Unit-II

Cardiovascular system:

* **Hypertension:** Arterial pressure is a product of cardiac output (CO) & peripheral resistance (resistance produced by arterial wall against blood).
  - A patient whose repeated measurement of BP denotes more than 90 mm Hg diastolic pressure & ≥140 mm Hg systolic pressure, patient is c/a hypertensive.

⇒ **Note: Blood pressure:** Blood pressure is the pressure of circulating blood on the walls of blood vessels.
- Most of this pressure is due to work done by the heart by pumping blood through the circulatory system.
- Blood pressure usually refers to the pressure in large arteries of the systemic circulation.
- Normal BP range: 120/80 mmHg to 140/90 mmHg.
- Sphygmomanometer is used to measure the BP.

- **Sign and symptoms:** Headache, ringing of ears (tinnitus), faint (unconscious), postural unsteadiness, hyperventilation symptoms are induced by anxiety in patient.
- **Types of hypertension:** 3 types:
  A) 1° hypertension (90% case)
  B) 2° hypertension (10% cases)
  C) Pulmonary hypertension.

A) **Primary (1°) hypertension:** It is further subdivided into 4 subtypes according to the rate at which the disease progresses:

a) **Mild hypertension:** BP → Systolic pressure: ≥140 to 159 mm Hg
→ Diastolic pressure: 90 to 99 mm Hg.

b) **Moderate hypertension:** Systolic BP: ≥160 to 179 mm Hg.
Diastolic BP: 105 to 114 mm Hg.

c) **Hypertension during pregnancy:** Systolic BP: ≥135 mm Hg
Diastolic BP: 85 mm Hg

d) **Hypertensive emergency & urgency:** Systolic BP: ≥210 mm Hg.
Diastolic BP: 120 mm Hg.

B) **Secondary (2°) hypertension:** It results from other disease account for 10% of all cases. Factors involved in it are:

a) **Kidney disease:** Raised BP is complication of kidney disease. The vasoconstriction effect of more renin released by damaged kidney is one of the causative factor.

b) **Endocrine disorder:** Secretion of more aldosterone (mineralocorticoid) and cortisol stimulates the retention of Na & H_2O by kidney leading to ↑ed blood volume and pressure (BP). Over stimulation of aldosterone hormone is due to a hormone secreting tumour. Over stimulation of cortisol may be due to more stimulation of gland by adrenocorticotrophic hormone (ACTH) released from anterior lobe of pituitary gland.
- Pheochromocytoma is adrenal gland tumour. Therefore, secretion of more adrenaline and noradrenaline leads to ↑ed BP.

c) **Structure of aorta:** Hypertension develops in branching arteries. Elastic tissue in tunica media is replaced by inelastic fibres as a part of ageing.

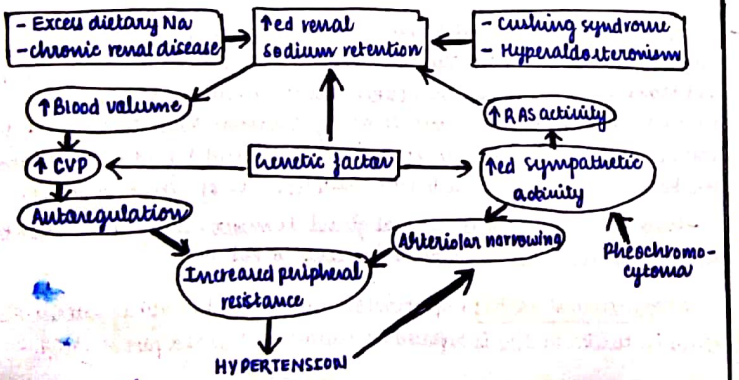
d:) **Aspirin drug or oral contraceptive:** consumption of aspirin and oral contraceptive responsible for 2° hypertension.

c:) **Pulmonary hypertension:** ↑ed BP in pulmonary circulation is secondary to change in the architecture of blood vessels, disease of heart, cirrhosis in liver failure, thrombosis of portal vein cause ↑ed blood pressure in the left side of the heart leads to left ventricular failure (LVF).

- **Pathogenesis of pulmonary hypertension:**

Vasoconstriction ⇒ Intimal smooth muscle cell proliferation
⇓
Initial thrombosis ⇒ Inflammation ⇒ Fibrous thickening of pulmonary vasculature
⇓
Vascular occlusion.

