PHARMACOLOGY-II

UNIT 1 NOTES

PHARMACOLOGY OF CARDIOVASCULAR DISEASES

- ANTIHYPERTENSIVE AGENTS
- DRUGS USED IN CHF
- ANTIANGINAL AGENTS
- ANTIARRHYTHMIC AGENTS
- ANTIHYPERLIPIDEMIC AGENTS

IMPERFECT PHARMACY

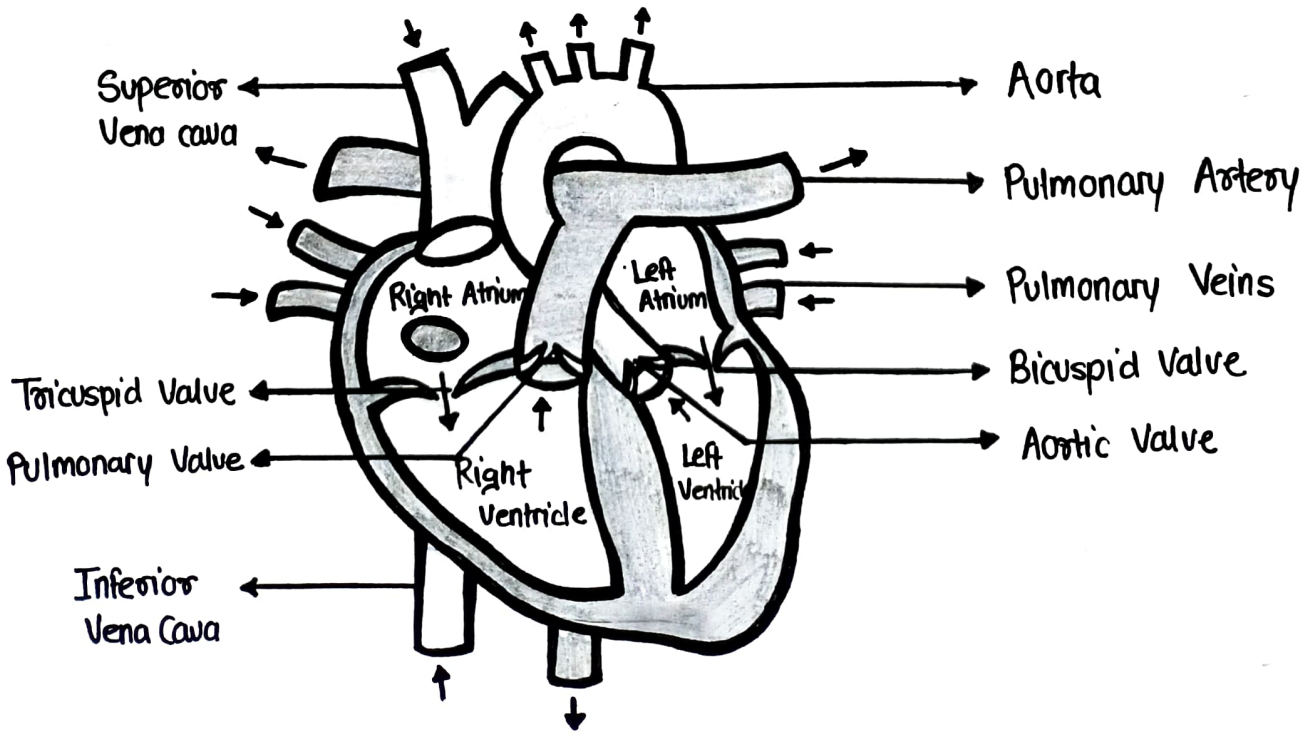
CARDIOVASCULAR SYSTEM

- The word cardiovascular is made from two words
  Cardio - heart
  Vascular - Blood Vessels
- The human cardiovascular system is a system of organs that includes heart, blood vessels and blood.
- Heart pumps the blood into blood vessels and blood vessels circulate the blood throughout the whole body.

- Cardiovascular System + Lymphatic System → Circulatory System.

HEART

- Heart is a hollow muscular organ that pumps the blood throughout the ~~whole~~ ~~body~~ blood vessels.
- It is a small structure, roughly having the size of person's closed fist.



Shape : Cone shape (Like closed fist)
Dimensions : 12 cm x 9 cm x 6 cm
Location : Mediastinum (Space between the lungs)
Weight : About 250 g in females and 300 g in males.

LAYERS OF HEART

The wall of the heart consist of three layers :

① Pericardium
② Myocardium
③ Endocardium

Pericardium

- It is the uppermost layer of the heart that encloses the heart and roots of the blood vessels.
- It surrounds and protect the heart.
- It is also divided into two main layers :

(1) Fibrous Pericardium
(2) Serous Pericardium

Fibrous Pericardium : It is a tough external layer made of dense irregular connective tissue

Serous Pericardium : It is a thin internal layer which is itself divided into two main layers

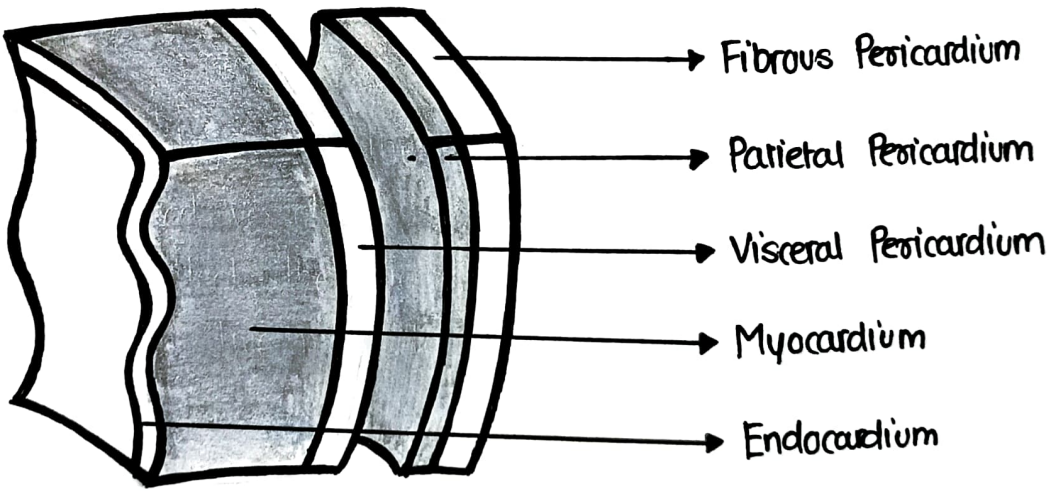
① Parietal Layer
② Visceral Layer (Epicardium)
- It secret serous fluid which maintains the lubrication of heart.

Myocardium

- It is the middle layer of the heart made of cardiac muscle tissue.
- It makes up the bulk of the heart.
- The myocardium is responsible for pumping of heart.

Endocardium

- It is the innermost layer of the heart.
- It is made up of thin layer of epithelial tissue.
- It provides smooth lining for chambers of heart and covers the values of heart.



Chambers Of The Heart

- The heart mainly consist of 4 chambers :

① Right Atrium
② Left Atrium
③ Right Ventricles
④ Left Ventricles

- The thickness of wall of the 4 chambers varies according to their functions.
- The left side of the heart has much larger work load than the right side of the heart, hence wall of left side is much thicker compared to right side of the heart.

Right Atrium

- It is present on the upper right side of the heart.
- It receives deoxygenated blood from superior and inferior venacava
- Superior vena cava present on the upper side and Inferior Vena cava present on the lower side of right atrium.
- The average thickness of wall is 2-3 mm.

Left Atrium

- It is present on the upper left side of the heart.
- It receive oxygenated blood from lungs through pulmonery veins.
- It is smaller in shape compared to Right atrium.
- 4 pulmonary veins opens in the left atrium.
- The average thickness of wall is 3-5 mm.

Right Ventricle

- It is present below the right atrium.
- It recieves Deoxygenated blood from the right atrium.
- It forms a large part of heart.
- The average thickness of wall is 3-5 mm

Left Ventricle

- It is present below the left atrium.
- It receives Oxygenated blood from left atrium.
- The wall of left ventricle is two - three times thicker than right ventricle.
- The average thickness of wall is 10- 15 mm.

VALVES OF HEART

Heart consist of 4 types of valve :

① Tricuspid Valve
② Bicuspid Valve
③ Pulmonary Valve
④ Aortic Valve

Tricuspid Valve

- It is also known as Right atrioventricular valve.
- It separates the right atrium from right ventricle.
- It prevents backflow of blood into atrium.

Bicuspid Valve

- It is also known as left atrioventricular valve.
- It lies between left atrium & left ventricle.
- It prevents backflow of blood into atrium.

Pulmonary Valve

- It can also be known as semilunar valve.
- It lies between the right ventricle and pulmonary artery.
- It prevents backflow of blood into pulmonary artery.

Aortic Valve

- It is also known as semilunar valve.
- It lies between aorta and left ventricle
- It prevents backflow of blood in Aorta.

BLOOD VESSELS

- The heart pumps the blood into blood vessels that vary in structure size and function
- Blood vessels are of mainly three types

① Arteries
② Veins
③ Capillaries

Arteries

- Arteries are the blood vessels that carry blood away from the heart and supply to the whole body.
- They generally carry oxygenated blood (except pulmonery Arteries)
- They are composed of three layers.

(1) Tunica Intima
(2) Tunica Media
(3) Tunica Externa

- According to their shape and size they can be further divided into two class :

AORTA : Aorta is the largest artery of the body that carries blood from the heart to the circulatory system.

ARTERIOLES : These are the smaller sub branches of arteries

Veins

- These are the blood vessels that carry the blood from body back to heart.
- They generally carry deoxygenated blood (except pulmonery veins)
- They are also composed of three layers same as artery.
- Their wall is thin compared to artery wall.
- Their lumen size is larger compare to artery.

- According to their shape and size, they are divided into two sub classes

VENA CAVA: Vena cava is the large vein that carry blood to the heart from the body.

VENULES: These are the smaller sub branches of vein.

