Pharmacy Technician

Fundamentals of Pharmacology

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Fundamentals of Pharmacology

For the students of Pharmacy Technicians (Category-B)

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UNIT-I

Introduction/ Basic Concepts Of Pharmacology

Pharmacology

Definition of Pharmacology

It is defined as the study of substances, that interact with living systems through chemical processes, especially by binding to regulatory molecules and activating or inhibiting the normal body processes.

Branches of Pharmacology

Pharmacokinetics
Study of effects the body has on drugs, includes absorption, distribution, metabolism and excretion is called Pharmacokinetics.

Pharmacodynamics
Study of effects of drugs on the body is called Pharmacodynamics.

Pharmacokinetics

Before discussing the Pharmacokinetics, it is important to understand about the routes of drug administration.

Routes Of Drug Administration

The route of drug administration is determined primarily by

- The properties of drug (water or lipid solubility, ionization etc)
- The therapeutics objectives (the desirability of a rapid onset of action or the need for long term administration)

There are three major routes of drug administration

1. **Enteral (oral, sublingual)**
2. **Parenteral (IV, IM, SC etc.)**
3. **Others (inhalation, intranasal, topical etc.)**

Enteral

Enteral administration is the simplest and most common means of administration drug, enteral route includes…

1. **Oral**
2. **Sublingual**

Oral route
Giving drug by mouth is called oral route.

Advantages

- Most convenient and most acceptable
- Used for local as well as systemic action of drugs.
- Dosage forms do not require sterile techniques for administration.

- Delivery of drug into circulation is slow, so that rapid, high blood concentration are avoided and adverse effects are less

Disadvantages

- Rate of absorption is variable
- Irritation of mucosal surfaces can occur
- Extensive hepatic metabolism (first pass effect) may occur before the drug reaches its site of action
- Onset of action is delayed, thus unsuitable in emergency situation
- Drugs destroyed by digestive enzymes (insulin, pituitary hormones) or by gastric acidity (benzyl penicillin) cannot be administration

Sublingual

Placement of drug under the tongue is called sublingual, it allows a drug to diffuse into the capillary network and, therefore, to enter the systemic circulation directly.

Advantages

- Rapid absorption and effect (eg, glyceryl trinitrate in angina)
- Spitting out tablet can terminate effect
- Low incidence of infection
- Avoidance of first pass metabolism

Disadvantages

- Inconvenient (discomfortable) for frequent use
- Irritation of oral mucosa, and excessive salivation

Parenteral

Parenteral administration is used for drugs that are poorly absorbed from the GIT (heparin) and for agents that are unstable in the GIT (insulin). Parenteral administration is also used for treatment of unconscious patients and under situations that require a rapid onset of action.

Examples

- Intravenous (IV)
- Intramuscular (IM)
- Intra dermal (ID)
- Subcutaneous (SC)
- Intra peritoneal (IP)
- Intra arterial (IA)
- Intra cardiac (IC)
- Intra thecal (IT)
- Intra articular or joint (IJ)
- Intra bone marrow (IBM)

The tree major parental routes are intravenous, intramuscular and subcutaneous

Advantages

- Drugs get to the site of action more rapidly, providing a rapid response, which may be required in an emergency
- Dose can be more accurately delivered
- Suitable for drugs that are not absorbed from GIT

Disadvantages

- More rapid absorption can lead to increased adverse effects
- Local irritation may occur at the site of injection
- These routes are irreversible and may cause pain, fear, and infection

Other Routes Of Drug Administration

- **Inhalation**
- **Intranasal**
- **Topical**
- **Rectal**

Drug Absorption

Absorption is transfer of a drug from its site of administration to the bloodstream. The rate and efficiency of absorption depend on the route of administration. For IV delivery, absorption is complete, that is the total dose of drug reaches the system circulation.

Transport Of A Drug From The GI Tract

Depending on their chemical properties, drug may be absorbed from the GI tract by either passive diffusion or active transport.

Passive Diffusion

It refers to passage of drug molecules by diffusing a un-ionized moiety through lipid membrane. The drug moves from a region of high concentration to one of lower concentration. The vast majority of drug gains access to the body by this mechanism.

Active Transport

Active transport is energy dependent and is driven by the hydrolysis of adenosine triphosphate (ATP). It is capable of moving drugs against a concentration gradient that is from a region of low drug concentration to one of higher drug concentration.

Endocytosis And Exocytosis

This type of drug delivery transports drugs of exceptionally large size across the cell membrane. Endocytosis involves engulfment of a drug molecule by the cell membrane and transport into the cell by pinching off the drug filled vesicle. Exocytosis is the reverse of endocytosis and is used by cells to secrete many substances by a similar vesicle formation process.

Drug Distribution

Drug distribution is the process by which a drug reversibly leaves the bloodstream, and enters the interstitium (extracellular fluid) and/ or the cell of the tissues.

Blood Flow

The rate of blood flow to the tissue capillaries varies widely as a result of the unequal distribution of cardiac output to the various organs. Blood flow to the brain, liver, and kidney is greater than that to the skeletal muscles; adipose tissue has a still lower rate of blood flow. More drugs are delivered to greater blood flow areas.

Capillary Permeability

- It varies widely in various tissues
- In brain capillary endothelial cells are continuous and have no slit junction, so that only lipid soluble (unionized) drug can cross.

- In liver and spleen a large part of basement membrane is exposed by large discontinuous capillary through which large plasma protein can pass.

Binding Of Drug To Plasma Protein
Drug molecules may bind to plasma protein (usually albumin). Bound drugs are pharmacologically inactive, only the free, unbound drug can act on target site in the tissues. Bound drug stays in vascular space and is not metabolized or eliminated.

Apparent Volume Of Distribution
A drug rarely associates exclusively with only one of the water compartments of the body. Instead, the vast majority of drugs distribute into several compartments, often avidly binding cellular compartments. For example, lipids (abundant in adipocytes and cell membranes), protein (abundant in plasma and within cells), or nucleic acids (abundant in the nuclei of cells). Therefore, the volume into which drugs distribute is called the apparent volume of distribution.

VD = Dose administered / Plasma Concentration of drug

Drug Metabolism

Drugs are most eliminated by biotransformation and/or excretion into the urine or bile. The process of metabolism transforms lipophilic drugs into more polar readily excretable products. The liver is the major site for drug metabolism, but specific drug may undergo biotransformation in other tissues, such as the kidney and the intestine.

Reaction Of Drug Metabolism
The kidney cannot efficiently eliminate lipophilic drugs that readily cross cell membrane and are reabsorbed in the distal tubules. Therefore lipid soluble agents must first be metabolized in the liver using two general sets of reaction, called Phase I and Phase II.

Phase I
Phase-I reaction function to convert lipophilic molecules into more polar molecules by the exposing a polar functional group. Mainly it is oxidation, but sometimes there is reduction or hydrolysis.

Phase II
This phase consists of conjugation reactions. If the metabolites from Phase I metabolism is sufficiently polar, it can be excreted by the kidneys, However, many Phase I metabolites are too lipophilic to be retained in the kidneys tubules. A subsequent conjugation reaction with an endogenous substrate such as sulfuric acid, acetic acid, or amino acid result in polar and more water soluble compounds, that excreted by the kidney.

Drug Elimination

Removal of a drug from the body occurs via a number of routes, the most important being through the kidney into the urine. Other routes include the bile, intestine, lung or milk in nursing mothers. A patient in renal failure may undergo extracorporeal dialysis, which removes small molecules such as drug.

Routes of Elimination

Kidney
Excretion of drug and their metabolites into urine involves:

- Glomerular filtration e.g. of water soluble and polar components (less than 500 dalton)
- Active tubular secretion
- Passive tubular reabsorption

Liver
It can secrete drugs or their metabolites into bile that are lost in feces. However, some drug may be reabsorbed in intestine to again enter the circulation.

GIT
Some drugs are excrete through GIT
Thiocynates, iodides and mercury in saliva
Morphine through passive diffusion in stomach

Lungs
Gaseous and volatile general anesthetic is excreted in expired air.

Others Routes
- Sweat
- Tears
- Breast milk
- Salivary secretion

Pharmacodynamics

Most drugs exert their effects, both beneficial and harmful, by interacting with receptors that are, specialized target macromolecules present on the cell surface or intracellulraly. Receptors bind drugs and initiate events leading to alterations in biochemical and / or biophysical activity of a cell and consequently, the function of an organ. Drugs may interact with receptors in many different ways. Drugs may bind to enzymes, nucleic acids or membrane receptors.

Major Receptors Families

Pharmacology defines receptors as any biologic molecule to which a drug binds and produces a measurable response. Thus, enzymes and structural protein can be considered to be pharmacological receptors.

Ligand-Gated Ion Channels Receptors
These are responsible for regulation of the flow of ion across cell membrane. The activity of these channels is regulated by the binding of a ligand to the channel.
Nicotinic receptor (Nn, Nm) and Gamma aminobutyric acid (GABA) receptors are important examples of ligand-gated receptors.

G-Protein Coupled Receptors
A second family of receptors consists of G protein-coupled receptors. These receptors contain a single peptide; these receptors are linked to a G protein having three subunits, alpha, beta, and gamma subunit. Binding of the appropriate ligand to the extra-cellular region of the receptor activates the G protein.

Enzyme Linked Receptors
A third major family of receptors consists of those having cytosolic enzyme activity as an integral component of their structure or function. Binding of a ligand activates or inhibits this cytosolic enzyme activity.

Intracellular Receptors
The fourth family of receptors is called intra cellular receptors. These receptors are either in the cytoplasm or in the nucleolus gives response by increasing the gene transcription.

UNIT-II

Posology

It is the branch of pharmacology, which deals with dosage of drugs.

Drug
It refers to any substance that brings about a change in biological function through its chemical action.

Pro-Drug
It refers to compounds that, on administration, must undergo chemical conversion by metabolic processes before becoming an active pharmacological agent. (Levodopa into dopamine)

Placebo
It refers to an inactive substance or preparation given to satisfy the patients symbolic need (psyche need) for drug therapy, and used in controlled studies to determine the efficiency of medicinal substance.

Dose

Amount of drug taken each time by an individual or a quantity to be administrated at one time. (20mg, 10mg, 2drops etc)

Dosage

The amount of a drug given to an individual per unit body weight or the determination and regulation of the size, frequency and number of doses.

Dosage Types

Therapeutic Dose
Average dose for an adult to produce a therapeutic effect is called therapeutic dose.

Loading Dose
A large dose initially used to produce an effective concentration as quickly as possible is called loading dose.

Maintenance Dose
A dose used to maintain the therapeutic effect or concentration in blood plasma is called maintenance dose.

Maximal Tolerated Dose
Largest dose of a drug that can be taken safely.

Toxic Dose
Amount of drug, which produces undesirable harmful effect of serious nature, is called toxic dose.

Fatal Dose
A dose that produces death is called fatal dose.

Dose Calculation
Adult dose is for a person between the age of 18-60years. Children are given small dose. Children dose may be calculated as a fraction of adult dose.

Young's Formula

Young's formula is used to calculate doses for children (2-17years old) based on the adult dose.

$$\text{Child's Dose} = \frac{\text{age in years} \times \text{Adult dose}}{\text{age in years} + 12}$$

Clark's Formula

Clark's formula is used to calculate doses especially for infants (birth to 1year old) by using weight of infant in pounds (lbs).

$$\text{Infant Dose} = \frac{\text{infant weight in pounds} \times \text{adult dose}}{150}$$

Factors Modifying The Action And Dosage Of Drug

Many factors influence the dosage and action of drug. If the drug is too small, the drug will not produce the desired action. If it is too large it will produce toxic effects, which are not desirable. Following are important factors, which influence the action and dosage of drug.

