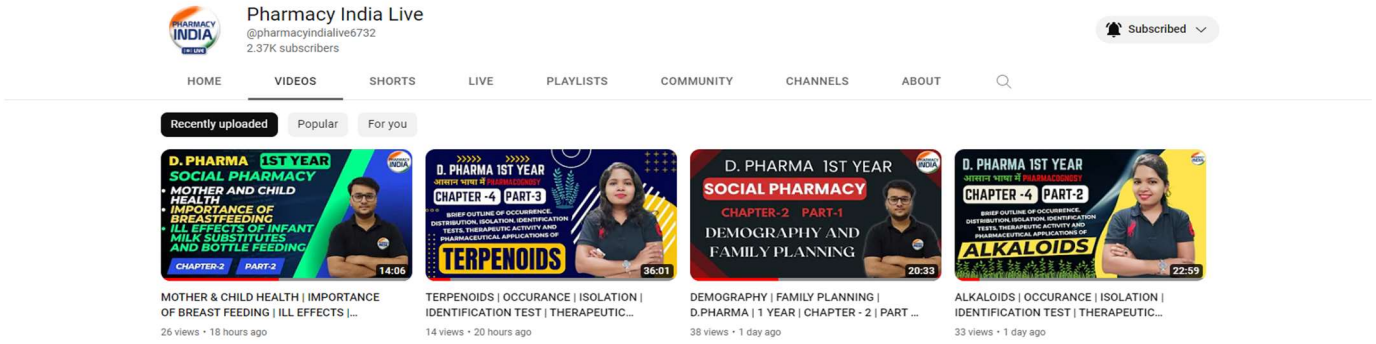
PHARMACOLOGY

MODEL PAPER – 1

Syllabus to be covered in this module are-

- ❖Chapter-1 General Pharmacology
- ❖Chapter-2 Drugs Acting on the Peripheral System
- ❖Chapter-3 Drugs Acting on the Eye
- ❖Chapter-4 Drugs Acting on the Central Nervous System



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Questions

Long Questions-

Ques.1 Explain factors affecting absorption in detail.

Ques.2 Discuss drug distribution.

Ques.3 Write in detailed about factors modifying drug action.

Ques.4 Explain in detail about adrenergic drugs.

Ques.5 Discuss anti-adrenergic drugs in detail.

Ques.6 Explain drugs acting on the eye.

Ques.7 Write in detailed about general anaesthetics.

Ques.8 Discuss sedatives and hypnotics.

Short Questions

Ques.1 Write a short note on pharmacology.

Ques.2 What are the scopes of pharmacology?

Ques.3 Write a short note on local routes of administration.

Ques.4 What are physio-chemical properties of drug substance.

Ques.5 What are patient related factors?

Ques.6 Give the factors influencing drug metabolism.

Ques.7 Give the general mechanism of drug action.

Ques.8 What is the effect of combination of drugs?

Ques.9 Write a short note on pharmacological actions of cholinergic agonists.

Ques.10 Define anti-cholinergic drugs. Give the classification of anti-cholinergic drugs.

Ques.11 What is anti-cholinesterase poisoning?

Ques.12 What are the pharmacological actions of anti-cholinergic drugs?

Ques.13 Give the classification of non-steroidal anti-inflammatory drugs (NSAIDS).

Ques.14 Give the pharmacological actions of aspirin.

Ques.15 Write a short note on angle closure glaucoma.

Ques.16 What are intravenous anaesthetics?

Ques.17 What are the complications of anaesthetics?

Ques.18 Give the therapeutic uses & treatment of barbiturates.

Ques.19 Give the mechanism of action of general anaesthetics.

Ques.20 Give the classification of epileptic seizures.

Ques.21 What are the advantages of benzodiazepines over barbiturates?

Ques.22 Write a short note on anti-anxiety drugs?

Ques.23 What are mood stabilizing agents?

Ques.24 Give the mechanism of action and adverse drug reactions of anti-psychotics.

Ques.25 What are the pharmacological actions of morphine?

