Name of Unit	Cardiovascular System, Respiratory System and Renal System
Subject /Course name	Pathophysiology
Subject/Course ID	BP204T
Class: B.Pharm. Semester	II
Course coordinator	Harsimran Singh / Devinder Kumar
Mobile No.	959249889/ 8219193104
Email id	harsimranjattana@gmail.com /devinderkumar1994.dk@gmail.com

Learning Outcome of Module 02

LO	Learning Outcome	Course Outcome Code
LO 1	To understand about the Cardiovascular System: Hypertension, congestive heart failure,	BP204T.2
LO 2	To understand about the Cardiovascular System: Hypertension, congestive heart failure,	BP204T.2
LO 3	To understand about the Ischemic Heart Disease (angina, myocardial infarction,	BP204T.2
LO 4	To understand about the atherosclerosis & arteriosclerosis).	BP204T.2
LO 5	To understand about the Respiratory System: Asthma, Chronic obstructive airways diseases.	BP204T.2
LO 6	To understand about the Renal System: Acute and chronic renal failure.	BP204T.2

Content Table

Topic
• Cardiovascular System: Hypertension, congestive heart failure, • Ischemic Heart Disease (angina, myocardial infarction, atherosclerosis & arteriosclerosis). • Respiratory System: Asthma, Chronic obstructive airways diseases. • Renal System: Acute and chronic renal failure.

CARDIOVASCULAR SYSTEM

Hypertension, Congestive heart failure

Ischemic heart disease (angina, myocardial infarction, atherosclerosis and arteriosclerosis)

HYPERTENSION

Hypertension (HTN or HT), also known as high blood pressure (HBP), is a long-term medical condition in which the blood pressure in the arteries is persistently elevated. The hypertension is defined as persistent increase in systolic blood pressure and diastolic blood pressure.

A well accepted definition of hypertension was suggested by **Evans and Rose: "Hypertension should be defined in the terms of blood pressure level above which investigation and treatments do well more than harm"**

The Systolic Blood Pressure will be more than or equal of 140 mmHg and Diastolic Blood Pressure will be more than or equal of 90 mmHg. A patient is said to be hypertensive when his SBP≥ 140 mm Hg & DBP ≥ 90 mm Hg provided that the patient is not on antihypertensive drugs.

Blood pressure is the pressure exerted by the blood on the arteries or blood vessels.

Blood Pressure = Cardiac output × Total peripheral resistance

BP = C.O × T.P.R

Total peripheral resistance is the resistance offered by arteries to flow of the blood.

Cardiac output is the blood pump by heart per minute.

Cardiac output = Stroke Volume× Heart Rate

C.O = S.V × H.R

Stroke volume: Volume of blood pumped out of the left ventricle of the heart during each systolic cardiac contraction.

Heart Rate: The speed at which the heart beats. The average heart rate is 72 beats per minute.

Long-term high blood pressure, however, is a major risk factor for coronary artery disease, stroke, heart failure, atrial fibrillation, peripheral arterial disease, vision loss, chronic kidney disease, and dementia. Hypertension is a hemodynamic disorder. A World Wide Epidemic. Hypertension is poorly controlled, with less than 25% controlled in developed countries and less than 10% in developing countries. Nearly 1 billion hypertensive in the world. Hypertension which is responsible for 3 million deaths annually. May 17th World Hypertension Day (WHD) is

celebrated to promote the public awareness of the importance of monitoring blood pressure with being awareness of its natural levels. The WHD was first inaugurated in May 2005 and initiated by The World Hypertension League (WHL),

CLASSIFICATIONON THE BASIS OF BLOOD PRESSURE

Category	Systolic Blood Pressure (mmHg)	Diastolic Blood Pressure (mmHg)
Optimal	<120	< 80
Normal	< 130	< 85
High Normal	130-139	85-89
Hypertension Stage-I	140-159	90-99
Hypertension Stage-II	160-179	100-109
Hypertension Stage-III	≥180	≥110

TYPES OF HYPERTENSION

Primary/Essential Hypertension	Secondary Hypertension
No specific medical cause ac be found to explain a patient's condition. 95% of the populations are suffered from primary hypertension	Less common cause HTN (5%). There is known cause, and thus the hypertension is known as Secondary Hypertension. It indicates that the high blood pressure is result of another condition such as kidney disease or certain tumors.

ETIOLOGY

Primary Hypertension:

i. **Salt sensitivity:** Approximately 60% of the primary hypertension population is responsive to sodium intake. This is due to the fact that increasing amount of salt in the blood stream causes the body to draw more water, increasing the pressure on the blood vessel walls.

ii. **Genetics:** Hypertension is one of the most complex disorders, which genetic heritability averaging 30%.

iii. **Role of Renin:** The high level of renin predispose to hypertension; Increased Renin → Increased Angiotensin II→ Increased Vasoconstriction, Thirst/ADH and Aldosterone → Increased Sodium Reabsorption in Kidneys (DCT and CD) →Increased Blood Pressure

iv. **Insulin Resistance:** Insulin regulates the levels of glucose in the body. It also exhibits vasodilatory properties. Insulin resistance or hyperinsulinemia have suggested as being responsible for the increased arterial pressure in some patients of hypertension.

v. **Sleep Apnea:** Sleep apnea is a common under recognized cause of hypertension. It is best treated with tonsillectomy, adenoidectomy, sinus surgery, or weight loss, or the Mandibular advancement splint (MAS).

vi. **Other Factors:** Cigarette smoking, obesity and lack of exercise, mental tension and excessive cholesterol intake may also contribute to development of primary hypertension.

Secondary Hypertension: Only in small minority of patients with elevated arterial pressure can a specific cause be identified.

i. **Renal Hypertension:** Hypertension produces by the disease of kidney. This includes diseases such as chronic glomerulonephritis. Hypertension can also be produced by disease of the renal arteries supplying the kidney, this is known as **renovascular hypertension.** It is thought that decreased perfusion of renal tissue due to stenosis of main or branch renal artery activities the renin-angiotensin system.

ii. **Pheochromocytoma:** In patients with ***Pheochromocytoma*** increased in secretion of catecholamines such as epinephrine and norepinephrine by a tumor cause excessive stimulation of adrenergic receptors, which results in peripheral vasoconstriction and cardiac stimulation.

iii. **Diet:** Diet that id high fat and salt has been proven to exacerbate hypertension. Patients placed on a strict vegetarian diet showed a significant benefit to their condition over the one year.

iv. **Age:** Over time, the number of collagen fibers in artery and arteriole walls increases, making blood vessels stiffer with the reduce elasticity comes a smaller cross sectional area in systolic and so raised mean arterial blood pressure.

CLINICAL FEATURES

Sometimes the high blood pressure does not cause any symptoms, so that it is known as silent killer disease.

Some Common Symptoms of Hypertension	
Head ache	Vomiting
Blurred vision	Fatigue
Dizziness	Confusion epistaxis
Nausea	Chest pain
Cyanosis	Irregular heart beat
Shortness of breath	Papilledema

PATHOPHYSIOLOGY

The normal blood pressure is maintained by different mechanisms

OVER ACTIVATION OF SYMPATHETIC NERVOUS SYSTEM:

When the BP is decreasing or increase then activation of sympathetic nervous system will occur. The increased sympathetic nervous system activity increases the heart rate and cardiac contraction.

The increased the heart rate and cardiac contraction produce vasoconstriction in the peripheral arterioles and promotes the release of renin from kidney.

The net effect of SNS activation is to increase the arterial blood pressure by increasing cardiac output and systemic vascular resistance.

NATRIURETIC HORMONE

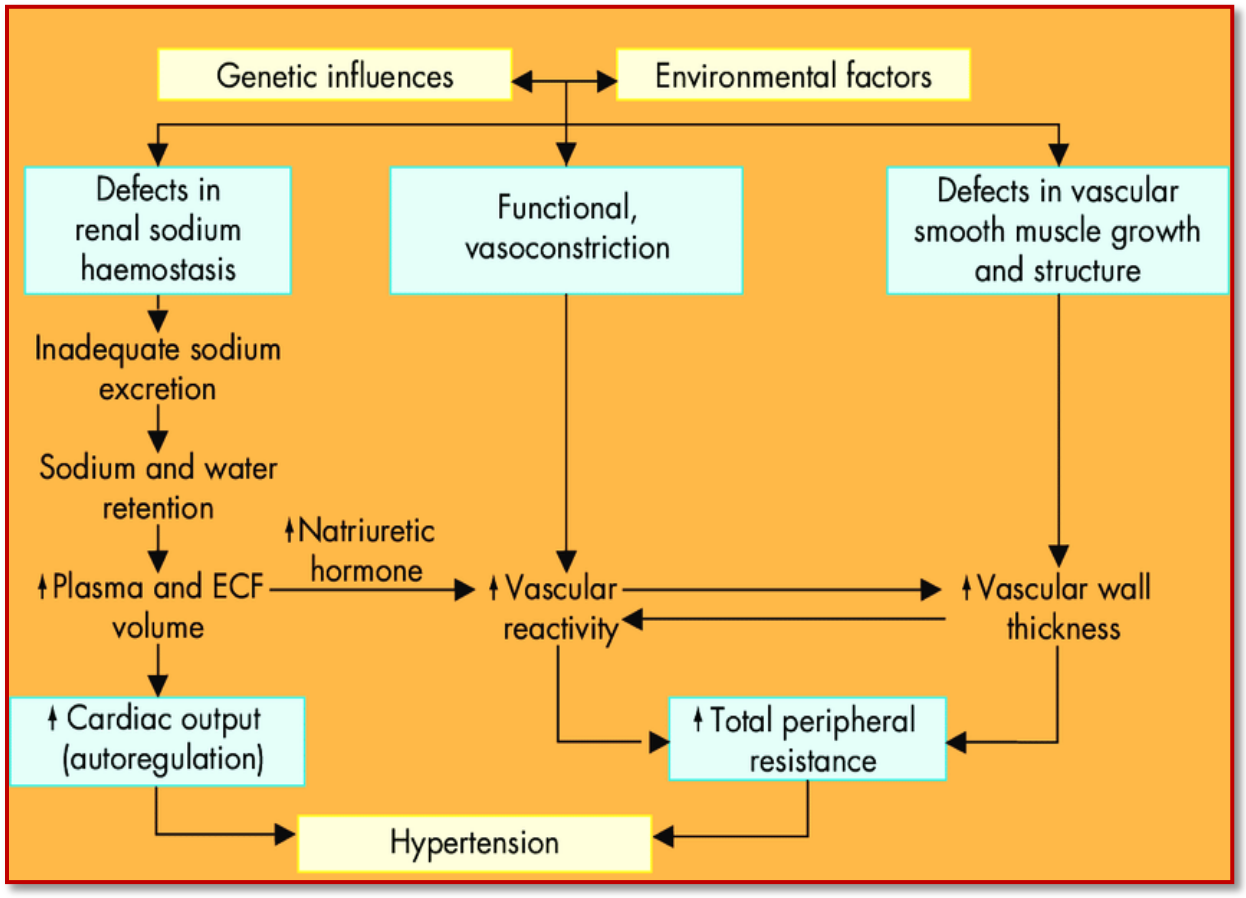
By inhibiting sodium and potassium ATPase → Block the activity transport of sodium →Increase intracellular concentration of sodium.

ACTIVITIES OF VASCULAR ENDOTHELIUM

The vascular endothelium is a single cell layer that lines the blood vessel. It will produce vasoactive substances and growth factors like nitric acid, endothelin etc.

These substances are potent vasoconstrictor peptide that has pronounced vasoconstrictor effects on the renal vasculature, promoting the retention of sodium.

The plasma concentration of endothelium-I is increased in proportion to the symptomatic and hemodynamic severity of heart failure.

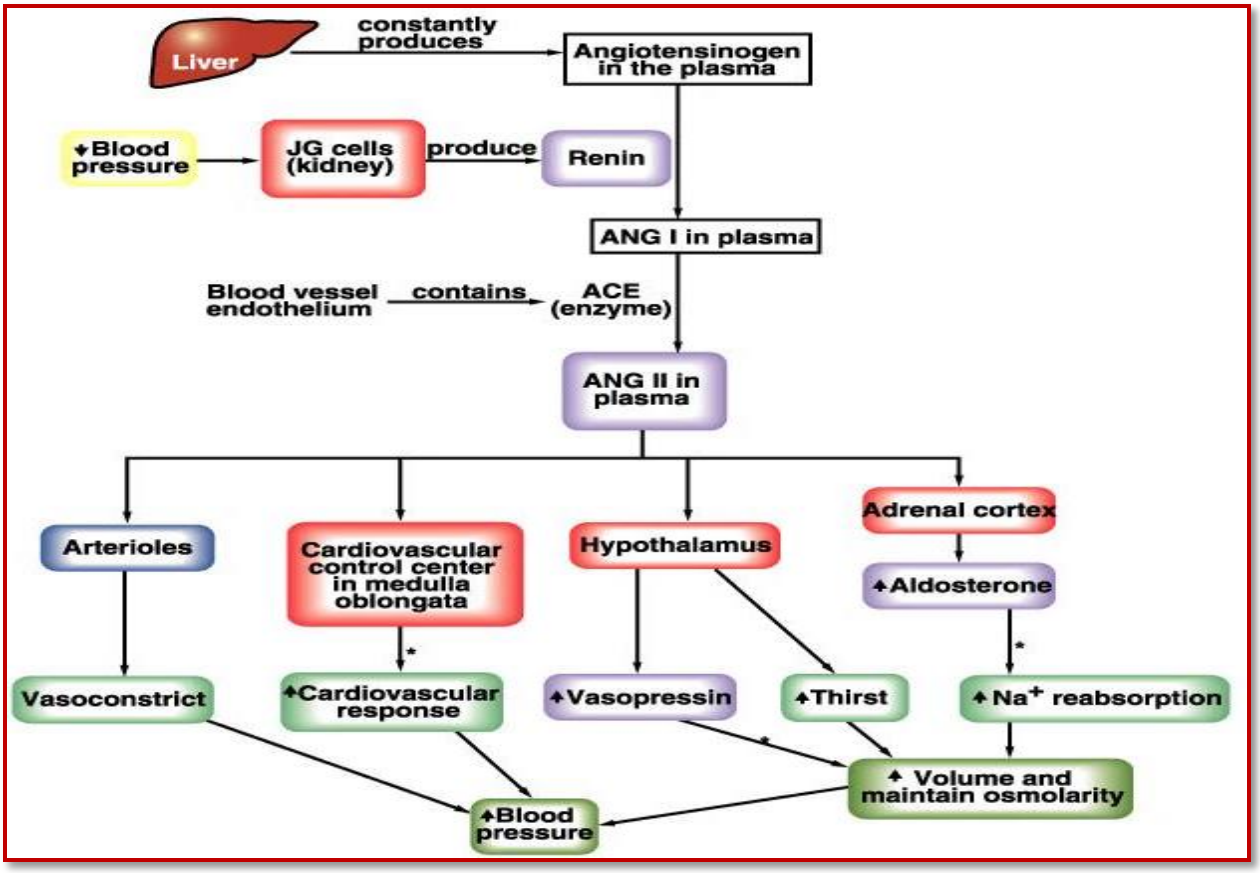


ACTIVITIES OF ENDOCRINE SYSTEM

When the angiotensin-II is stimulated in the adrenal cortex, it will secrete aldosterone. The aldosterone will stimulate the kidneys to retain sodium and water. Thus the BP and cardiac output will get increased.

OVER ACTIVATION OF RENIN-ANGIOTENSIN ALDOSTERONE SYSTEM (RAAS)

Over activation of RAAS lead to vasoconstriction and retention of sodium and water. The increase in blood pressure leads to hypertension as show below:



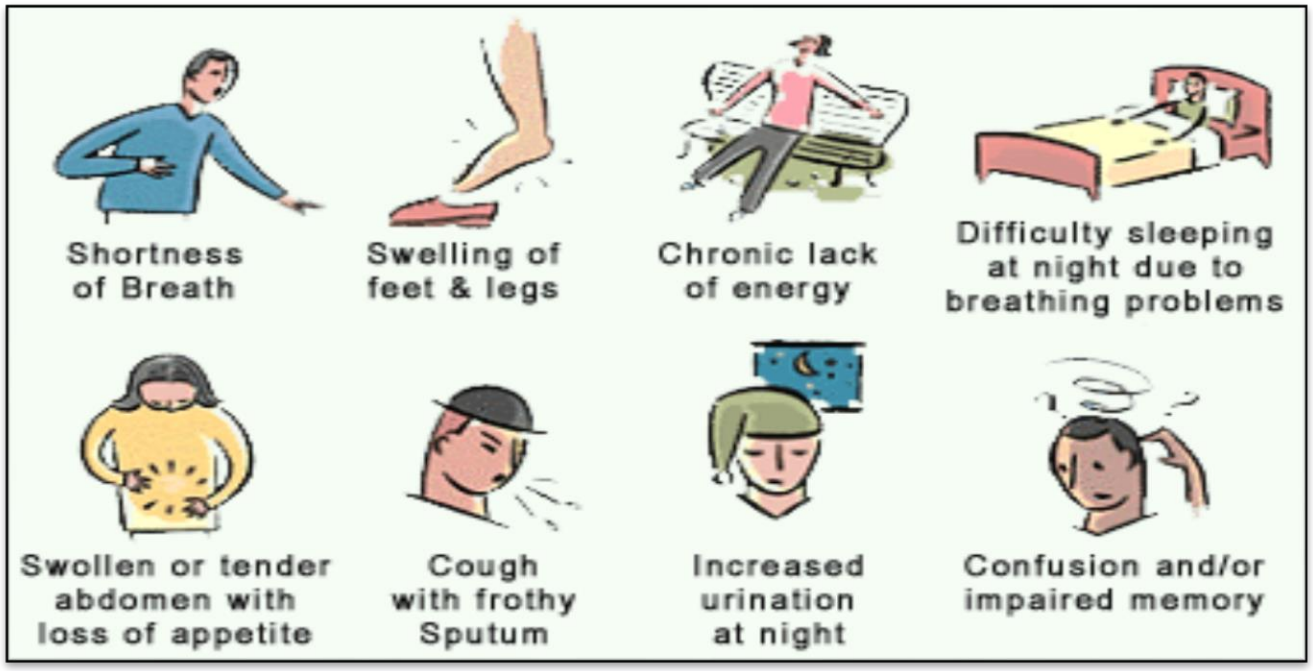
DIAGNOSIS	MANAGEMENT
Measuring blood pressure	**LIFE STYLE MODIFICATION**
Blood test: Creatinine,	Weight reduction
Electrolytes	Dietary sodium reduction
Glucose	Reduce alcohol
Cholesterol	Exercise
Additional test: Chest x-ray,	Stress management
ECG	**PHARMACOLOGICAL**
Testing of urine sample for proteinuria	

CONGESTIVE HEART FAILURE

Congestive heart failure (CHF), or heart failure, is a condition in which the heart is unable to pump sufficient blood to meet the metabolic demand of the body and also unable to receive it back because every time after a systole.