- **Age**
- **Body weight**
- **Sex**
- **Routes of administration**
- **Time of administration**
- **Dosage form**
- **Absorption, Distribution and excretion of drug**
- **Pathological condition**
- **Tolerance**
- **Combination of drugs (synergism, antagonism)**

Age
Adult dose is for a person between the ages of 18-60years. Children are given small dose. We use young's formula and Clark's formula to calculate dose for children and infant. Above 60years of age the dose should be decreased $3/4^{th}$ of adult dose.

Body Weight
For abnormal body weight the dose of the drug should be suitably adjusted according to the weight of the patient

Sex
Doses for the women should be less than man because women are usually having more effect than men. Pregnancy, menstruation and lactation periods should keep in mind while adjusting dosage.

Routes Of Administration
When drug is given intravenously onset of action is rapid orally given drug have slow onset action. Oral dose of drug always greater than when it is given parenterally and dose for subcutaneous or intramuscular injection is greater than intravenous.

Time Of Administration
Presence of food in stomach delays the absorption of drug onset action is slow some drugs can cause irritant, nausea and vomiting while given in empty stomach. Hypnotics are more effective when given at bedtime.

Dosage Form Of Drug (Preparation)
Onset action is rapid when the drug is given in liquid or as a powder as compared to drug given inform of a tablet of pill.

Absorption, Distribution And Excretion Of Drug
Drugs, which are rapidly absorbed and excreted quickly, cannot maintain effective concentration for therapeutic effect. Drugs, which are quickly absorbed but excreted slowly, may produce toxic effect.

Pathological Condition
When liver or kidneys are not functioning properly the dose should be decreased to avoid toxic effects.

Tolerance
It is unusual resistance to ordinary dose of the drug-increased dose is often required to obtain desired therapeutic effects

Combination Of Drugs
When two or more than two drugs are given together action may be increased or decreased.

UNIT-III

Autonomic Nervous System (ANS)

Autonomic Nervous System

ANS along with the endocrine system coordinates the regulation and integration of bodily function. ANS is concerned with regulation of visceral function. So it is otherwise called involuntary nervous system.

Neuron

Neuron is defined as the basic structural and functional unit of the nervous system.
Neuron is like any other cell in the body having nucleus and all the organelles in the cytoplasm.

However it is different from other cells by two ways:

1. **Neuron has branches or processes called axon and dendrites.**
2. **Neuron does not have centrosome, so it cannot undergo division.**

Classification Of Nerve Cells

On the basis of functions the nerve cells are classified into two types

1. **Motor Neuron (Efferent)**
2. **Sensory Neuron (Afferent)**

Motor Neuron (Efferent)

Neurons, which carry the motor impulses from central nervous system to the peripheral effectors organ like muscles, gland, and blood vessels. Motor neurons are also known as efferent nerve cells; generally these neurons have long axons and short dendrites.

Sensory Neuron (Afferent)

These neurons carry the sensory impulses from periphery to the CNS generally these have short axons and long dendrites.

Receptor

Pharmacology defines a receptor as any biological molecule to which a drug binds and produces a measurable response. Thus, enzymes and structural protein can be considered to be pharmacological receptors.

Neurotransmitters

Neurotransmitter is a chemical substance that acts as the mediator for the transmission of nerve impulse from one neuron to another neuron through a synapse.
Communication between nerve cells and between nerve cells and effector organs occurs through the release of specific chemical signals called neurotransmitters.

Local Mediators

Most cells in the body secrete chemicals that act locally. These chemical signals are rapidly destroyed or removed; therefore, they do not enter the blood and are not distributed throughout the body etc Histamine.

Hormones

Specialized endocrine cells secrete hormones into the bloodstream where they travel throughout the body exerting effects on broadly distributed target cells in the body.

Anatomy of ANS

Efferent Neurons

Efferent neurons carry nerve impulse from CNS to the effector organs by way of two types of efferent neurons.

The first nerve cell is called preganglionic neuron, its cell body is located within the CNS, and it emerges from brainstem or spinal cord, and makes a synaptic connection in ganglia. These ganglia function as relay station between preganglionic neuron and a second nerve cell called postganglionic neuron. Cell body of second neuron is originates from ganglion and terminates on effector organs such as smooth muscles of the viscera, cardiac muscle and the exocrine glands.

Afferent Neurons

Afferent neurons of ANS bring nerve impulse back to CNS from periphery

Sympathetic Neurons

The efferent ANS is divided into the sympathetic and parasympathetic nervous system, as well as the enteric NS.

Anatomically they originate in the CNS and emerge from two different spinal cord regions. The preganglionic neurons of the sympathetic system come from thoracic and lumber regions of the spinal cord. Preganglionic neurons are short in comparison to the postganglionic neurons. Axons of the postganglionic neurons extend from ganglia to the tissues that they innervate and regulate.

Parasympathetic Neurons

The parasympathetic preganglionic fibers arise from cranium (cranial nerve 3, 7, 9 and 10) and from sacral region of the spinal cord and synapse in ganglia near or on the effector organs. In contrast to the sympathetic system the preganglionic fibers are long and postganglionic ones are short, with the ganglia close to or within the organ innervated.

Enteric Neurons

The enteric nervous system (ENS) is the third division of the autonomic NS. It is a collection of nerve fibers that innervate the gastrointestinal tract (GIT), pancreas and gallbladder. This system functions independently of the CNS and controls the motility, exocrine and endocrine secretions and microcirculation of GIT.

Action of Sympathetic and Parasympathetic Nervous System on Effecter Organs

Organ	Sympathetic Action	Parasympathetic Action
Eye	Contraction of iris redial muscle (Pupil dilate) Relaxation of ciliary muscles	Contraction of iris sphincter muscle (Pupil contracts) Contraction of ciliary muscle (lens accommodates for near vision)
Heart	Increase rate Increase contractility	Decrease rate Decreased contractility
Blood Vessels (skeletal muscle)	Dilate	…
Blood Vessels (skin, mucous membrane)	Constriction	…
Kidney	Rennin secretion (β1 increase, α1 decrease)	…
Trachea & Bronchioles	Dilate	Constrict Increase secretions
Gastrointestinal	Contraction of sphincters Decrease in muscle motility and tone	Increased muscle motility and tone
Genitalia (male)	Stimulation ejaculation	Stimulates erection
Genitalia (female)	Relaxation of uterus	…
Salivary Gland	Thick, viscous secretion	Large watery secretion
Adrenal Medulla	Epinephrine & Nor-epinephrine secreted	…
Lacrimal Gland	…	Stimulates tears

Prototype Drugs of ANS

Prototype Drug Definition

A first or preliminary form of drug from which other forms of drugs are developed or copied is called prototype drug.

Drugs affecting the autonomic nervous system are divided into two groups according to the type of neuron involved in their mechanism of action.

Group#1

Cholinergic Drugs Or Parasympathetic Drugs

Group#2

Adrenergic Drugs Or Sympathetic Drugs

Now we will discuss cholinergic drug/parasympathetic drugs, these drugs are classified into…

1. **Colinergic agonist or parasympathetomimetic**
2. **Colinergic antagonist or parasympathetolytic**

Cholinergic Agonists

(Parasympathomimetics)

Here Is The List Of Prototype Cholinergic Agonists

Direct Acting
➔Acetylcholine

Indirect Acting (reversible)
➔Physostigmine

Indirect Acting (irreversible)
➔Echothiophate

Reactivation of Acetylcholine esterase
➔Pralidoxime

Available Brands in the Market
Contrathion inj. (Pralidoxime)

Acetylcholine (Direct Acting)

Acetylcholine is a quaternary ammonium compound that cannot penetrate membrane. It is neurotransmitter of parasympathetic and somatic nerves as well as autonomic ganglia. It is rapidly inactivate by acetylcholinesterase. Duration of action of acetylcholine is small (a few milliseconds) hence it is not used in therapeutics. Acetylcholine has both muscarinic and nicotinic activities.

Action of Acetylcholine

- It has following major actions
- Decrease in heart rate and cardiac output
- Decrease in blood pressure
- Other actions

Decrease In Heart Rate And Cardiac Output
Acetylcholine mimics the effect of vagal stimulation; as a result decrease in heart rate and cardiac output.

Decrease In Blood Pressure
Injection of acetylcholine causes vasodilation and lowering the blood pressure

Others Actions

- In GIT, acetylcholine increases salivary secretion intestinal secretions and motility
- It enhances the secretions in bronchioles
- It stimulates erection
- In eye, it causes contraction of iris sphincter muscle (pupil contraction), which is called miosis
- It causes contraction of ciliary muscle (lens accommodates for near vision)

Therapeutic Actions Of Acetylcholine

Acetylcholine (1% solution) is instilled into the eye to produce miosis during ophthalmic surgery.

Adverse Effects Of Cholinergic Drugs

Diarrhea, Miosis, Nausea, Urinary urgency, Bradycardia, Bronchoconstriction, AV block, Flushing, Salivation

Physostigmine (Indirect Acting, Reversible)

It is a natural alkaloid obtained from the plant physostigmine venenosum. It is a tertiary amine. It is absorbed from GIT. It can cross blood brain barrier. It stimulates CNS.

Mechanism Of Action

Physostigmine reversibly block acetylcholine esterase enzyme and prevent its breakdown. This action enhances the acetylcholine response by activating the postsynaptic receptors.

Action Of Physostigmine

Physostigmine has a wide range of effects. It acts on muscarinic and nicotinic receptors as well as on neuromuscular junction.
Its duration of action is about 2 to 4 hours. It can cross blood brain barrier and stimulate CNS.

Therapeutic Uses

- This drug increases intestinal and bladder motility
- It is used for treatment of glaucoma
- It produces miosis and spasm
- Physostigmine is also used in the treatment of overdose of drugs with anticholinergic actions

Adverse Effects Of Physostigmine

When high doses are used fall in cardiac output may occur. The cause of death in physostigmine poisoning is respiratory failure.

Echothiophate (Indirect Acting, irreversible)

A number of synthetic organophosphate compounds (organo-phosphorus compound) have the capacity to bind covalently to acetylcholinesterase. This result is a long lasting increase in acetylcholine at all sites where it is released.

Mechanism Of Action

Echothiophate is an organophosphate that covalently binds with acetylcholinesterase. After binding this enzyme permanently inactivated. Restoration of acetylcholinesterase activity requires the synthesis of new enzyme molecules.

Action Of Echothiophate

As acetylcholine released, it does not destroyed due to inactivation of acetylcholinesterase. Acetylcholine gets accumulated in the body to exert both muscarinic and nicotinic actions. Due to muscarinic action there will be miosis, salivation, sweating, bradycardia vasodilation and fall in blood pressure. Due to nicotinic actions there are muscle twitching in the whole body. Due to central effect there is restlessness confusion.

Therapeutic Uses

An ophthalmic solution of the drug is used directly in the eye for the chronic treatment of open angle glaucoma.

Cholinergic Antagonists

(Parasympatholytic Drugs)

Anti Muscarinic Agent
➔Atropine

Ganglionic Blockers
➔Mecamylamine

Neuromuscular Blockers
➔Succinylchoine
➔Tubocurarine

Available Brands in the Market

Atropa Drops (Atropine)
S-Cholin inj. (Succinylchoine)

Atropine (Anti Muscarinic Agent)

Mechanism Of Action

Atropine is a tertiary amine belladonna alkaloid. It has high affinity for muscarinic receptors, where it binds competitively, and preventing acetylcholine from binding to those sites. Atropine acts both centrally and peripherally. Its duration of action is about 4 hours except when placed topically in eye, where the action may last for days.

Action Of Atropine

Eye
Atropine dilate the pupil of eye (mydriasis) in patients with narrow angle glaucoma, intraocular pressure may rise dangerously.

GIT
Atropine can be used as an antispasmodic to reduce activity of the GIT.

Salivary Glands
Producing a dry effect, swallowing and talking become difficult.

Respiratory Tract
Atropine reduces secretions of the respiratory tract.

Cardiovascular System
At low doses it decrease cardiac rate (bradycardia). With high doses, cardiac rate increases.

Sweat Glands
Atropine inhibits activity of sweat glands. The skin becomes hot and dry.