- **Pathophysiology of hypertension:**



* **Congestive Heart Failure (CHF):** The heart is described as failing, when the cardiac output (C.O.) is unable to circulate sufficient blood to meet the demand of the body. In mild cases cardiac output (C.O.) is adequate at rest but becomes inadequate only when tissue needs are increased. e.g. during exercise.

- The term congestive Heart failure (CHF) is used for the chronic form of heart failure in which the patient has evidence of congestion of peripheral circulation and of lungs. CHF is the end-result of various forms of serious heart disease.

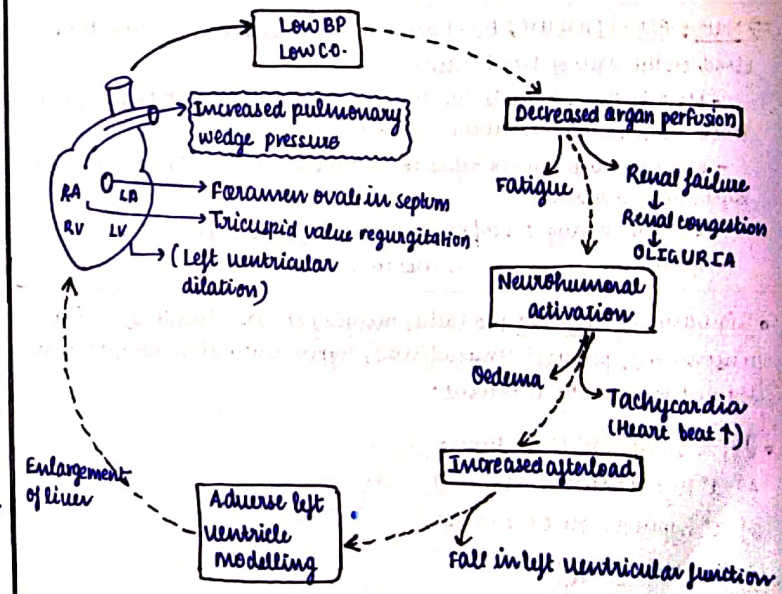


Fig: Neurohumoral adaptation in CHF

∵ Cardiac output (C.O.) = Stroke volume (ml) X Heart Rate (beats/min)

∵ **Regurgitation:** Back flow of blood from RV to RA.

Preload: Initial stretching of the cardiomyocytes prior to contraction.

Afterload: It is the pressure the heart must work against to eject blood during systole (ventricular contraction).

Oliguria: The production of abnormally small amounts of urine.

Anuria: Non passage of urine or stop urination.

- **Signs and symptoms:**

A) **Dyspnoea:** Labour breath (extra efforts needed for breathing).

B) Fatigue (हरुवा लाग्ने)

C) **Oliguria:** Led output of urine.

D) **Oedema:** Accumulation of fluid in extravascular space.

E) **Tachycardia:** Fed heart rate.

F) Fall in left ventricular function.

- **Aetiology:**

A) **Increased preload:** Resistance to flow of blood in vein.

B) **Increased afterload:** Arterial BP affects the stroke volume bcoz it creates resistance to flow of blood i.e., afterload.

C) Hypertension

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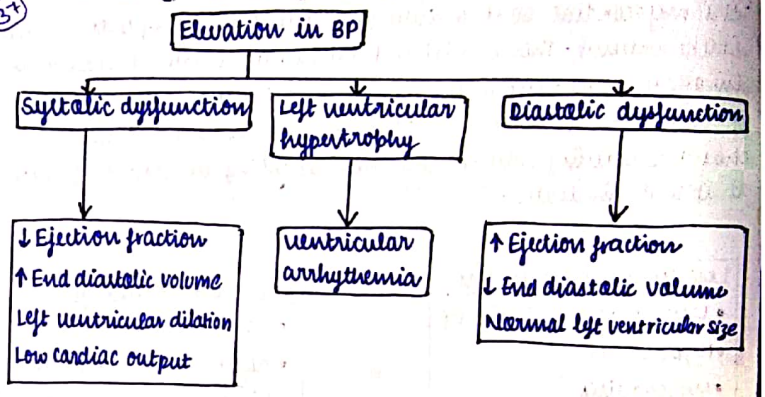

Fig; Alteration of haemodynamic status in hypertensive patient

-Left ventricular hypertrophy, stroke induced atherosclerosis formation in coronary artery with myocardial infarction and sudden mortality due to angina pectoris, arrhythemia and congestive heart failure results in hypertension.