A heart failure, heart has a reduced ability to pump blood. A normal heart pumps blood in a smooth and synchronized way.

Sign & Symptoms



ETIOLOGY

Heart failure may be caused by one of the following factors, either singly or in combination:

1. INTRINSIC PUMP FAILURE. The most common and most important cause of heart failure is weakening of the ventricular muscle due to disease so that the heart fails to pump sufficient quantity of blood. The various diseases may be:

i) Ischemic heart disease

ii) Myocarditis

iii) Cardiomyopathies

iv) Metabolic disorders e.g. beriberi

v) Disorders of the rhythm e.g. atrial fibrillation and flutter.

2. INCREASED WORKLOAD ON THE HEART.

Increased mechanical load on the heart results in increased myocardial demand resulting in myocardial failure.

Increased load on the heart may be in the form of pressure load or volume load.

i) Increased pressure load may occur in the following states:

a) Systemic and pulmonary arterial hypertension.

c) Chronic lung diseases.

ii) Increased volume load occurs when a ventricle is required to eject more than normal volume of the blood resulting in cardiac failure. This is seen in the following conditions:

a) Valvular insufficiency

b) Severe anemia

c) Thyrotoxicosis

e) Hypoxia due to lung diseases.

3. IMPAIRED FILLING OF CARDIAC CHAMBERS.

Decreased cardiac output and cardiac failure may result from extra-cardiac causes or defect in filling of the heart:

a) Cardiac tamponade e.g. haemopericardium, hydropericardium

b) Constrictive pericarditis.

TYPES OF HEART FAILURE

There are two main associations which are working on the governance of Research on heart failure.

- ***International Society for Heart Failure (ISHR)***
- ***New Yourk Heart Association (NYHA).***

According to NYHA heart failure is divided into four classes:

Class-I There is no structural and functional abnormalities but this class of people is prone to have heart failure. e.g. in diabetes and hypertension.

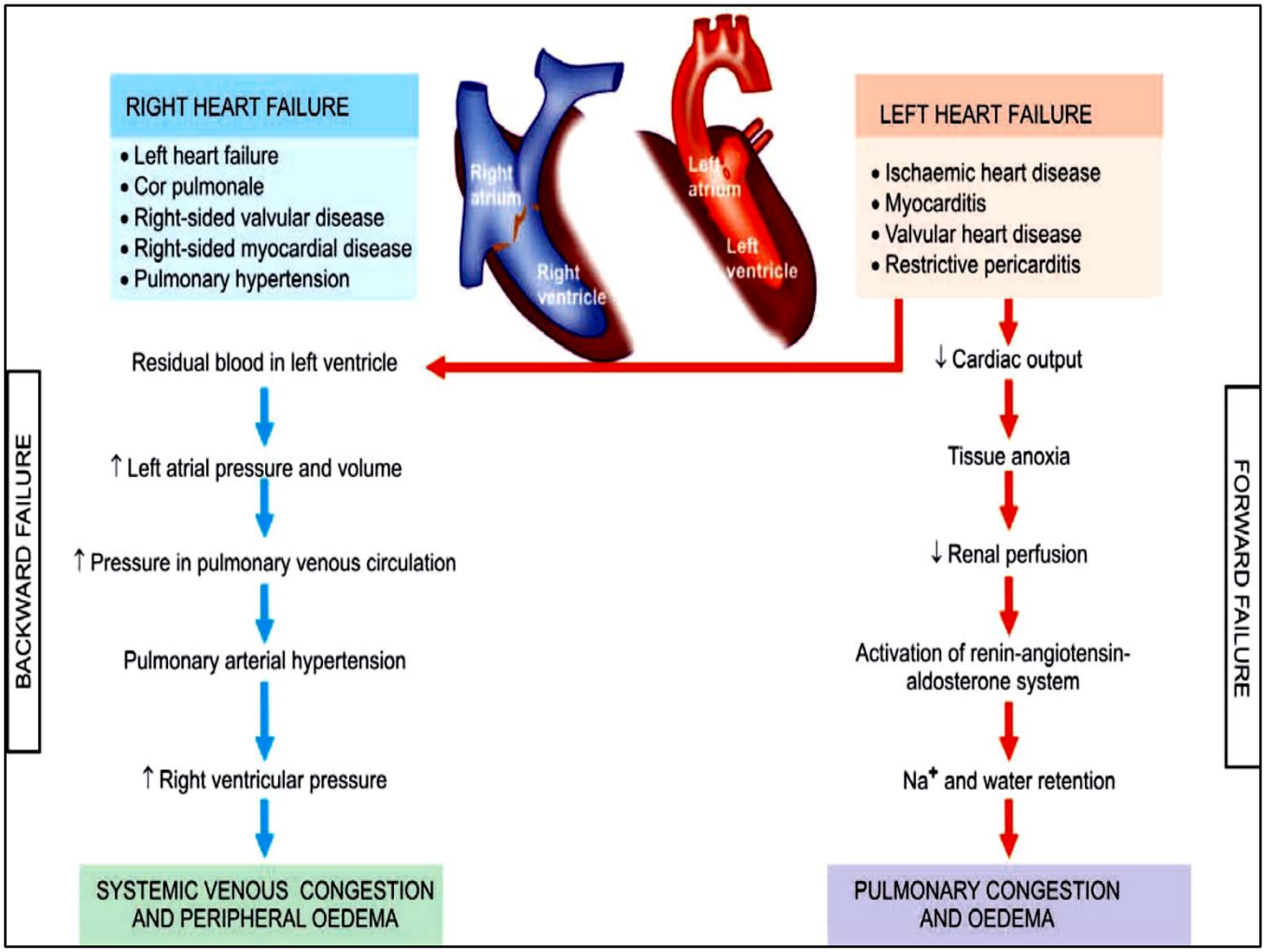
Class-II There is structural and functional abnormalities in the heart, but people of this class do not show any symptoms of heart failure. e.g. Dyspnea, fatigue, pulmonary hypertension.

Class-III These patients undergone or shows forceful contraction of heart muscle because of release of the catecholamines (e.g. adrenaline a noradrenaline). There are structural and functional abnormalities and these patients experience the symptoms

Class-IV It is a decompensated heart failure or also known as stage of clinical emergency. Patients belonging to this class, have to be hospitalized. In class IV, patients used to have cardiac hypertrophy. It is of two types:

► ***Concentric hypertrophy***: Wall thickness of left ventricle is increased, whereas volume of left ventricle is decreased

► ***Eccentric Hypertrophy*** In this case left ventricular wall thickness is decreased, whereas volume of left ventricle is increased



Other types of heart failure:

Heart failure may be acute or chronic, right-sided or left sided, and forward or backward failure.

A. ACUTE AND CHRONIC HEART FAILURE

Acute Heart Failure Sudden and rapid development of heart failure occurs in the following conditions:

i) Larger myocardial infarction

ii) Valve rupture

v) Acute viral myocarditis

vi) Acute bacterial toxaemia.

In acute heart failure, there is sudden reduction in cardiac output resulting in systemic hypotension but oedema does not occur. Instead, a state of cardiogenic shock and cerebral hypoxia develops.

Chronic Heart Failure More often, heart failure develops slowly as observed in the following states:

i) Myocardial ischemia from atherosclerotic coronary artery disease

ii) Multivalvular heart disease

iii) Systemic arterial hypertension

iv) Chronic lung diseases resulting in hypoxia

v) Progression of acute into chronic failure.

In chronic heart failure, compensatory mechanisms like tachycardia, cardiac dilatation and cardiac hypertrophy try to make adjustments so as to maintain adequate cardiac output. This often results in well-maintained arterial pressure and there is accumulation of oedema.

B. LEFT-SIDED AND RIGHT-SIDED HEART FAILURE.

From clinical point of view, therefore, it is helpful to consider failure of the left and right heart separately. The clinical manifestations of heart failure result from accumulation of excess fluid *upstream* to the left or right cardiac chamber whichever is initially affected.

Left-Sided Heart Failure It is initiated by stress to the left heart. The major causes are as follows:

i) Systemic hypertension

iii) Ischaemic heart disease

iv) Myocardial diseases e.g. cardiomyopathies, myocarditis.

v) Restrictive pericarditis.

The clinical manifestations of left-sided heart failure result from decreased left ventricular output and hence there is accumulation of fluid *upstream* in the lungs.

Right-Sided Heart Failure some conditions affect the right ventricle primarily, producing right-sided heart failure. These are as follows:

i) As a consequence of left ventricular failure.

iii) Pulmonary or tricuspid valvular disease.

iv) Pulmonary hypertension secondary to pulmonary thrombo-embolism.

v) Myocardial disease affecting right heart.

vi) Congenital heart disease with left-to-right shunt.

Whatever be the underlying cause, the clinical manifestations of right-sided heart failure are *upstream* of the right heart such as systemic and portal venous congestion, and reduced cardiac output.

C. BACKWARD AND FORWARD HEART FAILURE

The mechanism of clinical manifestations resulting from heart failure can be explained on the basis of mutually interdependent backward and forward failure.

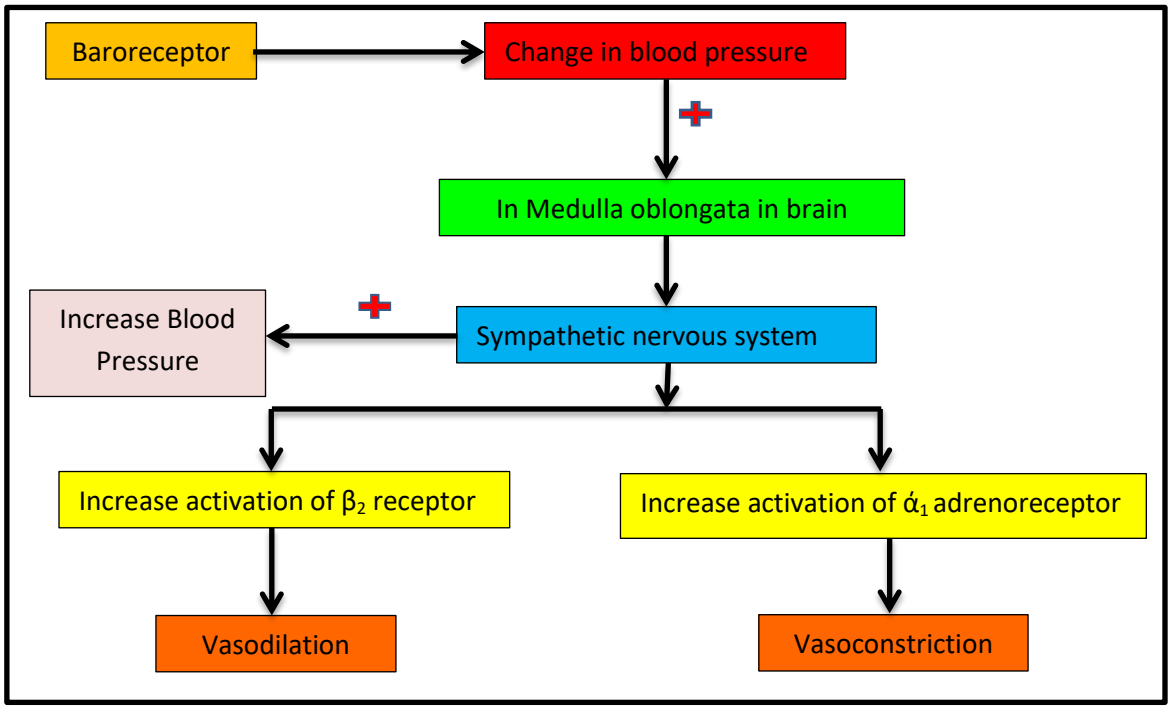
Backward Heart Failure According to this concept, either of the ventricles fails to eject blood normally, resulting in rise of end-diastolic volume in the ventricle and increase in volume and pressure in the atrium which is transmitted *backward* producing elevated pressure in the veins.

Forward Heart Failure According to this hypothesis, clinical manifestations result directly from failure of the heart to pump blood causing diminished flow of blood to the tissues, especially diminished renal perfusion and activation of renin angiotensin-aldosterone system.

PATHOPHYSIOLOGY

Over activation of Sympathetic Nervous System:

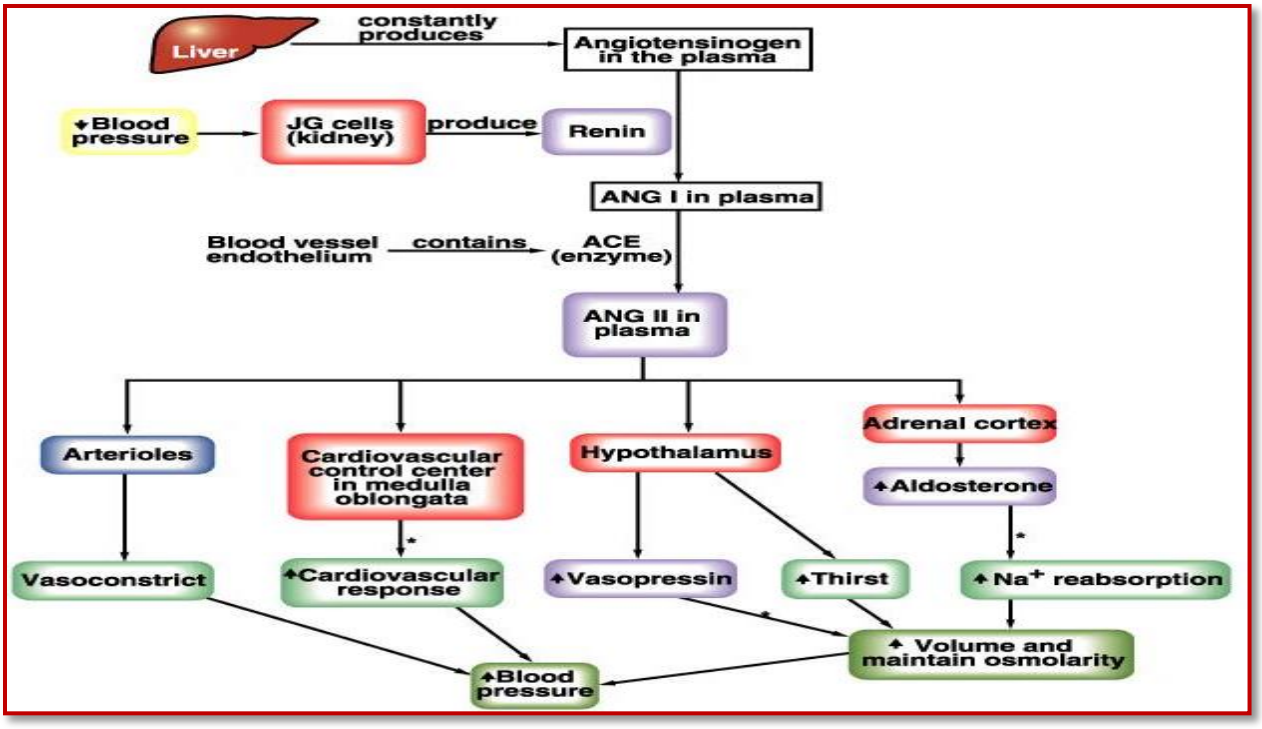
The sympathetic nervous system is activated in heart failure via low and high pressure baroreceptors, as an early compensatory mechanism which provides inotropic support and maintains cardiac output. Chronic sympathetic activation, however, has deleterious effects causing a further deterioration in cardiac function.