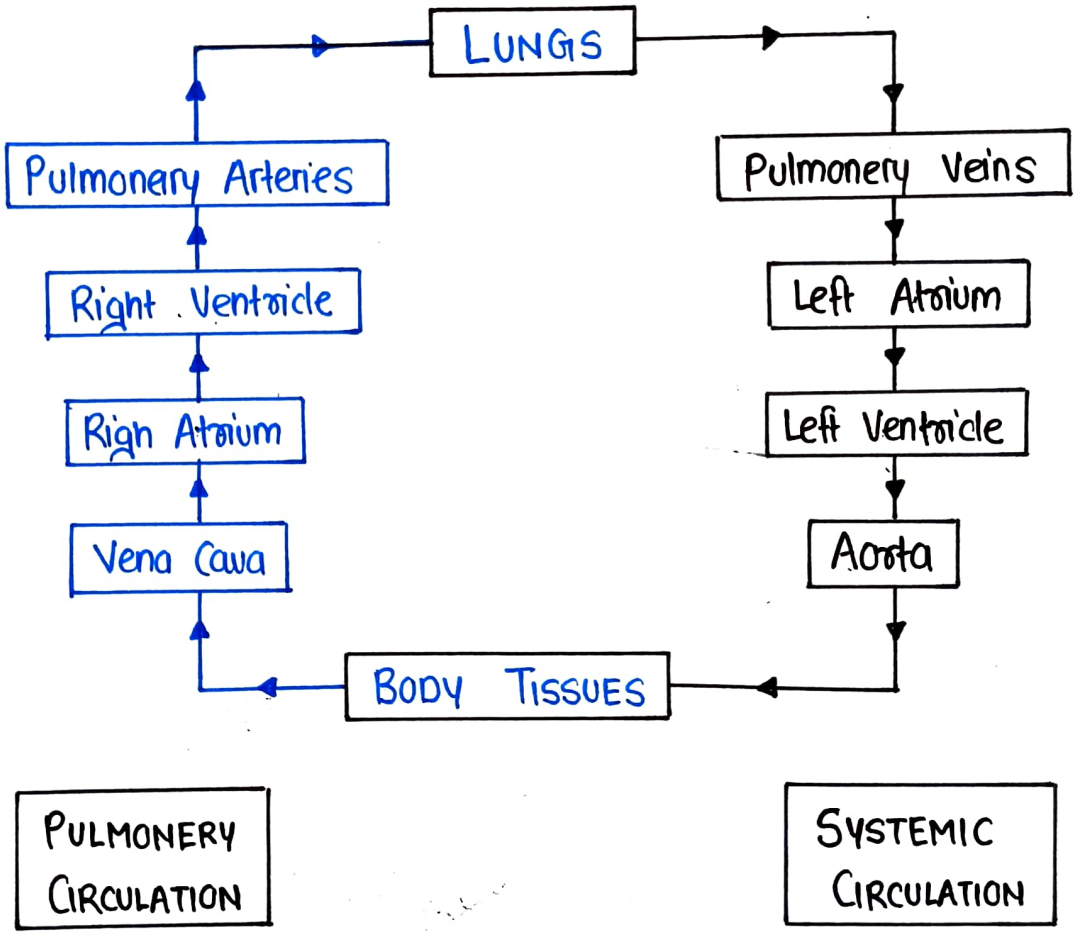
Cappillaries

- Capillaries are the smallest blood vessels that forms when arterioles and venules further subdivided into smallest branches:
- These are the smallest vessels that connects arterioles to venules.
- They are the sites of nutrients and waste exchange between the blood & body tissues.

Blood Circulation

- By the blood circulation , nutrients, respiratory gases (O_2) and other essential products supplied throughout the body and deoxygenated blood sends back to the heart.
- There are two types of circulation occurs in our body.

① Systemic Circulation
② Pulmonery Circulation



Conducting System Of Heart

- It is a specialized system of Heart made of cardiac muscle fibres.
- They produce and conduct the electrical impulses through heart.
- The conducting system of heart work as Auto Rythmicity.
- This system consist of 4 major parts :

① SA Node
② AV Node
③ Bunde of His
④ Purkinje Fibres

SA Node

- The full form of SA Node is Sinoatrial Node.
- It is also known as Natural Pacemaker of Heart.
- It prooduces the electrical impulses which is responsible for the contraction / relaxation of heart.
- It produce electrical impulses approx 100 times per minute
- It lies at walls of right atrium just below the opening of superior vena cava.

AV Node

- The full form of AV Node is Atrioventricular Node.
- It is also known as Second Pacemaker of Heart.
- It collects impulses from the SA Node and transfer them to bundle of HIS.
- Impulses from SA Node to AV Node reach in 0.09 second (approx)
- It lies at the bottom of right atrium.

Bunde of HIS

- It is also known as AV Bundles.
- It receives the impulses from AV Node and transmit to Purkinje Fibres
- It lies at the septum of heart.

Purkinje Fibres

- The purkinje fibres are branches of specialized nerve cells.
- It receives electrical impulses from Bundle of HIS and transfer them very quickly to your right and left heart ventricles.
- They lies at the wall of right and left ventricles.

CARDIAC CYCLE

- Cardiac cycle is defined as sequences of events taking place during each heart beat.
- Now 1 heart beat includes :

① 1 Systole (contraction)
② 1 Diastole (Relaxation)

- So we can also say cardiac cycle is the time when 1 systole and 1 Diastole takes place.
- During Systole heart contracts
- During Diastole heart relaxes

Time Period of Cardiac Cycle : 0.8 Second
Normal Heart Beat : 70-75 beat per minute

Stages of Cardiac Cycle

Cardiac Cycle includes 3 main stages :

① Atrial Systole
② Ventricular Systole
③ Complete Cardiac Diastole

Arterial Systole

- Its time duration is 0.1 second.
- During arterial systole superior vena cava and inferior vena cava transports deoxygenated blood into right atrium and at the same time 4 pulmonary veins brings oxygenated blood into left atrium
- Finally in the last step tricuspid valve (atrioventricular valve) open and as a result of arterial systole blood transfer into ventricles.

Ventricular Systole

- Its time duration is 0.3 seconds.
- When blood comes into left and right ~~atrium~~ ventricles then as a result of ventricular systole, blood from the both ventricles transferred into pulmonary artery and Aorta.
- After arterial and ventricular systole all the values get closes.
- Arterial and Ventricular systole occurs due to electrical impulses generated by SA Node and trasferred by AV Node.

Complete Cardiac Diastole

- Its time duration is 0.4 seconds.
- When both arterial and ventricular systole completed there is a complete diastole of 0.4 seconds, when ~~aorta~~ atrium and ventricles get relaxed.
- Cardiac diastole occurs so that heart get ready for next cardiac cycle

Electrophysiology Of Heart

- Electrophysiology of heart refers to the study of electrical processes that govern the function of the heart, particularly how the generates and conduct electrical impulses
- These electrical impulses coordinate the contraction of the heart muscles, ensuring proper blood flow.
- It consit of 5 Phases :

① Phase 0
② Phase 1
③ Phase 2
④ Phase 3
⑤ Phase 4

~~Phase~~

Phase 0

- The phase is characterized by a rapid upstroke in membrane potential.
- It is caused by sudden opening of voltage gated sodium (Na^+) channels, leading to a large influx of Na^+ ions
- The cell membrane potential becomes more positive, moving around -90 mV to + 30 mV.
- This triggers muscle contraction.

Phase 1

- Na^+ channels closes, and there is a transient outward flow of potassium ions (K^+) through k^+ channels
- This creates a little, small dip in membrane potential.
- This phase is known as Initial or Partial Repolarization.

Phase 2

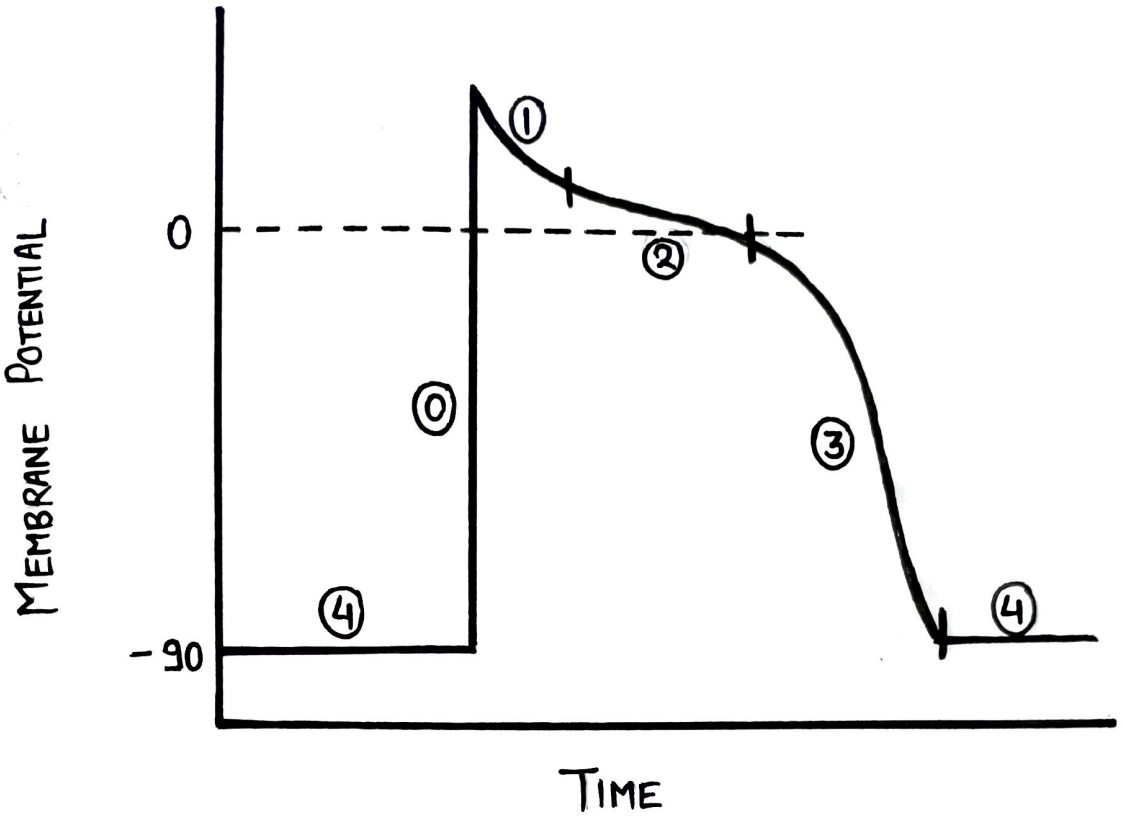
- It is known as Plateau Phase.
- Ca^{2+} channels, allowing Ca^{2+} to enter the cell slowly, while K^+ continues to exit.
- L-type Ca^{2+} channels open, while some K^+ channels remain open.
- The inflow of Ca^{2+} balances the outflow of K^+, causing the membrane potential to remain relatively stable.
- This Plateau phase prolongs the action potential, ensuring sustained contraction of heart muscle necessary for effective pumping.