Ques.26 Write a short note on opioid analgesics.

Ques.27 Explain centrally acting muscle relaxants.

Long Answers

Ques.1 Explain factors affecting absorption in detail.

Ans- FACTORS AFFECTING ABSORPTION

These are the factors, which influence the diffusion of the drug molecule across the membrane. The rate of absorption is determined by the following

1. Pharmaceutical Factors

(A) Physio-chemical properties of drug substances

Drug solubility & dissolution rate: The rate determining steps in absorption of orally administered drugs are:

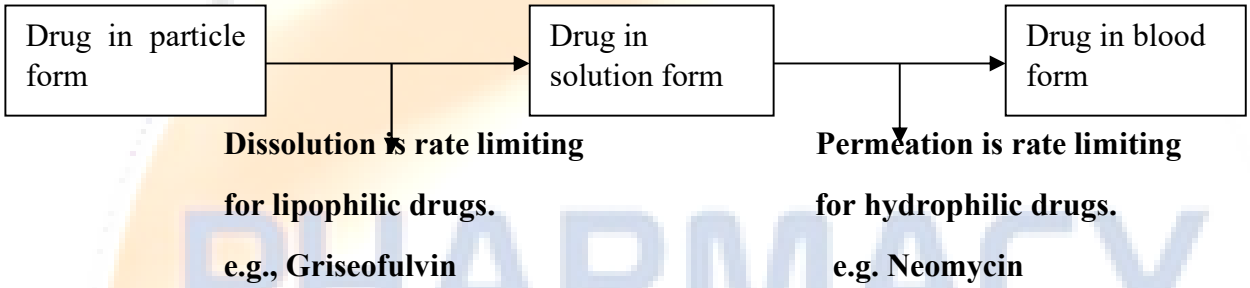

Fig. 1.2: Rate determining steps

- **Particles size & effective surface area:** The smaller the particle size (by micronization), the greater is the effective surface area, more intimate contact between solid surface and aqueous solvent, the higher is the dissolution rate and increase in absorption efficiency, e.g., soluble non-hydrophobic drugs like Griseofulvin, chloramphenicol whose dissolution is rate limited.
- **Polymorphism & amorphism:** Many compounds form crystals with different molecular arrangements, or polymorphs. These polymorphs may have different physical properties, such as dissolution rate and solubility. Amorphous form has greater aqueous solubility than the crystalline forms because the energy required to transfer a molecule from crystal lattice is greater than that required for non-crystalline solid.
- **Solvates & hydrates:** The stoichiometric type of adducts where the solvent molecule is incorporated with the crystal lattice of the solid are called as solvates. The solvates can exist in different crystalline forms called as pseudomorphs and the phenomenon is pseudo polymorphism. When the solvent in association with drug is water, the solvate is known as hydrate. e.g., anhydrous form of theophylline and ampicillin are more bioavailability than their monohydrate & trihydrate forms.
- **Salt form of drug:** At given pH, the solubility of drug, whether acidic/basic or its salt, is a constant. While considering the salt form of drug, pH of the diffusion layer is important not the pH of the bulk of the solution. e.g., salt of weak acid, which increases the pH of the diffusion layer, promotes the solubility and dissolution of a weak acid and absorption is bound to be rapid.
- **Ionization state:** Unionized state is important for passive diffusion through membrane so important for absorption. Ionized state is important for solubility.
- **Drug pK, & lipophilicity & GI pH** (pH partition hypothesis)

(B) Formulation Factors

- **Disintegration time (D.T):** Rapid disintegration is important to have a rapid absorption so lower D.T. is required. D.T. of tablet is directly proportional to amount of binder and compression force. Also, if the disintegrated drug particles do not dissolve then absorption and ultimately bioavailability is not achieved.
- **Manufacturing variables:**

(1) Method of granulation depending on the method wet/dry granulation can be used to produce tablets that dissolve at a faster rate.

(2) Compression force influence the hardness, density, porosity, disintegration & dissolution of tablet.