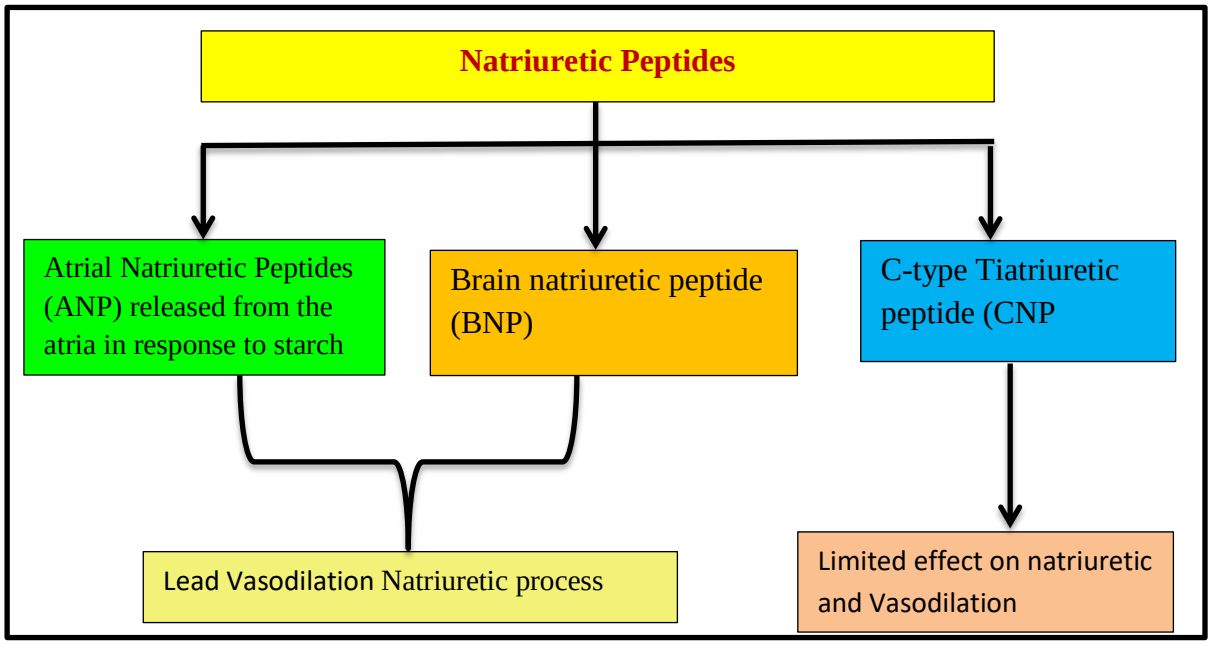
Over activation of Renin-Angiotensin aldosterone System (RAAS):

Stimulation of the renin-angiotensin-aldosterone system leads to increased concentrations of renin, plasma angiotensin-II and aldosterone. Angiotensin-II is a potent vasoconstrictor of the renal (efferent arterioles) and systemic circulation, where it stimulates release of noradrenaline from sympathetic nerve terminals, inhibits vagal tone, and promotes the release of aldosterone.

This leads to the retention of sodium and water. In addition, angiotensin-II has important effects on cardiac myocytes and may contribute to the endothelial dysfunction that is observed in chronic heart failure.

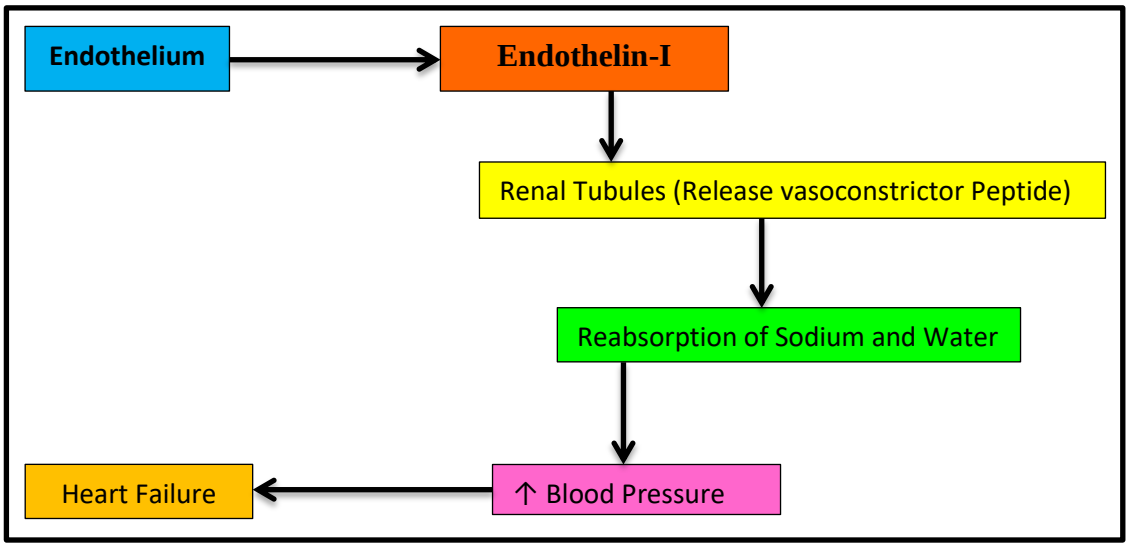


Down Regulation of Natriuretic Peptides: There are three natriuretic peptides, of similar structure, and these exert a wide range of effects on the heart, kidneys, and central nervous system. Atrial natriuretic peptide (ANP) is released from the atria in response to stretch, leading to natriuresis and vasodilatation.

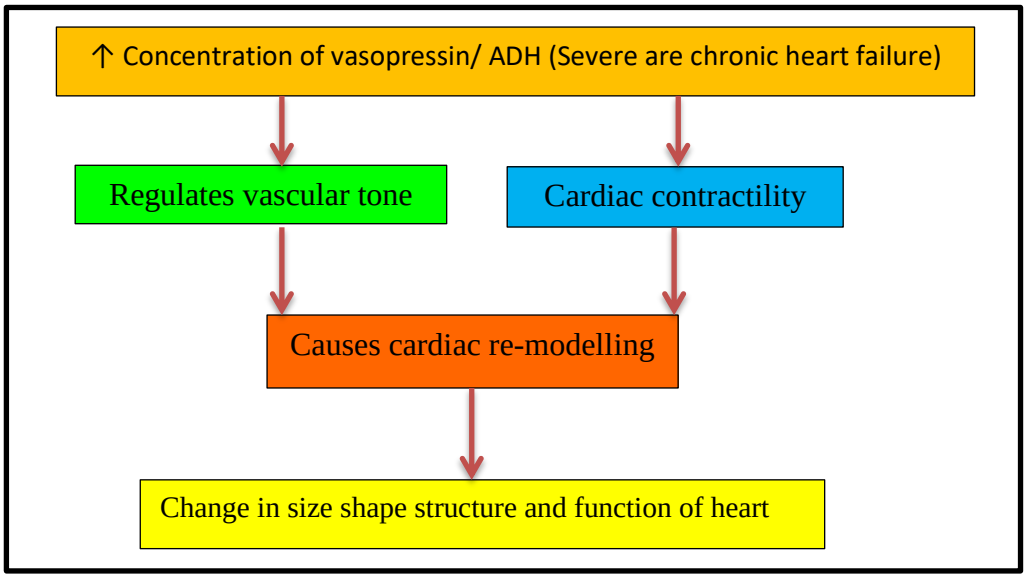


In humans, brain natriuretic peptide (BNP) is also released from the hear predominantly from the ventricles, and its actions 2 similar to those of atrial natriuretic peptide C-type Tiatriuretic peptide (CNP) is limited to the vascule endothelium and central nervous system and has gain limited effects on natriuresis and vasodilatation. The atrial and brain natriuretic peptides increase in response to volume expansion and pressure overload of the heart and act as physiological antagonists to the effects of angiotensin II on vascular tone, aldosterone secretion and renal-tubule sodium reabsorption In heart failure there is down regulation of natriuretic peptides.

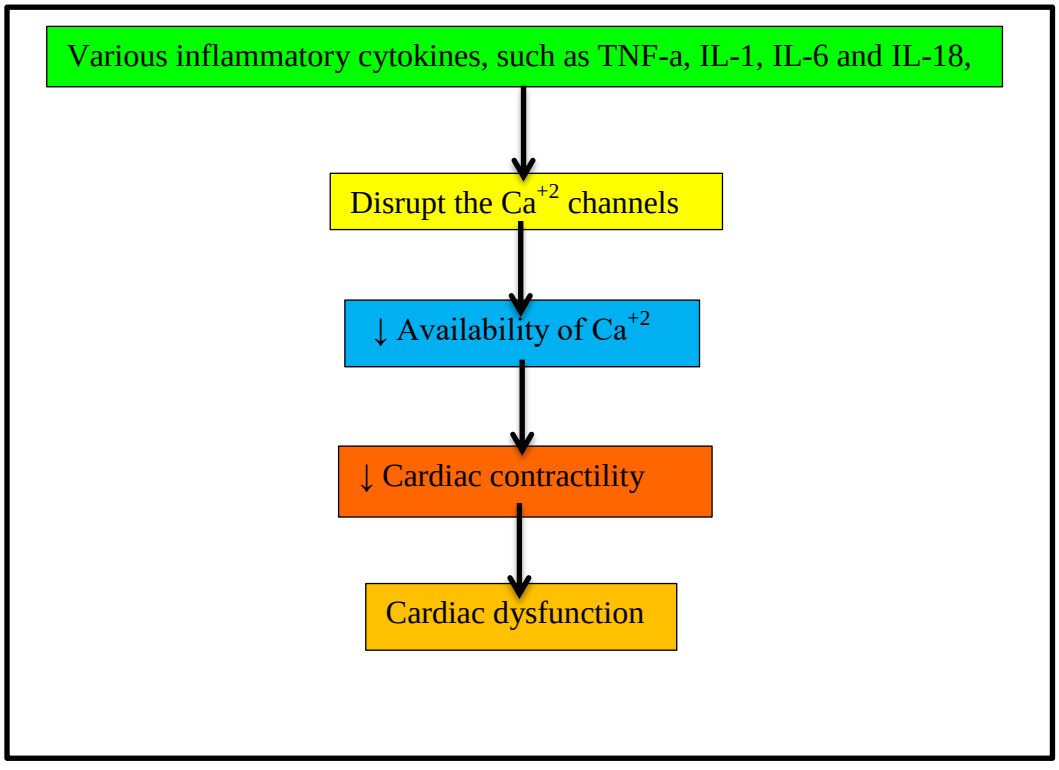
Endothelin-I: Endothelin-l is secreted by vascular endothelial cells and is a potent vasoconstrictor peptide that has pronounced vasoconstrictor effects on the renal vasculature, promoting the retention of sodium. Importantly, the plasma concentration of endothelin-1 is of prognostic significance and is increased in proportion to the symptomatic and haemodynamic severity of heart failure.



Over Activation of Arginine Vasopressin (AVP) or Antidiuretic Hormone: AVP concentrations are also increased in severe chronic heart failure. It regulates vascular tone and cardiac contractility and causes cardiac re-modelling it also regulates free water reabsorption. The increase in AVP level will deteriorate cardiac function and it is the potential biomarker for heart failure. High concentrations of hormones are common in patients receiving diuretic treatment, and this may contribute to the development of hypernatremia.



Over expression of inflammatory cytokines: There are various inflammatory cytokines, such as TNF-a, IL-1, IL-6 and among recently discovered IL-18, which are over-expressed in CHF. These cytokines disrupt the Ca^{+2} channels and reduce the availability of Ca^{+2} which decreases cardiac contractility and produce cardiac dysfunction. Moreover, these cytokines also cause apoptosis of cardiac muscles.



DIAGNOSES

1. Chest X-ray Film. This is very helpful in identifying the build-up of fluid in the lungs. Also, the heart usually enlarges in CHF, and this may be visible on the x-ray film

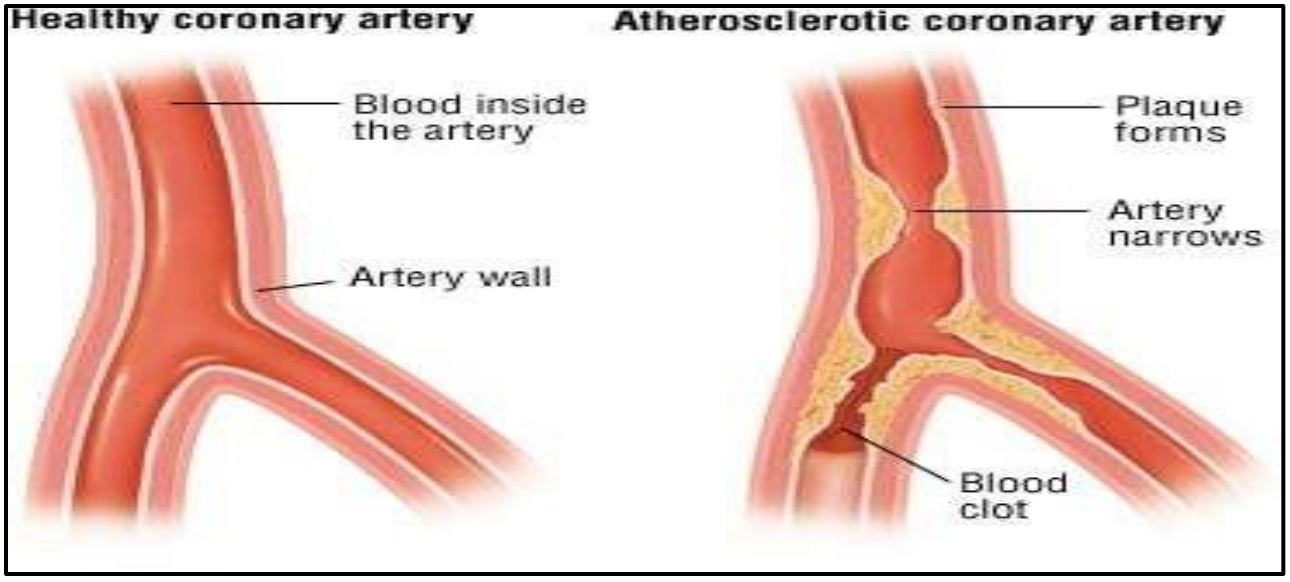
2. Electrocardiogram (ECG). This painless test measures the electrical activity (rhythm) of the heart. It can reveal several different heart problems that can cause heart failure, including heart attacks, rhythm disorders, long- standing strain on the heart from high blood pressure, and certain valve problems.

3. MUGA Scan. This stands for multiple-gated acquisition scanning. A small amount of a mildly radioactive dye is injected into a vein and travels to the heart. As the heart pumps the blood with the dye in it, pictures are taken. The pumping performance of the left and right ventricles can be determined.

4. Stress Test. A treadmill or medication (non-walking) stress test is used to help evaluate the cause or causes of heart failure, in particular, regarding coronary artery disease. This test is frequently combined with nuclear imaging or echocardiography to improve accuracy.

ANGINA PECTORIS

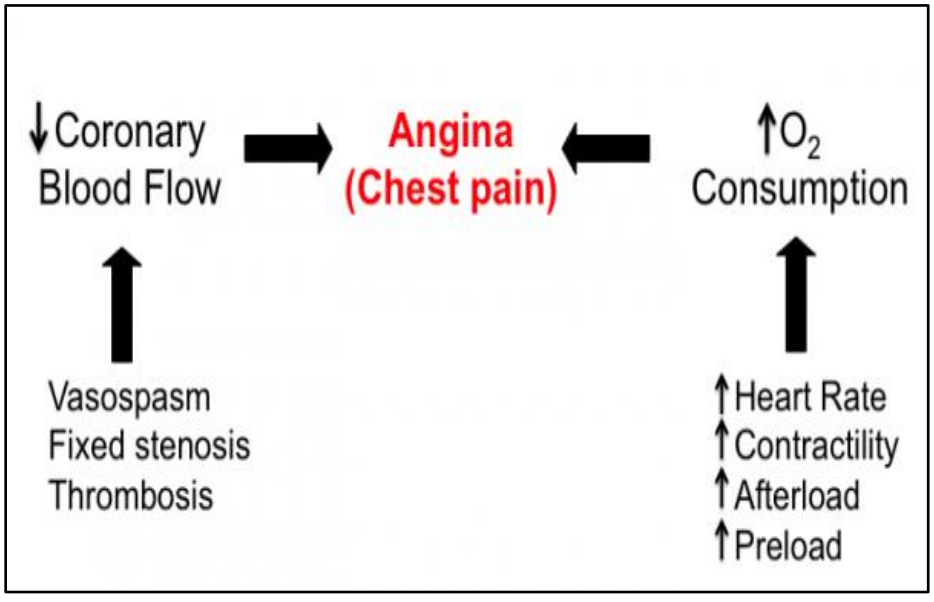
- Chest pain due to imbalance between the oxygen requirement of the heart and oxygen supplied to it via the coronary vessels.
- It is the principal symptoms of patient with ischemic heart disease. Angina is not a disease itself, but a symptom of heart disease.
- The pain often also spreads to the shoulders, arms, jaw, neck and back.
- It is a pain syndrome occurs due to adverse induction in oxygen supply and demand, situation in a portion of the myocardium.
- ***Ischemia*** is defined as lack of blood supply or no blood supply, resulting in decrease in O_2 supply and accumulation of metabolic end products (mainly acidic in nature).
- ***Anoxia*** is defined as absence of O_2 to myocardium and hypoxia is decrease in O_2 supply.



Etiology

- Coronary atherosclerosis
- Coronary thrombus
- Coronary vasospasm
- Transient platelet aggregation
- Adrenergic system stimulation and coronary vasoconstriction
- Accumulation of potent vasoconstrictor at the site of endothelial injury.

Oxygen Supply and Demand



TYPES OF ANGINA PECTORIS

Mainly angina Pectoris is of following three types:

1) Stable Angina (Typical Angina)
2) Variant angina (Prinzmetal's Angina)
3) Unstable angina (Crescendo Angina)

1. Stable angina (Typical Angina):

- It is due to deposition of atherosclerotic plaques in the coronary arteries.
- It results in narrowing of the lumen of the arteries. So, whenever, demand of the heart increases such as in exercise, emotional reactions, the pain or angina develops.
- This is because the coronary arteries cannot supply enough blood to heart due to reduced lumen size. The pain is relieved after taking rest because it will result in decreased demand of heart.

2. Variant angina (Prinzmetal's Angina)

- In this case, there is transient vasospasm of the coronary arteries.
- It will result in decreased blood flow to heart.
- The demand of heart is not changed, but because blood supply has reduced, so there will be angina pain.
- Attacks occur at rest or during sleep and are unpredictable

3. Unstable angina (Crescendo Angina)

- In this case, there is atherosclerotic deposition in arteries.
- These plaques will rupture and will block the coronary arteries.
- There is also a vasospasm of the coronary arteries. So, combination of both atherosclerotic plaques and vasoconstriction (vasospasm) of blood vessels will decrease blood flow to heart.
- It will then lead to development of angina
- Chronically, reduced blood supply causes atrophy of cardiac muscle with fibrosis replacement (reduced myocardial capacity work leads to CHF) and may damage conducting tissue to produce unstable cardiac arrhythmia.