Phase 3

- Ca^{2+} channels close, while K^+ continues to leave the cell.
- K^+ channels dominate as Ca^{2+} channels close.
- The membrane potential returns to its resting state due to continued efflux of K^+.
- The cell repolarizes, preparing for next cycle of depolarization.

Phase 4

- The cell remains at its resting membrane potential until it is depolarize again by a new stimulus.
- K^+ channels maintain the resting membrane potential by allowing K^+ to flow out, while (Na^+/K^+ ATPase) actively maintain ion gradients.
- The cell is in its resting state at round -90 mV, awaiting the next depolarization phase.



Phases Of Action Potential

HAEMODYNAMICS

- Haemodynamics refers to study of blood flow and forces involved in the circulation of blood throughout the body.
- It focuses on understanding how heart pumps blood & how blood flows through the circulatory system.

① Cardiac Output

- It is defined as amount of blood that heart pumps in 1 minute.

C.O. = Heart Rate X Stroke Volume

② Heart Rate

- It is defined as number of heart beats per minute.
- Normal Range : 60 - 100 beat per minute.

③ Stroke Volume

- It is defined as amount of blood pumped by left ventricle in one contraction.

④ Blood Pressure

- It is defined as force that blood exerts against wall of blood vessels.
- It is of two types

(1) Systolic Pressure
(2) Diastolic Pressure

HYPERTENSION

- The term Hypertension referred to 'High Blood Pressure'.
- It is a chronic medical condition that arises when blood pressure is abnormally high.
- It occurs when blood vessels gets narrowed & cause blood to exert more pressure on heart's wall.
- Heart & Blood vessels can tolerate high blood pressure for months & years but eventually high B.P. ended up damaging walls of heart that leads to Heart Failure.
- As per the world health statistics, approx 1.5 billion adult population across the world is suffering from Hypertension.

STAGES OF HYPERTENSION

	STAGES	SYSTOLIC BP	DIASTOLIC BP
•	Normal	< 120 mm Hg	< 80 mm Hg
•	Pre- Hypertension	120-139 mm Hg	80-89 mm Hg
•	Stage I	140- 159 mm Hg	90-99 mm Hg
•	Stage II	≥ 160 mm Hg	≥ 100 mm Hg

TYPES OF HYPERTENSION

Hypertension is of mainly two types:

① Primary Hypertension

② Secondary Hypertension

Primary Hypertension

- It is also known as Essential Hypertension.
- 95% people with High B.P. suffered with Primary Hypertension.
- Generally causes behind this are unidentified.

Secondary Hypertension

- Secondary Hypertension is often arised by other medical conditions such as kidney, artery, heart or endocrine system disorders.
- It's less common than primary hypertension affecting 5-10% of Hypertensive patients.
- It's more common in younger people.

Etiology / Causes Of Hypertension

As we discussed early, it is very difficult to find the exact cause of Hypertension. but here are some following reasons that can be responsible for Hypertension.

- Inactive Life Style
- Stress
- Obesity
- High sodium (salt) diet
- Alcohol
- Smoking
- kidney Diseases.
- Diabetes
- Age
- Family History
- Certain Medications

PATHOGENESIS OF HYPERTENSION

Pathogenesis of hypertension is often multifactorial & complex, it can be described by following mechanism

- Increased Arteriolar Resistance
- Chronic Renal Failure
- Sympathic Activation
- Activation of RAAS System

① Increased Arteriolar Resistance

- An increase in arteriolar resistance can lead to Hypertension by raising blood pressure within arteries.
- An increase in arteriolar resistance can be occur due to many reasons including thining & fracturing of elastin, increased collagen deposition & increased wall thickness.
- It further increases risk of stroke, coronary artery disease & CHF.

② Chronic Renal Failure

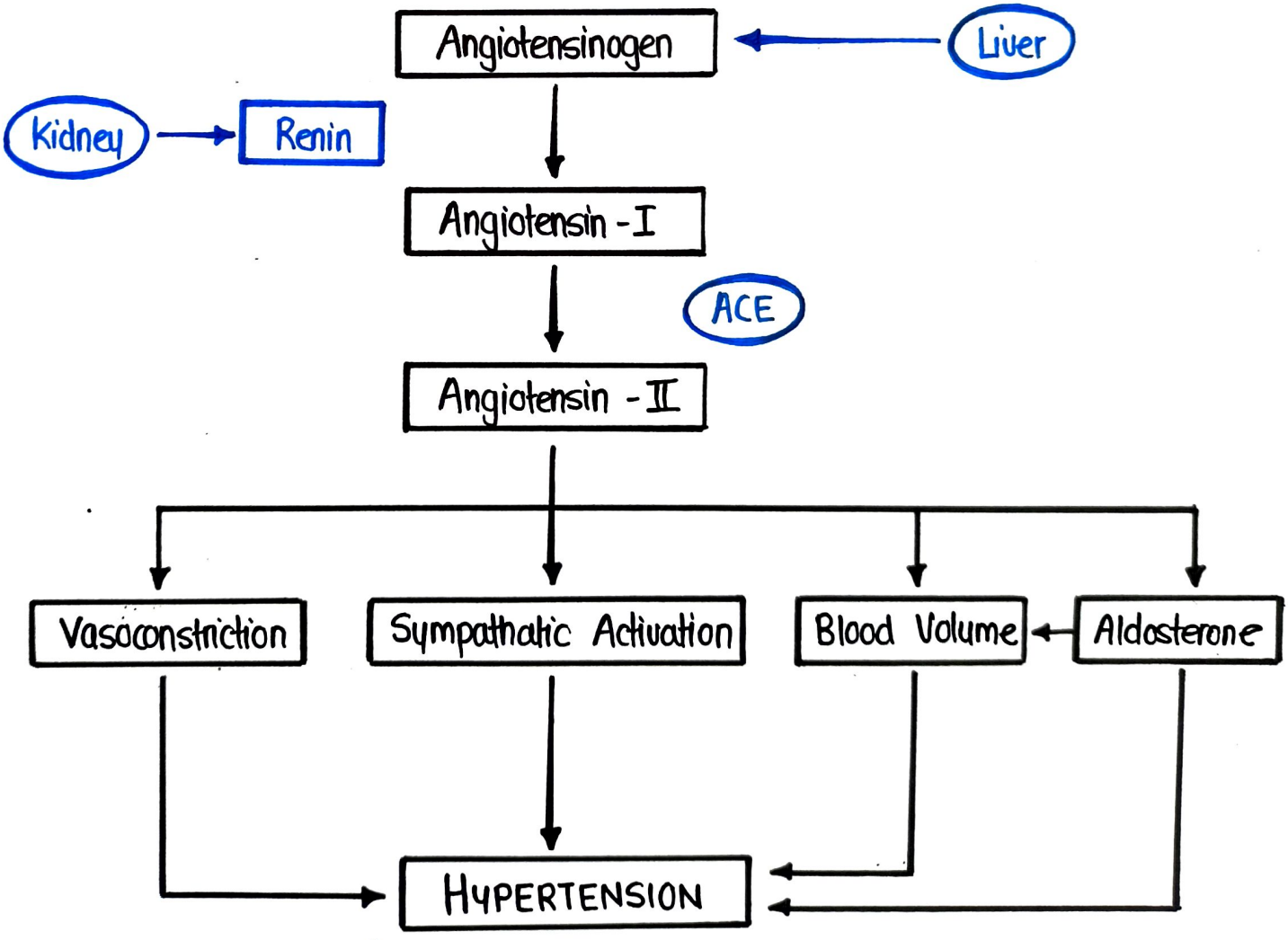
- When kidney doesn't function properly then it fails to excrete normal amount of sodium that leads to sodium retention.
- Now this sodium retention causes water retention that increases the blood volume that leads to Hypertension.

③ Sympathatic Activation

- Stress & various other factors leads to the activation of sympathatic nervous system that causes increased release of nor-epinephraine
- Now this leads to increase cardiac output & systemic vascular resistance.

④ Activation Of RAAS System

- RAAS stands for Renin Angiotensin Aldosterone System.
- Renin is a harmone released by kidney while Angiotensin is released by liver & when they both combines activates Aldosterone.



Sign & Symptoms

- Headache
- Dizziness
- Blurred Vision
- Nausea & Vomiting
- Fatigue
- Chest Pain
- Irregular Heartbeat

Complications

- Heart Attack
- Heart Failure
- kidney Failure
- Stroke
- Retinopathy

Treatment / Management

① Non Pharmacological

- Weight Loss
- Exercise
- Meditation
- Healthy Diet

② Pharmacological

- Diuretics
- α, β Blockers
- Vasodilators, ACE Inhibitors

Classification Of Anti Hypertensive Agents

Antihypertensive Drugs are classified as follows :

① Diuretics

- Thiazides : Hydrochlorothiazide
  Chlorthalidone
  ~~Id~~ Indapamide
- High Ceiling : ~~Fuse~~ Furosemide
- K^+ Sparing : Spironolactone, Amiloride

② ACE Inhibitors

- Captopril
- Lisinopril
- Enalopril
- Perindopril
- Ramipril
- Fosinopril

③ Angiotensin (AT_1) Blockers

- Losartan
- Candesartan
- Irbesartan
- Valsartan
- Telmisartan

④ Direct Renin Inhibitors

- Aliskiren

⑤ Calcium Channel Blockers

- Verapamil
- Diltiazem
- Nifedipine
- Felodipine
- Amlodipine
- Nitrendipine
- Lacidipine

⑥ β Adrenergic Blockers

- Propranolol
- Metoprolol
- Atenolol

⑦ α Adrenergic Blockers

- Prazosin
- Terazosin
- Doxazosin
- Phentolamine
- Phenoxybenzamine

⑧ α + β Adrenergic Blockers

- Labetalol
- Carvedilol

⑨ Central Sympatholytics

- Clonidine
- Methyldopa

⑩ Vasodilators

- Arteriolar : Hydralazine
  Minoxidil
  Diazoxide
- Arteriolar + Venous : Sodium Nitroprusside.