Therapeutic Uses

Opthalmic: Atropine is used topically for examination of retina and optic disc for accurate measurement of refractive errors. It is used as mydriasis.

Antispasmodic
Atropine is used as an antispasmodic agent to relax the GIT and bladder.

Antisecretory
Atropine is used as an antisecretory agent to block secretions in the upper and lower respiratory tract and salivary secretions before the surgery.

Motion Sickness
Atropine is an effective prophylactic agent for motion sickness during short journey (4 to 6 hours).

Antidote For Cholinergic Agonists
Atropine is used for the treatment of overdoses of acetylcholinesterase inhibitors, insecticides and some types of mushroom poisoning.

Pharmacokinetics Of Atropine
Atropine is absorbed rapidly from the GIT. Partially metabolized by the liver and eliminated primarily in the urine, it has a half-life of about 4 hours.

Adverse Effects
Depending on the dose atropine may cause dry mouth, blurred vision, constipation, increase in temperature, effect on the CNS include restlessness, confusion.

Mecamylamine (Ganglionic Blockers)

Ganglionic blockers specifically act on the nicotinic receptors of both parasympathetic and sympathetic autonomic ganglia. These drugs block the entire output of the ANS at the nicotinic receptor. Ganglionic blockers rarely used therapeutically. However they often serve as tools in experimental pharmacology.

Mechanism Of Action
Mecamylamine produces a competitive nicotinic blockade of the ganglia.

Pharmacokinetics
The duration of action is about 10 hours after a single administration. It has good oral absorption.

Therapeutic Actions
It is primarily used to lower blood pressure in emergency situations.

Neuromuscular Blockers

These drugs blocks acetylcholine at neuromuscular junctions. These neuromuscular blockers are structural analogs of acetylcholine. These drugs are clinically useful during surgery for producing complete muscle relaxation.

Tubocurarine (Non-Depolarizing (Competitive) Blockers)

Mechanism Of Action
Non-depolarizing neuromuscular blocking drugs interact with the nicotinic receptors to prevent the binding of acetylcholine. These drugs thus prevent depolarizing of the muscles and inhibit muscular contraction. Because these agents compete with acetylcholine at the receptor that's why also called competitive blockers.

Therapeutic Uses
These blockers are used therapeutically as adjuvant drugs in anesthesia during surgery to relax skeletal muscle. These agents are also used to facilitate intubations as well as during orthopedic surgery.

Pharmacokinetics
All neuromuscular blocking agents are injected intravenously. They penetrate membrane very poorly and do not enter cells or cross the blood brain barrier, many drugs are not metabolized. They excreted in urine unchanged.

Succinylcholine (Depolarizing Agents)

Mechanism Of Action
The depolarizing neuromuscular blocking drug succinylcholine attaches to the nicotinic receptor and act like acetylcholine. This drug remains attached to the receptor for longer time and providing a constant stimulation of the receptor.

Action
Succinylcholine initially produces short lasting twitching of the muscle (fasciculation) followed within a few minutes by paralysis. The drug does not produce a ganglionic block except at high doses.

Therapeutic Uses
Because of its rapid onset and short duration of action, succinylcholine is useful when rapid endotracheal intubation is required during the anesthesia. For example if aspiration of gastric contents is to be avoided during intubations.

Pharmacokinetics
Succinylcholine is injected intravenously its duration of action is short therefore usually given by continuous infusion.

Adverse Effects
Hyperthermia, Hyperkalemia

Adrenergic Agonists
(Sympathomimetics)

The adrenergic drugs affect receptors that are stimulated by norepinephrine or epinephrine. Some adrenergic drugs act directly on the adrenergic receptors (adrenoceptor) by activating it and said to be sympathomimetics.

Sympathomimetic drugs stimulate postganglionic sympathetic adrenergic nerves. Adrenergic agonists may act directly on adrenergic receptors or indirectly through release of norepinephrine or may have mixed action (act directly and indirectly)

Direct Acting Agonists
➔Epinephrine

Indirect Acting Agonists
➔Amphetamine

Mixed Action Agonists
➔Ephedrine

Available Brands in the Market

Adrenaline Injection (Epinephrine)
Efedra Tab. (Ephedrine)

Epinephrine Or Adrenaline (Direct Acting Agonists)

Epinephrine or other direct acting agonists have direct action on tissues supplied by postganglionic sympathetic nerve ending. They interact with receptor sites on the cell

membranes. The drugs are effective even when the sympathetic nerves have been cut or inhibited by other drugs.

Adrenaline/epinephrine is produced in the body by the adrenal medulla and released along with small amount of norepinephrine into the blood stream.

Epinephrine interacts with both alpha and beta-receptors. At low doses, it act on beta-receptors (vasodilatation), and at high doses it act on alpha-receptors (vasoconstriction).

Pharmacological Actions

CVS
Epinephrine is a powerful cardiac stimulant (B1 receptor). Force of myocardial contraction increased, also increased in heart rate.

Respiratory Tract
Epinephrine causes powerful bronchodilation by acting directly on bronchial smooth muscle (B2 receptor).

Blood Vessels
Epinephrine causes powerful vasodilatation in skeletal muscles and coronary vessels (B2 receptor).

GIT
Smooth muscles of GIT are generally relaxed by epinephrine and contract the sphincter muscle.

Therapeutic Uses

Bronchospasm (Bronchial Asthma)
Epinephrine is the primary drug used in the emergency treatment of any condition of the respiratory tract. Improved respiratory exchange observed within few minutes after subcutaneous administration of epinephrine.

Glaucoma
2% epinephrine solution may be used topically to reduce intraocular pressure in open angle glaucoma.

Cardiac Arrest
Epinephrine may be used in patient. Intra cardiac injection may be used in case of cardiac arrest due to anesthetic, electric shock.

Anesthetic
Local anesthetic solution usually contains 1:100000 part epinephrine. The effect of the drug is to greatly increase the duration of the local anesthesia. It does this by producing vasoconstriction at the site of injection.

Pharmacokinetics Of Epinephrine

Epinephrine is ineffective when given orally because it rapidly destroyed in GIT.
It is administered subcutaneously or intra muscularly.
It is not given intravenously as it is highly dangerous. It may be applied topically to produce vasoconstriction and stop oozing of blood.

Adverse Effects
CNS disturbance, Hemorrhage, Cardiac arrhythmias, pulmonary edema

Amphetamine (Indirect Acting)

Amphetamine is a non-catecholaminergic sympathetic amine that shows quite similar effects as cocaine.

Mechanism Of Action
Amphetamine has indirect action on the CNS and peripheral nervous system. Effects on CNS and peripheral nervous system depend upon the level of catecholamine neurotransmitters in synaptic space. Amphetamine shows their effect on CNS and peripheral nervous system by releasing intra cellular stores of catecholamine. Amphetamine also inhibits monoamine oxidase (MAO) that's why high levels of catecholamine are readily released into synaptic spaces and response increased.

Pharmacological Action Of Amphetamine
Amphetamine has more powerful effects on the CNS but less affects at all other sites. It has both alpha and beta effects and are largely indirectly.
Amphetamine increases both systolic and diastolic blood pressure. Large doses produce cardiac arrhythamias. It produces mydriasis.

Therapeutic Uses
Therapeutic uses of Amphetamine are limited due to psychological and physiological dependence and the development of tolerance.

Attention deficit hyperactivity disorder (ADHD)
Some young children are lack the ability to be involved in any one activity for longer than few minutes. Amphetamine and their derivatives are able to improve attention. The drug prolongs the patient's span of attention.

Narcolepsy
Narcolepsy is a rare sleep disorder. Patient is usually treated with drugs such as amphetamine.

Pharmacokinetics
Amphetamine is completely absorbed from the GIT, metabolized by the liver and excreted in the urine.

Adverse Effects
Undesirable side effects of amphetamine include insomnia, irritability, weakness, dizziness, and tremor. Amphetamine can also causes confusion suicidal tendencies especially in mentally ill patients.
Amphetamine causes cardiac arrhythmias, hypertension, angina pain, headache, excessive sweating, nausea, and diarrhea.

Adrenergic Antagonists

(Sympatholytic Agents/Drugs)

A large number of drugs inhibit the activity of the sympathetic nervous system. These drugs are called adrenergic antagonists or sympatholytics.
These adrenergic blocking drugs may be classified into groups based on their site of action.

Adrenergic Blockers Prototype Drugs

Alpha-Blocker
➔Prazosin

Beta-Blocker
➔Propranolol

Drugs Affecting Neurotransmitter Uptake Or Release
➔Reserpine

Available Brands in the Market

Minipress Tab. (Prazosin)
Inderal Tab. (Propranolol)
Betanol Tab. (Propranolol)
Reserpine Tab. (Reserpine)

Prazosin (Alpha-Blockers)

Prazosin is selective competitive blocker of α1 receptor. This drug is useful in the treatment of hypertension.

Pharmacological Actions

Prazosin decreases peripheral vascular resistance and lower arterial blood pressure by causing the relaxation of both arterial and venous smooth muscle. They prevent the response of effector organs to adrenaline, nor adrenaline. It also causes miosis in eye.

Therapeutic Uses

Hypertension
Usefulness of prazosin in hypertension is due to its lack of potency in inhibiting α 2 receptors. The first doses of these blockers may cause hypotensive response that can result fainting. This action termed a first-dose effect. It may be minimize by adjusting the first dose to one-third or one-fourth of the normal dose.

Adverse effect

α 1 blockers may cause dizziness, lack of energy, nasal congestion, headache, orthostatic, hypotension.

Propranolol (Non-Selective Beta Antagonists Or Beta-Blockers)

All the clinically available β-Blockers are competitive antagonists. Non-selective β-Blocker acts at both β 1 and β 2 receptors.
B-Blockers are useful in hypertension angina, cardiac arrhythmias, congestive heart failure and glaucoma. The names of all β -Blockers ends in 'olol' except for labetalol and carvedilol.

Propranolol is the prototype β -adrenergic antagonists block both β 1 and β 2 receptors. Sustained release preparation for once a day dosing is available.

Pharmacological Actions

Cardiovascular
Propranolol decreases the force of myocardial contraction. Cardiac output, work, and oxygen consumption are decreased. It is used in the treatment of angina and heart failure.

Respiratory Tract
Propranolol acts on B receptors and causes broncho-constriction.

Eye
Propranolol reduces intraocular pressure especially in glaucoma.

Increased Na+ Retention
Due to the decrease in blood pressure there is decrease in renal perfusion, resulting in an increase in Na+ retention and plasma volume.

Disturbance In Glucose Metabolism
B-Blocker leads to decreased glucose secretion. Therefore if type-I diabetic is to be given Propranolol very careful monitoring of blood glucose is essential.

Therapeutic Uses

Hypertension
Propranolol lowers blood pressure in hypertension. Decreased cardiac output is the primary mechanism.

Glaucoma
B-Blocker particularly topically applied and effective in diminishing intraocular pressure in glaucoma.

Migraine
Propranolol is also effective in reducing migraine episodes when used prophylactically.

Treatment Of Angina
Propranolol decreases the oxygen requirement of heart muscle and therefore is effective in reducing the pain.

Adverse Effects
Broncho-constriction, disturbance in metabolism, sexual impairment

Reserpine (Drugs Affecting Neurotransmitter Release Or Uptake)

Mechanism Of Action
Reserpine blocks the Mg^{2+} ATP-dependent transport of biogenic amine, norepinephrine, dopamine and serotonin from the cytoplasm into storage vesicles in the adrenergic nerves of all body tissues.

Therapeutic Uses
Reserpine is used in the treatment of hypertension mild to moderate. Reserpine causes a slowly developing falling blood pressure.

UNIT-IV

Central Nervous System (CNS)

Drugs Affecting The CNS

Drugs acting on CNS may be CNS depressants or CNS stimulants. Depressants are more important pharmacologically and therapeutically than stimulants. Most drugs that affect the CNS act by altering some step in the neurotransmission process.
Drugs affecting the CNS may act presynaptically by influencing the production, storage, release or termination of action of neurotransmitters. Other agents may activate or block postsynaptic receptors.