SYMPTOMS

- Pain and discomfort are the main symptoms and these are often described as
- Pressure, squeezing burning or tightness in the chest
- Pain usually starts in the chest, behind the breast bone
- Pain may also occur in arms, shoulders, neck, jaw throat or back
- Person may feel like Indigestion
- Various symptoms such as nausea, fatigue, short ness of breath, sweating, light headache, or weakness may also occur.

PATHOPHYSIOLOGY

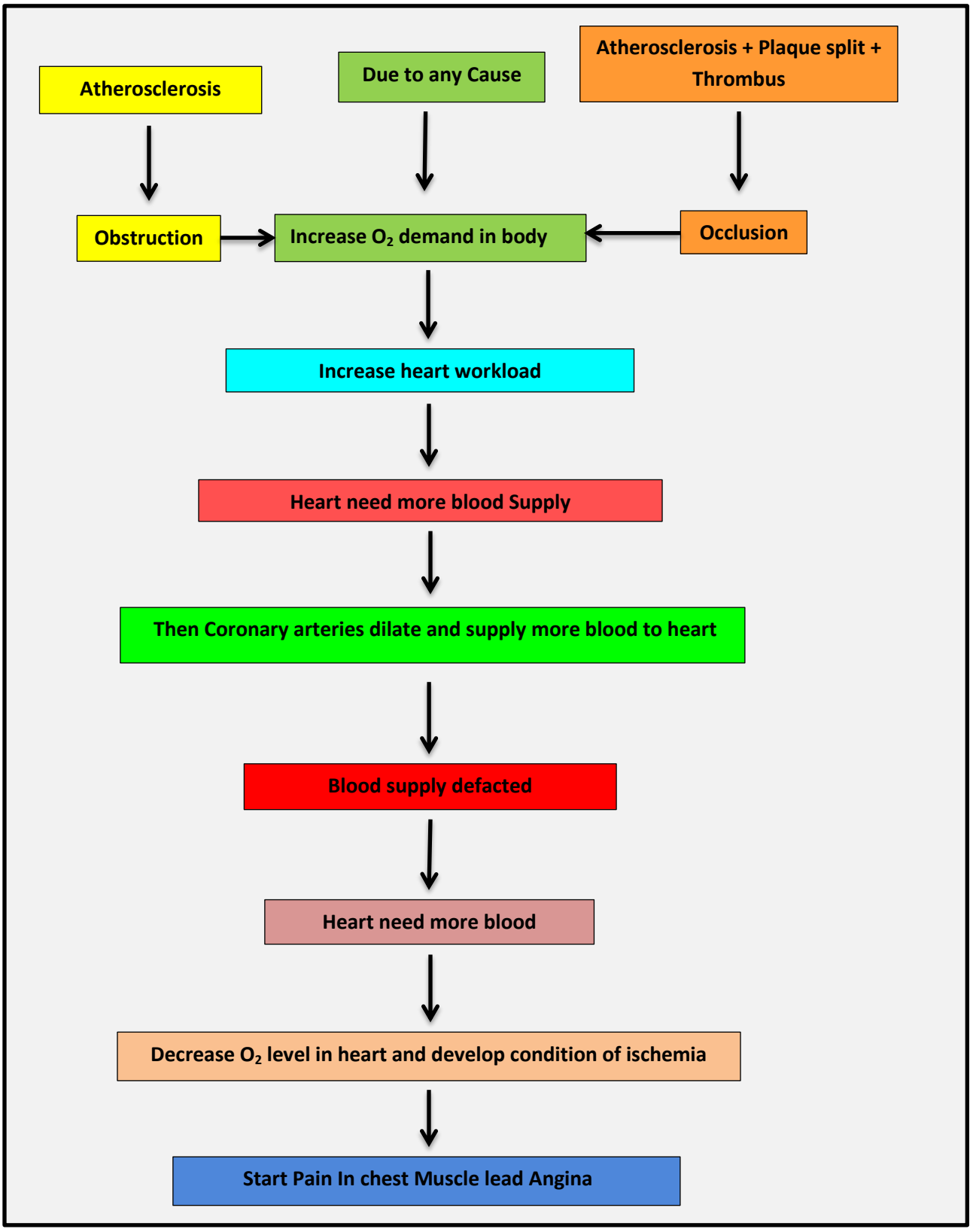
Pathophysiology of angina is dynamic, evolutionary and complex It can be explained on the basis of various factors i.e. factors which lead to decreased blood supply and factors which cause increased O_2 demand.

- **Factors responsible for increased oxygen demand**
- **Factors responsible for decreased oxygen supply**
- **Factors responsible for increased oxygen demand**
    - Heart rate
    - Contractility
    - Intra-myocardial wall tension
- **Factors responsible for decreased oxygen supply**
    - Stenosis due to atherosclerosis.

Collateral blood flow: It means during any obstruction of the blood vessels, an alternate blood vessel is generated due to angio-genesis. So blood bypass the obstruction pathway and hence it can also affect the coronary blood flow and leads ischemia.

- Shortening of diastole time.
- Increased heart rate.
- Loss of vascular endothelium by PTCA (Percutaneous Trans Coronary Angioplasty) leads to loss of protective factors like NO, prostaglandins PGH2, PGE2.Sympathetic stimulation by action on ά-1 receptors.

PATHOPHYSIOLOGY OF ANGINA PECTORIS



DIAGNOSIS

PHYSICAL EXAMINATION:

The primary diagnosis is based upon description of symptoms by the patient (viz – kind of pain, duration of pain, its association with other factors like exertion, meal, weather, etc.).

ECG EXAMINATION:

(a) Resting ECG: It is helpful to find previous myocardial infarction and is a little useful. 'T' wave flattening is occasionally seen.

(b) Exercise ECG: A standard formal exercise tolerance test is performed to increase workload on heart followed by recording of ECG during exercise stress. Changes in 'ST' segment, abnormal pumping motion of wall of left ventricles are common findings.

CORONARY ANGIOGRAPHY:

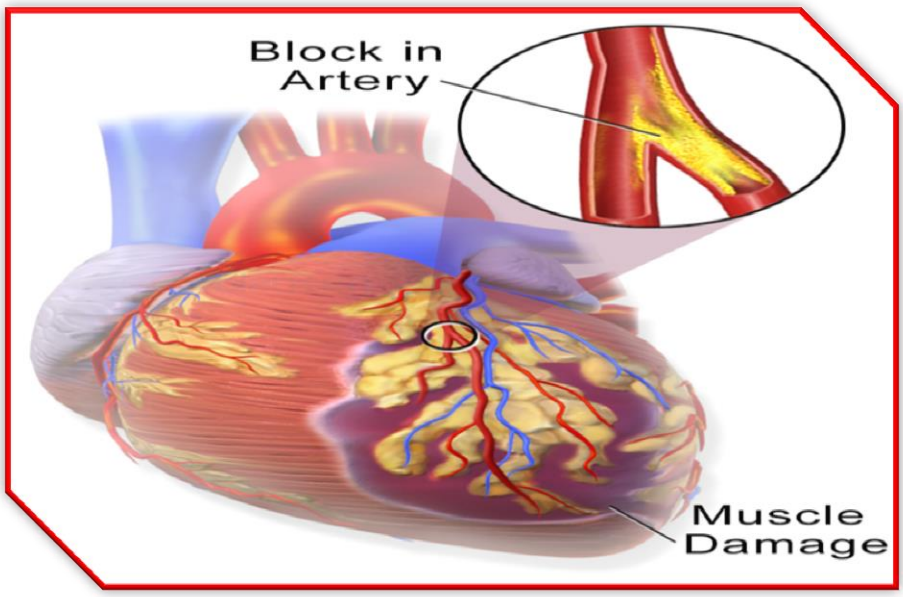
It is generally used when other non-invasive tests have failed to diagnose angina pectoris. Angiography reveals the severity of the disease and gives a view regarding need of coronary angioplasty.

RADIONUCLIDE IMAGING:

This technique confirms the presence of ischemia along with the region and number of cells affected.

MYOCARDIAL INFARCTION

- Myocardial infarction (MI) refers to the process by which areas to the process by which areas of myocardial cells in the heart are permanently destroyed.
- It occurs when myocardial tissues are abruptly and severely deprived of oxygen.
- Myocardial infarction (MI) refers to tissue death (infarction) of the heart muscle (myocardium) caused by ischemia, that is lack of oxygen delivery to myocardial tissue.
- It is a type of acute coronary syndrome, which describes a sudden or short-term change in symptoms related to blood flow to the heart.
- Myocardial infraction is a diseased condition which is caused by reduced blood flow in a coronary artery due to atherosclerosis and occlusion of an artery by an embolus or thrombus.



TYPES OF MYOCARDIAL INFRACTION

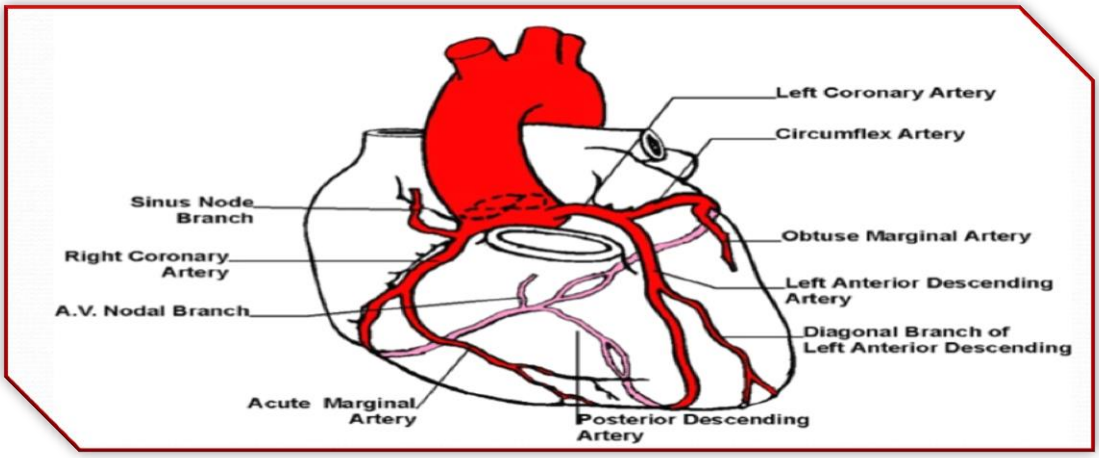
The two main types of acute MI based on pathology are:

Transmural infraction: It extends through the whole thickness of heart muscle and is usually a result of complete occlusion of the area's blood supply.

Subendocardial infraction: It involves a small area in the subendocardial wall of the left ventricle septum, or papillary muscles.

LOCATION OF MYOCARDIAL INFRACTION

- Obstruction of left anterior descending artery (LAD) results in anterior or septal wall MI
- Obstruction of the circumflex artery results in posterior wall MI and Lateral MI.
- Obstruction of the right coronary artery results in inferior wall MI.



ETIOLOGY:

Modifiable		**Non- Modifiable**
Hyperlipidemia	Hypertension,	Age- More than 40 years
Obesity	Physical inactivity	Family history: Myocardial infraction can be inherited from parents to children.
Stress, Smoking	Diabetes Mellitus	Gender: Myocardial infarction is 3 times more in men than women.

Hyperlipidemia:

Cholesterol is a major component of the atherosclerotic plaque that is associated with MI. An elevated level of total cholesterol is associated with an increased risk of coronary atherosclerosis and MI. Elevated levels of low density lipoprotein (LDL) cholesterols are associated with an increased incidence of both atherosclerosis and MI.

Diabetes Mellitus:

Patients who are diabetic have a substantially greater risk of atherosclerotic vascular disease in the heart as well as in other areas of the vasculature. Diabetes increases the risk of MI because it increases the rate of atherosclerotic progression and adversely affects blood cholesterol levels. This accelerated form of atherosclerosis occurs regardless of whether a patient has insulin-dependent or non-insulin-dependent diabetes mellitus.

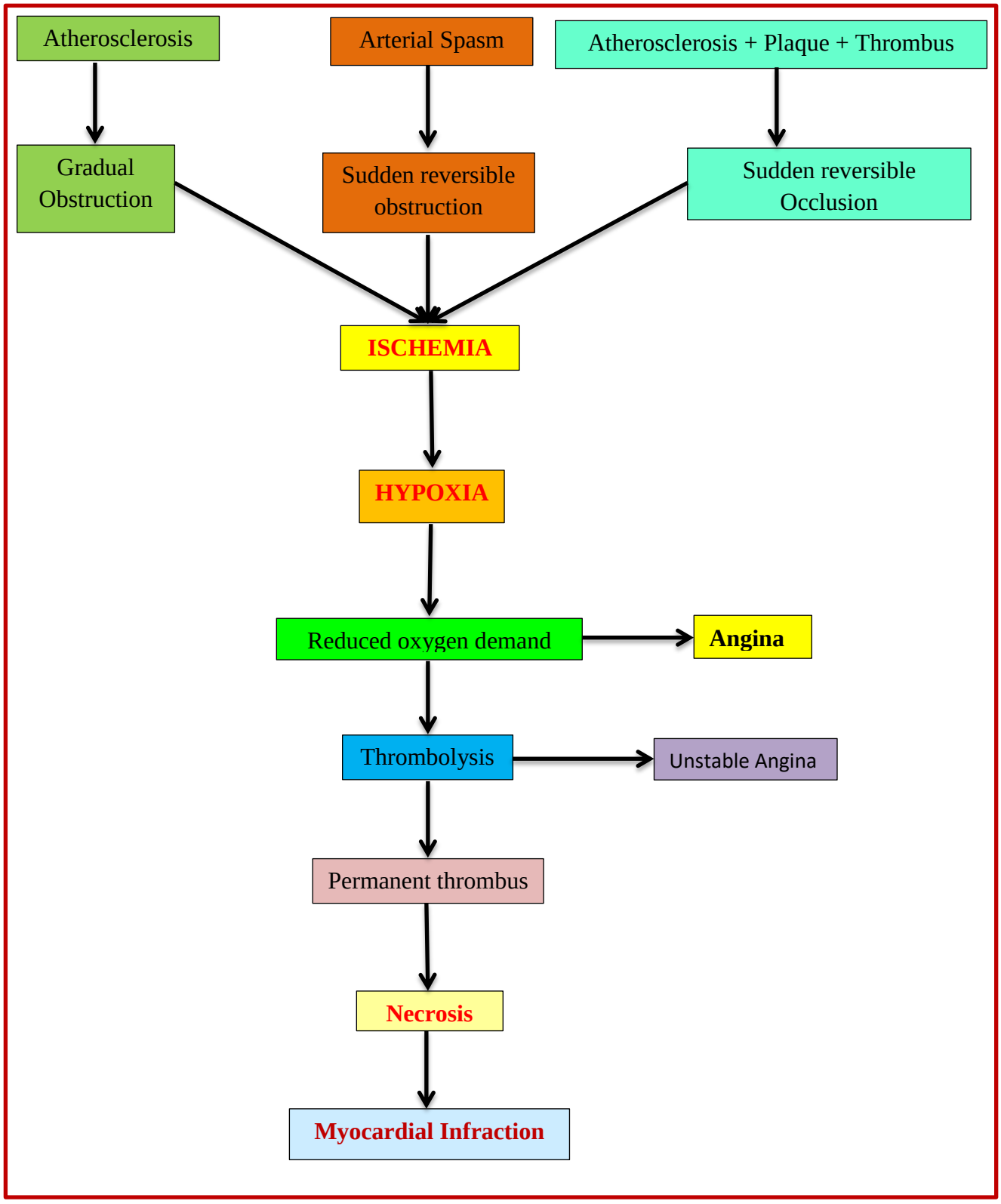
Hypertension:

High blood pressure has consistently been associated with an increased risk of MI.This risk is associated with both systolic and diastolic hypertension. The control of hypertension with appropriate medication has been shown to significantly reduce the risk of MI.

Tobacco Use:

Certain components of tobacco and tobacco combustion gases are known to damage blood vessel walls. The body's response to this type of injury elicits the formation of atherosclerosis and its progression, thereby increasing the risk of MI.

PATHOPHYSIOLOGY OF MI



SIGNS AND SYMPTOMS

- Chest pain described as a pressure sensation, fullness, or squeezing in the mid portion of the thorax.
- Radiation of chest pain into the jaw/teeth, shoulder, arm, and/or back.
- Associated dyspnea or shortness of breath.
- Associated epigastric discomfort with or without nausea and vomiting
- Associated diaphoresis or sweating
- Syncope or near-syncope without other cause
- Impairment of cognitive function without other cause

DIGNOSIS

Once a patient's clinical picture raises a suspicion of a MI, several confirmatory tests can be performed rapidly. These tests include-

- Electrocardiography
- Blood testing
- Echocardiography

1. Electrocardiography (ECG)

The first test is the ECG, which may demonstrate that a MI is in progress or has already occurred Thus ECG changes are one of the most important parameter such as ST-segment elevation, T-wave inversion and appearance of wide deep Q-wave.

2. Blood Tests

Blood tests can be performed to detect evidence of myocardial cell death Living heart cells contain certain enzymes and proteins (eg, creatine phosphokinase, troponin. And myoglobin) within cell membranes associated with specialized cellular functions such as contraction. When a heart muscle dies, cellular membranes lose integrity and intracellular enzymes and proteins slowly leak into the bloodstream. These enzymes and proteins can be detected by a blood sample analysis. The concentration of enzymes in a blood sample and more importantly, the changes in concentration found in samples taken over time correlates with the amount of heart muscle that has died. Normal values are given below –

Normal Values of Blood Tests to Detect Myocardial Infarction

Blood Test	Normal Values
Total Creatinine Phosphokinase (CPK)	30-200 U/L
CPK, MB fraction	0.0-8 8 ng/ml
CPK, MB fraction percent of total CPK	0-4%
CPK, MB2 fraction	< 1 U/L
Troponin 1	0.0-0.4 ng/mL
Troponin T	0.0-0.1 ng/ml

3. Echocardiography

An echocardiogram may be performed in order to compare areas of the left ventricle that are contracting normally with those that are not. The echocardiogram can be helpful in identifying which portion of the heart is affected by a MI, and which of the coronary arteries is most likely to be occluded unfortunately, the presence of wall motion abnormalities on the echocardiogram may be due to an acute MI or previous (old) MI or other myopathic processes. Thus, the usefulness of echocardiography in the diagnosis of MI is limited

ATHEROSECROLOSIS

Atherosclerosis is a condition when the arteries become narrowed and hardened due to a buildup of plaque (fatty material) around the artery wall. Plaque is basically made up of fat, cholesterol, calcium, and other cellular waste product and substances found in the blood. Arteries are blood vessels are same pipe like structure which carry vital nutrients for our body including water- oxygen, vitamins and many other.