DIURETICS

- Diuretics are a class of drugs commonly used as Antihypertensive agents due to their ability to lower blood pressure.
- They achieve this by promoting the excretion sodium and water through urine, which decreases the volume of blood circulating in the body, ultimately lowering blood pressure:

① THIAZIDES

- It is most commonly prescribed diuretics for Hypertension.
- These diuretics are inexpensive first line antihypertensive agents.

Mechanism Of Action

- Thiazide diuretics such as Hydrochlorothiazide and Chlorthalidone lower blood pressure by acting primarily on the kidneys, reducing blood volume.
- Thiazides inhibit the sodium - chloride symporter in the Distal Convulated Tubule of kidney.
- By blocking this transporter, thiazides prevent the reabsorbtion of sodium & chloride from urine to Blood.
- This leads to increased excretion of sodium, chloride and water, reducing bleed volume.

PHARMACOKINETIC PROFILE

Absorption :
- Thiazides are well absorbed orally.
- However, absorption may vary between different drugs.

Distribution :
- They are moderately bound to plasma proteins and have variable volume of distribution

Onset of Action :
- Typically 2-3 hours after oral administration.

Peak Effect :
- Occurs within 4-6 hours

Duration of Action :
- Ranges between 12-24 hours for Hydrochlorothiazide, but can last upto 48 hours for Chlorthalidone.

Metabolism & Excretion :
- Thiazides are not extensively metabolized and are primarily excreted unchanged by the kidneys.

THERAPEUTIC USES

- Thiazide or thiazide-like diuretics are effective in reducing the incidences of strokes, heart failure etc.
- Diuretics can be effectively used in obese, elderly and diabetic patients.
- They are used in patients with systolic heart failure and excess sodium intake.
- Thiazide diuretics increases calcium level and decrease osteoporosis.

Adverse Effect of Thiazide Diuretics

- They can lead to low levels of potassium and sodium, as well as elevated calcium levels
- Excessive fluid loss can result in dehydration, which may cause dizziness, headaches or low blood pressure.
- Thiazides may impair glucose tolerance, potentially increasing blood sugar levels, which is particularly concerning for diabetic patients.
- There can be a risk of decreased kidney function, especially in individuals with pre-existing kidney issues.

Hydrochlorthiazide

This prototype thiazide diureti reduces electrolyte reabsorbtion from renal tubules, thus increases excretion of water & electrolytes.
It is used in several disorders like oedema, Hypertension, diabetes, hypoparathyroidism.

② HIGH CEILING DIURETICS

High ceiling diuretics also known as loop diuretics, are a class of diuretics that are highly effective in promoting diuresis.

Mechanism of Action

- They act primarily on ascending loop of Henle to prevent reabsorbtion of Cl^- & Na^+ & K^+.
- This result in a significant excretion of these electrolytes along with water. & lowering in blood volume.

PHARMACOKINETICS

① **Absorbtion** : • The absorbed relatively quick when administered orally, although bioavailibility varies in different drugs.

② **Distribution** : • Loop diuretics are highly bound to plasma proteins, means only a little fraction is pharmacologically active.
• Onset of action occurs within 30-60 minutes after oral administration

③ **Metabolism** : • Furosemide is minimally metabolized and primarily excreted unchanged by kidneys.

④ **Excretion** : • The majority of loop diuretics are excreted via the kidneys either unchanged or as metabolites.

POTASSIUM SPARING DIURETICS

- These diuretics have comparatively low efficacy
- They are class of diuretics that promote diuresis without causing significant loss of potassium that is typically associated with other diuretics like loop & thiazide diuretics.
- They are generally used in combination with Hydrochlorothiazides

TYPES OF POTASSIUM - SPARING

Potassium - Sparing Diuretics are divided into two categories based on their Mechanism of Action:

① Aldosterone Antagonist
② Sodium Channel Blockers

MOA

① Aldosterone Antagonist

- These drugs block the action of aldosterone at the mineralocorticoid receptors in the distal convoluted tubule and the collecting duct of the nephron in the kidney.
- Aldosterone is a hormone that promotes sodium reabsorption and potassium excretion.
- By blocking aldosterone, these drugs reduce sodium & water reabsorption, leading to mild diuresis and lowering blood pressure.
- At the same time, they conserve potassium by preventing its excretion, which is particularly important in patients at risk of hypokalemia.

Sodium Channel Blockers

- These drugs inhibit the epithelial sodium channels in the distal part of nephron, reducing sodium reabsorbtion and promoting mild diuresis.
- They also retain potassium because sodium reabsorbtion is linked to potassium excretion, so by inhibiting sodium reabsorbtion, potassium excretion is reduced.

PHARMOCOKINETICS

① **Absorbtion**: They are generally well absorbed when taken orally.

② **Distribution**: These drugs are widely distributed throughout the body.

③ **Metabolism**: Spironolactone is extensively metabolized in liver while drugs such as Amiloride is not extensively metabolized and is mostly excreted unchanged.

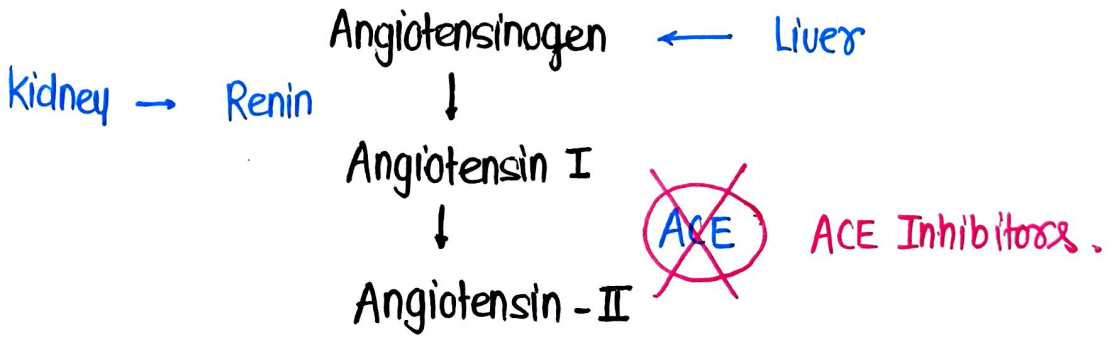
④ **Excretion**: These drugs are primarily excreted in the urine through kidneys.

ACE Inhibitors

- Angiotensin converting enzyme inhibitors are class of medications commonly used to manage hypertension & other cardiovascular conditions.
- They act by inhibiting the action of ACE enzyme.

Mechanism of Action

- ACE inhibitors block the ACE enzyme, which is responsible for converting Angiotensin I into Angiotensin II.
- Angiotensin II is a potent vasoconstrictor, By inhibiting ACE, these drugs reduces level of angiotensin II, leading to vasodilation.



Pharmacokinetics

- **Absorption**: Most ACE inhibitors are well absorbed from GIT. For instance, enalapril is converted to its active form, enalaprilat, after absorption.

- **Distribution**: They are distributed throughout the body, with varying degree of protein binding.

- **Metabolism**: Many ACE Inhibitors, like enalapril & lisinopril, are prodrug and require conversion to their active forms in the body.

- **Excretion**: ACE Inhibitors are primarily excreted by the kidneys, either unchanged or as metabolites.

THERAPEUTIC USES

- They are effectively used in Hypertension.
- They are also used in Heart failure.
- ACE Inhibitors also help to protect renal function.
- They are particularly beneficial in diabetic patients to prevent or delay progression of kidney damage.

ADVERSE EFFECTS

- Cough
- Hyperkalemia
- Hypotension
- Rashes
- Itching
- Loss of Taste sensation

Some Individual Drugs

Captopril

- Captopril is an ACE Inhibitor, widely used for the treatment of Hypertension, Heart failure, Diabetic nephropathy etc.
- It was the first ACE Inhibitor & have relatively short half-life. compare to other drugs in class.
- It is rapidly absorbed from oral route.
- Bioavalibility : About 60-75 %.
- It is not a prodrug like other ACE inhibitors.
- It is excreted via kidneys.
- Half Life : 2-3 hours.
- Duration of Action : 6-12 hours
- Doses : Need to administered 2-3 times daily.

Some Important Points

- All ACE Inhibitors are prodrug except captopril & lisinopril.
- Captopril is shortest & fastest acting ACE Inhibitor.
- Ramipril & perindopril are longest acting drugs.
- ACE Inhibitors are teratogenic : Contraindicated in preganancy.

VASODILATORS

Vasodilatoors are a class of Antihypertensive Agents that work by relaxing the smooth muscles in the blood vessel walls, leading to vasodilation.

Mechanism Of Action

- Vasodilatoors cause vasodilation by directly relaxing the vasculars smooth muscles because it does not depend nervous or receptor control.
- Vasodilatoors reduce total peripheral resistance, thus correct elevated BP in primary hypertension.
- They also act by increasing the level of Nitric Oxide which is a potent vasodilators.
- They also act by opening potassium channels leading to hyperpolarization & relaxation of smooth muscles.

PHARMACOKINETICS

- **Absorbtion**: • They are rapidly absorbed from oral administration, bioavailibility varies widely among individuals, typically between 25-50%.
- **Distribution**: ACE Inhibitoors are widely distributed throughout the body
- **Metabolism**: They are extensively metabolized by liver, primarily through acetylation.

Excretion : Excreted primarily in the urine, with some biliary excretion.

Half Life : Typically 3-7 hours.

MINOXIDIL

- Minoxidil is a potent vasodilator used as an antihypertensive agent for severe and resistant cases of Hypertension, while it is more commonly known for its use in treating hair loss.
- Absorption : Well absorbed orally, with nearly 90% bioavailibility.
- Distribution : Extensively distributed into tissues, with a large volume of distribution.
- Metabolism : Primarily metabolized by liver to inactive metabolites. via glucuronidation.
- Excretion : Metabolites are excreted mainly in urine.
- Half Life : Nearly 4 hours.

SODIUM NITROPRUSSIDE

- Sodium Nitroprusside is a potent and fast-acting vasodilator used primarily in acute situations where rapid reduction of blood pressure is needed.
- Absorption : Given intravenously, so absorption is immediate.
- Distribution : Rapidly distributes in extracellular fluids.
- Metabolism : Rapidly metabolized in red blood cells and tissues to nitric ~~acid~~ oxide & cyanide.
- Excretion : The primary metabolite is excreted in the urine.
- Half Life : Very Short Half Life.

Excretion : The metabolites are excreted primarily via the kidneys although some are excreted in feaces.