- **Pathophysiology of congestive heart failure (CHF):** In order to maintain normal cardiac output, several compensatory mechanisms play a role as under:

– Compensatory enlargement in the form of cardiac hypertrophy, cardiac dilatation, or both

– Tachycardia (i.e. increased heart rate) due to activation of neurohumoral system e.g., release of norepinephrine and atrial natriuretic peptide, activation of renin-angiotensin-aldosterone mechanism.

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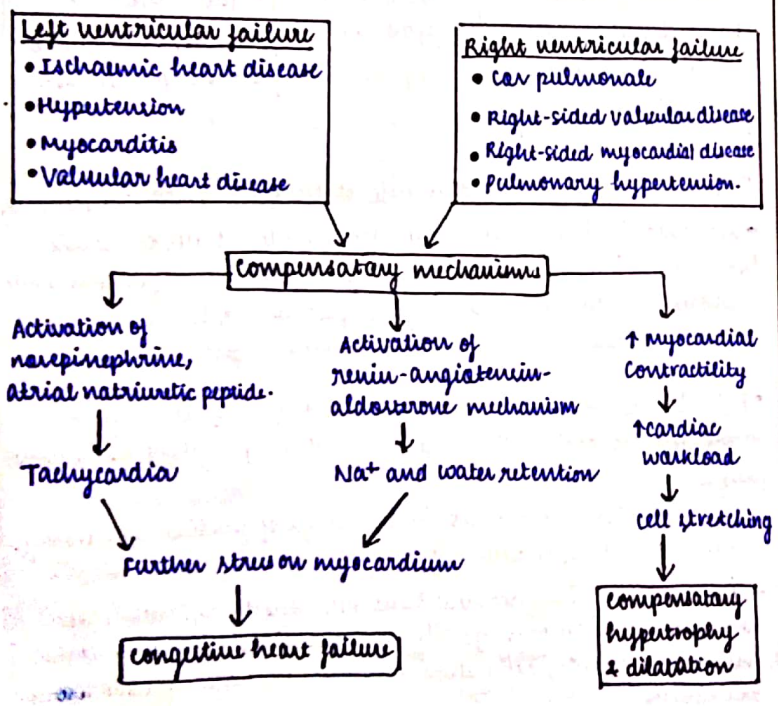
According to Starling's law on pathophysiology of heart, the failing dilated heart, in order to maintain cardiac performance, the

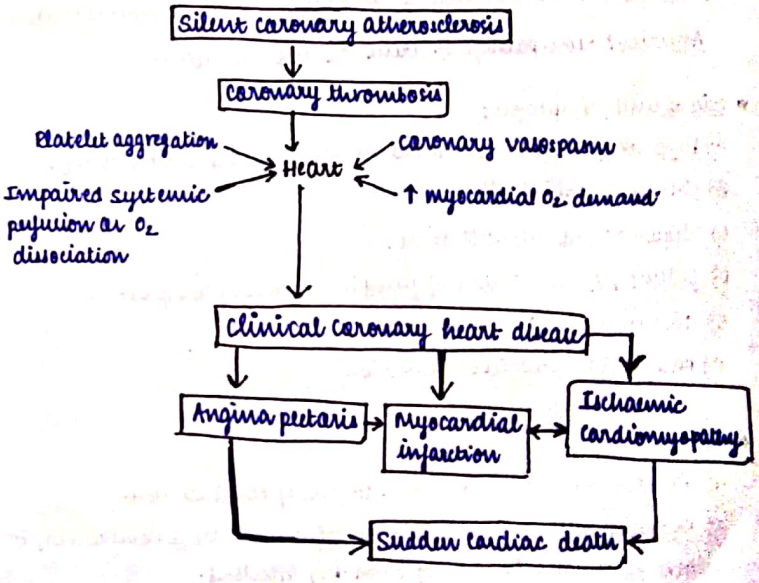
the myocardial contractility and thereby attempts to maintain stroke volume. This is achieved by ↑ing the length of sarcomeres in dilated heart. Ultimately, however dilatation ↓ces the force of contraction & leads to residual volume in the cardiac chambers causing volume overload resulting in cardiac failure that ends in death.