However, we will discuss prototype drugs used in different CNS related diseases.

1. **Neurodegenerative Diseases**
2. **Anxiolytic And Hypnotic Drugs**
3. **CNS Stimulants**
4. **Antidepressant**
5. **Neuroleptics Drugs**
6. **Antiepileptic Drugs**

Neurodegenerative Diseases

Levodopa (Antiparkinson)

Levodopa is a metabolic precursor of dopamine. It decreases the rigidity, tremors and other symptoms of Parkinsonism. Because Parkinsonism results from insufficient dopamine in specific regions of the brain, attempts have been made to restore the dopamine deficiency.

Available Brands in the Market

Larodopa Tab. (Levodopa)

Mechanism Of Action

Dopamine itself does not cross the blood brain barrier, but its precursor Levodopa is actively transported into the CNS and is converted to dopamine in the brain.

Therapeutic Uses

Levodopa in combination with carbidopa is currently available to treat Parkinson's disease. It reduces the severity of the disease for the first few years of treatment.

Pharmacokinetics

The drug is absorbed rapidly from the small intestine. Levodopa should be taken on an empty stomach. Levodopa has an extremely short half-life (1 to 2 hours).

Adverse Effects

- **Peripheral Effects**

Trachycardia, Nausea, vomiting, hypotension, brownish color of saliva and urine.

- **CNS Effect**

Abnormal involuntary movements, mood change, depression

Anxiolytic And Hypnotic Drugs

Benzodiazepines

Barbiturates
➔Phenobarbitone

Other Anxiolytic drugs
➔Buspirone

Available Brands in the Market

Xanax Tab. (Benzodiazpines)
Valium Tab. (Benzodiazpines)
Busron Tab. (Buspirone)
Phenobarbitone Tab. (Phenobarbitone)

Benzodiazepines

Benzodiazepines are the most widely used Anxiolytic drugs. These are safer and effective than others like barbiturates.

Mechanism Of Action

The targets of benzodiazepine actions are GABAa receptors. Benzodiazepine modulate the GABA effects by binding to a specific site, these binding sites are sometimes labeled benzodiazepine receptors.

Actions Of Benzodiazepine

Reduction Of Anxiety
At low doses, the benzodiazepines are Anxiolytic. They reduce anxiety by selectively enhancing GABAergic transmission in neurons.

Sedative And Hypnotic Action
Benzodiazepines also have sedative properties and some can produce hypnosis (artificially produced sleep) at higher doses.

Muscle Relaxant
At high doses, the benzodiazepines relax the skeletal muscle.

Therapeutics Uses

Anxiety Treatment
Benzodiazepines are effective for the treatment of the anxiety disorder, social anxiety disorder, performance anxiety etc. The drug should not be used to reduce the normal stress of everyday life. They should be used for short periods of time.

Muscular Disorders
These agents are useful in the treatment of skeletal muscle spasms.

Seizures
These agents are also used in the treatment of certain types of epilepsy.

Sleep Disorders
Not all benzodiazepines are useful as hypnotic agents, although all have sedative or calming effects. These agents are also used in the treatment of insomnia.

Pharmacokinetics

The benzodiazepines are lipophilic and they are rapidly and completely absorbed after oral administration and distribute throughout the body.

Adverse Effects
Drowsiness and confusion early morning insomnia

Barbiturates

Mechanism Of Action
The sedative-hypnotic action of the barbiturates is due to their interaction with GABAA receptors, which enhances GABAnergic transmission.

Actions

Depression of CNS
At low doses, the barbiturates produce sedation (Have a calming effect and reduce excitement). At higher doses, the drugs cause hypnosis, followed by anesthesia (loss of feeling or sensation), and, finally, coma and death. Thus, any degree of depression of the CNS is possible, depending on the dose.

Respiratory Depression
Barbiturates suppress the hypoxic and chemoreceptor response to CO_2 and over dosage is followed by respiratory depression and death.

Therapeutic Uses

Anesthesia
Selection of a barbiturate is strongly influenced by the desired duration of action. The ultra short-acting barbiturates, such as thiopental, are used intravenously to induce anesthesia.

Anticonvulsant
Barbiturates are used in long-term management of seizures, status epilepticus, and eclampsia.

Anxiety
Barbiturates have been used as mild sedatives to relieve anxiety, nervous tension, and insomnia.

Pharmacokinetics
Barbiturates are absorbed orally and distributed widely throughout the body. These agents are metabolized in the liver, and inactive metabolites are excreted in urine.

Adverse Effects
Drowsiness, impaired concentration, and mental and physical sluggishness tremors, anxiety, weakness, restlessness, nausea and vomiting, death can occur due to overdoses for many decades.

Buspirone (Other Anxiolytic Agents)

Buspirone is useful in the treatment of generalized anxiety disorder. Buspirone lack the anticonvulsant and muscle relaxant property. Most common adverse effects are headache, dizziness, and nervousness.

CNS Stimulants

Large number of drugs may stimulate different parts of brain and in large doses they may stimulate all parts of brain. CNS stimulants have diverse clinical uses and are important as drugs of abuse.

Following prototype drugs are used as CNS stimulants.

Psychomotor Stimulants
➔Cocaine
➔Nicotine

Hallucinogens
➔Lysergic Acid Diethylamide (LSD)

Available Brands in the Market

Coramin-G Cap. (Nicotine)

Cocaine (Psychomotor Stimulants)

Cocaine is a widely available and highly addictive drug that is currently abused daily by more than 3million people.

Mechanism Of Action

Cocaine inhibits the reuptake of monoamines (nor epinephrine, serotonin and dopamine). The inhibition of reuptake of monoamine by the cocaine potentiates and prolongs the CNS and peripheral action of these monoamines.

Actions

CNS

The behavioral effects of cocaine result from powerful stimulation of cortex and brainstem. It also causes tremors and convulsions.

Hyperthermia

Hyperthermia can also cause by cocaine.

Therapeutics Uses

Cocaine has a local anesthetic action. Cocaine is applied topically as a local anesthetic during eye, ear, nose and throat surgery. Cocaine is the only local anesthetic that causes vasoconstriction.

Pharmacokinetics

Cocaine is often self-administered by chewing, intranasal, smoking or intravenous onset of action is most rapid.

Adverse Effects

Anxiety, depression, seizures, cardiac aarrhythmias.

Nicotine (Psychomotor Stimulants)

Nicotine is the active ingredient in tobacco. It is most widely used CNS stimulant.

Mechanism Of Action

In low doses, nicotine causes ganglionic stimulation by depolarization. At high doses, nicotine causes ganglionic blockade.

Action

CNS
Nicotine is highly lipid soluble and readily cross the blood brain barrier. It improves attention, learning, problem solving and reaction time.

Peripheral Effects
The peripheral effects of nicotine are complex. It increases blood pressure and heart rate. Use of tobacco is harmful in hypertensive patients.

Pharmacokinetics
Because nicotine is highly lipid soluble absorption readily occur via oral mucosa, lungs, GIT and skin. Clearance of nicotine involves metabolism in the lung and the liver and urinary excretion.

Adverse Effects
High blood pressure trachycardia, diarrhea, tremors

Hallucinogens (Lysergic Acid Diethylamide, LSD)

Mechanism Of Actions
Multiple sites in the CNS are affected by lysergic acid diethylamide (LSD). The drug shows serotonin agonist activity at presynaptic receptor in the midbrain.

Pharmacological Effects
Activation of the sympathetic nervous system causes pupillary dilation, increased blood pressure and increased body temperature.

Adverse Effects
Adverse effects include hyper-reflexia, nausea and muscular weakness.

Antidepressants

Depression is a serious disorder and its symptoms are intense feeling of sadness, hopelessness and inability to experience pleasure in usual activities.

Here is the list of Prototype Antidepressant

Selective Serotonin Re-uptake Inhibitors
➔Fluoxetine

Serotonin/norepinephrine Re-uptake Inhibitors
➔Duloxetine

Atypical Antidepressant
➔Mirtazapine

Tricyclic Antidepressants
➔Amitriptyline

Monoamine Oxidase Inhibitors
➔Phenelzine

Available Brands in the Market

Depex Tab. (Fluoxetine)
Depricap Tab. (Fluoxetine)
Dulan Tab. (Duloxetine)
Zeubar Tab. (Duloxetine)
Mirtazep Tab. (Mirtazapine)
Mipine Tab. (Mirtazapine)
Tryptanol Tab. (Amitriptyline)

Fluoxetine (Selective Serotonin Re-Uptake Inhibitors)

Selective serotonin re-uptake inhibitors are a group of antidepressant drugs that specifically inhibit serotonin uptake.

Mechanism Of Action

The SSRI block the reuptake of serotonin, leading to increased concentration of the neurotransmitter in the synaptic cleft and increased postsynaptic neuronal activity

Therapeutic Uses

SSRI are used for the treatment of depression. It also used for generalized anxiety disorder, panic disorder.

Pharmacokinetics

All SSRI are well absorbed after oral administration. All agents are well distributed. Their half-life range between 16 to 36 hours

Adverse Effects

Headache, sweating, sleep disturbance, sexual dysfunction

Duloxetine (Serotonin/ Norepinephrine Re-Uptake Inhibitors)

Duloxetine inhibits serotonin and norepinephrine reuptake at all doses. It metabolized in the liver. Duloxetine should not be administered to patients with hepatic insufficiency. Metabolites are excreted in the urine. Food delays the absorption of the drug. The half-life is 12 hours.

Mirtazapine (Atypical Antidepressants)

This drug enhances serotonin and norepinephrine neurotransmission. Via mechanism related to its ability to block presynaptic ALPHA2 receptors. It does not cause the antimuscarinic side effects. It increased appetite and weight gains frequently occur. Mirtazapine is sedating, which may be used in sleeping disorder.

Amitriptyline (Tricyclic Antidepressants)

Mechanism Of Action

The Tricyclic antidepressants block serotonin and norepinephrine reuptake into the neuron.
Tricyclic antidepressants also block serotonergic, alpha adrenergic, histaminic and muscarinic receptors.

Actions

Tricyclic antidepressants elevate mood, improve mental alertness, and increase physical activity.

Therapeutics Uses

Tricyclic antidepressants are effective in treating moderate to severe major depression. Some patients with panic disorder also respond to these agents.

Pharmacokinetics

Tricyclic antidepressants are well absorbed upon oral administration because of their lipophilic nature. They are widely distributed in body. These drugs have variable half-lives from 4 to 17 hours metabolism occurs in liver and excreted from urine.

Adverse Effects

Blurred vision, dry mouth, urinary retention, and constipation

Phenelzine (Monoamine Oxidase Inhibitors)

Monoamine oxidase (MAO) is mitochondrial enzyme found in nerve and other tissues. In the neuron, MAO functions a safety valve as MAO inactivate any excess neurotransmission.

Mechanism Of Action

Most MAO inhibitors form a stable complex with the enzyme to increase the storage of norepinephrine. Serotonin and dopamine within the neuron.

Actions

These drugs are used to inhibit the action of MAO and enhance the activity of neurotransmitters.

Therapeutics Uses

MAO inhibitors are used for the treatment of depression. Patients with low psychomotor activity may also use these agents.

Pharmacokinetics

These drugs are well absorbed after oral administration. MAO inhibitors are metabolized and excreted rapidly in the urine.

Adverse Effects

Headache, stiff neck, tachycardia, hypertension are common adverse effects of MAO inhibitors.

Neuroleptics Drugs OR Antipsychotic Drugs

Neuroleptics drugs are used primarily to treat schizophrenia. They are also used in other psychotic states such as manic states.

Schizophrenia

Schizophrenia is caused by increased dopamine activity in mesolimbic pathway and mesocortical pathway. During schizophrenia, glutamic acid activity in mid brain is decreased and now there is a new emergence of role of serotonin in the development of schizophrenia.