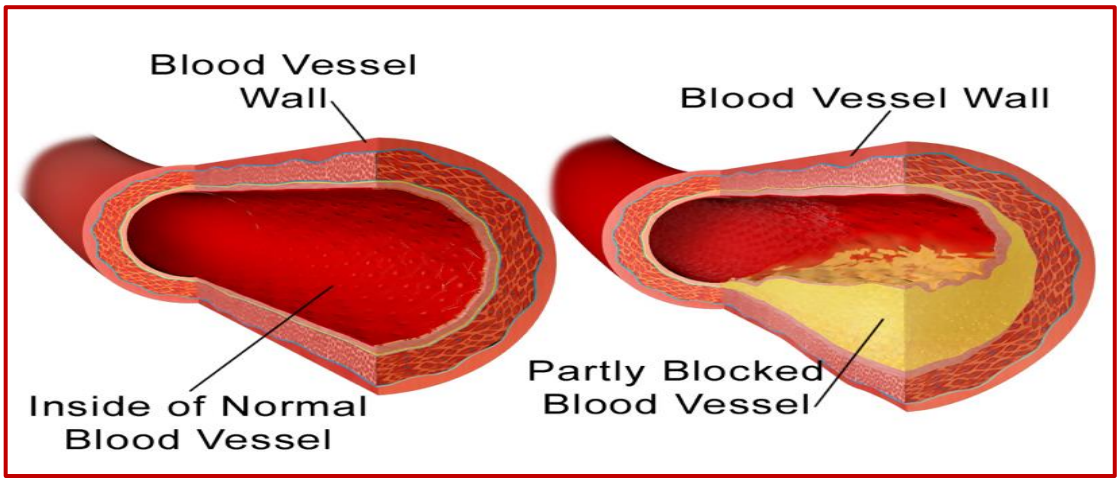
The term atherosclerosis is derived from Greek word i.e;

athero- (meaning: gruel or Paste) *sclerosis* (meaning: hardness).

Atherosclerosis is a hardening of artery specifically due to an athromatous plaque.

Athromatous plaque: It is an abnormal accumulation of material in the inner layer of the wall of artery. The material consists of mostly macrophage cells, or debris, containing lipids, calcium and a variable amount of fibrous connective tissues

The term atherogenic is used for substances of processes that cause formation of Atheroma.



If Plaques causing agents continues to buildup they will accumulate and start forming hardness inside the blood vessels and then blood vessels will be narrow.

This limits the flow of oxygen-rich blood to our organs and other parts of body.

Atherosclerosis is not a common problem, it may lead to serious problems, including heart attacks, stroke, and peripheral vascular disease or even death. Atherosclerosis is now become the most common cause of human morbidity and death in the modern world.

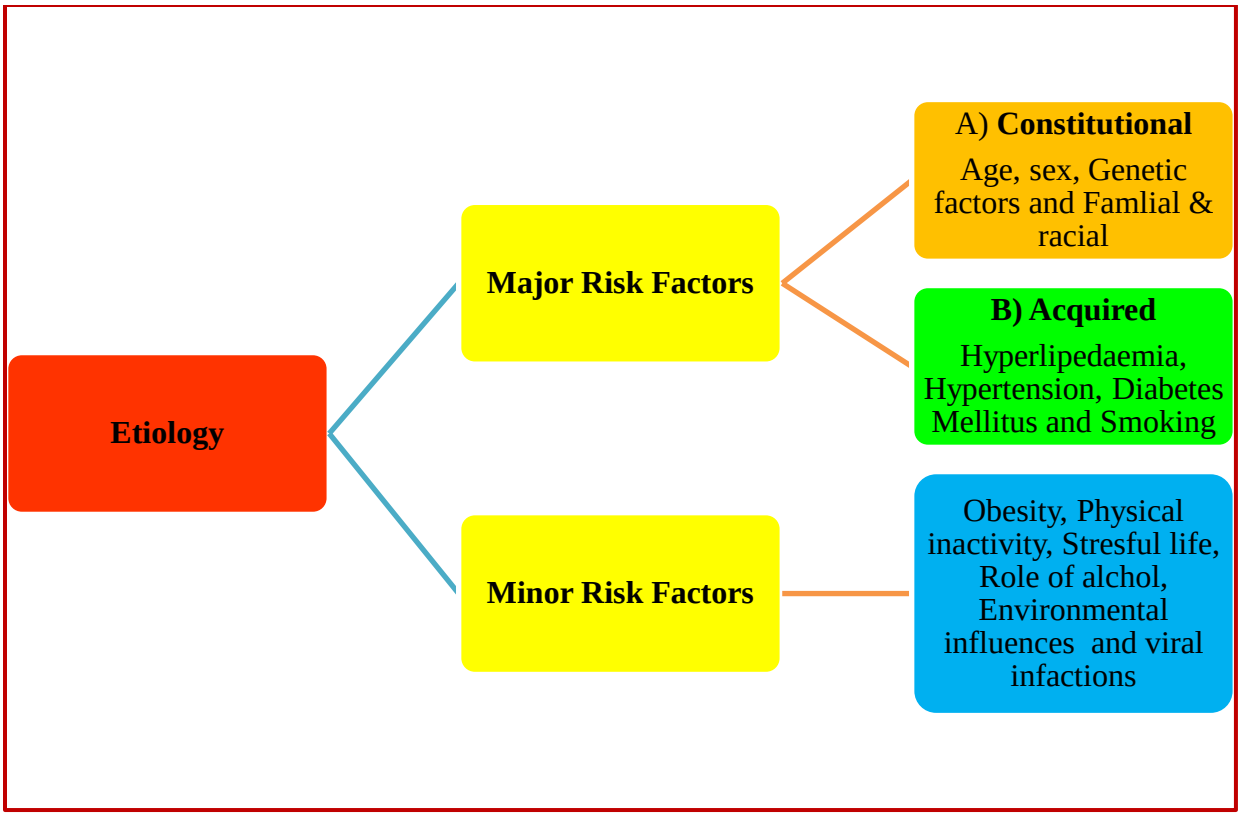
CLINICAL MANIFESTATIONS	
Chest pain	Ischemia of heart muscles
Inadequate cardiac output	Heart failure
Dyspnea	MI
Sudden cardiac death	Diaphoresis
Increased cardiac enzyme level	Difficulty in speaking
Palpitation	Arrhythmia

Etiology

A number of risk factor are associated with increased risk of developing clinical atherosclerosis often, these risk factor are in combination rather than single.

The risk factor are divided into two groups

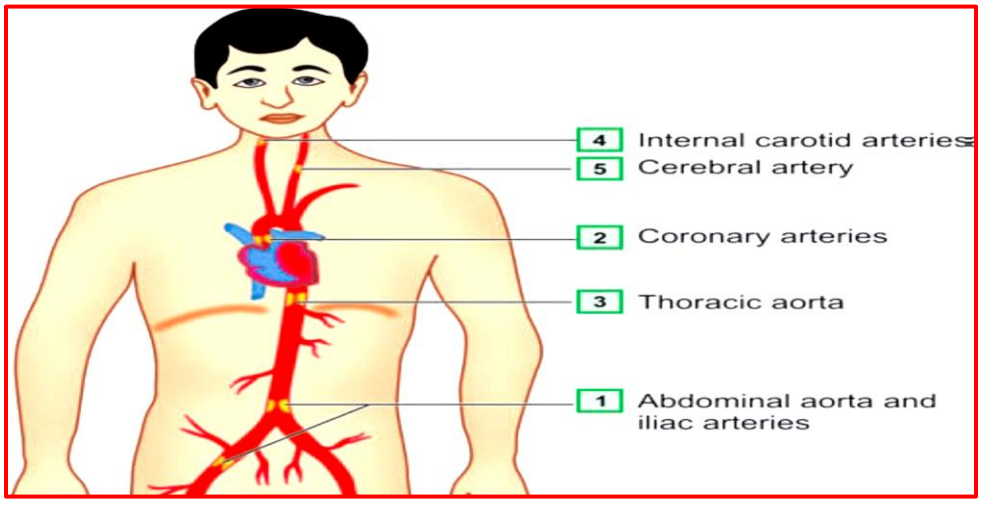
I. Major Risk Factors
II. Minor Risk Factors



Etiology of Atherosclerosis

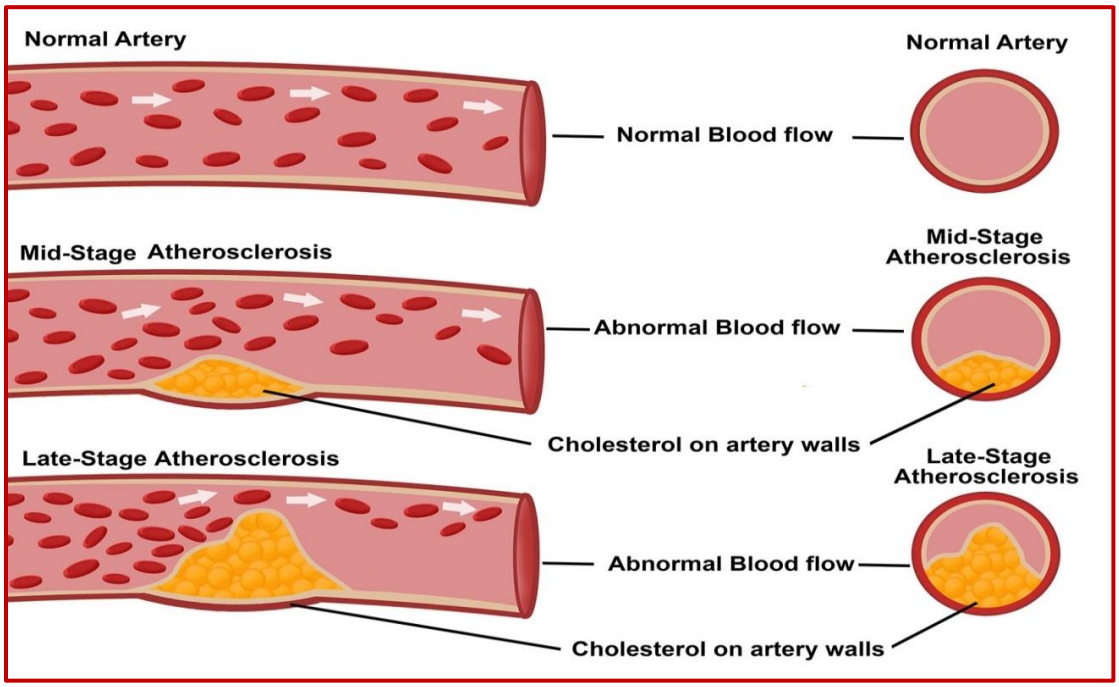
MAJOR TARGETS

The major targets are the aorta, the coronary and cerebral arteries. Begins in infants and childhood and progresses slowly over the decades. Often produces critical ischemia of the intestines and lower extremities, a major cause of abdominal aortic aneurysms.



Major sites of atherosclerosis

STAGES OF ATHEROSECROLOSIS



PATHOPHYSIOLOGY

NORMAL ARTERIAL WALL

- The normal arterial wall consists of smooth muscles and connective tissue with an endothelial covering.

FORMATION OF FATTY STREAK

- The fatty streaks will develop in the coronary arteries at the age of 15 onwards.
- When the fatty streak develop a yellow ting will be appear in the wall of blood vessels.

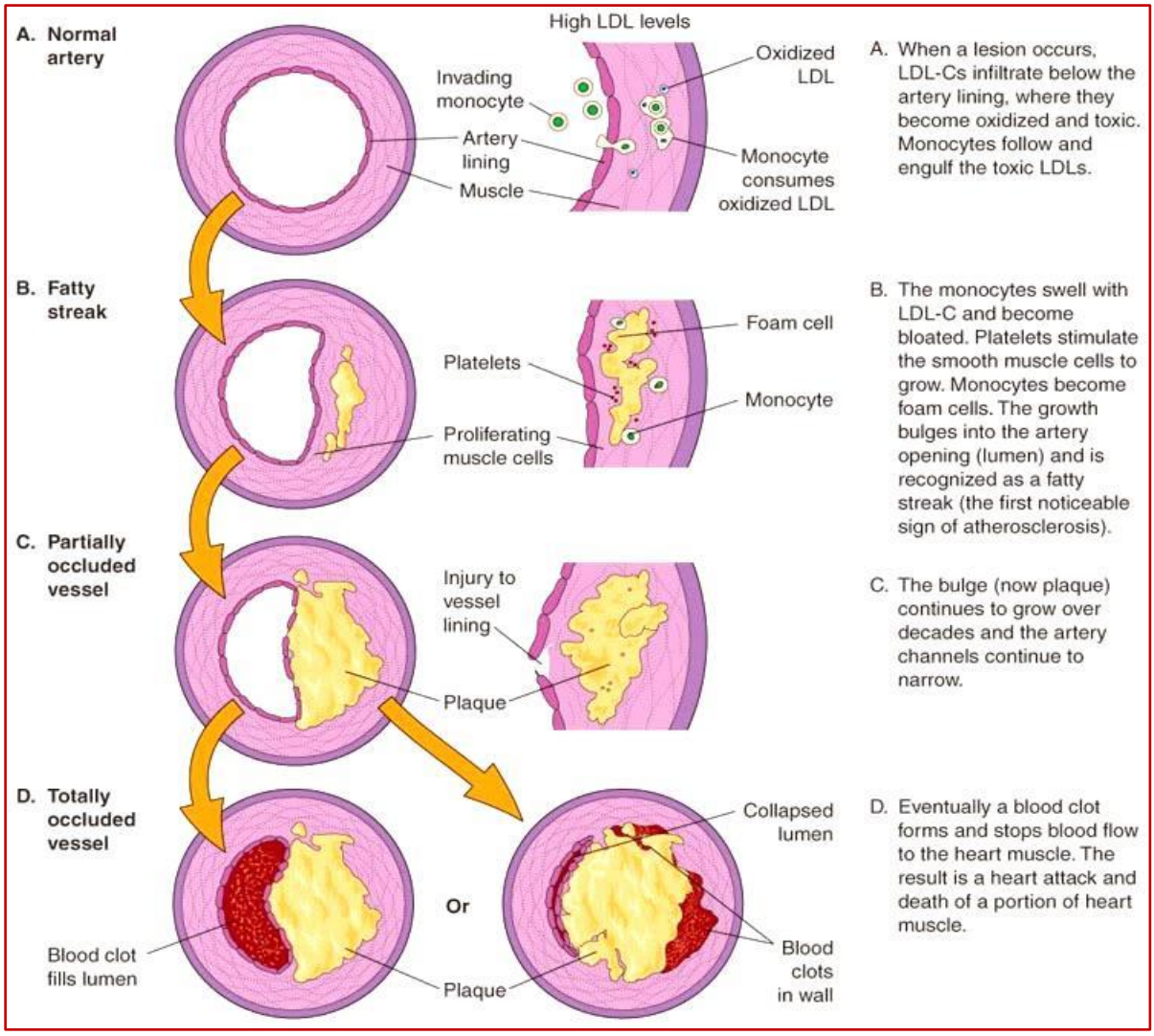
STABLE PLAQUE (FIBROUS PLAQUE FORMATION)

- The fibrous plaque stage is the beginning of progressive changes in the endothelium of arterial wall.
- This change will appear in the age of 13 and increase with age.
- Normally the endothelium repairs immediately after injury but, in persons with CAD the endothelium is not rapidly replaced.
- It allows the accumulation of LDL and growth factor which causes the thickening of the arterial wall.
- Then the fatty streak is eventually covered by collagen and forming a fibrous plaque which is greyish or whitish in colour.

VULNERABLE PLAQUE OR COMPLICATED LESIONS

- It is the final stage of development of atherosclerotic lesions and it is the most dangerous stage. As fibrous plaque grows, the continuous inflammation can cause plaque instability, ulceration and rupturing.
- When rupturing occurs the bleeding will be get started and as a result aggregation of platelets will occur which will leads to the formation of thrombus.
- Further, growth of thrombus and accumulation of platelets will leads to the total accumulation of platelets and the total occlusion of the arteries.

DIAGRAMMATIC REPRESENTATIONS



DIAGNOSIS

History collection and physical examination: The family history, nutritional history and personal history should be collected from the patient. During physical examination the nurse should check the characteristics of pulse.

Blood studies: it is necessary to check the complete lipid profile of the patient.

Electrocardiogram (ECG): An electrocardiogram records electrical signals as they travel through the heart. An ECG can often reveal evidence of a previous heart attack or one that's in progress.

Echocardiogram: An echocardiogram uses sound waves to produce images of heart. During an echocardiogram, the doctor can determine whether all parts of the heart wall are contributing normally to the heart's pumping activity.

Exercise stress test: If the signs and symptoms occur most often during exercise, doctor may ask to walk on a treadmill during an ECG. This is known as an exercise stress test. In some cases, medication to stimulate the heart may be used instead of exercise.

Cardiac catheterization or angiogram. To view blood flow through heart, the doctor may inject a special dye into coronary arteries. This is known as an angiogram.