Half Life : Drugs like Amlodipine have long half lives (30-50 hours) etc.
Veramapil & dilthiazem have shorter half-lives

CLINICAL USES

- Hypertension
- Angina
- Arrythmias
- Migrain etc.

ADVERSE EFFECT

- Peripheral Edema
- Bradycardia
- Heart failure
- Constipation

VERAMAPIL

- It is categorised under phenyl alkylamine class of organic compounds.
- It is well absorbed orally
- Bioavailibility : 20-35%.
- Widely distributed due high protein binding.
- Metabolized in liver by cytochrome P-450 enzyme.
- Primarily excreted in urine

Congestive Heart Failure

- Congestive Heart Failure is defined as failure of heart capacity to pump sufficient blood that required for proper functioning of body.
- The term CHF used for chronic form of Heart Failure.
- Heart Failure leads the blood to move through body & heart at slower rate.
- CHF is the end result of various forms of serious heart disease.
- It can be further classified into 3 types :

① Left Sided Heart Failure
② Right Sided Heart Failure
③ Both Sided Heart Failure

Types Of CHF

Congestive Heart Failure is of mainly two types :

① Systolic Heart Failure
② Diastolic Heart Failure

Systolic Heart Failure

- In systolic heart failure Heart muscles becomes too weak & enlarged & fails to contract properly.
- In systolic heart failure.
  - Stroke Volume ↓
  - Cardiac Output ↓
  - Ejection Factor ↓

Diastolic Heart Failure

- In diastolic heart failure Heart muscles becomes stiff, thick & enlarged hence the ventricles fails to fill properly.
- In Diastolic Heart Failure :
- Preload ↓
- Cardia Output ↓
- Stroke Volume ↓

Etiology / Causes

- Ischemic Heart Disease / Coronary Artery Disease
- Hypertension
- High Sodium Diet
- Diabetes
- Overweight
- Smoking
- Alcohol
- Myocarditis
- Arrythemia

PATHOGENESIS

Failure of Heart is frequently seen in elderly patients suffering from Hypertension, Angina pectoris etc. Following factors can be responsible for Heart Failure.

① Intrinsic Pump Failure

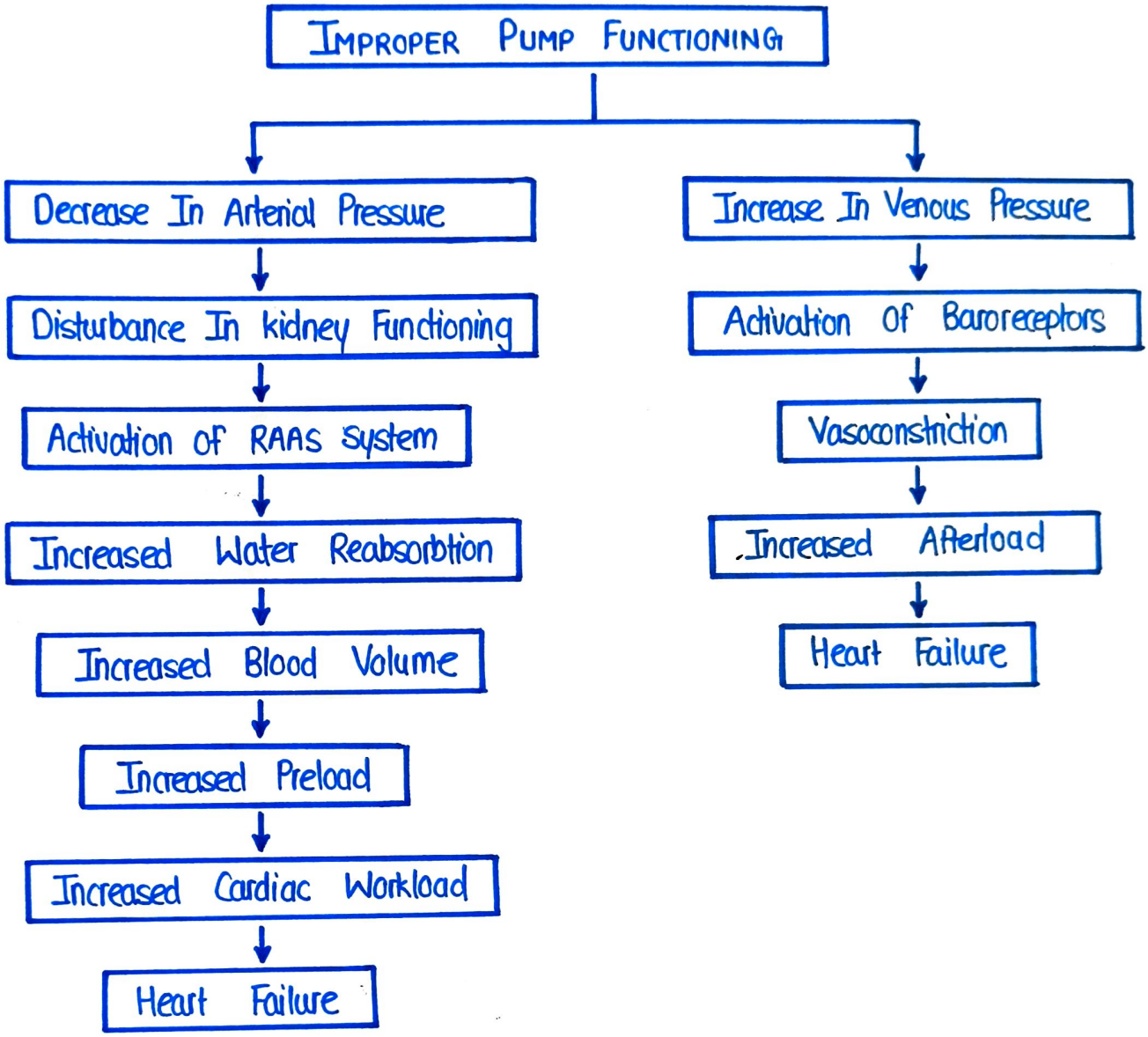
- The most common & most important cause of Heart Failure is weakening of ventricular muscle due to various diseases that leads to failure of efficient pumping of blood by heart.
- It can be occur due to :
  - Ischemic Heart Disease
  - Myocarditis
  - Beriberi Disorder
  - Various kidney Diseases

② Increased Workload On Heart

- An increase in the workload on Heart can also be a major cause of Heart Failure.
- It can be occur due to :
  - Increased Pressure Load
  - Increased Volume Load

③ Improper Pump Functioning

Improper pump functioning can leads to heart failure through following mechanism.



Sign & Symptoms

- Chest Pain
- Fatigue
- Irregular Heartbeat
- Headache
- Blurred Vision
- Cough
- Shortness of Breath
- Swelling

Complications

- kidney Damage
- Lungs Disorders
- Heart Attack
- Liver Damage
- Heart Valve Problems

Treatment / Management

① Non Pharmacological :

- Exercise
- No Smoking
- Healthy Diet / Proper Lifestyle

② Pharmacological :

- β Blockers
- ACE Inhibitors
- Diuretics / Vasodilators

CLASSIFICATION

The following drugs are use in the treatment of Congestive Heart Failure.

① Ionotropic Drugs

- Cardiac Glycosides : Digoxin, Digitoxin, Oubian
- Sympathomimetics : Dobutamine, Dopamine
- PDE 3 Inhibitors : Inamrinone, Milrinone

② Diuretics

- High Ceiling : Furosemide, Bumetanide
- Thiazide like : Hydrochlorthiazide, Metalozone, Xipamide

③ B- Blockers

- Metoprolol
- Bisoprolol
- Nebivolol
- Carvedilol

④ Aldosterone Antagonist

- Spironolactone
- Eplerenone

⑤ ACE Inhibitors

- Enalapril
- Ramipril

⑥ Vasodilatoors

- Glyceryl Trainitroate
- Isosorbide Dinitrate
- Sodium Nitroposside
- Hyralazine

CARDIAC GLYCOSIDES

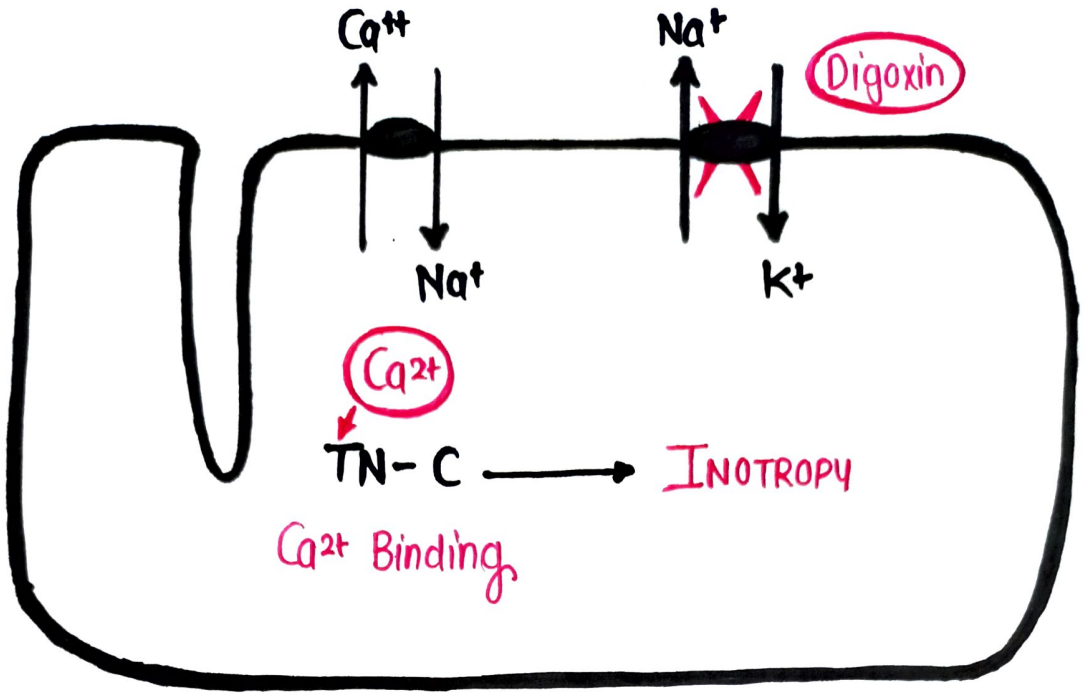
- Cardiac Glycosides are class of medications that are used to treat heart failure, particularly congestive heart failure (CHF).
- They work by increasing force of heart's contraction & slowing heart rate.
- This improves heart's efficiency and helps relieve symptoms of Heart Failure.
- Digoxin is most well known and effective cardiac Glycoside.