Prototype Neuroleptics Drugs

Typical Neuroleptics (Low Potency)
➔Chlorpromazine

Typical Neuroleptics (High Potency)
➔Haloperidol

Atypical Neuroleptics
➔Clozapine

Available Brands in the Market

Chlorotil Tab. (Chlorpromazine)
Halodol Tab. (Haloperidol)
Clozaril Tab. (Clozapine)

Here is the general introduction of Neuroleptics drugs

Mechanism Of Action

Dopamine Receptor Blocking In The Brain

All of the older and new Neuroleptics drugs block dopamine receptor in the brain and the periphery. The Neuroleptics drugs bind to these receptors to varying degrees.

Serotonin Receptor Blocking Activity In The Brain

Some of these drugs also inhibit serotonin receptors.

Actions

Antipsychotic Actions

All of the Neuroleptics drugs can reduce the symptoms of schizophrenia by blocking dopamine receptors in the brain.

Antiemetic Effects
Most of the drugs have antiemetic effects.

Antimuscrinic Effects
Some of the Neuroleptics produce anticholinergic effects

Therapeutics Uses
The Neuroleptics are considered to be the only efficacious treatment for schizophrenia.

Prevention Of Severe Nausea And Vomiting
Old Neuroleptics are useful in the treatment of drug-induced nausea and vomiting.

Other Uses
The Neuroleptics drugs can be used as tranquilizers. These drugs with combination also used for treatment of chronic pain and severe anxiety.

Pharmacokinetics
After oral administration the Neuroleptics show variable absorption. These agents readily pass into the brain.

Adverse Effects
Movement disorder, tremors, constipation, urinary retention, confusion, sexual dysfunction

Antiepileptic Drugs

Epilepsy

In epilepsy there is a sudden excessive and rapid discharge in grey matter of the brain. Epilepsy is not a single entity it is collection of different seizure types and syndromes originating from several mechanisms. This abnormal electrical activity may result in variety of events including loss of consciousness, abnormal movements, and odd behavior.
Seizures have been classified into two groups.

1. **Partial or focal seizures**
2. **Generalized seizures**

Partial Or Focal Seizures
Partial seizures involve one portion of the brain. Partial seizures may progress, becoming generalized seizures.

Generalized Seizures
Generalized seizures may begin locally, producing abnormal electrical discharge throughout both hemisphere of the brain.

Mechanism Of Action Of Antiepileptic Drugs
These drugs inhibit the neuronal discharge or its spread, by altering cell permeability to ions and by enhancing the activity of natural inhibitory neurotransmitter such as GABA.

Prototype Antiepileptic Drugs

Benzodiazepines
(See In Anxiolytic And Hypnotic Drugs)

GABA Analogues
➔Gabapentin

Phenytoin

Available Brands in the Market

Xanax Tab. (Benzodiazpines)
Valium Tab. (Benzodiazpines)
Neogab Tab. (Gabapentin)
Epinat Tab. (Phenytoin)

Gabapentin (GABA Analogues)

Gabapentin is an analog of GABA. However it does not act at GABA receptors nor enhance GABA actions, nor it converted into GABA. Its precise mechanism of action is not known. Gabapentin does not bind to plasma protein and is excreted unchanged through kidneys.

Phenytoin

Mechanism of Action
Phenytoin blocks voltage-gated sodium channels. At very high concentration, Phenytoin can block voltage-dependent calcium channel.

Therapeutic Uses
Phenytoin is used in the treatment of partial seizures and generalized seizures.

Adverse Effects
The side effects may include gum hypertrophy, skin rashes.

UNIT-V

Cardiovascular System (CVS)

Prototype Drugs Affecting The CVS

In this chapter we will discuss the prototype drugs used in major diseases of CVS.

Major Diseases Related To Cardiovascular System

1. **Heart Failure**
2. **Arrhythmias**
3. **Angina**
4. **Hypertension**

Now we will discuss prototype drugs of each disease.

Heart Failure

Heart is a unique organ that starts functioning before birth and continues till the death occurs. Heart acts as a pump to supply blood and thus oxygen and nutrients to all the body tissues.
Heart failure is a complex, progressive disorder in which the heart is unable to pump sufficient blood to meet the needs of the body. HF is due to the impaired ability of the heart to properly fill with blood or eject blood. It is often due to abnormal increases in blood volume and interstitial fluid.

Prototype Drugs Used To Treat Heart Failure

Renin Angiotensin System Blockers
➔Captopril (ACE inhibitor)
➔Losartan (angiotensin receptor blockers)

B-Blockers
➔Propranolol

Diuretics
(See in Genito Urinary System)

Direct Vasodilators
➔Sodium nitroprusside

Inotropic Agents
➔Digoxin/Digitalis

Available Brands in the Market

Capotein Tab. (Captopril)
Losar-k, Tab. (Losartan)
Losartan Tab. (Losartan)
Inderal Tab. (Propranolol)
Betanol Tab. (Propranolol)
Spiromide Tab. (Spironolactone)
Aldactone Tab. (Spironolactone)
Digox Tab. (Digoxin)

Captopril (ACE Inhibitors)

Captopril is ACE inhibiters agents that block the ACE activity. As ACE convert angiotensin-I into angiotensin-II, which is a powerful vasoconstrictor.
These agents also diminish the rate of bradykinin inactivation, which is a vasodilator.

Action On Heart
Captopril and other ACE inhibitors decrease vascular resistance and blood pressure.

Adverse Effect
Dry cough, abdominal pain, skin rash, hypotension, and renal insufficiency. ACE inhibitor should not be used in pregnant women, because they are fetotoxic.

Pharmacokinetics
ACE inhibitors absorbed in GIT. The presence of food may decrease absorption so they should be given empty stomach except for Captopril.

Losartan (Angiotensin Receptor Blocker)

Losartan and other angiotensin receptor blockers are competitive antagonist of angiotensin type 1 receptor (AT1 receptor).
Losartan have the advantage of more complete blockade of angiotensin action. These agents do not affect bradykinin level.

Action On CVS
All the angiotensin receptor blockers approved for treatment of hypertension. This agent is very useful in HF as they reduce the blood pressure.

Pharmacokinetics
All drugs are orally active and require only once a day dosing. Losartan undergoes extensive first pass hepatic metabolism. All drugs are highly plasma protein bound.

Adverse effects
Angiotensin receptor blockers have similar adverse effect of ACE inhibitor. However angiotensin receptor blockers do not produce cough.

Propranolol (B-Blockers)

See, B-Blocker prototype drug in adrenergic antagonist chapter.

Diuretics

(See in Genito Urinary System)

Sodium Nitroprusside (Direct Vasodilators)

Vasodilators are used in the treatment of heart failure and hypertension. Vasodilators cause relaxation of smooth muscle of blood vessels by direct action. Sodium Nitroprusside is a mixed vasodilator.

Pharmacological Action
Sodium Nitroprusside is an emergency drug, which, acts directly to relax smooth muscle of both arterioles' and veins.

Pharmacokinetics
Onset of action occurs within 1 minute of intravenous administration.

Therapeutics Uses
Sodium Nitroprusside is used for treatment of heart failure and hypertension.

Adverse Effects
Headache, nausea, vomiting

Inotropic Agents (Digoxin or Digitalis)

Positive Inotropic agents enhance cardiac muscle contractility and thus increase cardiac output.

Mechanism Of Action

These agents increase cytoplasmic calcium concentration that enhances the contractility of cardiac muscle.

Pharmacological Action Of Digitalis

Digitalis has direct and indirect action on cardiovascular. The important actions are increasing contractility, conductivity and rate of the heart. Digitalis increases the cardiac output.

Therapeutic Uses

Digitalis is used for treatment of congestive heart failure. The drug is effective in right, left or both ventricular failures. In badly damaged heart the drug may not be so effective.

Adverse Effects

Nausea, vomiting, headache, blurred vision

Antianginal Drugs

Angina pectoris (pain or discomfort in the chest),(pectoris= chest or breast) is on of the major symptoms of heart disease. It is sudden, severe, pressing chest pain radiating to the neck, jaw and arms. It is caused by coronary blood flow that is insufficient to meet the oxygen demand of the myocardium leading to ischemia.

Types Of Angina

Angina occurs in the following forms

1. **Stable Angina/ Typical Angina**
2. **Unstable Angina**
3. **Variant Angina**

Stable Angina

It is the most common form of angina and therefore is called typical angina pectoris. It is characterized by a burning and heavy feeling in the chest. It is produced by physical activity, emotional excitement or any other cause of increased cardiac workload. Typical angina pectoris is promptly relieved by rest or nitroglycerin (a vasodilator).

Unstable Angina

Unstable angina lies between stable angina and myocardial infarction. In unstable angina chest pains occur with increased frequency. The symptoms are not relieved by rest or nitroglycerin. Unstable angina requires hospital admission.

Variant Angina

Variant angina is an uncommon pattern of episodic angina that occurs at rest and due to coronary artery spasm. Symptoms are caused by decreased blood flow to the heart muscles due to the spasm of coronary artery. Variant angina relieved by coronary vasodilators such as nitroglycerine and calcium channel blockers.

Antianginal Prototype Drugs

Organic Nitrate
➔Nitroglycerine

B-Blockers
➔Propranolol

Ca2+ Channel Blockers
➔Verapamil

Available Brands in the Market

Angised Tab. (Nitroglycerine)
Cardnit Tab. (Nitroglycerine)
Inderal Tab. (Propranolol)
Betanol Tab. (Propranolol)
Calan Tab. (Verapamil)

Nitroglycerine (Organic Nitrates)

Organic nitrates and nitrites used in the treatment of angina pectoris. These are simple nitric and nitrous acid esters of glycerol. These compounds cause a rapid reduction in myocardial oxygen demand, followed by rapid relief of symptoms. They are effective stable and unstable angina as well as in variant angina pectoris.

Pharmacological Effect
Nitrates decrease coronary vasoconstriction or spasm and increase blood flow by relaxing coronary arteries. In addition they relax veins, decreasing preload and myocardial oxygen consumption. Nitroglycerine, which is also known as glyceryl trinitrate, relaxes vascular smooth muscle by their intracellular conversion to nitrite ions and then to nitric oxide.

Pharmacokinetics
Nitroglycerine is commonly given by sublingually or via a transdermal patch because it has significant first pass metabolism.

Adverse Effects
The most common adverse effect of nitroglycerine and other organic nitrates are headache, postural hypotension, facial flushing and tachycardia.

Propranolol (B-Blockers)

(See in Adrenergic Antagonists)

Verapamil (Ca2+ Channel Blockers)

(See in Antiarrhythmic)

Antiarrhythmic Drugs

Any cardiac rhythm other than the normal is called arrhythmia. For example cardiac arrhythmias may cause the heart to beat too slowly (bradycardia) or to beat too rapidly (tachycardia) or to beat irregularly.

Causes Of Arrhythmias
Most arrhythmias arise due to abnormal automaticity or due to defect in impulse conduction.

Prototype Drugs

Class I (Na+ channel blockers)
➔Quinidine

Class II (B-Adrenoceptor blockers)/ B-Blockers
➔Propranolol

Class III (K+ channel blockers)
➔Amiodarone

Class IV (Ca2+ channel blockers)
➔Verapamil

Available Brands in the Market

Inderal Tab. (Propranolol)
Betanol Tab. (Propranolol)
Cordarone Tab. (Amiodarone)
Sedacoron Tab. (Amiodarone)
Calan Tab. (Verapamil)

Quinidine (Class-I Anti Arrhythmic Drug Or Na+ Channel Blockers)

Quinidine is an alkaloid and shows many of the action of quinine such as anti malarial, antipyretic, depression. The action on the heart is more marked and specific as compared to quinine.

Pharmacological Action
In general quinine is a cardiac depressant. It decreases automaticity, excitability and conduction velocity and depressed contractility.