Fig; Schematic pathophysiology of patho CHF

* Ischaemic heart disease (IHD): It is defined as acute or chronic form of cardiac disability arising from imbalance b/w the myocardial supply and demand for oxygenated blood. Narrowing or obstruction of the coronary arterial system is the most common cause of myocardial anoxia.

– IHD is also k/n as coronary heart disease (CHD).



Fig; Schematic representation of multiple mechanism that leads to clinical coronary heart disease (CHD) and inter-relationship of the various clinical patterns

- Ischaemic heart disease is due to the effect of the atheroma (deposition of fibrofatty plaque) on to the intima portion. It leads to occlusion of one or more coronary arteries branches. coronary atherosclerosis includes ischaemic heart disease (IHD) that results from an imbalance b/w the cardiac need for an oxygenated blood and its supply when the atrial lesions are complicated by thrombosis. (Thrombus is a clot that adhere to vessel wall). Thrombus may block blood vessels, deprived tissue of O_2 and nutrients. Arterial thrombosis often involves medium sized vessels. Vasospasm and platelet aggregate also contribute to the ischaemia.

- **Angina pectoris:** It is the acute 'chest pain' due to induction of adverse O_2 supply in the portion of myocardium.
- **Myocardial infarction:** A prominent ischaemic heart disease.
- **Infarct:** It is an area of tissue that has died bcoz of lack of oxygenated blood, the myocardium is affected when a branch of coronary artery is occluded or blocked. Sub-endocardial zone is normally least perfused region of myocardium.

- Myocardial infarction is usually accompanied by crushing chest pain behind the sternum which continues even after taking rest. It may leads to fatal complications such as severe arrhythemia such as cardiac failure, rupture of ventricular wall, pulmonary or cerebral embolism.

The effect of complication is greatest when left ventricle is involved.

- Chronic ischaemic heart disease is k/n as ischaemic cardiomyopathy.
- Sudden cardiac death is an unexpected mortality from cardiac dysfunction caused within 1 to 2 hours of onset of acute symptoms which may be superimposed on any of the other 3 conditions (i.e., angina pectoris, myocardial infarction and ischaemic cardiomyopathy)

⇒ **Arteriosclerosis:** Arteriosclerosis is an arterial disorder cause thickening and inelasticity of arterial wall. Arteriosclerosis is the generic term for 3 patterns of vascular disease i.e.,

A) Arteriosclerosis
B) Monckeberg's arteriosclerosis (medial calcific sclerosis)
C) Atherosclerosis

A) **Arteriosclerosis:** It includes thickening and hardening of the arterial walls due to degenerative changes.

- **Complications of arteriosclerosis:** Arteriosclerosis is the disease of small artery and arterioles. small vessels secretes sclerosis in patient with hypertension and diabetes. Hyaline and hyperplastic both anatomical variants depending on the cause and the rate of progression of a disease leads to thickening of vessel wall with narrowing of lumen in aggregate and consequently induce ischaemic injury to the tissue and organ like nephropathy of kidney.

a) **Hyaline arteriosclerosis:** vascular wall becomes thick and lamina becomes narrow due to eosinophilic hyaline material in intima and media.

b) **Hyperplastic sclerosis (lesion):** Endothelial injury induced by systemic malignant hypertension, hypoxia and proliferation of smooth muscle cell with fibrosis leads to the pathological changes i.e., onion skin lesion (the diseased intima due to atherosclerotic plaque in the aorta and coronary artery cracks like an egg shell when vessel is incised open).

mucinous intimal thickening (means deposition of proteoglycans with scanty cells), fibrous mucinous intimal thickening (occurs due to deposition of collagen bundles, elastic fibres and hyaline in intima).

B.) Monckeberg's medial calcific sclerosis: It is the calcification of the media of large and medium-sized muscular arteries, especially of the extremities and of the genital tract, in persons past the age of 50, without associated inflammatory rxn is noted while adventitia and intima are spared due to prolonged vasoconstriction.

— It is characterised by deposits of calcium salts in the media without associated inflammatory reaction while the intima and the adventitia are spared.