- **Nature & type of dosage form:** Drug formulations are designed to provide an attractive, stable, and convenient method to use products Conventional dosage forms may be broadly characterized in order of decreasing dissolution rate as solutions, solid solutions, suspensions, capsules and tablets, coated capsules and tablets, and controlled release formulations
- **Pharmaceutical excipients:** The more the number of excipients in the dosage form, the more complex it is & the greater the potential for absorption and bioavailability problems Commonly used excipients in various dosage forms are vehicle, diluents, binders & granulating agent, disintegrants, lubricants, suspending/viscosity agents, surfactants, and colorants.
- **Product age & storage conditions:** Product aging and storage conditions can adversely affect the bio-availability by change in especially the physio-chemical properties of the dosage forms. For example: precipitation of the drug in solution, hardening of tablet & change in particle size of suspension

II. Patient Related Factors

(A) Physiological Factors

1. Membrane physiology: Nature of cell membrane & Transport processes (discussed earlier in the chapter)

2. Gastro-Intestinal motility:

(a) Gastric emptying rate: Gastric emptying is a first order process by which food leaves the stomach and enters the duodenum. Rapid gastric emptying is required when the drug is best absorbed from distal part of the small intestine. Delayed gastric emptying is required when drugs are absorbed from proximal part of the small intestine and prolonged drug absorption site contact is desired. Factors that influence gastric emptying rate are

- Volume of meal (bulky material tends to empty more slowly than liquids)
- Composition of meal (carbohydrates> proteins > fats)
- Physical state and viscosity of meal (Solutions or suspensions of small particles empty more rapidly than do chunks of material that must be reduced in size prior to emptying)
- Body posture (Lying on the left side decreases emptying rate and right side promotes it)
- Emotional state (Anxiety promotes whereas depression retards it)
- Disease state (gastric ulcer, hypothyroidism retards it, while duodenal ulcer, hyperthyroidism promotes it)

(b) Intestinal motility: Normal peristaltic movements mix the contents of the duodenum, bringing the drug particles into intimate contact with the intestinal mucosal cells. The drug must have a sufficient time (residence time) at the absorption site for optimum absorption. In the case of high motility in the intestinal tract, as in diarrhoea, the drug has a very brief residence time and less opportunity for adequate absorption

(c) Drug stability in GIT: Metabolism or degradation by enzymes or chemical hydrolysis may adversely affect the drug absorption and thus reduces bioavailability Generally, a problem with orally administered drugs which can be destructed by gastric acid

(d) Intestinal transit: Long intestinal transit time is desirable for complete absorption of drug e.g for enteric coated formulation & for drugs absorbed from specific sites in the intestine, Peristaltic contraction promotes drug absorption by increasing the drug membrane contact and by enhancing dissolution especially of poorly soluble drugs.

(e) Blood flow to GIT: It continuously maintains the concentration gradient across the epithelial membrane. The GIT is extensively supplied by blood capillary network. Absorption of polar molecules doesn't depend on the blood flow but lipid soluble molecules highly depend on the blood flow. Food influences blood flow i.e., perfusion increases after meals & persist for few hours but absorption is not affected.

3. Age: In infants, the gastric pH is high and intestinal surface and blood flow to the GIT is low resulting in altered absorption pattern in comparison to adults. In elderly persons, altered gastric emptying, decreased intestinal surface area and GI blood flow impairs drug absorption.

BIOAVAILABILITY

Bioavailability is the Fraction of administered drug that reaches the systemic circulation. Bioavailability is expressed as the fraction of administered drug that gains access to the systemic circulation in a chemically unchanged form. For example, if 100 mg of a drug is administered orally and 70 mg of this drug is absorbed unchanged, the bioavailability is 70%.

Factors Affecting Bioavailability

1. First-pass hepatic metabolism: When a drug is absorbed across the GI tract, it enters the portal circulation before entering the systemic circulation. If the drug is rapidly metabolized by the liver, the amount of unchanged drug that gains access to the systemic circulation is decreased. Many drugs, such as propranolol or lidocaine, undergo significant biotransformation during a single passage through the liver.