DIGOXIN

- Digoxin is a cardiac glycoside commonly used in the treatment of congestive heart failure.
- Its mechanism of action in CHF primarily revolves around its positive inotropic effect, meaning it increases the force of heart contractions.

Mechanism Of Action

- Digoxin inhibits the Na^+/K^+ ATPase pump, which is located in the membranes of cardiac myocytes.
- By inhibiting this pump, digoxin increases the intracellular concentration of sodium.
- The increased intracellular sodium indirectly affects Na^+/Ca^{2+} exchanger; which pumps calcium out in exchange for sodium.
- Due to inhibition of Na^+/K^+ ATPase pump, the Na^+/Ca^{2+} exchanger become less effective, reducing calcium efflux.
- As a result more calcium remains inside the cell.



- The increased intracellular calcium allows for more calcium to be available during each heartbeat.
- During cardiac contraction, this extra calcium is released, leading to stronger contractions of the heart muscle.
- The increased contractility helps improve the heart's pumping efficiency.
- Digoxin also slows down conduction through AV node, which helps to control Heart Rate.

PHARMACOKINETICS

- **Absorption** : It is well-absorbed orally (60-80% bioavailibility) food can affect absorption.
- **Distribution** : It has large volume of distribution, especially in the heart, skeletal muscle and kidneys.
- **Metabolism** : Digoxin undergoes minimal metabolism, mainly in the liver.
- **Excretion** : Digoxin is primarily excreted unchanged via the kidneys.
- **Half Life** : Approximately 36-48 hours.

SIDE EFFECTS

- Nausea
- Vomiting
- Diarrhea
- Dizziness

USES

- CHF
- Atrial fibrillation
- Atrial flutter

Ischemic Heart Disease

- Ischemic Heat Disease is also known as Coronary Artery Disease.
- It is a condition in which supply of oxygen to the muscles of heart get reduced.
- IHD / CAD develops when coronary artery become diseased or damaged.
- In IHD blood supply reduced according to demand of myocardium.
- Building of Plaque & Inflammation in arteries are the major causes of Ischemic Heart Disease.
- Ischemic Heat Disease is further responsible for following heart diseases as follows :

① Angina Pectoris
② Myocardial Infarction
③ Atherosclerosis

Angina Pectoris

- Angina is a term used for 'Chest Pain' caused by reduced blood flow to the heart muscles.
- It is a symptom or complication of 'Coronary Artery Disease'.
- It is a condition that arised when there is an imbalance between the demand for oxygen and its supply to myocardium.

Types Of Angina Pectoris

① Stable Angina
② Unstable Angina
③ Variant Angina

STABLE ANGINA

- It is also known as Chronic Angina.
- It generally occurs when heart is working harder than it works in normal conditions i.e., during exercises.
- It occurs due to building of plaque / fat deposition in Coronary Arteries.
- Pain of stable angina releived by proper rest or medication.

UNSTABLE ANGINA

- The pain of unstable angina occurs even during period of rest, sleeping or suddenly.
- It is considered more serious than stable angina as rest or medication is not enough for its relief.
- It generally occurs due to rupturing of coronary arteries.

VARIANT ANGINA

- It is a rare type of angina, its pain generally occurs at resting stage.
- It occurs due to narrowing of coronary arteries.
- This narrowing or spasm leads to decreased blood flow to the heart and increases the risk of Heart Attack.

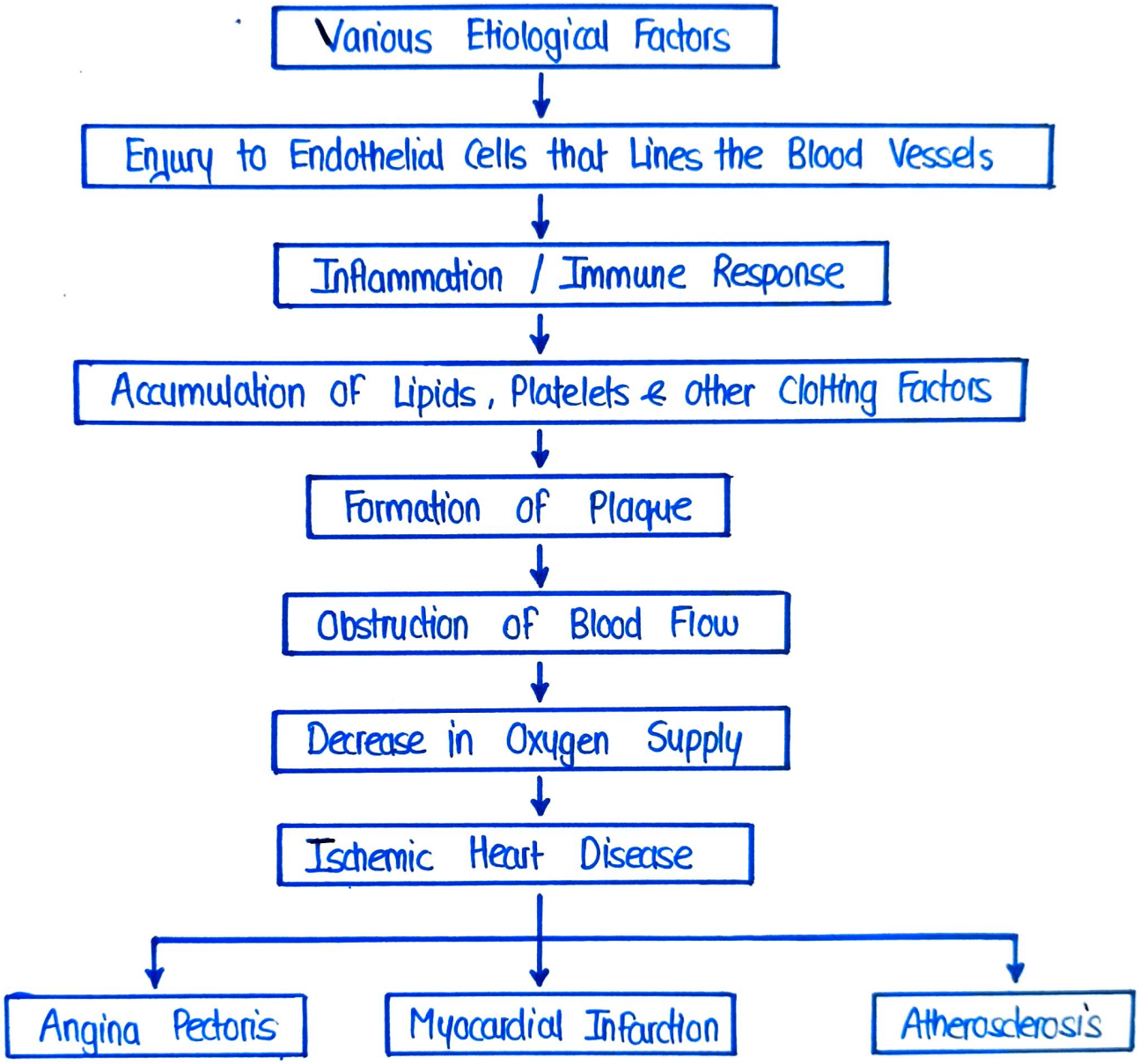
CAUSES

The various causes for Ischemic Heart Disease including Angina Pectoris, Myocardial Infarction & Atherosclerosis are as follows:

- Hypertension
- High Cholesterol
- Smoking
- Alcohol
- Obesity
- Diabetes
- Age
- Stress
- Genetics

PATHOGENESIS

The most common mechanism / pathogenesis behind all the Ischemic Heart Diseases are as follows :



Sign & Symptoms

- Chest Pain
- Fatigue
- Anxiety
- Headaches
- Shortness of Breath
- Irregular Heartbeat
- Blurred Vision

Complications

- Heart Attack
- Heart Failure
- kidney Failure
- Eye Problems
- Various Metabolic Disorders.

Treatment / Management

① Non Pharmacological

- Exercise
- Healthy Diet
- No Tobacco / Alcohol
- Healthy Lifestyle

② Pharmacological :

- Anticoagulants
- Beta Blockers
- ACE Inhibitors / Vasodilators

ANTI-ANGINAL DRUGS

- Anti-Anginal Drugs are medications used to treat Angina Pectoris, a condition marked by chest pain or discomfort that occurs when heart muscles doesn't get enough oxygen rich blood.
- The primary goal of these drugs is to improve blood flow to the heart or reduce heart's oxygen demand.

CLASSIFICATION

Anti-Anginal Drugs are classified as follows:

① NITRATES

- Short Acting: Glyceryl Trinitrate
- Long Acting: Isosorbide Dinitrate, Isosorbide Mononitrate, Erythrityl Tetranitrate, Pentaerythritol Tetranitrate.

② β BLOCKERS

- Propranolol
- Metoprolol
- Atenolol etc.

③ CALCIUM CHANNEL BLOCKERS

- Phenyl Alkylamine: Verapamil
- Benzothiazepine: Diltiazem
- Dihydropyridines: Nifedipine, Felodipine, Amlodipine, Nitrendipine, Nimodipine, Lacidipine, Lercanidipine, Benidipine.