Mechanism Of Action
Quinidine blocks sodium channels. It reduces the maximal rate of depolarization (phase o) depresses spontaneous phase 4 diastolic depolarization slow conduction and prolong the effective refractory period of arterial and ventricular.

Therapeutic Uses
Quinidine is used in the treatment of a wide variety of arrhythmias.

Pharmacokinetics
Quinidine is rapidly and almost completely absorbed after oral administration. It undergoes extensive hepatic metabolism forming active metabolites.

Adverse Effects
Quinidine may cause SA and VA block or a systole. At toxic level the drug may induce ventricular tachycardia. Nausea, vomiting and diarrhea are commonly observed.

Propranolol (Class-II, B-Adrenoceptor Blocker)

See in Adrenergic Antagonists

Amiodarone (Class-III, K+ Channel Blockers)

Action
Amiodarone contains iodine and is related structurally to thyroxin. It has complex effect showing class I, II, III and IV actions.
Its dominant effect is prolongation of the action potential duration and the refractory period. Amiodarone has anti anginal as well as anti arrhythmic activity.

Therapeutic Uses
Amiodarone is effective in the treatment of severe refractory supra ventricular and ventricular trachy arrhythmias. Despite its side effect Amiodarone is the most commonly employed antiarrhythmic.

Pharmacokinetics
Amiodarone is incompletely absorbed after oral administration. The drug is unusual in having prolonged half-life of several weeks and it distributes extensively in adipose tissue.

Adverse Effects
Amiodarone shows a variety of toxic effects. Some common side effects are GIT disturbance, tremor, dizziness, lover toxicity, photosensitivity, muscle weakness, skin discoloration caused by iodine accumulation in the skin.

Verapamil (Class-IV, Ca2+ Channel Blockers)

Mechanism Of Action
Verapamil inhibits slow channel calcium ion transport across the myocardial cell membrane it also reduces intracellular calcium concentration in smooth muscle cells of the coronary and peripheral vasculature.

Pharmacological Action
Verapamil depress SA and AV nodal functions. Slow AV conduction is its major action making it useful as anti arrhythmic agent. It reduces coronary and peripheral vascular resistance. It increases coronary blood flow. Verapamil increases myocardial oxygen supply by increasing coronary blood flow. Simply we can say Verapamil has anti arrhythmic, anti anginal and antihypertensive properties.

Pharmacokinetics
Verapamil is rapidly and almost completely absorbed after oral administration. It undergoes extensive first pass metabolism in the liver. It is highly bound by plasma proteins. Its half-life is 3 to 6 hours.

Therapeutics Uses
Verapamil is more effective in the treatment of arterial arrhythmias than ventricular arrhythmias. It is also very useful in the treatment of angina pectoris and hypertension.

Adverse Effects
Constipation is the most common side effect. Nausea, vomiting, headache, weakness and gastric disturbance may occur when given IV; Verapamil may cause severe hypotension, and bradycardia.

Antihypertensive

Hypertension is group of symptoms, characterized by elevated blood pressure. Cardiac output and total peripheral resistance determine the blood pressure.
Anti hypertensive therapy involves non-pharmacological intervention as well as specific drugs treatments. Dietary sodium restriction, exercise, weight loss, behavior are some factors that effect B.P.

Prototype Drugs Of Hypertension

Diuretics
(See in Genito Urinary System)

B-Blockers
➔Propranolol

ACE Inhibitors
➔Captopril

Angiotensin Receptor Antagonist
➔Losartan

Rennin Inhibitors
➔Aliskiren

Ca2+ Channel Blocker

Alpha Blockers

Available Brands in the Market

Spiromide Tab. (Spironolactone)
Aldactone Tab. (Spironolactone)
Acetofen Tab. (Acetazolamide)
Acetopril Tab. (Acetazolamide)
Osmotol Tab. (Mannitol)
Medisol Tab. (Mannitol)
Inderal Tab. (Propranolol)
Betanol Tab. (Propranolol)
Capotein Tab. (Captopril)
Losark-k Tab. (Losartan)
Rasilez Tab. (Aliskiren)

Diuretics

➔See in Genito urinary system

Propranolol (B-Blockers)

➔See in adrenergic antagonist

Captopril (ACE inhibitors)

➔See in Heart failure

Losartan (Angiotensin Receptor Antagonist)

➔See in Heart failure

Alpha Blockers

➔See in adrenergic antagonist

Ca2+ Channel Blockers

➔See in antiarrhythmic

UNIT-VI

Gastrointestinal Drugs

Gastro Intestinal Tract is concerned with the function of ingesting and absorbing nutrients and excreting unabsorbed and waste products.

Here we will discuss prototype drugs used to treat three common medical conditions involving the gastrointestinal (GI) tract:

1. **Peptic ulcers and gastroesophageal reflux disease**
2. **Diarrhea**
3. **Constipation**
4. **Emesis**

Drugs Used To Treat Peptic Ulcer Disease

Antimicrobial Agents
➔Metronidazole

H2 – Histamine Receptor Blockers
➔Cimetidine

Proton Pump Inhibitors
Omeprazole

Prostaglandins Analogue
➔Misoprostol

Antacids
➔Aluminum Hydroxide

Mucosal Protective Agents
➔Sucralfate

Available Brands in the Market

Flagyl Tab. (Metronidazole)
Klint Tab. (Metronidazole)
Cimet Tab. (Cimetidine)
Ulcirex Tab. (Cimetidine)
Risek Cap. (Omeprazole)
Omega Cap. (Omeprazole)
Cytotec Tab. (Misoprostol)
Misoclear Tab. (Misoprostol)
Dijex-MP Syrup. (Aluminum Hydroxide)
Dimeco Syrup (Aluminum Hydroxide)
Sucmed Tab. (Sucralfate)
Sucfate Tab. (Sucralfate)

Metronidazole (Antimicrobial Agents)

Patients with peptic ulcer disease (both duodenal and gastric ulcers) who are infected with H. pylori, which is a Gram- negative, microaerophilic bacterium found in the stomach requires antimicrobial treatment. (See Antiprotozoals Drugs in Chemotherapy topic)

Cimetidine (H2 – Histamine Receptor Blockers)

Mechanism Of Actions

The histamine H2-receptor antagonists cimetidine, act selectively on H2 receptors in the stomach, blood vessels, and other sites, but they have no effect on H1 receptors. They are competitive antagonists of histamine and are fully reversible.

Therapeutic Uses

Peptic Ulcers
Histamine H2-receptor antagonists are equally effective in promoting the healing of duodenal and gastric ulcers.

Acute Stress Ulcers
These drugs are typically given as an intravenous infusion to prevent and manage acute stress ulcers associated with high-risk patients in intensive care units.

Gastroesophageal Reflux Disease
Gastroesophageal reflux disease is a chronic symptom of mucosal damage caused by stomach acid coming up from the stomach into the esophagus.
Low doses of H2 antagonists, currently available for over-the-counter sale, appear to be effective for the prevention and treatment of heartburn (gastroesophageal reflux).

Pharmacokinetics
Cimetidine and the other H2 antagonists are given orally, distribute widely throughout the body and are excreted mainly in urine. Cimetidine normally has a short serum half-life, which is increased in renal failure.

Adverse Effects
The most common side effects are headache, dizziness, diarrhea, and muscular pain.

Omeprazole (Proton Pump Inhibitors)

Mechanism Of Actions
Proton pump inhibitors act by irreversibly blocking the H+/K+ ATPase, or more commonly just gastric proton pump of the gastric parietal cell.

Therapeutic Uses
Proton pump inhibitors are used in the treatment of peptic ulcer, these agents suppressing acid production and healing peptic ulcers. These agents are also successfully used with antimicrobial agents for the peptic ulcer treatment.

Pharmacokinetics
All these agents are delayed-release formulation and effective orally. Metabolites of these agents are excreted in urine and feces.

Adverse Effects
These agents are generally well tolerated. Increased concentration of viable bacteria in the stomach has been reported with continued use of these agents.

Misoprostol (Prostaglandins Analogue)

Mechanism Of Action
Misoprostol seems to inhibit gastric acid secretion by a direct action on the parietal cells through binding to the prostaglandin receptor. It Increases secretion of mucus and bicarbonate.

Therapeutic Action
It is an effective anti-ulcer agent. It is clinically effective only at higher doses that diminish gastric acid secretion.

Adverse Effects
The most common adverse effects of misoprostol are uterine contractions, diarrhea and nausea.

Aluminum Hydroxide (Antacids)

An antacid is a substance, which neutralizes stomach acidity.

Mechanism Of Action
Antacids are weak bases that react with gastric acid to form water and a salt to diminish gastric acidity.

Therapeutic Uses
Aluminum hydroxide antacids are used in the treatment of peptic ulcer disease, and they may also promote healing of duodenal ulcers. They are used as last-line therapy for acute gastric ulcers.

Adverse Effects
Aluminum hydroxide tends to cause constipation, stomach pain, loss of appetite, and muscle weakness.

Pharmacokinetics
Aluminum hydroxide mostly excreted in feces. Small amounts absorbed are excreted by the kidneys.

Sucralfate (Mucosal Protective Agents)

These agents have several actions that enhance mucosal protection mechanisms, they are useful in mucosal injury, reducing inflammation, and healing existing ulcers.

Mechanism Of Action
Sucralfate creates a physical barrier that impairs diffusion of HCl and prevents degradation of mucus by pepsin and acid. It also stimulates prostaglandin release as well as mucus and bicarbonate output, and it inhibits peptic digestion.

Therapeutic Uses
Sucralfate effectively heals duodenal ulcers and is used in long-term maintenance therapy to prevent their recurrence.

Pharmacokinetics
Little of the drug is absorbed systemically. It is very well tolerated; it has a very short serum half-life of 1 h and is excreted almost completely by the kidneys.

Adverse Effects
Less serious side effects of sucralfate may include stomach pain, constipation, diarrhea, nausea, and vomiting.

Prototype Drugs Used To Treat Diarrhea

Increased motility of the gastrointestinal tract and decreased absorption of fluid are major factors in diarrhea. Most common antidiarrheal drugs used to treat acute diarrhea include antimotility agents, and adsorbents.

Available Brands in the Market

Imodium Tab. (Loperamide)
Floramex Tab. (Loperamide)
Dijex-MP Syrup. (Aluminum Hydroxide)
Dimeco Syrup (Aluminum Hydroxide)

Antimotility Agents
➔Loperamide

Adsorbents
➔Aluminum Hydroxide

Loperamide (Antimotility Agents)

Loperamide is widely used to control diarrhea. They inhibit acetylcholine release and decrease peristalsis. At the usual doses, they lack analgesic effects. Side effects include drowsiness,

abdominal cramps, and dizziness. They should not be used in young children or in patients with severe colitis.

Aluminum Hydroxide (Adsorbents)

Adsorbent agents, such as aluminum hydroxide are used to control diarrhea. Presumably, these agents act by adsorbing intestinal toxins or microorganisms and/or by coating or protecting the intestinal mucosa. They can interfere with the absorption of other drugs.

Prototype Drug Used To Treat Constipation

Laxatives are commonly used for constipation to accelerate the movement of food through the gastrointestinal tract. Most common and important laxatives are listed below.

Irritants And Stimulants
➔Castor oil

Saline And Osmotic Laxatives
➔Lactulose

Stool Softeners
➔Docusate

Available Brands in the Market

Castor Oil
Duphalc Syrup (Lactulose)
Lilac Syrup (Lactulose)
Abolitium Tab. (Docusate)

Castor Oil (Irritants And Stimulants)

This agent is broken down in the small intestine to ricinoleic acid, which is very irritating to the stomach and promptly increases peristalsis. This agent is used for the treatment of constipation.

Lactulose (Saline And Osmotic Laxatives)

Lactulose is a semisynthetic disaccharide sugar that also acts as an osmotic laxative. It is a product that cannot be hydrolyzed by intestinal enzymes. Oral doses are degraded in the colon by colonic bacteria into lactic, formic, and acetic acids. This increases osmotic pressure, causing fluid accumulation, colon distension, and soft stools.

