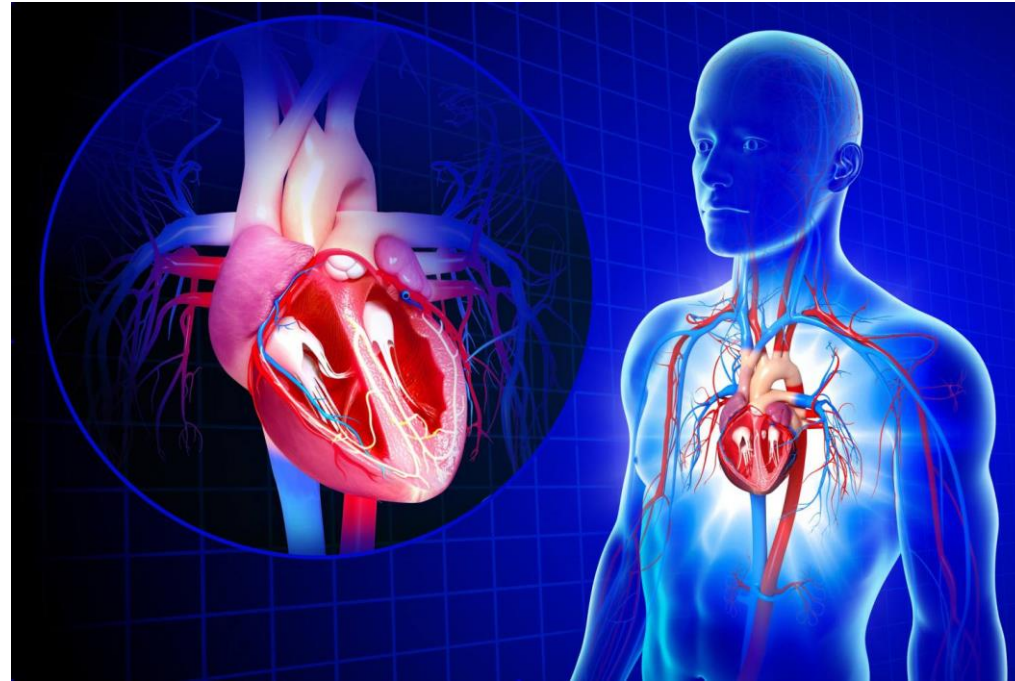


DISORDERS of Cardiovascular System (Heart Failure)



Lec.Dr. Aseel Ghassan Daoud

Ph.D in Pharmacy

Definitions:

- **Cardiac reserve:** The ability to increase cardiac output during increased activity .
- **The cardiac output:** is the amount of blood that the heart pumps each minute. It reflects how often the heart beats each minute (heart rate) and how much blood the heart pumps with each beat (stroke volume) and can be expressed as the product of the heart rate and stroke volume (cardiac output = heart rate \times stroke volume).
- **Preload:** It is the volume of blood stretching the resting heart muscle and is determined mainly by the venous return to the heart.

- **After load:** Afterload represents the force that the contracting heart must generate to eject blood from the filled heart. The main components of afterload are ventricular wall tension and the peripheral vascular resistance.
- **Cardiac contractility:** refers to the mechanical performance of the heart: the ability of the contractile elements (actin and myosin filaments) of the heart muscle to interact and shorten against a load. Contractility increases cardiac output independent of preload filling and muscle stretch.

- **An inotropic influence:** is one that increases cardiac contractility. Sympathetic stimulation increases the strength of cardiac contraction (i.e., positive inotropic action), and hypoxia and ischemia decrease contractility (i.e., negative inotropic effect). The inotropic drug (digitalis), which is used in the treatment of heart failure, increases cardiac contractility such that the heart is able to eject more blood at any level of preload filling.

Compensated heart failure:

- With a decrease in cardiac performance, tissue and organ perfusion is largely maintained through compensatory mechanisms such as the :
 1. Activation of the sympathetic nervous system
 2. Renin-angiotensin-aldosterone mechanism, and
 3. Myocardial hypertrophy.

1. Activation of the sympathetic nervous system leading to direct stimulation of heart rate and cardiac contractility (An inotropic effect). The negative aspects of increased sympathetic activity include an increase in peripheral vascular resistance and the afterload.

2. Renin-angiotensin-aldosterone mechanism : With decreased renal blood flow, there is a progressive increase in renin secretion by the kidneys along with parallel increases in circulating levels of angiotensin II. The increased concentration of angiotensin II contributes to a generalized vasoconstriction and serves as a stimulus for aldosterone production by the adrenal cortex. Aldosterone, in turn, increases tubular reabsorption of sodium, with an accompanying increase in water retention.

3. Myocardial hypertrophy: Increase in myocardial size.

Cardiac Hypertrophy:

- This is an adaptive response to mechanical load on the heart in which there is an increase in the rate of protein (myofilaments) synthesis within each cell.

Causes :

1. Pressure overload

- a. Systemic or pulmonary hypertension
- b. Aortic or pulmonary stenosis

2. Volume overload

- a. Aortic or pulmonary regurgitation
- b. Abnormal communication between the two sides of the heart congenital or acquired

3. Excessive stimulation as of beta-adrenergic receptors example in hyperthyroidism leading to an increase in heart rate.