④ Potassium Channel Opener

- Nicorandil

⑤ Others

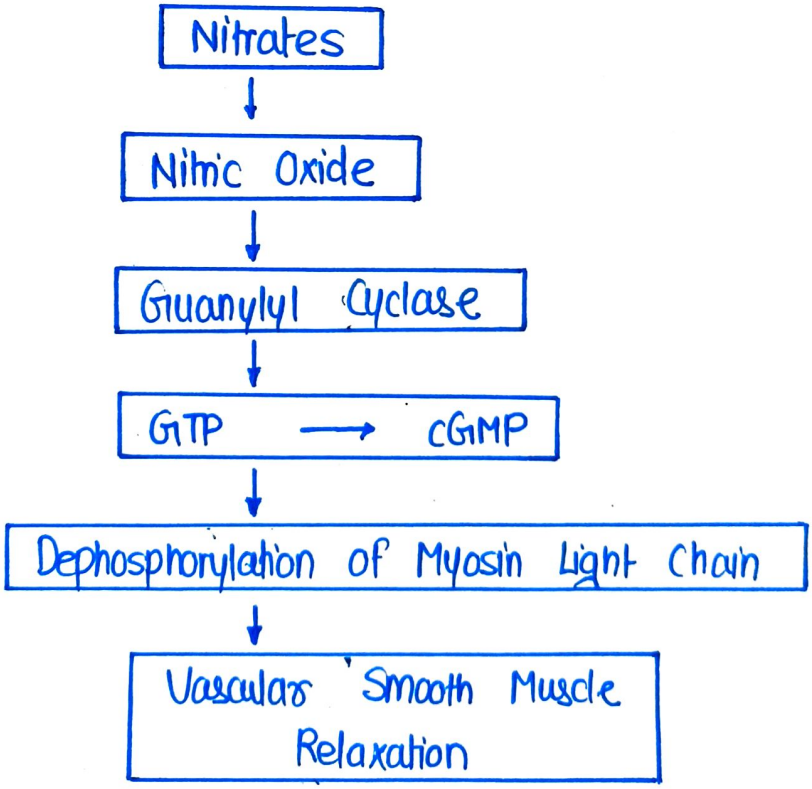
- Dipyridamole
- Trimetazidine
- Ranolazine
- Ivabradine
- Oxyphedrine

NITRATES

- Nitrates are class of medications primarily used to treat angina pectoris by dilating blood vessels, which improves blood flow to the heart & reduces its workload.
- They are often used both for immediate relief and for long term prevention.
- They are one of the oldest and most widely used treatments for Angina.

MECHANISM OF ACTION

- Nitrates work by converting into Nitric Oxide, which is potent vasodilator.
- They reduced Preload, which decreases heart's oxygen demand.
- Dilates Coronary Artery, improving oxygen supply to heart.



PHARMACOKINETICS

- **Absorption :**
  - Nitroglycerine is rapidly absorbed when taken sublingually.
  - Isosorbide Dinitrate & mononitrate are well absorbed orally.
- **Distribution :**
  - Nitrates relatively have low volume of distribution.
- **Metabolism :**
  - Nitroglycerine & isosorbide dinitrate undergo extensive first pass metabolism in liver when taken orally.
- **Excretion :**
  - They are primarily excreted via kidneys.
- **Half Life :**
  - Nitroglycerine : 1-4 minute
  - Isosorbide Dinitrate : 1-2 hour
  - Isosorbide Mononitrate : 4-5 hour

Uses

- Angina Pectoris
- Myocardial Infarction
- CHF
- Acute Coronary Syndrome
- Cyanide Poisoning

SIDE EFFECT

- Headaches
- Dizziness / Hypotension

Individual Drugs

① Nitroglycerine

- It is the drug of choice for Angina Pectoris since it is effective, fast acting & economic.
- If taken via sub-lingual route, it acts rapidly and its action lasts for an hour.

MOA

- Nitroglycerine acts by dilating the blood vessels, thus affecting the vascular smooth muscles.
- It decreases the cardiac oxygen demand in case of stable angina and increases oxygen supply in variant angina.

Therapeutic Uses

- Nitroglycerine sublingually used for treatment of acute anginal pain or for prevention of angina.

Adverse Effect

- Headache
- Blurred Vision
- Weakness
- Vertigo
- Dizziness

② Isosorbide Mononitrate & Dinitrate

These drugs provide longer duration of action than Nitroglycerine. Both isosorbide mononitrate & isosorbide dinitrate are long acting nitrates.

Mechanism of Action

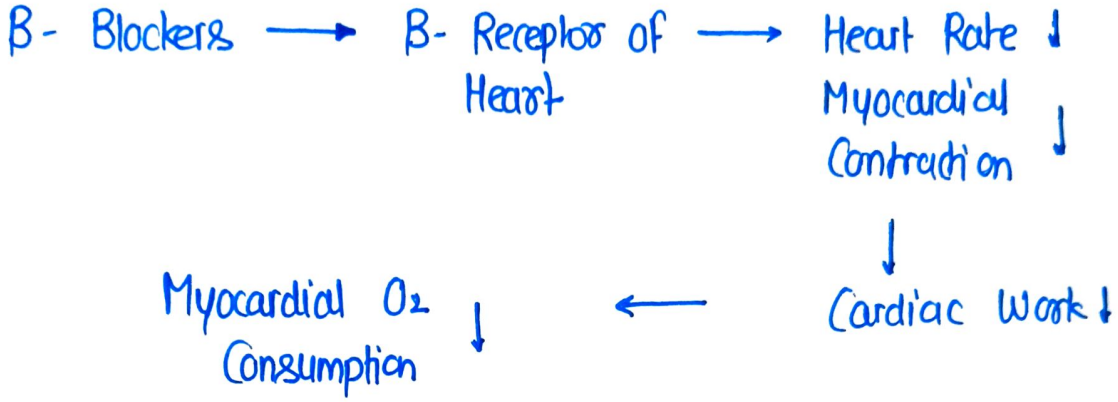
Isosorbide monitrate decreases pre-load, left ventricular end volume, diastolic pressure & thus myocardial oxygen consumption.

Pharmacological Action & Adverse Effect

It is similar to Nitroglycerine.

β - Blockers

- β- Blockers have slow onset of action & are useful in exercise induced asthama
- They act by decreasing cardiac work & O_2 consumption.



CALCIUM CHANNEL BLOCKERS

- Calcium channel blockers are widely used as antianginal agent due to their ability to relax vascular smooth muscles.
- Smooth muscle depolarizes primarily by inward Ca^{2+} ions through L- type channels.
- The CCBs cause relaxation by decreasing intracellular availibility of Ca^{2+}
- Blocking Ca^{2+} influx into cardiac muscle decreases contractility & cause vasodilation.

K^+ Channel Openers

- Potassium Channel openers are a class of drugs used as antianginal agents due to their ability to cause vasodilation.

K^+ Channel Opener ⟶ Open ATP sensitive K^+ Channels

↓

Hyperpolarization

↓

Smooth Muscle Relaxation.

ANTI-ARRHYTHMIC AGENTS

- Anti-Arrythmic Agents are medications used to treat Arrythmias. which are abnormal heart beats that can be too fast, too slow or irregular.
- These drugs work by modifying the electrical activity of the Heart to restore or maintain a normal rythm.

ARRYTHMIA

- Arrythmia refers to an abnormality in the rythm of heart's electrical activity, which can cause the heart to beat too fast, too slow or irregularly
- Generally Arrythmias are harmless, However long term may result into a weak or damaged heart.

CARDIAC ELECTROPHYSIOLOGY

- Deviation from normal pattern of cardiac rythm of heart is known as Arrythmia.
- The resting membrane potential of cardiac cell as about -90 mV.
- It is determined mainly by Sodium, Potassium, Calcium & Chloride Ions.
- Normally K^+ is more in intracellular fluid while Na^+ is more in Extracellular fluid.

ELECTROPHYSIOLOGY OF HEART

- Electrophysiology of heart refers to the study of electrical processes that govern the function of the heart, particularly how the generates and conduct electrical impulses
- These electrical impulses coordinate the contraction of the heart muscles, ensuring proper blood flow.
- It consit of 5 Phases :

① Phase 0
② Phase 1
③ Phase 2
④ Phase 3
⑤ Phase 4

~~Phase~~

Phase 0

- The phase is characterized by a rapid upstroke in membrane potential.
- It is caused by sudden opening of voltage gated sodium (Na^+) channels, leading to a large influx of Na^+ ions
- The cell membrane potential becomes more positive, moving around -90 mV to + 30 mV.
- This triggers muscle contraction.

Phase 1

- Na^+ channels closes, and there is a transient outward flow of potassium ions (K^+) through k^+ channels
- This creates a little, small dip in membrane potential.
- This phase is known as Initial or Partial Repolarization.

Phase 2

- It is known as Plateau Phase.
- Ca^{2+} channels, allowing Ca^{2+} to enter the cell slowly, while k^{+} continues to exit.
- L- type Ca^{2+} channels open, while some k^{+} channels remain open.
- The inflow of Ca^{2+} balances the outflow of k^{+}, causing the membrane potential to remain relatively stable.
- This Plateau phase prolongs the action potential, ensuring sustained contraction of heart muscle necessary for effective pumping.

Phase 3

- Ca^{2+} channels close, while k^{+} continues to leave the cell.
- k^{+} channels dominate as Ca^{2+} channels close.
- The membrane potential returns to its resting state due to continued efflux of k^{+}.
- The cell repolarizes, preparing for next cycle of depolarization.

Phase 4

- The cell remains at its resting membrane potential until it is depolarize again by a new stimulus.
- k^{+} channels maintain the resting membrane potential by allowing k^{+} to flow out, while (Na^{+}/k^{+} ATPase) actively maintain ion gradients.
- The cell is in its resting state at round -90 mV, awaiting the next depolarization phase.

Phase 2

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Types

Generally it is of 4 types :

- Bradycardia
- Tachycardia
- Atrial Fibrillation
- Ventricular Fibrillation

Causes

- Electrolyte Imbalances (potassium, Calcium)
- Coronary Artery Disease
- High Blood Pressure
- Stress
- Thyroid Disorders.
- Medications

Symptoms

- Palpitations (Feeling of Fast or Irregular Heartbeat)
- Dizziness
- Shortness of Breath
- Chest Pain
- Fatigue

Classification Of Anti Arrythmic Agents

Anti - Arrythmic Agents are classified as follows :

① Class - I (Na+ Channel Blockers)

- Moderate : Quinidine , Procainamide , Disopyramide
- Weak : Lidocaine , Mexiletine
- Strong : Propafenone , Flecainide

② B- Blockers (Class - II)

- Propranolol
- Metoprolol
- Esmolol
- Sotalol

③ Potassium Channel Blockers (Class - III)

- Amiodarone
- Dronedarone

④ Calcium Channel Blockers (Class - IV)

- Verapamil
- Diltiazem

Na^+ Channel Blockers

- Sodium Channel Blockers are a class of Antiarrythmic Agents used to manage various cardiac arrythmias.
- They work by inhibiting the influx of sodium ions during depolarization phase of cardiac action potential, which stabilizes the cardiac membrane & reduces excitability.

Mechanism Of Action

They work by blocking Na^+ channels & slows down the rate of depolarazition, which can prolong the refractory period & prevent abnormal electrical activity.