The dye is injected into the arteries of the heart through a long, thin, flexible tube (catheter) that is threaded through an artery, usually in the leg, to the arteries in the heart.

This procedure is called cardiac catheterization. The dye outlines narrow spots and blockages on the X-ray images.

If the patients have a blockage that requires treatment, a balloon can be pushed through the catheter and inflated to improve the blood flow in coronary arteries.

A mesh tube (stent) may then be used to keep the dilated artery open.

CT scan. Computerized tomography (CT) technologies can help the doctor see calcium deposits in arteries that can narrow the arteries. If a substantial amount of calcium is discovered, coronary artery disease can be suspect.

PREVENTION

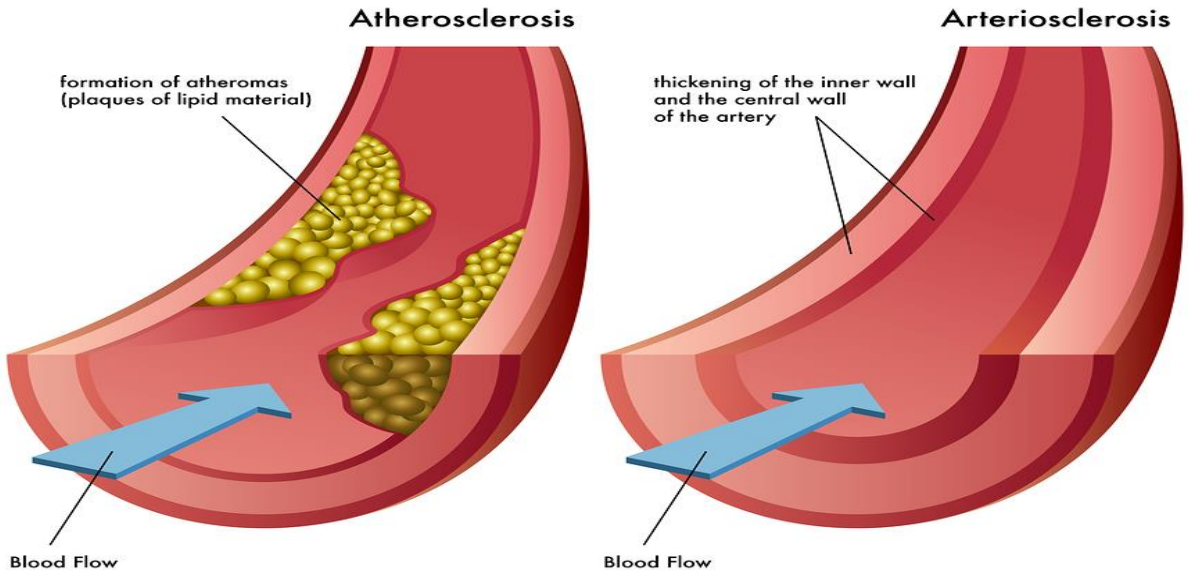
Feed your heart healthy food, Quit Tobacco smoking and Have regular physical activity

Others like: Control blood pressure, Check cholesterol, Manage stress.

ARTERIOSCLEROSIS

Arteriosclerosis occurs when the blood vessels that carry oxygen and nutrients from your heart to the rest of your body (arteries) become thick and stiff — sometimes restricting blood flow to your organs and tissues.

Arteriosclerosis refers to a group of disorders which causes the thickening, hardening and loss of elasticity in arterial walls.



FACTORS THAT CAUSE ARTERIOSCLEROSIS

- Old age → Loss of protein called elastin → Loss of elasticity of the arterial musculature → Thickening of the arterial walls→ Arteriosclerosis
- Genetic trait.

CAUSE OF ARTERIOSCLEROSIS

- Deposition of cholesterol beneath the endothelium of arteries.
- Deposition of fibers and calcium ions in the cholesterol.
- Deposits will calcify & become hard.
- Atheromatous plaques formed & cause the narrowing of arterial lumen.

TYPES OF ARTERIOSCLEROSIS

1) Arteriolosclerosis, unlike atherosclerosis, is a sclerosis that only affects small arteries and arterioles, which carry nutrients and blood to the cells.

2) Atherosclerosis is the narrowing of arteries from a buildup of plaque, usually made up of cholesterol, fatty substances, cellular waste products, calcium and fibrin, inside the arteries. This affects large and medium-sized arteries; however, its positioning varies person to person.

3) Monckeberg's arteriosclerosis or medial calcific sclerosis is seen mostly in the elderly, commonly in arteries of the extremities.

4) Hyperplastic: Hyperplastic arteriosclerosis refers to the type of arteriosclerosis that affects large and medium-sized arteries.

5) Hyaline type: Hyaline arteriosclerosis, also referred to as arterial hyalinosis and arteriolar hyalinosis, refers to lesions that are caused by the deposition of homogenous hyaline in the small arteries and arterioles.

SYMPTOMS

Plaque buildup happens gradually. Mild arteriosclerosis may not have any symptoms.

Symptoms of moderate to severe arteriosclerosis depend on the arteries affected; moderate to severe arteriosclerosis symptoms include:

- Chest pain or angina
- Pain in your leg, arm, and anywhere else that has a blocked artery
- Shortness of breath
- Fatigue
- Confusion, which occurs if the blockage affects circulation to your brain
- Muscle weakness in your legs from lack of blood circulation

DIAGNOSIS

History collection and physical examination: The family history, nutritional history and personal history should be collected from the patient. During physical examination the nurse should check the characteristics of pulse.

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Exercise stress test: If the signs and symptoms occur most often during exercise, doctor may ask to walk on a treadmill during an ECG. This is known as an exercise stress test. In some cases, medication to stimulate the heart may be used instead of exercise.

COMPLICATIONS

Arteriosclerosis can cause the following conditions:

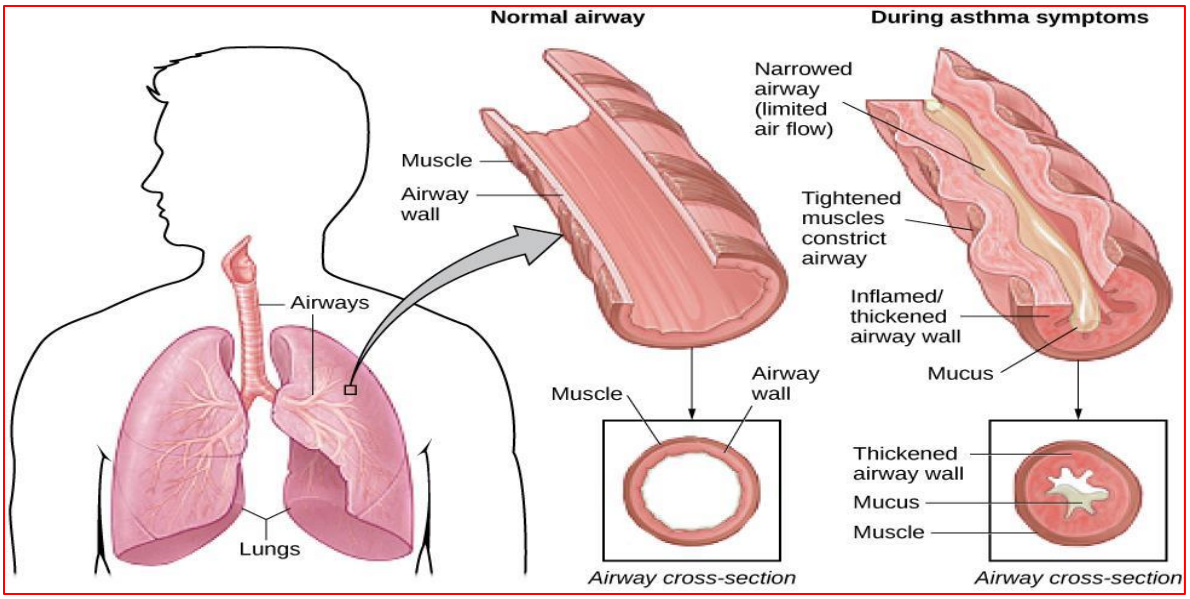
- **Coronary artery disease:** plaque deposits in coronary artery blocks the blood flow.
- **Carotid artery disease:** Carotid artery present in neck and the supply of blood to the brain get affected due to plaque buildup in the arteries.
- **Peripheral artery disease:** Narrowing of the arteries present in the lower body.
- **Kidney disease:** Plaque deposition in renal arteries. Arteriosclerosis of these arteries may lead to kidney failure.

RESPIRATORY SYSTEMS

ASTHMA AND COPD

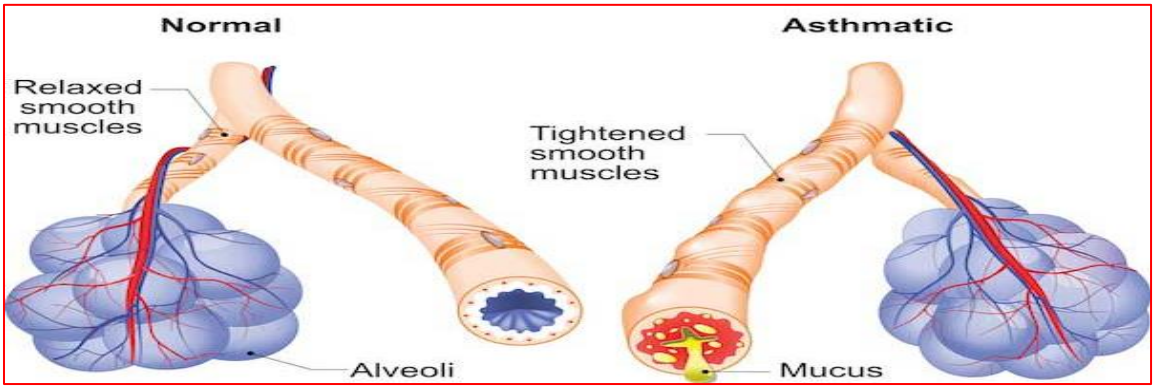
ASTHMA

Asthma is an inflammatory disorder with airway obstruction. Asthma is characterized by airway inflammation and hyper responsiveness of the bronchial smooth muscle to the stimuli that produce bronchoconstriction.



Trriger Factors:

- Cold air
- Allergens
- Exercise
- Emotional stress
- Cigarette smoking

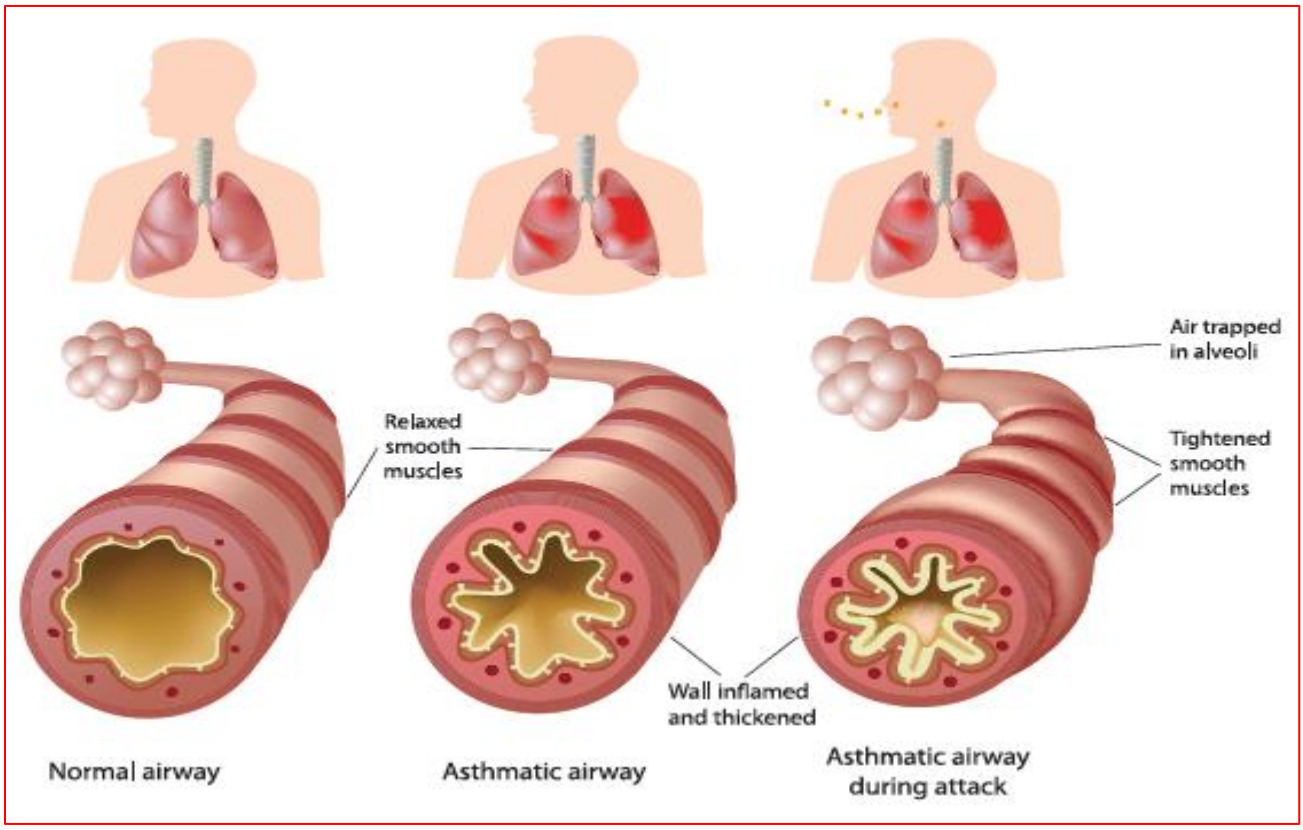


Hyperresposiveness of trachiobronchial smooth muscle to variety of stmuli. Which result in the narrowing of air tube, increase secretion, mucosal edema, mucus plugging.

Exposure to a stimulus causes the release of sub-stances from the activated mast cell, eoosinophills, neutrophills and macrophages.

Inflammatory substances released are histamine, bradykinin, and major basic proteins. Some other substances are formed and released immediately in response to asthmatic stimuli like arachidonic acid derived leukotrienes, prosta-glandins.

All these mediators cause the net inflammation of the airway, edema and hypertrophy of smooth muscle of the respiratory tract.



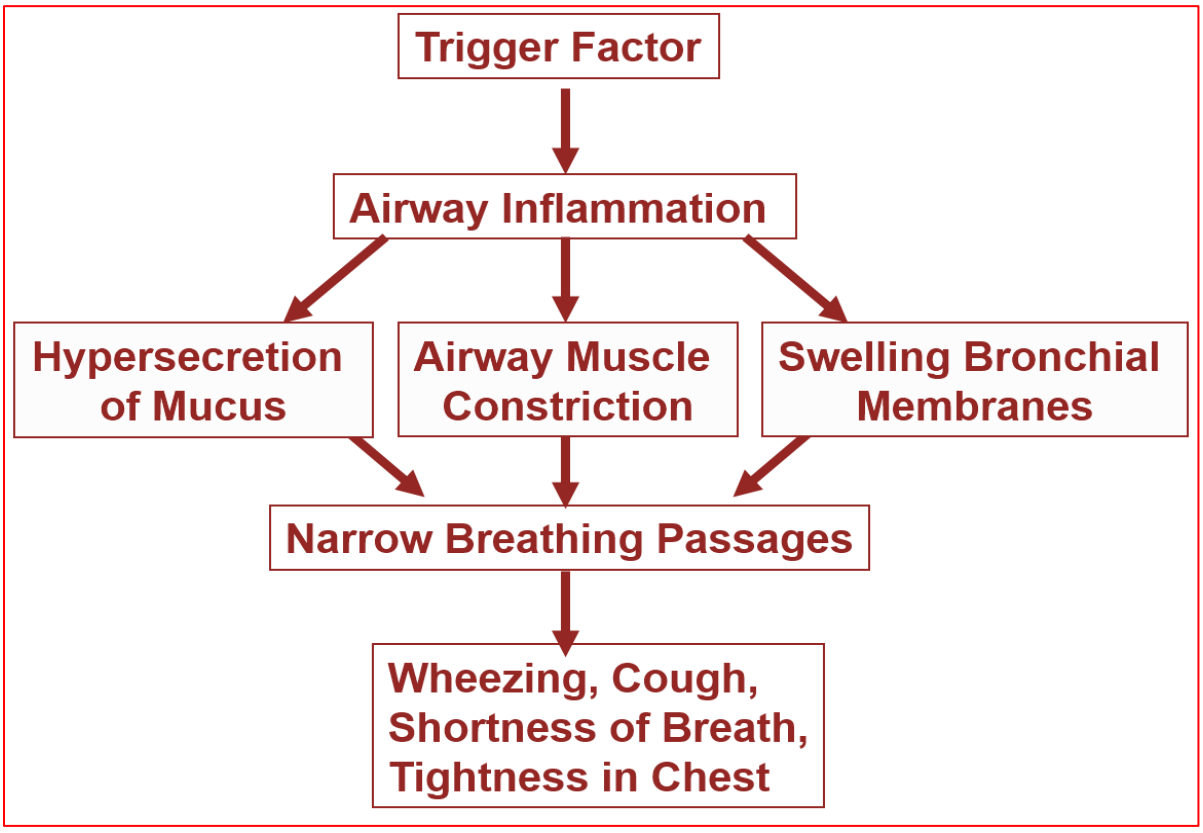
Asthma can be characterized by as:

Pathologically - Bronchial inflammation

Physiologically - Bronchial hyper reactivity and hyper responsiveness

Clinically- Variable cough, chest tightness and wheeze

ETIOLOGY	
Exercise	Night and early moming
Cold air, fog, humid climate	Viral respiratory tract infection
Allergens like house dust, mite etc.	Non specific irritants like cigarette smoking
Emotional stress	Occupational exposure



SYMPTOMS

Symptoms of asthma vary from person to person:

- Most common symptoms of asthma are dyspnoea or laboured breathing, audible wheezing, tightness of chest and coughing.
- Patients usually exhibit very low systolic blood pressure and abnormally rapid breathing during an attack.
- Wheezing sounds may accompany both inspiration and expiration or expiration alone.
- Episodic cough.