Docusate (Stool Softeners)

Stool softeners emulsified with the stool produce softer feces and ease passage. They may take days to become effective and are often used for prophylaxis rather than acute treatment. Stool softeners should not be taken with mineral oil because of the potential for absorption of the mineral oil.

Antiemetics

Vomiting is a protective reflex mechanism for eliminating irritant of harmful substances from upper GIT.

Causes Of Vomiting

- **Pregnancy**
- **Motion sickness**
- **GI obstruction**
- **Peptic ulcer**
- **Drug toxicity**
- **Renal failure**
- **Hepatitis**

Prototype Drug Used To Treat Emesis

D_2 Receptor Antagonist
➔Metoclopramide
➔Domperidone

Sedative Hypnotics
➔Barbiturates
➔Benzodiazepines
(See in Anxiolytic And Hypnotic Drugs)

Antimuscarinics
➔Scopolamine

H1 Receptor Antagonists
➔Meclizine
➔Dimenhydrinate

Available Brands in the Market

Metoclopramide Syrup (Metoclopramide)
Emetus Tab. (Domperidone)
Gravinate Syrup (Dimenhydrinate|)

Metoclopramide (D_2 Receptor Antagonist)

Mechanism Of Action
Metoclopramide centrally block dopamine D_2 receptors in CTZ, it also enhances action of acetylcholine at muscarinic nerve ending in gut.

Therapeutic Uses
Metoclopramide is used in the treatment of nausea and vomiting associated with GI disorders, before emergency anesthesia and in gastroesophageal reflux.

Adverse Effects
Restlessness, diarrhea

Dimenhydrinate (H1 Receptor Antagonists)

Mechanism Of Action
Dimenhydrinate is a H1 antihistaminic or antiemetic agent.

Therapeutic Uses
It provides relief of symptoms of vomiting, allergic reactions such as rash, watery eyes, runny nose, itchy eyes and sneezing. It may also be used to treat motion sickness, relief of anxiety or tension and sleeplessness.

Adverse Effects
Dizziness, Headache, Drowsiness, and Fatigue

UNIT-VII

Respiratory System

Prototype Drugs Affecting The Respiratory System

In this chapter we will discuss the prototype drugs used in common diseases of respiratory system.

Common Diseases Related To Respiratory System

1. **Asthma**
2. **Allergic Rhinitis**
3. **Cough**

Now we will discuss prototype drugs of each disease…

Asthma

Asthma is an inflammatory disease of the airways characterized by episodes of acute bronchoconstriction causing shortness of breath, cough, chest tightness, wheezing, and rapid respiration.

Prototype Drugs Used To Treat Asthma

β 2-Adrenergic Agonists

Corticosteroids

Leukotriene Antagonists
➔Montelukast

Xanthine Oxidase Inhibitor
➔Theophylline

Available Brands in the Market

Betnesol Cream (Corticosterioids)
Kanadex Cream (Corticosterioids)
Montika Tab. (Montelukast)
Myteka Tab. (Montelukast)
Theograde Tab. (Theophylline)
Respro-SR Cap. (Theophylline)

B2-Adrenergic Agonists

Inhaled adrenergic agonists with β2 activity are the drugs of choice for mild asthma; Direct-acting β2 agonists are potent bronchodilators that relax airway smooth muscle.

Most clinically useful β2 agonists have a rapid onset of action (5 to 30 minutes) and provide relief for 4 to 6 hours. They are used for symptomatic treatment of bronchospasm, providing quick relief of acute bronchoconstriction. Adverse effects are tachycardia, hyperglycemia, hypokalemia and hypomagnesemia.

Corticosteroids

Inhaled corticosteroids (ICS) are the drugs of first choice in patients with any degree of persistent asthma (mild, moderate, or severe). No other medications are as effective as ICS in the long-term control of asthma in children and adults. These are also effective when administered as nasal sprays for the treatment of Allergic Rhinitis.

Actions On Lung
Inhaled corticosteroids do not directly affect the airway smooth muscle. They directly targets underlying airway inflammation by decreasing the inflammatory cascade, reversing mucosal edema, decreasing the permeability of capillaries, and inhibiting the release of leukotrienes.

Montelukast (Leukotriene Antagonists)

Montelukast is selective, reversible inhibitor of the cysteinyl leukotriene-1 receptor, it block the effects of cysteinyl leukotrienes. Montelukast is used as a prophylaxis of asthma but are not effective in situations in which immediate bronchodilation is required. montelukast is also used for treatment of both seasonal and perennial allergic rhinitis.

Pharmacokinetics

The drug is orally active. Greater than 90 percent of drug is bound to plasma protein. The drug is extensively metabolized, and their metabolites undergo biliary excretion.

Adverse Effects

Elevations in serum hepatic enzymes, headache and dyspepsia

Theophylline (Xanthine Oxidase Inhibitor)

Theophylline is a bronchodilator that relieves airflow obstruction in chronic asthma and decreases its symptoms. Theophylline is well absorbed by the gastrointestinal tract, and several sustained-release preparations are available.

Allergic Rhinitis

Rhinitis is an inflammation of the mucous membranes of the nose and is characterized by sneezing, itchy nose/eyes, watery rhinorrhea, and nasal congestion. An attack may be due to inhalation of an allergen such as dust, pollen, or animal dander. The foreign material interacts with mast cells which, release mediators, such as histamine that promote bronchiolar spasm and mucosal thickening from edema and cellular infiltration.

Prototype Drugs Used To Treat Allergic Rhinitis

- **β -Adrenergic Agonists**
- **Antihistamines**
- **Corticosteroids (see in Asthma)**
- **Montelukast (see in Asthma)**

Available Brands in the Market

Antial (Antihistamines)
Softin (Antihistamines)

β-Adrenergic Agonists

Short-acting β-Adrenergic agonists constrict dilated arterioles in the nasal mucosa and reduce airway resistance. Longer-acting β-Adrenergic agonists are also available. When administered as an aerosol, these β-Adrenergic agonists nasal formulations should be used no longer than 3 days due to the risk of rebound nasal congestion.

Antihistamines (H1-Receptor Blockers)

Antihistamines are the most frequently used agents in the treatment of sneezing and watery rhinorrhea associated with allergic rhinitis. H1-histamine receptor blockers are useful in treating the symptoms of allergic rhinitis caused by histamine release.

Cough

Prototype Drugs Used To Treat Cough

- **Codeine**
- **Dextromethorphan**

Available Brands in the Market

Brufen-Plus (Codeine)
Codamin-P (Codeine)
Dextromethorphan Syrup (Dextromethorphan)
Pacific DM Syrup (Dextromethorphan)

Codeine

Codeine decreases the sensitivity of cough centers in the central nervous system to peripheral stimuli and decreases mucosal secretion. These therapeutic effects occur at doses lower than those required for analgesia but still have common side effects, such as constipation, dysphoria, and fatigue, as well as having addictive potential.

Dextromethorphan

Dextromethorphan is a synthetic derivative of morphine that suppresses the response of the central cough center. It has no analgesic effects in antitussive doses. It has a low addictive profile. Dextromethorphan has a significantly better side effect profile than codeine and has been verified to be equally effective for cough suppression.

UNIT-VIII

Genitourinary System

The term "genitourinary" actually refers to two different systems. Urinary refers to the system responsible for removal waste products of metabolism from the bloodstream. Genito refers to the genital organs and the reproductive system.

Diuretics

Uterine Muscles Relaxant
Beta-2 Agonist
➔Ritodrine

Uterine Muscles Contractants
➔**Misoprostol** (see in autacoids)
➔**Oxytocin**
Ergot Alkaloid
➔Ergotamine

Available Brands in the Market

Yutopar Inj. (Ritodrine)
S.T Mom Tab. (Misoprostol)
Oxytocin Inj (Oxytocin)
Cafergot Tab. (Ergotamine)

Diuretics

A drug that increases the volume of urine produced by promoting the excretion of salts and water form the kidney.
Diuretics can be used as first-line drug therapy for hypertension. Low-dose diuretic therapy is safe, inexpensive, and effective in preventing stroke, myocardial infarction, and congestive heart failure. Recent data suggest that diuretics are superior to β-blockers for treating hypertension in older adults.

Prototype Diuretics Drugs

Depending upon the site of action, diuretics can be classified as…

Thiazide Diuretic
➔Chlorothiazide

Loop Diuretic
➔Bumetanide
➔ Furosemide

Potassium Sparing Diuretic
➔Spironolactone

Carbonic Anhydrase Inhibitor
➔Acetazolamide

Osmotic Diuretic
➔Mannitol

Available Brands in the Market

Xurin-k (Bumetanide)
Spiromide (Spironolactone)
Aldactone (Spironolactone)
Acetofen (Acetazolamide)
Acetopril ((Acetazolamide)
Osmotol (Mannitol)
Medisol (Mannitol)

Chlorothiazide (Thiazide Diuretic)

Mechanism Of Action
They inhibit Na+ reabsorption in distal convoluted tubule decreased Na+ reabsorption increase the concentration of urine.

Therapeutic Uses
These agents are important in the treatment of hypertension, congestive heart failure and hypercalciuria.

Adverse Effects
Most of the adverse effects involved problems in fluid and electrolyte balance.

Pharmacokinetics
These drugs are effective orally half-life is 40 hours these drugs secreted by urine.

Bumetanide (Loop Diuretic)

Mechanism Of Action
These agents inhibit Na, K, Cl contrasport in the ascending limb of loop of Henley.

Therapeutic Uses
The loop diuretics are the drugs of choice for reducing the acute pulmonary edema of heart failure. The drug is useful in emergency situation.

Pharmacokinetics
Loop diuretics are administered orally or parenterally. They are secreted into the urine.

Adverse Effects
Hypotension, Hypokalemia, Hypomagnesaemia,Ototoxicity

Spironolactone (Potassium Sparing Diuretic)

Mechanism Of Action
Spironolactone antagonizes aldosterone at intracellular cytoplasmic receptor sites result in inhibit mediator protein that stimulate the Na/K exchange in collecting tubule. This prevents the Na reabsorption and therefore K and H secretion.

Therapeutic Uses
These agents are used as diuretics with an additional advantage that is retention of K.

Adverse Effects
Gastric upset, peptic ulcer, Hypokalemia, nausea, confusion

Pharmacokinetics
Spironolactone is completely absorbed orally and strongly bound to protein.

Acetazolamide (Carbonic Anhydrase Inhibitor)

Mechanism Of Action
Acetazolamide inhibits carbonic anhydrase located intra-cellularly and on proximal tubular epithelium, results in increased urine volume.

Therapeutic Uses
The most common use of acetazolamide is to reduce elevate intraocular pressure of open angle glaucoma. Less commonly, acetazolamide can be used in the prophylaxis of acute mountain sickness.

Pharmacokinetics
It is given orally. It is secreted by the proximal tubule.

Adverse Effects
Potassium depletion, renal stone formation

Mannitol (Osmotic Diuretic)
Osmotic diuretics are used to affect increased water excreted rather than Na excretion. They are not useful for treating conditions in which Na retention occurs. They are used to maintain urine flow. Mannitol is not absorbed when given orally and should only be given intravenously. Adverse effects include dehydration

Ritodrine (Beta-2 Agonist, Uterine Muscles Relaxant)

Mechamism of Action
Ritodrine is a selective beta-2 receptor agonist that developed specifically for use as a uterine relaxant.

Therapeutic Uses
Ritodrine used for smooth muscle (uterine muscle) relaxant to decrease uterine activity and delay uncomplicated premature labor.

Side Effects
Fast heart rate, headache, nervousness, anxiety, nausea and vomiting

Oxytocin (Uterine Muscles Contractants)

Mechamism of Action
Oxytocin increase in intracellular calcium levels thus stimulates rhythmic contractions of the uterus.

Therapeutic Uses
Oxytocin use as a smooth muscle (uterine muscle) contractant.