CLASSES

They are mainly classified into 3 groups:

① Class IA

- They are intermediate sodium channel blockers.
- They block the Na^+ channel & also block K^+ channels &
- prolong the action potential & slow conduction.
- Example: Quinidine, Procainamide.
- Uses: Treat both Atrial & Ventricular Arrythmias.

② Class IB

- They are weak sodium channel blockers.
- They shorten the action potential duration.
- Example : Mexiletin , Lidocaine.
- Uses : Ventricular Arrythmias.

③ Class Ic

- They are strong sodium channel blockers.
- They slows conduction with minimal effect on action potential duration.
- Example : Flecainide Propafenone.
- Uses : Life threatening Atrial & ventricular arrythmias.

Pharmacokinetics

- Absorbtion : Varies by drug : Some are well absorbed orally (Flecainide) while others may be administered intravenously.
- Distribution : Generally have high volume of distribution.
- Metabolism : Most are metabolised by liver through CYTP450 enzyme
- Excretion : They are mainly excreted via kidneys.

Side Effect

- Proarrythmia
- Dizziness
- Seizures
- Hypotension

CLASS-II (β-BLOCKERS)

- β-Blockers are commonly used as antiarrythmic agents due to their ability to block the effects of adrenaline & other stress hormones by inhibiting beta-adrenergic receptors, which helps in stabilizing heart rythm.
- They are particularly effective in managing arrythmias that originates from excessive sympathatic nervous system stimulation.

MOA

- β Blockers inhibit β_1 adrenergic receptors in heart, reducing the effect of catecholamines like adrenaline, which slows down heart rate, decreases contrachility & reduces risk of abnormal electrical activity.

Examples

- Metoprolol
- Atenolol
- Esmolol
- Propranolol

Uses

- Atrial fibrillation
- Atrial flutter
- Ventricular Arrythmias.

K^+ CHANNEL BLOCKERS (Class III)

Potassium Channel Blockers are class of antiarrythmic drugs that primarily work by prolonging repolarization phase of cardiac action potential.

MOA

- Potassium Channel Blockers inhibit the outward potassium flow during repolarization phase of cardiac action potential.
- By blocking these ~~calcium channels~~ potassium channels, they delay repolarization, thereby prolonging action potential duration.

Uses

- Atrial fibrillation
- Atrial Flutter
- Ventricular Arrythmia

Ca^{2+} BLOCKERS

Calcium Channel Blockers are a class of antiarrythmic drugs that work by inhibiting calcium ions influx into cardiac cells, primarily affecting AV node & SA node, which are crucial for regulating heart rythm.

MOA

- Calcium Channel Blockers inhibit L-type calcium channels in cardiac & smooth muscle cells.
- This leads to reduced calcium entry into these cells, which slows down action potential, particularly in Nodal Tissues (SA Node & AV Node).

Uses

- Atrial Fibrillation
- Atrial Flutter

ANTI - HYPERLIPIDEMIC DRUGS

- Anti - Hyperlipidemic agents are medications designed to lowers lipid levels in the blood, particularly Cholesterol & Triglycerides.
- They help manage conditions like, Hyperlipidemia, which is associated with an increased risk of cardiovascular disease

HYPERLIPIDEMIA

- Hyperlipidemia is a medical condition characterized by abnormally high levels of lipid in blood, which include cholesterol & triglycerides.
- These elevated lipid levels can increase the risk of developing cardiovascular diseases such as coronary artery disease, stroke & peripheral artery disease.

Types Of Lipid Involved

- Cholesterol
  - Low Density Lipoprotein
  - High Density Lipoprotein
- Triglycerides

Symptoms

It itself has no specific symptoms, However long term elevated lipid levels can lead to development of atherosclerosis which can cause :

- Chest Pain
- Heart Attack / Stroke etc.

Classification Of Anti- Hyperlipidemic Drugs

Anti- Hyperlipidemic Drugs can be classified as follows :

① HMG - CoA Reductase Inhibitors (Statins)

- Lovastatin
- Simvastatin
- Pravastatin
- Atorvastatin
- Rosuvastatin
- Pitavastatin

② Bile Acid Sequestrants (Resins)

- Cholestyramine
- Colestipol

③ Lipoprotein Lipase Actuator (Fibrates)

- Clofibrate
- Gemfibrozil
- Bezafibrate
- Fenofibrate

④ Lipolysis & Triglyceride Synthesis Inhibitor

- Nicotinic Acid

⑤ Sterol Absorbtion Inhibitor

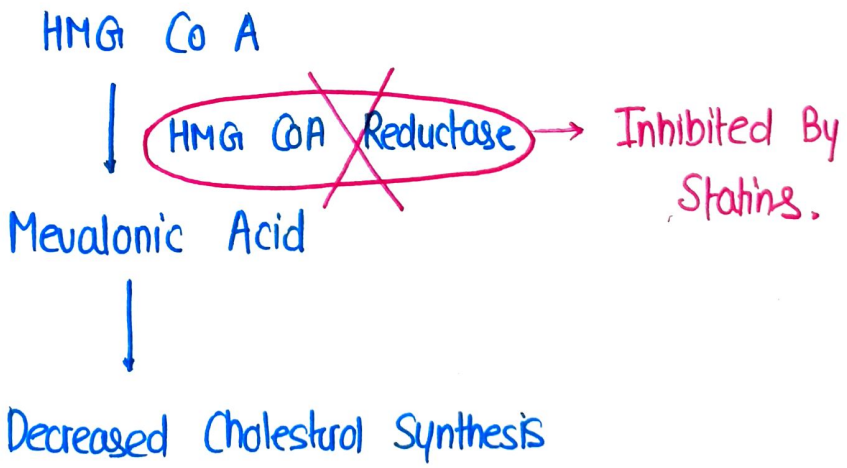
- Ezetimibe

HMG CoA Reductase Inhibitors

HMG Co-A reductase inhibitors, commonly known as Statins, are class of drugs that reduce cholesterol levels by inhibiting HMG Co-A reductase enzyme.

Mechanism Of Action

- HMG - CoA reductase is an enzyme responsible for converting HMG - CoA into mevalonate, an early & essential precursor in cholesterol biosynthesis pathway.
- Statins act as competitive inhibitors of HMG Co-A reductase, effectively lowering production of cholesterol in liver.
- This inhibition leads to a decrease in intracellular cholesterol levels, which triggers an upregulation of LDL Receptors on hepatocyte surfaces.
- These receptors increase the uptake of LDL cholesterol from blood thereby reducing LDL levels.
- They shows maximum activity in midnight.



PHARMACOKINETICS

- **Absorbtion**
  - They are generally administered orally
  - Some statins, such as Atorvastatin & Fluvastatin, are highly absorbed, while others like prawastatin are less absorbed.
- **Distribution**
  - Statins are highly protein-bound in plasma, hence widely distributed.
- **Metabolism**
  - Most statins undergo extensive hepatic metabolism.
  - Atorvastatin, Simvastatin and lovastatin are metabolized primarily by CYP3A4.
  - Rosuvastatin & Fluvastatin are metabolized by CYP2C9.
- **EXCRETION**
  - Statins are primarily excreted by the liver into bile, and to a lesser extent, through the kidneys.

SIDE EFFECT

- Muscle Pain / Weakness
- Type-2 Diabetes
- Cognitive Effects
- Digestion Issues
- Allergic Reactions

SOME INDIVIDUAL DRUGS

- **Lovastatin**
- This is the frost clinically used statin which is lipophilic & given orally.
- It work by inhibiting HMG CoA reductase.
- It is primarily used to treat Hyperlipidemia.
- It is typically taken once daily with evening meal to enhance absorption.
- Common side effects include muscle pain, liver enzyme elevation, GIT issues & increased blood sugar levels.

Simvastatin

- More efficious & twice potent than Lovastatin.

Atorvastatin

- It is newer statin
- It work by inhibiting HMG Co-A reductase.
- It is most widely used Anti-Hyperlipidimeic drug now a days.
- Side effects include Muscle Pain, Elevated Liver Enzyme, Increased Blood sugar levels.

Bile Acid Sequestrants

Bile Acid sequestrants are a class of medications that used to lower cholesterol levels.

Mechanism of Action

- They work by binding to bile acids in the intestine.
- This binding forms an insoluble complex that prevents the reabsorption of bile acids into blood stream.
- As a result, the liver must convert more cholesterol into bile acids to replace those lost, leading to decrease LDL levels.

Common Drugs

- Cholestyramine
- Colestipol
- Colesevelam

Side Effects

- Constipation
- Bloating
- Interference with absorbtion of fat soluble vitamins (A, D, E, k)

LIPOPROTEIN LIPASE ACTIVATOR

Lipoprotein Lipase Activatorss are a class of agents designed to enhance the activity of LPL, which plays a key role in lipid metabolism.

Mechanism Of Action

- Lipoprotein Lipase Activatorss enhance the enzyme's activity. leading to increased hydrolysis of triglycerides in lipoproteins (like chylomicrons & VLDL) into free fatty acids & glycerol.
- By facilitating the breakdown of triglycerides, these agents promote the clearance of triglyceride-rich lipoproteins from the bloodstream, thereby reducing overall triglyceride levels.

SIDE EFFECTS

- Gastrointestinal Disturbances
- Allergic Reactions

Lipolysis & Triglyceride Synthesis Inhibitors

Lipolysis & Triglyceride synthesis inhibitors are anti-hyperlipidimic agents that target the process of fat breakdown (lipolysis) & fat production (triglyceride synthesis)

MOA

Nicotinic Acid ⊖

- ↑se Lipoprotein Lipase activity
  - ↑ Hydrolysis of triglycerides of VLDL
    - ↓se VLDL levels
- Triglycerides → Free fatty Acids (Adipose Tissue)
  - Triglycerides → VLDL (Liver)

Adverse Effect

- Flushing
- GIT Issues.
- Muscle Pain

STEROL ABSORPTION INHIBITORS

Sterol- Absorption inhibitors are a class of lipid - lowering agents that specifically block the absorption of cholesterol in small inteshine.

MOA

- Sterol absorption inhibitors work by targeting & inhibiting. Niemann - Pick C1 - like 1 protein, a transporter located on the brush border of & enterocytes (cells lining the small intestine)
- This protein is essential for uptake of cholesterol from diet & bile into enterocytes.

Adverse Effect

- Diarrhea
- Abdominal Pain
- Fatigue
- Headache.

THANK YOU

FOR CHOOSING IMPERFECT PHARMACY AS YOUR STUDY PARTNER

IMPERFECT PHARMACY

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