C.) Atherosclerosis: Due to deposition of lipid in coronary artery and may be due to senile (i.e. age above 65 years).

— Changes in structure of artery: Progressive changes in artery affect the intima, media and elastic lamina:

a) Intimal thickening in coronary artery, abdominal aorta, and large artery of lower limb due to accumulation of fatty droplets in the intima.

b) Medial fibrosis: There is increased amount of collagen and ground substance at the expense of smooth muscle fibres of the media from an early age onwards. e.g., muscular arteries of viscera and arterioles.

c.) Elastic degeneration: Degeneration of elastic tissue is Dnt in the elastic lamina and media. In elastic content a calcium salt in the arterial wall are fused with the progressive age.

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**Note: Creatine kinase (CK) and lactate dehydrogenase (LDH) are released in blood vessel during myocardial infarction.

Respiratory system:

* **Asthma:** It is a common inflammatory disorder of airway associated with episodes of reversible over reactivity of smooth muscle of airway.

– Bronchial asthma is a syndrome characterized by periodic reversible spasm of tracheo-bronchial smooth muscle in response to noxious (unpleasant) stimuli such as infection, pollutant, exercise, exposure to cold air, psychogenic increased secretion, mucosal oedema and muscle plugging.

– Because of spasm retention of large volume of air in alveoli decreases tidal volume & vital capacity leading to Dyspnoea (difficulty in breathing out), cough and wheezing. It more inflammatory condition rather than Broncho-constriction leading to hypersensitivity (abnormal sensitivity to wide range of stimuli).

• **Pathophysiology of asthma:** The wall swell and thicken with inflammatory exudate and influx of inflammatory cells especially eosinophil.

During asthmatic attack spasmodic contraction of bronchial muscle (broncho-spasm) constrict the airway and their is excessive secretion of thick, sticky mucus, which further narrow the airway. Only partial respiration is achieved so, the lungs becomes hyper-inflated and there is severe dyspnoea and wheezing. The duration of attack usually vary from a few minutes to hours.

In severe acute attack bronchi may be obstructed by mucus plug, blocking air flow and leading to acute respiratory failure, hypoxia and possible mortality.

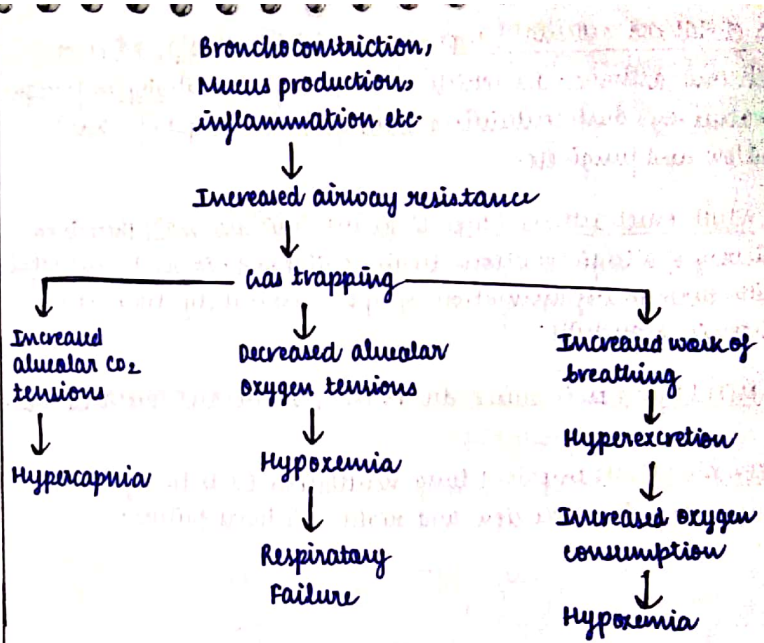

Fig: Pathophysiology of asthma

• **Aetiology | causes:** Infection, excessive exercise, pollution, exposure to cold air, respiratory tract infection and emotional stress.

• **Types of asthma:** It is of 3 types:

A) Childhood asthma / Type-I / Extrinsic (atopic, allergic) asthma.

B) Adult onset asthma / Type-II / Intrinsic (idiosyncratic, non-atopic) asthma

C) Mixed type

A) Childhood asthma (type-I or extrinsic asthma): Onset of (b2) Chronic asthma. In which there is hypersensitivity to foreign protein. eg, dust containing mites from the carpet, feather pillow and fungi etc.