Respiratory failure may result in patients:

- Becoming unconscious
- Becoming cyanotic
- Having a systolic blood pressure of more than 15 mmHg (normal systolic pressure is 120 mmHg)
- Having oxygen saturation of less than 90%
- Having hyperinflation- Patients with chronic asthma may have a barrel-shaped thorax caused by hyper inflammation

Types of Asthma

Intrinsic Asthma

- It is non-immune.
- Start middle age, Assums as chronic form.
- There is no family history of allergens.
- Bronchospasm occurs due to factors like aspirin, pulmonary infections, inhaled irritants, SO_2 etc.

Extrinsic Asthma

- Start in an early age.
- Episodic.
- Patients has history of allergies (Family)
- Caused byType -I hyper-sensitivity
- Induced by allergic antigens.

Extrinsic Asthma can be further classified into 3 classes:

- **Atopic Asthma:** Most common form of allergic asthma. Atopic means hereditary tendency to develop allergen.
- **Occupational Asthma**: Due to occupation.
- **Allergic:** Developed due to foreign external allergens.

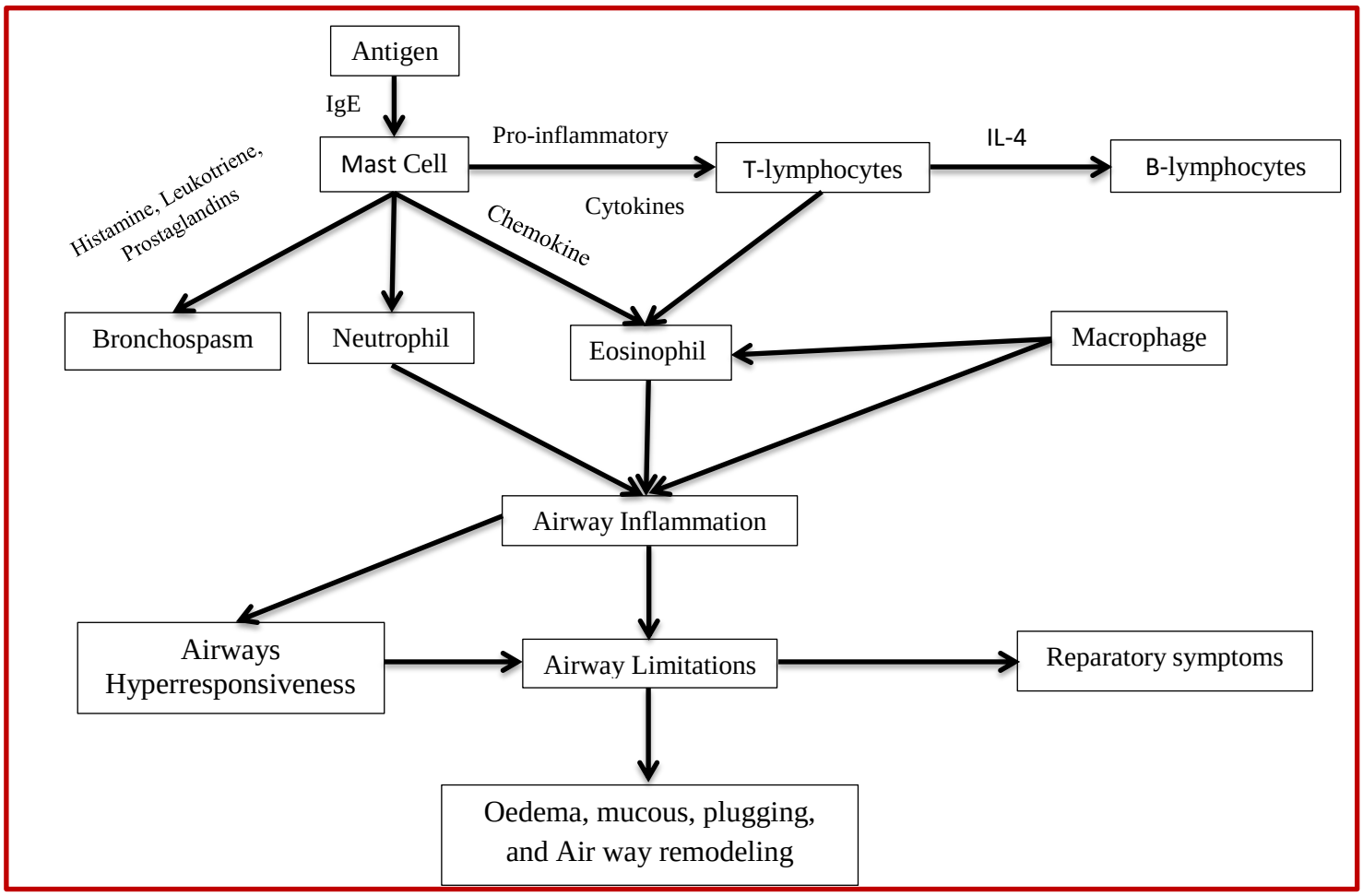
INITIATION OF ASTHMA

- Inflamation start with mast cell (present in lungs)
- Infamation produces following mediators- Release of intracellular granules like Histamine and protease enzymes.
- Release of phospholipids from cell membrane – Prostaglandins and leukotrienes.
- Activation of genes followed by protein synthesis- IL and TNF-ά

PATHOPHYSIOLOGY OF ASTHMA

Following steps involves in inflammation reactions:

- Allergens inhaled → Asthma Atthack → ↓ Breathing.
- Allergens bind to IgE (Immunoglobulin E) that have binding site for allergens.
- Allerens+ IgE → Trigger the release of Histamine and Leukotriens.
- Leukotrines → Bronchial smooth muscle contraction, ↓Luman.



DIAGNOSIS

Several tests can be performed in order to diagnose asthma. Tests may include:

1. Spirometry

A lung function test to measure breathing capacity and how well you breathe. The spirometer is used in this test.

2. Peak Expiratory Flow (PEF)

This test is performed with the help of peak flow meter device, patient forcefully exhales into the tube to measure the force of air he can expend out of lungs.

3. Chest X-ray

In order to check the infections and severity of the disease some other tests are also performed like- Blood examination (for leukocytosis), Sputum examination (for infections), pulmonary function test.

4. Methacholine challenge test:

Methacholine is known to trigger asthma. This test is conducted when spirometry results are normal.

5. Sputum eosinophils:

The count of eosinophils, a type of white blood cells, found in the sputum (mixture of mucus and saliva), helps in the diagnosis.

6. Allergy blood test:

This is done to identify triggers.

Complications of Asthma

- Infection of lungs i.e Pneumonia
- A collapse of part of all the lung.
- Respiratory failure where the level of oxygen in the blood become low and volume of co_2 is high.

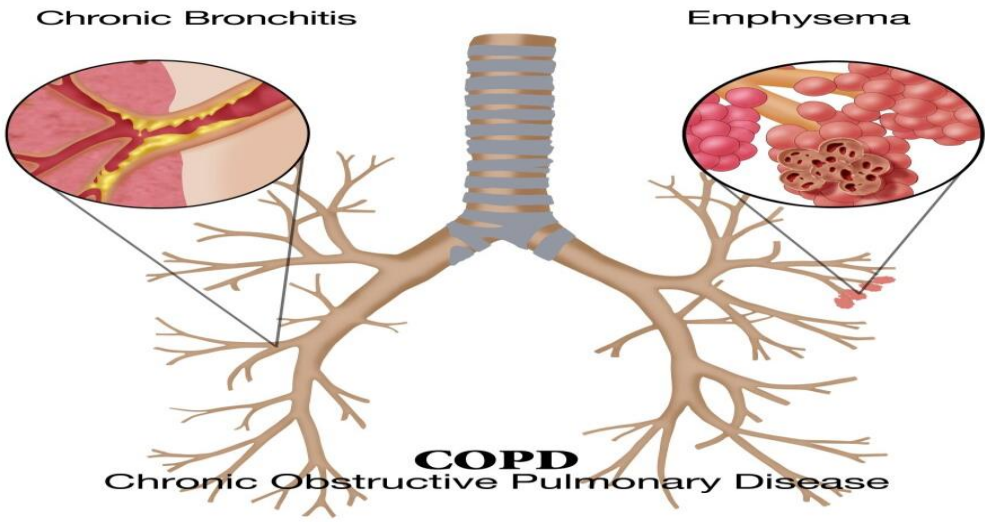
CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

COPD, a common preventable and treatable disease, is characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases.

It is a persistent obstruction of the airways which is either partially reversible or completely irreversible. It is usually caused by chronic bronchitis and or emphysema.

Chronic bronchitis is characterized by cough with or without expectoration for at least four months of a year for two consecutive years.

Emphysema is an enlargement of alveoli with destruction of alveolar septa. Chronic bronchitis and emphysema frequently co-exist as persistent chronic bronchitis often gets complicated by emphysema. Inflammation of smaller airways, spasm of smooth muscles, swelling of linings of airways, may further worsen the condition.



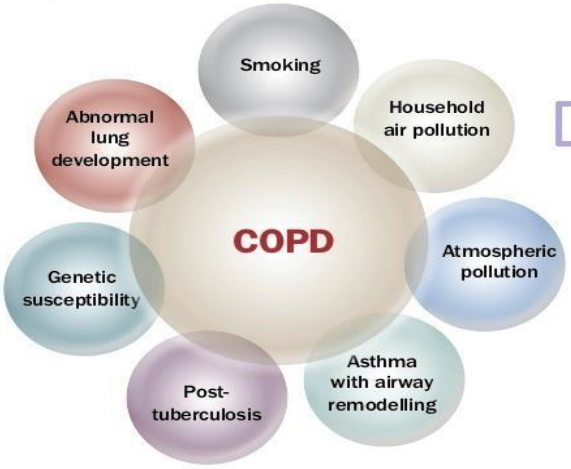
CAUSES:

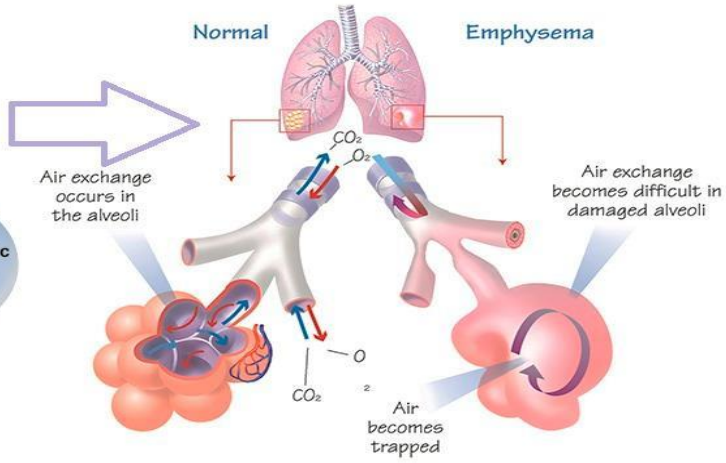
1 Smoking: It is most common factor that impairs mucociliary defence mechanism and leads to over activity of mucus producing glands.

2. Air pollution: Continuous exposure to various pollutants like industrial effluents, vehicle smoke, fire smoke, etc and occupational exposure to organic or inorganic dusts result in COPD.

3. Infections: Repeated infection of respiratory tract (e.g. viral infection, common cold) especially in infancy may lead to COPD.

4. Genetic make-up: Inborn deficiency of a body protein, called alpha, antitrypsin (A protease inhibitor) results in easy damage of alveoli to develop emphysema.





PATHOPHYSIOLOGY

Precipitating factors / causative agents

↓

Accumulation of alveoli

↓

Collection of WBC in inflamed area

↓

Release of enzymes (especially neutrophil elastase)

↓

Damage of connective tissue in the walls of alveoli

↓

Chronic obstructive pulmonary disease

SYMPTOMS:

- Repeated attacks of productive cough especially in winter.
- Wheezing, breathlessness and tightness in the chest usually in the morning.
- Progressive increase in respiratory disability with yellow or green sputum.
- Shortness of breath during normal activity like washing, dressing, toileting etc.
- Severe weight loss and generalized edema.

DIAGNOSIS:

Physical examination: It is usually normal at initial stages while in later stages, breathing sound becomes hard along with some wheezing sound.

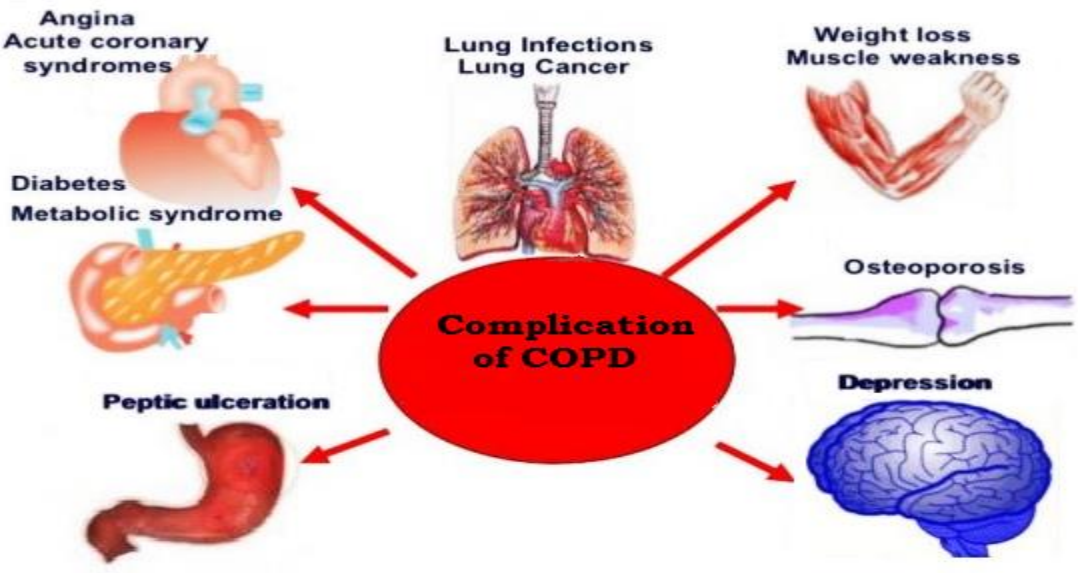
X-ray examination: It shows the presence of pulmonary abnormality, if any.

Pulmonary function tests: Recording of forced expiratory volume in one second (FEVD) and its ratio to vital capacity, volume of lungs, etc. reveal the pathological extent of the disease.

Exercise tests: Standard exercise tests are carried out to check day-to-day disability.

Blood Examination: Blood level of ά antitrypsin is estimated to check its involvement in the disease.

COMPLICATIONS OF COPD:



RENAL FAILURE

Renal failure is defined as a significant loss of renal function in both kidneys to the point where less than 10 to 20% of normal GFR remains.

Renal failure may occur as an acute and rapidly progressing process or may present as a chronic form in which there is a progressive loss of renal function over a number of years.

Acute renal failure has an abrupt onset and is potentially reversible.

Chronic failure progresses slowly over at least three months and can lead to permanent renal failure.

Accordingly, major groups of renal diseases are as under

1. Glomerular diseases: These are most often immunologically- mediated and may be acute or chronic.

2. Tubular diseases: These are more likely to be caused by toxic or infectious agents and are often acute.

3. Interstitial diseases: These are likewise commonly due to toxic or infectious agents and quite often involve interstitium as well as tubules (tubulo-interstitial diseases).

4. Vascular diseases: These include changes in the nephron as a consequence of increased intra-glomerular pressure such as in hypertension or impaired blood flow.

Regardless of cause, renal disease usually results in the evolution of one of the two major pathological syndromes: acute renal failure and chronic renal failure.

Pathophysiology of Renal Failure

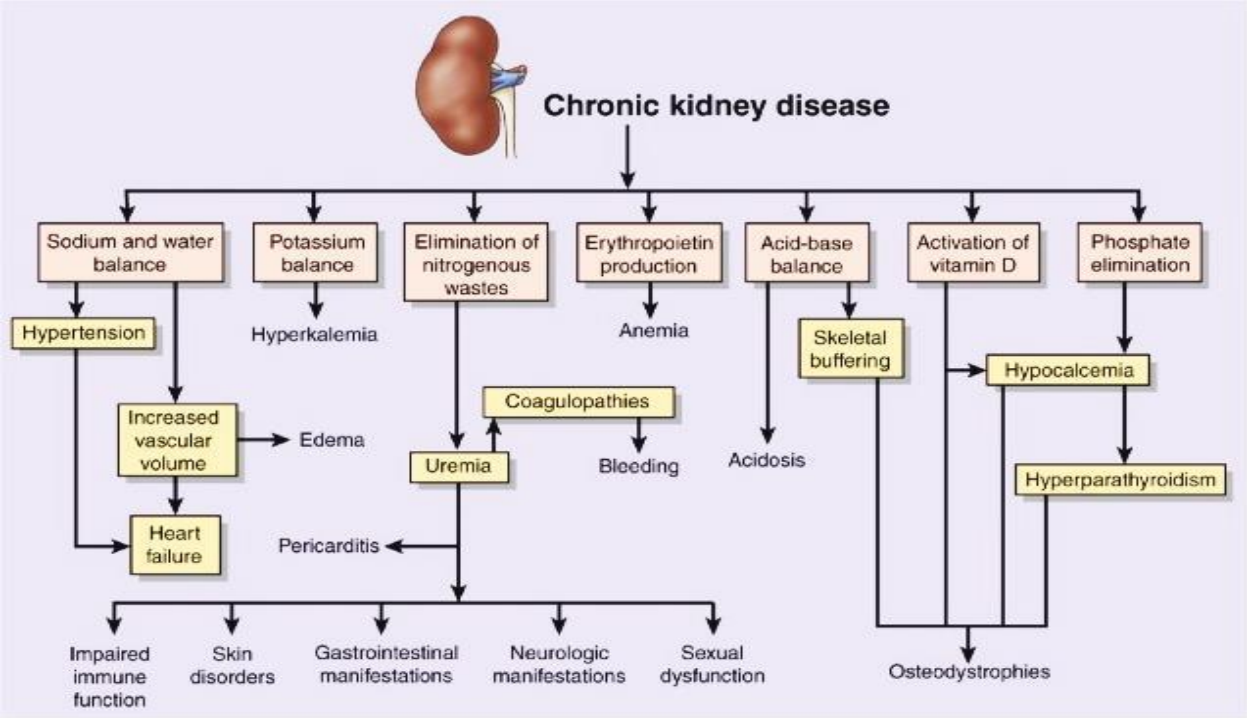
In renal failure there is either glomerular or tubular dysfunction e.g. – glomerulonephritis primarily causes of glomerular damage – aminoglycoside nephrotoxicity is mainly in tubular

Glomerular dysfunction-

As the main function of glomeruli is filtration; glomerular dysfunction leads to fall in GFR with retention of those substances usually cleared by filtration, including water

Tubular Dysfunction-

As the main function of tubules is reabsorption tubular failure results in the voiding of large volumes of dilute urine (polyuria) of low specific gravity, along with electrolytes and nutrients.



