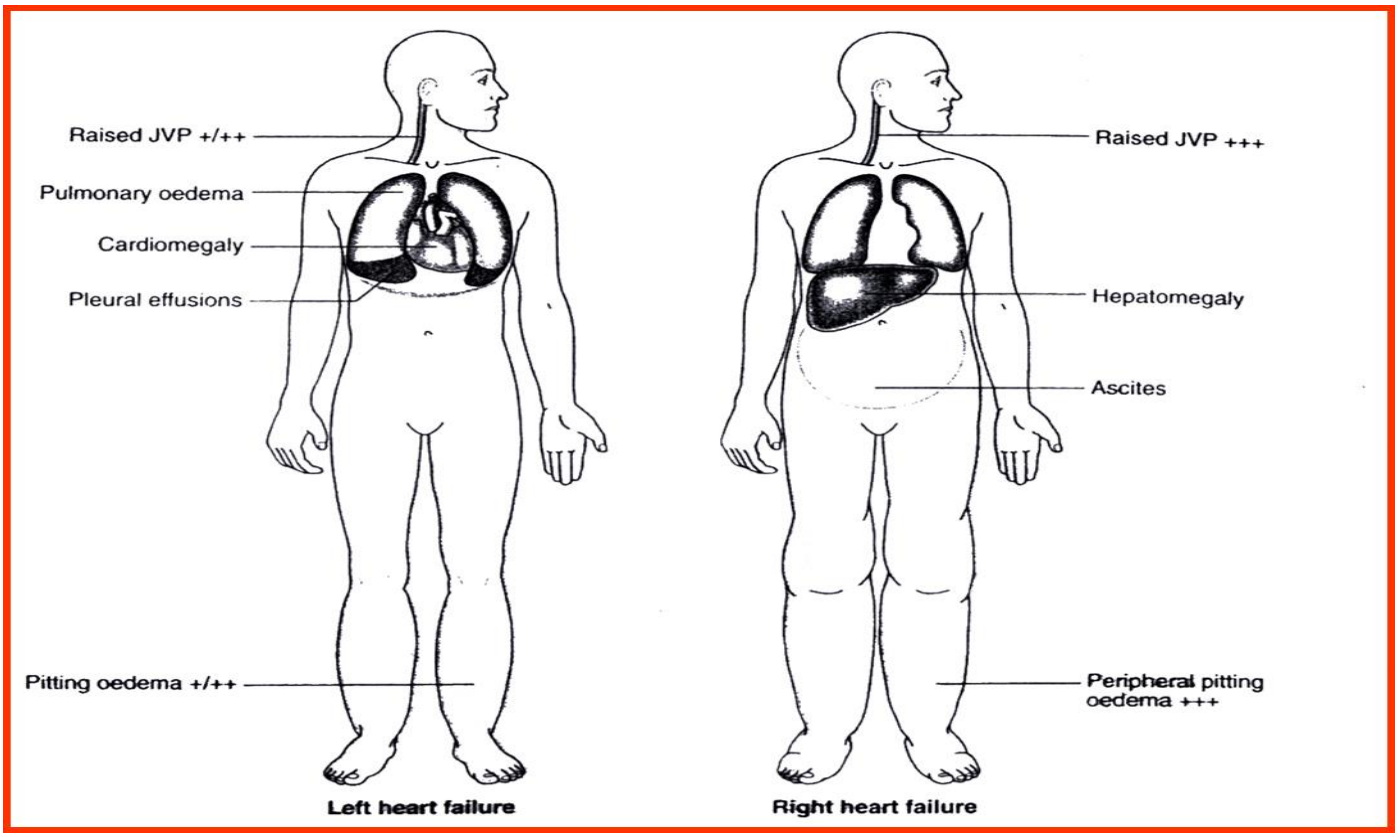
1- Contractility of the heart.
2- Preload.
3- Afterload.



The term ***preload*** means the volume and pressure of blood in the ventricle at the end of diastole.

The term ***afterload*** means the volume and pressure of blood in the ventricle during systole. The pressure in the ventricle should be greater than in the Vessels.





Seen with pulmonary hypertension, large RV infarctions.