B) Adult onset asthma (type-II or intrinsic asthma): There is no history of allergic reaction during childhood. It can be associated with chronic inflammation of upper respiratory tract. eg, Chronic bronchitis.

C) Mixed type: It is caused due to cold, exercise and emotional stress.

• Complications: Impaired lung ventilation leads to hypoxia, pulmonary hypertension and right side heart failure.

* Chronic obstructive airway diseases (COAD): Chronic obstructive airway disease (COAD) or chronic obstructive pulmonary disease (COPD) is commonly used clinical term for a group of pathological conditions in which there is chronic, partial or complete obstruction to the air flow at any level from trachea to the smallest airway resulting in functional disability of lung. i.e. they are diffused lung disease. Following entities are included in COPD:

A) Chronic bronchitis
B) Emphysema
C) Bronchial asthma
D) Bronchiectasis
E) Small airways disease (bronchiolitis).

Table; Contrasting features of all 5 conditions in COPD:

Feature	Chronic bronchitis	Emphysema	Bronchial asthma	Bronchiectasis	Small airways disease
1) Location	Bronchus	Acinus	Bronchus	Bronchus	Bronchiole
2) Age of diagnosis	Adults	Adults	Extrinsic: Childs Intrinsic: Adults	Adults	Childrew
3) Etiology	Smoking, air pollution	Smoking, air pollution	Extrinsic: allergy Intrinsic: viral infection	Infection, obstruction.	viral infection, smoke.
4) Pathogenesis	Impaired ciliary movement	Deficiency of α-1-antitrypsin	IgE-sensitised mast cells.	Damaged airways	Damage to surfactant.
5) Major gross feature	Thickened bronchial wall	Distended air sacs	Overdistended lungs	Dilated bronchi & bronchioles	Occluded bronchioles
6) Main histology	Hyperplasia of mucus gland	Broken alveolar septa	Mucus plugs in bronchioles	Inflammed bronchi	Fibrous plugs in bronchioles
7) Major clinical feature	Persistent cough with expectoration	Exertional dyspnoea	Bronchospasm	Copious foul-smelling expectoration	Cough, dyspnoea

A) **Chronic bronchitis:** Chronic bronchitis is a common condition defined clinically as persistent cough with expectoration on most days at least for 3 months of the year for 2 or more consecutive years.

- The cough is caused by the oversecretion of mucus in middle-aged male than females; approximately 20% of adult man and 5% of adult women have chronic bronchitis.

- **Etiopathogenesis:** The aetiologic factors associated with cigarette smoking, atmospheric pollution, occupation (cotton mills), infection, familial & genetic factors.

- Chronic bronchitis is associated with emphysema.

- **Morphological changes in bronchitis:** The bronchial wall is thickened, hyperaemic (↑ hyperreactivity of bronchi) and oedematous (i.e., deposition of fluid), lumen of bronchi & bronchioles may contain mucus plug and pus like matter (purulent exudate).

B) **Emphysema:** Pulmonary emphysema as combination of permanent dilation of airspaces distal to the terminal bronchioles and the destruction of the walls of dilated airspaces.

- **Classification of emphysema:** It is classified into 5 categories i.e., centriacinar, panacinar (panlobular), para-septal (distal acinar), irregular (para-cicatricial) and mixed (unclassified) emphysema.

- **Etiopathogenesis:** The causes of emphysema include tobacco smoke, air pollutants, occupational exposure, infection and genetic factors.

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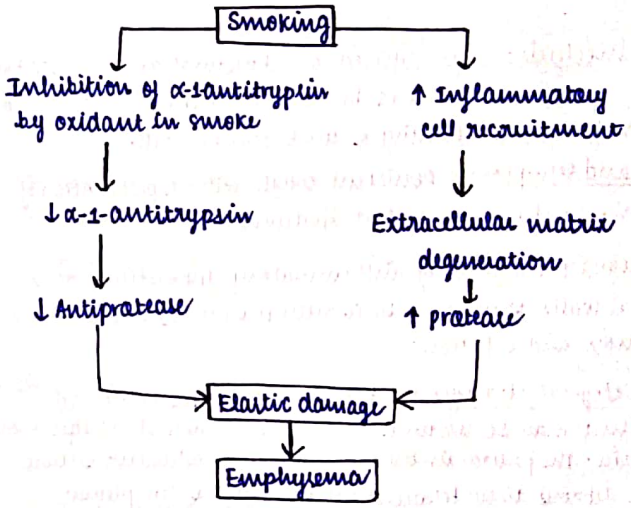
In emphysema destruction of the alveolar walls, is not linked to bronchial changes but is closely related to deficiency of serum α-1-antitrypsin.