ACUTE RENAL FAILURE (ARF)

Sudden decrease in renal function. Acute renal failure may be pre-renal, intra-renal or post-renal in nature. Acute renal failure is often reversible so long as permanent injury to the kidney has not occurred.

ETIOPATHOGENESIS

Myocardial infarction, Decreased blood flow, Obstruction, Hemolytic uremic syndrome, Glomerulonephritis are common causes of acute renal failure.

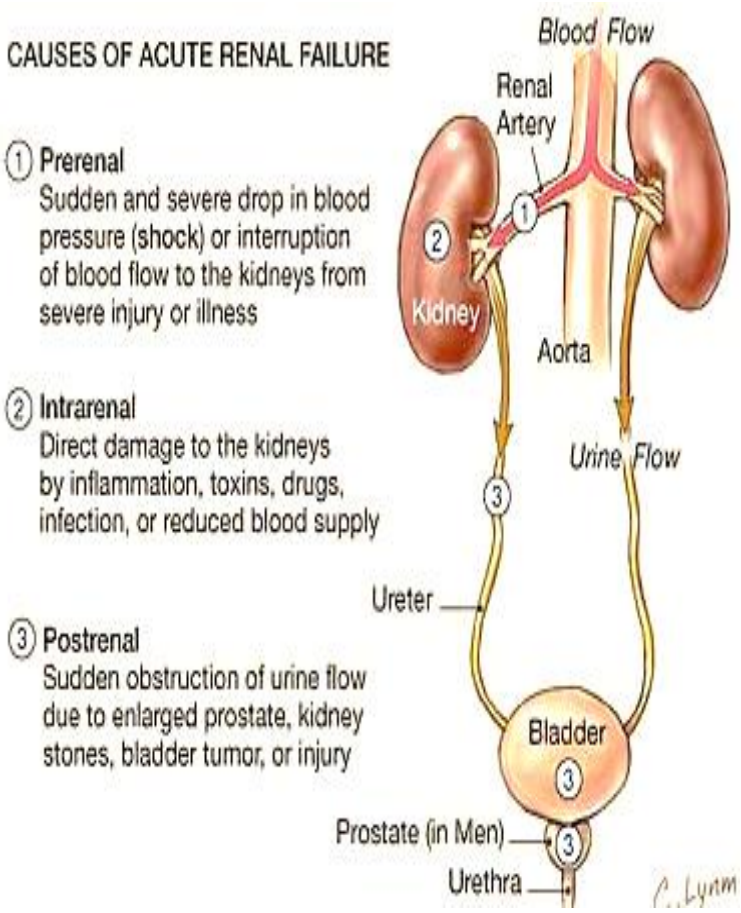
Manifestations: Oliguria (reduced urine output), Possible edema and fluid retention, Elevated blood urea nitrogen levels (BUN) and serum creatinine, Alterations in serum electrolytes, Acute Renal Failure classified as pre-renal failure, intra-renal failure and post-renal failure

1. Pre-renal causes: Pre-renal diseases are those which cause sudden decrease in blood flow to the nephron. Renal ischemia ultimately results in functional disorders or depression of GFR, or both. These causes include inadequate cardiac output and hypovolaemia or vascular disease causing reduced perfusion of the kidneys.

2. Intra-renal causes: Intra-renal disease is characterized by disease of renal tissue itself. These include vascular disease of the arteries and arterioles within the kidney, diseases of glomeruli, acute tubular necrosis due to ischaemia, or the effect of a nephrotoxin, acute tubulointerstitial nephritis and pyelonephritis.

3. Post-renal causes: Post-renal disease is characteristically caused by obstruction to the flow of urine anywhere along the renal tract distal to the opening of the collecting ducts. This may be caused by a mass within the lumen or from wall of the tract, or from external compression anywhere along the lower urinary tract—ureter, bladder neck or urethra.

It is important to note that ARF originating in pre- and post-renal disease such as by renal ischaemia or renal infection, eventually leads to intra-renal disease. Thus, full-blown ARF reflects some degree of nephron damage.



CLINICAL FEATURES

Decreased kidney function (electrolyte imbalance), Obstruction in the urinary tract, Blood in urine, Reduced urine output, Dehydration, Detectable abnormal mass, Pale skin, Poor appetite. The clinical features will depend to a large extent on the underlying cause of ARF and on the stage of the disease at which the patient presents.

1. Syndrome of acute nephritis

This is most frequently associated with acute post-streptococcal glomerulonephritis and rapidly progressive glomerulonephritis.

Renal dysfunction results from extensive proliferation of epithelial cells in the glomeruli with consequent mild increase in glomerular permeability and decrease in GFR.

The characteristic features are: mild proteinuria, haematuria, oedema and mild hypertension.

Fluid retention in acute nephritis syndrome appears to be due to both diminished GFR and increased salt and water reabsorption in distal nephron.

2. Syndrome accompanying tubular pathology

When the ARF is caused by destruction of the tubular cells of the nephron as occurs in acute tubular necrosis, the disease typically progresses through 3 characteristic stages from oliguria to diuresis to recovery:

i) Oliguric phase:

The initial oliguric phase lasting on an average from 7 to 10 days is characterised by urinary output of less than 400 ml per day.

The decline in formation of the urine leads to accumulation of waste products of protein metabolism in the blood and resultant azotaemia, metabolic acidosis, hyperkalemia, hypernatremia and hypervolemia.

ii) Diuretic phase:

With the onset of healing of tubules, there is improvement in urinary output.

This is believed to occur due to drawing of water and sodium by preceding high levels of creatinine and urea as they move through the nephron so as to be excreted.

Since tubular cells have not regained normal functional capacity, the urine is of low.

iii) Phase of recovery:

Full recovery with healing of tubular epithelial cells occurs in about half the cases, while others terminate in death. The process of healing may take up to one year with restoration of normal tubular function.

3. Pre-renal syndrome

The ARF occurring secondary to disorders in which neither the glomerulus nor the tubules are damaged, results in pre-renal syndrome.

Typically, this pattern is seen in marginal ischaemia caused by renal arterial obstruction, hypovolaemia, hypotension or cardiac insufficiency.

Due to depressed renal blood flow, there is decrease in GFR causing oliguria, azotaemia (elevation of BUN and creatinine) and possible fluid retention and oedema.

Since the tubular cells are functioning normally, the nephron retains its ability to concentrate the glomerular filtrate according to the adaptive needs.

Treatment of acute renal failure

- Prevention of acute renal failure through support of blood pressure and blood volume
- Correction of fluid and electrolyte imbalances
- Dialysis, which may be employed while the kidneys are in the recovery phase
- Low protein, high carbohydrate diet to minimize the formation of nitrogenous wastes

CHRONIC RENAL FAILURE (CRF)

Chronic renal failure is a syndrome characterised by progressive and irreversible deterioration of renal function due to slow destruction of renal parenchyma. Chronic renal failure is the end result of progressive kidney damage and loss of function. Chronic renal failure is often classified into four progressive stages based on the loss of GFR.

Stages of Chronic Renal Failure Diminished renal reserve — GFR decreased to 35 to 50% of normal Renal insufficiency — GFR decreased to 20 to 35% of normal Renal failure — GFR reduced to less than 20% of normal End-Stage Renal Disease — GFR is less than 5% of normal

ETIOPATHOGENESIS

Chronic glomerulonephritis, Chronic infections, Renal obstruction (prolonged), Exposure to toxic chemicals, Toxins or drugs (aminoglycoside antibiotics and nephrotoxicity), Diabetes Hypertension, Nephrosclerosis (atherosclerosis of the renal artery), Diabetic nephropathy Alport syndrome (inherited disorder causes deafness progressive kidney damage and eye defects), Polycystic kidney disease, Interstitial nephritis or pyelonephritis

All chronic nephropathies can lead to CRF. The diseases leading to CRF can generally be classified into two major groups:

- Those causing glomerular pathology,
- Those causing tubulointerstitial pathology.

1. Diseases causing glomerular pathology

A number of glomerular diseases associated with CRF have their pathogenesis in immune mechanisms. Glomerular destruction results in changes in filtration process and leads to development of the nephrotic syndrome characterised by proteinuria, hypo albuminaemia and oedema.

The important examples of chronic glomerular diseases causing CRF are covered under two headings: primary and systemic.

i) Primary glomerular pathology: The major cause of CRF is chronic glomerulonephritis, usually initiated by various types of glomerulonephritis such as membranous glomerulonephritis, membranous proliferative glomerulonephritis, lipoid nephrosis (minimal change disease) and anti-glomerular basement membrane nephritis.

ii) Systemic glomerular pathology: Certain conditions originate outside the renal system but Induce changes in the nephrons secondarily. Major examples of this type are systemic lupus erythematosus, serum sickness nephritis and diabetic nephropathy.

2. Diseases causing tubulointerstitial pathology

Damage to tubulointerstitial tissues results in alterations in reabsorption and secretion of important constituents leading to excretion of large volumes of dilute urine.

i) Vascular causes: Long-standing primary or essential hypertension produces characteristic changes in renal arteries and arterioles referred to as nephrosclerosis. Nephrosclerosis causes progressive renal vascular occlusion terminating in ischaemia and necrosis of renal tissue.

ii) Infectious causes: A good example of chronic renal infection causing CRF is chronic pyelonephritis. The chronicity of process results in progressive damage to increasing number of nephrons leading to CRF.

iii) Toxic causes: Some toxic substances induce slow tubular injury, eventually culminating in CRF. The most common example is intake of high doses of analgesics such as phenacetin, aspirin and acetaminophen (chronic analgesic nephritis). Other substances that can cause CRF after prolonged exposure are lead, cadmium and uranium.

iv) Obstructive causes: Chronic obstruction in the urinary tract leads to progressive damage to the nephron due to fluid backpressure. The examples of this type of chronic injury are stones, blood clots, tumours, strictures and enlarged prostate.

Regardless of the initiating cause, CRF evolves progressively through 4 stages:

1. Decreased renal reserve

At this stage, damage to renal parenchyma is marginal and the kidneys remain functional.

The GFR is about 50% of normal,

BUN and creatinine values are normal

The patients are usually asymptomatic except at times of stress.

2. Renal insufficiency

At this stage, about 75% of functional renal parenchyma has been destroyed.

The GFR is about 25% of normal.

There is elevation in BUN and serum creatinine.

3. Renal failure

At this stage, about 90% of functional renal tissue has been destroyed.

The GFR is approximately 10% of normal.

Tubular cells are essentially non-functional.

As a result, the regulation of sodium and water is lost resulting in oedema, metabolic acidosis, hypocalcaemia, and signs and symptoms of uraemia.

4. End-stage kidney (chronic kidney disease)

The GFR at this stage is less than 5% of normal

Results in complex clinical picture of uraemic syndrome with progressive primary (renal) and secondary systemic (extra-renal) symptoms.

CLINICAL FEATURES

Until very kidney function remains, chronic renal failure may not developed, Anemia, increased levels of phosphates (in blood) are complications of kidney failure, Malaise, Dry skin, Poor appetite, Vomiting, Bone pain, metallic taste in mouth, detectable abdominal mass.

Clinical manifestations of full-blown CRF culminating in uraemic syndrome are described under 2 main headings:

1. Primary (renal) uraemic manifestations
2. Secondary (systemic or extra-renal) uraemic manifestations

1. Primary uraemic (renal) manifestations

Primary symptoms of uraemia develop when there is slow and progressive deterioration of renal function. The resulting imbalances cause the following manifestations:

a. Metabolic acidosis As a result of renal dysfunction, acid-base balance is progressively lost. Excess of hydrogen ions occurs, while bicarbonate level declines in the blood, resulting in metabolic acidosis.

b. Hyperkalaemia A decreased GFR results in excessive accumulation of potassium in the blood since potassium is normally excreted mainly in the urine. The clinical features of

hyperkalemia are: cardiac arrhythmias, weakness, nausea, intestinal colic, diarrhoea, muscular irritability.

c. Sodium and water imbalance As GFR declines, sodium and water cannot pass sufficiently into Bowman's capsule leading to their retention. Release of renin from juxtaglomerular apparatus further aggravates sodium and water retention. The main symptoms referable to sodium and water retention are: hypervolaemia and circulatory overload with congestive heart failure.

d. Hyperuricaemia Decreased GFR results in excessive accumulation of uric acid in the blood. Uric acid crystals may be deposited in joints and soft tissues resulting in gout.

e. Azotaemia: The waste-products of protein metabolism fail to be excreted resulting in elevation in the blood levels of urea, creatinine, phenols and guanidines causing biochemical abnormality, azotaemia.

2. Secondary uraemic (extra-renal) manifestations

A number of extra-renal systemic manifestations develop secondarily following fluidelectrolyte and acid-base imbalances. These include the following:

a. Anaemia Decreased production of erythropoietin by diseased kidney results in decline in erythropoiesis and anaemia.

b. Integumentary system Deposit of urinary pigment such as urochrome in the skin causes sallow-yellow colour. The urea content in the sweat as well as in the plasma rises.

c. Cardiovascular system Fluid retention secondarily causes cardiovascular symptoms such as increased workload on the heart due to the hypervolaemia and eventually congestive heart failure.

d. Respiratory system Hypervolaemia and heart failure cause pulmonary congestion and pulmonary oedema due to back pressure.

e. Digestive system Azotaemia directly induces mucosal ulcerations in the lining of the stomach and intestines. Subsequent bleeding can aggravate the existing anaemia.

f. Skeletal system The skeletal manifestations of renal failure are referred to as renal osteodystrophy. Two major types of skeletal disorders may occur:

i) Osteomalacia occurs from deficiency of a form of vitamin D which is normally activated by the kidney. Since vitamin D is essential for absorption of calcium, its deficiency results in inadequate deposits of calcium in bone tissue

ii) Osteitis fibrosa occurs due to elevated levels of parathormone. How parathormone excess develops in CRF is complex. As the GFR is decreased, increasing levels of phosphates accumulate in the extracellular fluid which, in turn, cause decline in calcium levels.

Decreased calcium level triggers the secretion of parathormone which mobilises calcium from bone and increases renal tubular reabsorption of calcium thereby conserving it.

Manifestations of chronic renal failure –

System	Effect	Cause
Body fluids	Polyuria Metabolic acidosis Abnormal levels of Na^+, K^+, $Ca^{2+,}$ PO^{4-}	Metabolic acidosis Reduced H+ excretion Loss of tubular function
Hematologic	Anemia, excess bleeding	Impaired erythropoietin
Cardiovascular	Hypertension, edema	Activation of renin–angiotensin system
Gastrointestinal tract	Anorexia, nausea	Accumulation of metabolic wastes
Neurologic	Uremic encephalopathy	Accumulation of ammonia and nitrogenous waste
Musculoskeletal	Muscle and bone weakness ("Renal Osteodystrophy")	Loss of calcium and minerals

Treatment of chronic renal failure

- Careful management of fluids and electrolytes
- Prudent use of diuretics
- Careful dietary management; restriction of dietary protein intake
- Recombinant erythropoietin to treat anemia
- Renal dialysis
- Renal transplantation

Diagnosis

- Routine laboratory test (creatinine and blood urea nitrogen)
- Ultrasound of the kidney helps to determine whether kidney problem is acute or chronic.
- Kidney biopsy
- Computed tomography scan

Long Answer Questions: 10 MARKS

1. Define hypertension. Discuss the pathogenesis of essential hypertension in detail.
2. Define the angina pectoris. Briefly discuss the types and pathogenesis of angina.
3. What is Atherosclerosis? Explain the pathogenesis involved in Atherosclerosis.
4. What is CHF? What are the various types? Describe the pathogenesis of CHF.
5. Explain etiology, types, pathology and clinical features of Renal Failure.
6. Write a note on Ischemic Heart disease.

Short Answers Questions 5 Marks

1. Explain the pathogenesis of Asthma.
2. Describe the Pathophysiology of hypertension.
3. Explain the pathogenesis and clinical symptoms of CHF.
4. Explain the pathophysiology of congestive cardiac failure.
5. Explain the pathogenesis and clinical symptoms of Asthma.
6. Write a note on pathophysiology of atherosclerosis.
7. Write a note on the myocardial infarction and its clinical diagnosis.
8. Write a note on COAD and arteriosclerosis.

Very short Answers Questions. 2 Marks

1. What is Emphysema?
2. What is hypertension?
3. What is variant and unstable angina?
4. Etiology of CHF.
5. Write a note diagnosis of Asthma.
6. Write down symptoms of Angina and MI
7. Define Prizemental angina and its cause.
8. Define chronic bronchitis.
9. Define renal failure and its types.
10. Write down cause and symptoms of chronic renal failure.