The Pathophysiology of heart failure

Cardiac and Vascular Changes Accompanying Heart Failure

Cardiac

- Decreased stroke volume & cardiac output.
- Increased end-diastolic pressure.
- Ventricular dilation or hypertrophy.
- Impaired filling (diastolic dysfunction).
- Reduced ejection fraction (*systolic dysfunction*).

Vascular

- Increased systemic vascular resistance
- Decreased arterial pressure
- Impaired arterial pressure
- Impaired organ perfusion
- Decreased venous compliance
- Increased venous pressure
- Increased blood volume

The changes in cardiac function associated with heart failure result in a decrease in cardiac output. This results from a decline in stroke volume that is due to systolic dysfunction, diastolic dysfunction, or a combination of the two.

Briefly, **systolic dysfunction** results from a loss of intrinsic inotrope (**contractility**), most likely due to ***alterations in signal transduction mechanisms*** responsible for regulating inotrope. Systolic dysfunction can also result from the ***loss of viable, contracting muscle*** as occurs following acute myocardial infarction.
Diastolic dysfunction refers to the diastolic properties of the ventricle and occurs when the ventricle becomes less compliant (i.e., "**stiffer**"), which impairs ventricular filling. Both systolic and diastolic dysfunction result in a **higher ventricular end-diastolic pressure**, which serves as a compensatory mechanism by utilizing the **Frank-Starling mechanism** to augment **stroke volume**. In some types of heart failure (e.g., dilated cardiomyopathy), the ventricle dilates as preload pressures increase in order to recruit the Frank-Starling mechanism in an attempt to maintain normal stroke volumes.
Therapeutic interventions to improve cardiac function in heart failure include the use of **cardio-stimulatory drugs** (e.g., *beta-agonists and digitalis*) that stimulate heart rate and contractility, and vasodilator drugs that reduce ventricular afterload and thereby enhance stroke volume.

Systemic Vascular Function

In order to compensate for reduced cardiac output during heart failure, feedback mechanisms within the body try to maintain normal arterial pressure by *constricting arterial resistance vessels* through **activation of the sympathetic** adrenergic nervous system, thereby increasing systemic vascular resistance. Veins are also constricted to elevate venous pressure. Arterial baroreceptors are important components of this feedback system. Humoral activation, particularly the renin-angiotensin system and antidiuretic hormone (vasopressin) also contribute to **systemic vasoconstriction**.
Heightened sympathetic activity, and increased circulating angiotensin II and increased vasopressin contribute to an increase in systemic vascular resistance. Drugs that block some of these mechanisms, such angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, improve ventricular stroke volume by reducing afterload on the ventricle. Arterial and venous dilators such as **hydralazine and sodium nitroprusside** are also used to reduce afterload on the ventricle.

Blood Volume

In heart failure, there is a compensatory increase in blood volume that serves to increase ventricular preload and thereby enhance stroke volume by the Frank-Starling mechanism. Blood volume is augmented by a number of factors. Reduced renal perfusion results in decreased urine output and retention of fluid. Furthermore, a combination of reduced renal perfusion and sympathetic activation of the kidneys stimulates the release of renin, thereby activating the renin-angiotensin system. This, in turn, enhances aldosterone secretion. There is also an increase in circulating arginine vasopressin (antidiuretic hormone) that contributes to renal retention of water. The final outcome of humoral activation is an increase in renal reabsorption of sodium and water. The resultant increase in blood volume helps to maintain cardiac output; however, the increased volume can be deleterious because it raises venous pressures, which can lead to pulmonary and systemic edema. When edema occurs in the lungs, this can result in exertional dyspnea (shortness of breath during exertion). Therefore, most patients in heart failure are treated with diuretic drugs to reduce blood volume and venous pressures in order to reduce edema.

Clinical Presentation of Heart Failure

A. Due to excess fluid accumulation:

- **a)** Dyspnea (most sensitive symptom).
- **b)** Edema.
- **c)** Hepatic congestion.
- **d)** Ascites.
- **e)** Orthopnea, Paroxysmal Nocturnal Dyspnea (PND).

B. Due to reduction in cardiac output:

- **a)** Fatigue (especially with exertion).
- **b)** Weakness.

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