Fig; Pathogenesis of alveolar wall destruction in emphysema

- **Morphological changes in emphysema:** There is dilatation of airspaces and destruction of septal walls of part of acinus involved i.e., respiratory bronchioles, alveolar ducts and alveolar sacs.

C) **Bronchial asthma:** Bronchial asthma is a syndrome characterized by periodic reversible spasm of tracheo-bronchial smooth muscle in response to noxious stimuli. Because of spasm, retention of larger

volume of air in alveoli ↓ the tidal volume and vital capacity, consequently leading to dyspnoea (difficulty in breathing out), wheezing and cough. (For detailed description see Section asthma).

D.) **Bronchiectasis:** It is defined as abnormal and irreversible dilation of the bronchi and bronchioles developing secondary to inflammatory weakening of the bronchial wall.

- **Sign and symptoms:** Persistent cough with expectoration of infection, smelling of purulent sputum.
- **Aetiology:** The origin of inflammatory destructive process of bronchial walls occurs by 2 basic mechanisms i.e, endobronchial obstruction and infection.
- **Morphological changes in bronchiectasis:** The bronchial epithelium may be normal, ulcerated or may show squamous metaplasia. The pleura in the affected area is adherent & there bands of fibrous tissue between the bronchus & the pleura

E.) **Small airways disease:** Bronchialitis & bronchialitis obliterans are the inflammatory conditions affecting the small airways occuring predominantly in older paediatric age & in quite elderly persons.

- **Aetiology:** Viral infection (frequently adenovirus & respiratory syncytial virus), bacterial infection, fungal infection, inhalation of toxic gases & aspiration of gastric contents.
- **Morphological changes in small airways disease:** The lumen of bronchioles are affected & becomes narrow and occluded by fibrous plugs. The bronchiolar wall are inflamed and are infiltered by lymphocytes and plasma cells.

Renal system:

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* **Renal failure:** Renal failure is defined as significant loss of renal function in both kidneys to the point when less than 10 to 20% of normal GFR (glomerular filtration rate) remains.

- Renal failure may occur as an acute and rapidly progressive 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 renal failure progresses slowly over at least 3 months & can leads to permanent renal failure.

• **Pathophysiology of Renal failure:** In renal failure their 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 filteration, glomerular dysfunction leads to fall in GFR with retention of those substances usually cleared by filteration, including water

- **Tubular dysfunction:** As the main function of tubules is re-absorption, tubular failure results in the voiding of large volumes of dilute urine (polyuria) of low specific gravity, along with electrolytes and nutrients.

• **Classification of renal failure:** It is of 2 types:

1) Acute renal failure (ARF)
2) Chronic renal failure (CRF)

1) **Acute renal failure:** ARF is a syndrome characterized by rapid onset of renal dysfunction, chiefly oliguria or anuria, and sudden increase in metabolic waste products (urea and creatinine) in the blood with consequent development of uraemia.

- ARF is 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 occured

- **Manifestations (symptoms):**
  a) Oliguria (reduced urine output)
  b) Possible oedema and fluid retention
  c) Elevated blood urea nitrogen levels (BUN) and serum creatinine.
  d) Alterations in serum electrolytes.