The **severity** of hypertrophy:

1 -Mild hypertrophy up to 2x ...ischemic heart disease

2 -Moderate hypertrophy 2 x to 3 x ...as in a systemic hypertension and aortic stenosis

3- Sever hypertrophy more than 3 xxas in aortic regurgitation and hypertrophic cardiomyopathy

- The **pattern** of hypertrophy reflects the **nature of the underlying cause** example in **pressure overload** hypertrophy there is **concentric hypertrophy** of the left ventricle this hypertrophy may reduce the cavity diameter i.e restrict diastolic filling. In **volume overload** hypertrophy there is dilatation and hypertrophy that increases the size of the ventricular cavity without increase in wall thickness.

Note: sustain pathological hypertrophy progress to cardiac failure, in contrast physiological hypertrophy as in athletes there is no harmful effect.

Heart failure [congestive heart failure]:

- Is a common condition with a poor prognosis. It represents the Endpoint of many cardiac diseases. The failing heart is unable to pump sufficient blood to meet the requirements of the body
- **Forward failure** mean that failing ventricles can no longer pump the whole blood delivered to it by the venous circulation that there is an associated increase in venous pressure and congestion of the venous circulation **backwards failure**.

- Heart failure can be **Left-sided HF, Right-sided HF** or **both**.

Causes of left-sided HF:

- Ischemic heart disease
- Systemic hypertension
- Mitral or aortic valve disease
- Primary diseases of the myocardium (cardiomyopathies).

- **The clinical effect of left-sided heart failure:**

Clinical effect primarily results from:

- Progressive damming of blood within the pulmonary circulation (pulmonary venous congestion)
- The consequences of diminished cardiac output i.e. multi organ ischemia.

- The morphological changes of Lt sided HF are divided into **cardiac** and **extra cardiac**
- **Cardiac changes:** left ventricle is usually hypertrophied and often dilated the later often leads to secondary enlargement of the left atrium with resultant **Atrial Fibrillation (AF)** that may lead to:
 - A/ further reduction of the stroke volume
 - B/ blood stasis with possible thrombus formation. Dislodgement of such thrombus carries a risk of embolism

- **Extra cardiac changes** are manifested most prominently in lung although the kidneys and the Brain may also be affected.
- **Lungs:** the pressure in the pulmonary veins increase and is ultimately transmitted retrograde to the capillaries and arteries that resulting in **pulmonary congestion and edema**. Lungs change includes in sequence:
 1. Progressive edematous widening of alveolar septa

2. Accumulation of edema fluid in the alveolar space

3. RBCs which leak from congested capillaries are phagocytosed by macrophages where their haemoglobin is converted to hemosiderin. Hemosiderin containing macrophages are accumulated in the alveoli (heart failure cells).

These anatomic changes are associated clinically at first with dyspnea (breathlessness) that progress to orthopnea (Dyspnea on laying down) then progress to paroxysmal nocturnal dyspnea (attacks of extreme dyspnea usually occurring at night).

- **Kidneys:** renal **hypoperfusion and hypoxia** will activate renin-angiotensin-aldosterone system and inducing retention of Salts and water which increases the pulmonary edema in left sided heart failure. in severe cases urea or other nitrogenous waste product increased in the blood.
- **Brain:** In far advanced left sided HF **cerebral hypoperfusion and hypoxia** may give rise to hypoxic encephalopathy, irritability, restlessness which may progress to comma.

Right-sided heart failure:

- Any increase in pressure within the pulmonary circulation secondary to Lt. side heart failure (backwards failure) leads to an increased burden on the Rt. side of the heart. The causes of Rt-sided heart failure must then include all those that induce Lt. sided heart failure. Pure right-sided heart failure most often occurs with the Chronic severe pulmonary diseases (COPD, pulmonary hypertension, valve defects in RT side of the heart) lead to a pressure overload on the Rt. ventricle and in such cases hypertrophy and dilatation are generally confined to the right ventricle and atrium.

Causes of right-sided heart failure:

1. Left ventricle failure the most common cause it is a due to its associated pulmonary congestion with elevation of pulmonary arterial pressure.
2. Intrinsic diseases of the lung parenchyma and or pulmonary vasculature. Rt side HF in this situation called (cor pulmonale).
3. Right sided valve disease
4. Congenital heart disease associated with left to right shunt.

- The major morphologic and the clinical effect of **pure** right-sided heart failure different from those of left sided heart failure in that
 1. Pulmonary congestion is minimum
 - 2 .Engorgement of the systemic and portal venous system is a prominent

Morphologic changes of right-sided heart failure :

A/cardiac changes: hypertrophy of Rt ventricle

B/extracardiac changes include:

- **Liver** includes the followings:
- Increased in size and weight(congestive hepatomegaly).
- Increased pressure in the portal vein and its tributaries (portal hypertension) .

- **Spleen** congestive splenomegaly
- **Bowel wall** : congestion and edema can occur and may interfere with the absorption of nutrients in addition accumulation of transudate in the peritoneal cavity may give rise to ascites
- **Kidneys** congestion of the kidneys is more marked with right-sided heart failure than with left-sided heart failure leading to greater fluid retention and edema and azotemia.

- **Brain** venous congestion and hypoxia of the central nervous system associated with symptoms essentially identical to those described in left sided heart failure.
- **Pleural and pericardial spaces** accumulation of fluid (effusion) in the pleural space (particularly right pleural space) and pericardial space may appear. **Thus while the pulmonary edema indicates left sided heart failure pleural effusion accompany right sided heart failure.**