Side Effects
Allergic reaction,nausea, vomiting, swelling of the mouth, face, lips, or tongue

Ergotamine (Ergot Alkaloid, Uterine Muscles Contractants)

Mechanism of Action
Ergotamine constricts smooth muscles like blood vessels and uterine muscles.

Therapeutic Uses
Ergotamine constricts uterine muscles. Ergotamine is also used to treat headache pain and other symptoms associated with migraines.

Side Effects
Allergic reaction, nausea, vomiting, swelling of the mouth, face, lips, or tongue

UNIT-IX

Introduction To Chemotherapy

Chemotherapy is a treatment of various diseases caused by pathogenic organism (bacteria, fungi, viruses, protozoa, and worm) with chemical substance, which due to their selective toxicity, destroy or remove the pathogenic organism without injuring the host. The chemical substances used for this purpose are called chemotherapeutics agents.

Drugs used for the treatment of neoplastic disease (anticancer drug) are also including in chemotherapy. Although cause of cancer is not known in most of the cases and anticancer drugs are most toxic to the patients as compare to anti microbial drugs. Anticancer chemotherapy does play important role in the treatment of cancer.

Drugs Used In Chemotherapy

1. **➔Antibacterial drugs**
2. **➔Antiviral drugs**
3. **➔Antiprotozoal drugs**
4. **➔Anthelmintics**
5. **➔Antifungal drugs**
6. **➔Antitubercular drugs**
7. **➔Antileprotic drugs**
8. **➔Anticancer drugs**

Antibacterial Drugs

Antibacterial drugs are used to treat infection caused by bacteria. These drugs posses selective toxicity against bacteria as compared to host cells. These drugs may be bacteriostatic or bacteriocidal in their activity.

Antiviral Drugs

Antiviral drugs are used to treat infections caused by viruses. Viruses do not contain cell wall and cell membranes and its replication depends on the metabolic processes of the host cell therefore they are not affected by antimicrobial agents.
Therefore clinically effective antiviral agents need to be given much earlier before the onset of the disease. Administration of drugs that block viral replication has limited effectiveness. However some antiviral agents are useful as prophylactic agents.

Antiprotozoal Drugs

Antiprotozoal Drugs used to treat protozoals infections. Protozoal infections are common among people in underdeveloped countries, where sanitary conditions, hygienic practices etc are inadequate with increased world travel protozoal diseases such as malaria, amebiasis, and trypanosomiases are spreading.

Many of the antiprotozoal drugs cause serious toxic effects in the host. Most Antiprotozoal agents have not proved to be safe for pregnant patients.

Anthelmintics Drugs

Anthelmintics are drugs used for eradication of worms from the body. An anthelmintic, which kills the worm, is called vermicide. If the drug is merely noxious to the worms and causes them to be expelled from the body, it is called a vermifuge.

Antifungal Drugs

Antifungal drugs are used treat fungal infections. Fungal infections are common. They may affect mucous membranes, skin hair and nails. Sometimes internal organs may be involved e.g lungs, intestine, liver, brain etc. Some antifungal drugs are for local application only. Other drugs are given orally or may be injected.

Antitubercular Drugs

Antitubercular drugs are used to treat tuberculosis. Tubercular is small rounded swellings or nodules. Tubercular is an infectious disease caused by the bacillus and characterized by formation of nodules. In pulmonary tuberculosis, the bacillus is inhaled into the lungs where it sets up a primary tubercle and spreads to the nearest lymph nodes.

Antileprotic Drugs

These drugs are used to treat leprosy. Leprosy is a chronic disease caused by bacteria that affect the skin mucous membranes and nerves causing discoloration and lumps on the skin.

Anticancer Drugs

These drugs are used to treat cancer, neoplasia or tumor. Cancer is a disease caused by an uncontrolled division of abnormal cells in the part of the body that then invade and destroy the surrounding tissues.

Spread of cancer cells (metastasis) may occur via the blood stream or the lymphatic channels. Cancer may be treated by surgery, radiotherapy or chemotherapy. Certain tumors are highly sensitive to chemotherapy but many tumors are not sensitive to such drugs.

UNIT-X

Introduction To Drugs Used In Anesthetics

Anesthesia is insensitivity to pain, especially as artificially induce by the administration of gases or drugs before a surgical operation.

General Anesthesia
General anesthesia is a total unconsciousness of the body achieved by the drugs that affects the whole body. It is used for major surgical operations.

Local Anesthesia
Anesthesia that affects a limited area of the body and is used for minor surgical operations e.g. dental procedures.

For patients undergoing surgical and other medical procedures, anesthesia provides these five important benefits…

1. **Sedation And Reduction Of Anxiety**
2. **Lack Of Awareness And Amnesia**
3. **Skeletal Muscle Relaxation**
4. **Suppression Of Undesirable Reflexes**
5. **Analgesia**

Stages Of Anesthesia

Anesthetic drug effects can be divided into four stages of increasing depth of central nervous system depression.

1. **Stage Of Analgesia**
2. **Stage Of Excitement**
3. **Stage Of Surgical Anesthesia**
4. **Stage Of Medullary Depression**

Drugs Used In Anesthetics

General Anesthetics
Inhaled (Halothane) and **Intravenous (**Benzodiazepines)

Local Anesthetics
➔Lidocaine

Halothane (General Anesthetics, Inhaled)

Mechanism Of Action

No specific receptor has been identified as the locus of general anesthetic action. General anesthetics increase the sensitivity of the GABA receptors at clinically effective concentrations of the drug. This causes a prolongation of the inhibitory chloride ion current after a pulse of GABA release. Postsynaptic neuronal excitability is, thus, diminished.

Halothane induces the anesthetic state rapidly, and quick recovery made it an anesthetic of choice.

Therapeutic Uses

Halothane is a potent anesthetic but a relatively weak analgesic. It is a potent bronchodilator. Halothane relaxes both skeletal and uterine muscle.

Pharmacokinetics

Halothane is oxidatively metabolized in the body to tissue. Halothane anesthesia is not repeated at intervals of less than 2 to 3 weeks.

Adverse Effects

Bradycardia, Malignant hyperthermia, Isoflurane, Desflurane, Sevoflurane

Benzodiazepines (General Anesthetics, Intravenous)

IV anesthetics cause the rapid induction of anesthesia. This is often described as occurring within one "arm-brain circulation time or the time it takes the drug to travel from the site of injection (usually the arm) to the brain, where it has its effect. Anesthesia may then be maintained with an appropriate inhalation agent.

(for detail, see in Anxiolytic And Hypnotic Drugs)

Lidocaine (Local Anesthetics)

Pharmacokinetics

Local anesthetics are usually administered by injection into dermis and soft tissues located in the area of nerves. Thus, absorption and distribution are not as important in controlling the onset of effect. Local anesthetics abolish sensation and, in higher concentrations, motor activity in a limited area of the body.

Mechanism Of Action

The primary mechanism of action of local anesthetics is blockade of voltage-gated sodium channels.

Therapeutic Uses

Lidocaine is probably the most commonly used. Local anesthetics cause vasodilatation, which leads to rapid diffusion away from the site of action and results in a short duration of action when these drugs are administered alone. By adding the vasoconstrictor epinephrine to the local anesthetic, the rate of local anesthetic diffusion and absorption is decreased. This both minimizes systemic toxicity and increases the duration of action.

Adverse Effects

Neural toxicity, allergic reactions, depresses cardiac pacemaker activity, excitability, and conduction.

UNIT-XI

Introduction To Autacoids And Their Antagonists

Autacoids

Autacoids are naturally occurring substances having widely different structures and pharmacological activities. The word autacoid comes from the Greek "autos (self) and "akos" (medicinal agent, or remedy).

Following are the most important autacoids

- **Prostaglandins (Misoprostol)**
- **Histamine**
- **Serotonin**

They have the common feature of being formed by tissues on which they act, thus they function as local hormones.

Prostaglandins

Prostaglandins are unsaturated fatty acids derivatives. They act on the tissues in which they are synthesized.

Therapeutics Uses Of Prostaglandins

Abortion
Several of the prostaglandins used as abortifacients (agents causing abortion). Prostaglandins have the advantages of stimulating uterine contractions at any stage of pregnancy.

Peptic Ulcer
Prostaglandins protect the mucous membrane of stomach. Misoprostol is sometimes used to inhibit the secretion of gastric acid.

Histamine

Histamine is also an autacoid. It is a chemical messenger that mediates a wide range of cellular responses including allergic and inflammatory reactions, gastric acid secretion and neurotransmission in parts of the brain.

Mechanism Of Action

Histamine binds with histamine receptors H1, H2, H3, and H4. Where H1 and H2 receptors are widely expressed and are targets of clinically useful drugs.

Antihistamines

H1 **Antihistamines**
These compounds are H1 receptor blockers. They do not influence the formation or release of histamine. They only block the histamine response at target tissue.

Therapeutic Uses

Allergic And Inflammatory Conditions
H1 receptor blockers are useful in treating allergies caused by antigens.

Motion Sickness And Nausea

Along with the antimuscarinic agents, H1 receptor blockers are the most effective agents for prevention of the symptoms of motion sickness, nausea.

Somnifacients

Many first generation antihistamines have strong sedative properties and are used in the treatment of insomnia.

H2 Antihistamine

These agents block the H2 histamine receptors. The chief clinical use is a inhibitors of gastric acid secretion in the treatment of ulcers and heartburn.

Serotonin

Serotonin is widely distributed in nature, being found in plant and animal tissues. Serotonin is an important neurotransmitter a local hormone in the gut, a component of the platelet clotting process and is thought to play a role in migraine headache.

UNIT-XII

Introduction To Toxicology

Toxicology is defined as the study of the adverse effects of chemicals on living organisms.

Toxicity

Toxicity is defined as the inherent capacity of a chemical to cause injury. All the chemicals, drugs have some degree of toxicity. All substances are poison there is none, which is not a poison. The right dose differentiates a poison from a remedy.

Toxicity may occur in three general ways

1. **Accidental**
2. **Intentional**
3. **Adverse Drug Reactions**

Accidental ingestion occurs most commonly in children. Intentional over dosage often with suicidal attempts, whereas adverse drug reactions occurs due to any wrong therapy.

Toxic Actions Of Chemicals

Toxic chemicals from the environment may contact the skin or absorbed after ingestion or inhalation. A chemical toxin can potentially affect any tissue or organ within the body.

Occupational And Specific Environmental Toxin

Occupational and specific environmental toxicity is caused by many types of toxic substances like Chloroform, Aromatic hydrocarbon, Alcohols, Pesticides, Heavy metals, Gases and inhaled particles,

Treatment

We can use three types of treatment in toxicity

1. **Supportive care**
2. **Decreasing the quantity of drug absorption**
3. **Enhancing drug elimination**

Supportive Care

Supportive care is first line treatment. The most important advance in the management of drug over doses was the replace the use of protected airway, mechanical ventilation and support of the circulations. With the excretion of a few intoxication that require a specific therapeutic approach, good supportive care alone will ensure a positive outcome in most patients.

Decreasing The Quantity Of Drug Absorption

Three types of procedure are widely used to decrease GI absorption of orally ingested poisons.

These procedures are called

1. **Induced emesis (vomiting)**
2. **GI lavage (washing out stomach)**
3. **Instillation of activated charcoal**

Enhancing Drug Elimination

Poisons normally are eliminated by hepatic biotransformation, renal excretion, or a combination of these mechanisms. We can enhance drug elimination by using forced dieresis, hemodialysis and hemoperfusion.

Antidotes

Antidotes are drugs that counteract the effect of a poison or have over dosage by another drug. Specific chemical antidotes for poisoning exist for only a small number of chemicals or classes of chemicals.

These Antidotes Perform Following Functions

- **Accelerate detoxification of toxic agent**
- **Pharmacological antagonize toxication**
- **Reduce metabolic activation**
- **Provide alternative target**
- **Chelators**