- **Causes of acute renal failure:** Myocardial infarction, decreased blood flow, rhabdomyolysis, obstruction, hemolytic uremic syndrome, glomerulonephritis are common causes of acute renal failure

- **Classification of ARF:** ARF is classified as:
  A) Pre-renal failure
  B) Intra-renal failure
  C) Post-renal failure

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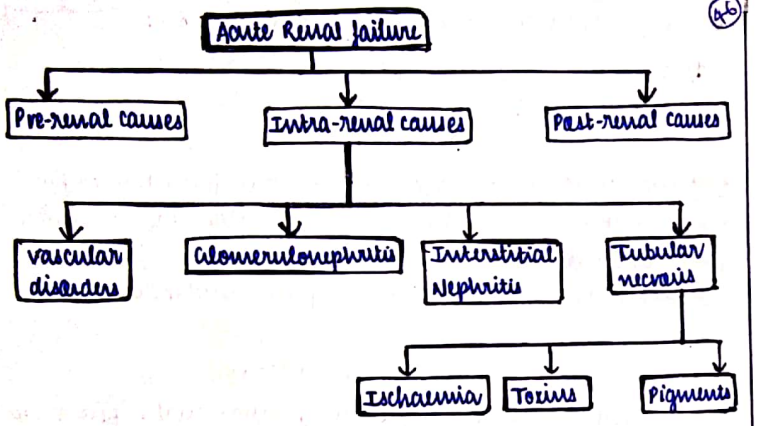

Fig; Aetiology and classification of acute renal failure

A.) **Pre-renal failure:** It results from impaired or reduced blood flow to the kidney. It occurs due to shock, hypotension, anaphylaxis, ischaemic formation

B.) **Intra-renal failure:** It results from acute damage to renal structures.

-**Aetiology:** a.) Acute glomerulonephritis, pyelonephritis.
b.) May also result from acute tubular necrosis (ATN).
c) damage of kidney structure from exposure to toxins, solvents, drugs and heavy metals; ATN is the most common cause of acute renal failure.

C.) **Post-renal failure:** It results from conditions block of urine outflow.

-**Aetiology:** Obstruction of urine outflow by calculi, tumors, prostatic hypertrophy

-**Sign and symptoms of ARF:**

a.) Decreased kidney function (electrolyte imbalance)
b.) Obstruction in the urinary tract.
c) Blood in urine
d.) Reduced urine output.
e.) Dehydration
f.) Detectable abnormal mass
g.) Pale skin
h.) Poor appetite.

2.) **Chronic Renal Failure (CRF):** Chronic renal failure is the end result of progressive kidney damage and loss of function. chronic renal failure is classified into 4 progressive stages based on the loss of GFR.

-**Stages of chronic renal failure:**

I.) Diminished renal reserve ⇒ GFR decreased to 35 to 50% of normal
II.) Renal insufficiency ⇒ GFR decreased to 20 to 35% of normal.
III.) Renal failure ⇒ GFR reduced to less than 20% of normal.
IV.) End-stage renal disease ⇒ GFR is less than 5% of Normal.

-**Aetiology of chronic renal failure:**

a.) Chronic glomerulonephritis.
b) chronic infections
c) Renal obstruction (pralonged)
d.) Exposure to toxic chemicals, toxins or drugs (aminoglycoside antibiotics and nephrotoxicity).

e.) Diabetes

f.) Hypertension

g.) Nephrosclerosis (atherosclerosis of the renal artery)

h.) Diabetic nephropathy

i.) Alport syndrome (inherited disorder caused deafness, progressive kidney damage and eye defects).

j.) Polycystic kidney disease.

k.) Interstitial nephritis or pyelonephritis.

- **Symptoms of chronic renal failure (CRF):**

a.) Anaemia, increased levels of phosphates (in blood) are complications of kidney failure.

b.) Malaise

c.) Dry skin

d.) Poor appetite

e.) Vomiting

f.) Bone pain

g.) Metallic taste in mouth

h.) Detectable abdominal mass.

- **Manifestations of chronic renal failure:** Renal failure is a multisystem disease. The manifestations of CRF are:

System	Effect	Cause
Body fluids	Polyuria	Metabolic acidosis
	Metabolic acidosis	Reduced H^+ excretion
	Abnormal levels of Na^+, K^+, Ca^{+2}, PO_4^{-}	Loss of tubular function
Haematologic	Anaemia, excess bleeding	Impaired erythropoietin.
Cardiovascular	Hypertension, oedema	Activation of renin-angiotensin system
Gastrointestinal tract	Anorexia, nausea	Accumulation of metabolic wastes.
Neurologic	Uremic encephalopathy	Accumulation of ammonia and nitrogenous waste
Musculoskeletal	Muscle & bone weakness ("Renal osteodystrophy")	Loss of calcium and minerals.