2. Solubility of drug : Very hydrophilic drugs are poorly absorbed because of their inability to cross the lipid-rich cell membranes. Paradoxically, drugs that are extremely hydrophobic are also poorly absorbed, because they are totally insoluble in the aqueous body fluids and, therefore, cannot gain access to the surface of cells. For a drug to be readily absorbed, it must be largely hydrophobic yet have some solubility in aqueous solutions.

3. Chemical instability: Some drugs, such as penicillin G, are unstable in the pH of the gastric contents. Others, such as insulin, may be destroyed in the GI tract by degradative enzymes.

4. Nature of the drug formulation: Drug absorption may be altered by factors unrelated to the chemistry of the drug. For example, particle size, salt form, crystal polymorphism, and the presence of excipients (such as binders and dispersing agents) can influence the ease of dissolution and therefore, alter the rate of absorption.

Bioequivalence: Two related drugs are bioequivalent if they show comparable bioavailability and similar times to achieve peak blood concentrations. Two related drugs with a significant difference in bioavailability are said to be bio-inequivalent.

Ques.2 Discuss drug distribution.

Ans- DRUG DISTRIBUTION

It refers to the reversible transfer of a drug between the blood and the extra vascular fluids and tissues of the body (for example, fat, muscle, and brain tissue). Only a free drug at its site of action can have a pharmacological effect, therefore it is important that a drug is distributed around the body effectively. When a drug is administered, it does not achieve an equal concentration throughout the body. Unless a drug is injected directly into the blood stream it will be absorbed from its site of administration, then enter the systemic circulation and be transported to the tissues in plasma. The body can be made up of aqueous and lipid compartments. Lipid compartments include all cell membranes and adipose tissue. Aqueous compartments include tissue fluid, cellular fluid, blood plasma and fluid in places like the central nervous system, the lymphatic system, joints and the gastrointestinal tract.

FACTORS AFFECTING DRUG DISTRIBUTION

The distribution of a drug into these different compartments depends on many factors:

(a) Aqueous solubility: It affects distribution because water-soluble drugs have difficulty crossing cell membranes and therefore tend to remain in the circulation. Consequently, water-soluble drugs are not well distributed throughout the body. They exist in large amounts in the plasma or tissue fluid and are rapidly cleared by the liver or kidney In practice, such drugs have little therapeutic use.

(b) Blood flow: At equilibrium, drugs are partitioned between plasma, plasma proteins and the different tissues. The rate of distribution to different tissues depends largely on the rate of blood flow through them. Some areas of the body have a relatively good blood supply, for example, the major organs, muscles, and skin have a moderate supply; and bone and adipose tissue have a poor supply. Thus, major organs receive a relatively high concentration of a drug whereas it can be difficult to get drugs into less well-perfused areas. Although the brain has a very good blood supply, distribution of drugs into the central nervous system is restricted. This is because of the so-called 'blood-brain barrier This is not an anatomical barrier as such, rather a combination of the tight junctions between endothelial cells of brain capillaries and the close association of glial cells with the outside of the capillaries. This arrangement makes diffusion of lipid-soluble drugs into the brain difficult and diffusion of water-soluble drugs almost impossible.

(c) Plasma protein binding: Many drugs have a high affinity for albumin and other plasma proteins. Binding to plasma protein inhibits distribution outside the blood since only unbound drug will be further distributed. Plasma protein binding therefore reduces active drug concentration and ultimate response to the drug. Drugs can compete for the same protein binding sites and this is a form of drug interaction. A well-known and important example is that of warfarin and aspirin. Warfarin is an anticoagulant, which binds extensively to plasma proteins, and this is taken into account when dosages are worked out. Aspirin taken with warfarin competes for the same protein binding sites, which means that they each displace the other and the amount of free drug in the plasma is increased for both drugs. Patients stabilized on warfarin should never take aspirin because the effect of increased free plasma concentration of warfarin can be severe haemorrhaging. Coincidental increased activity of aspirin is not as serious.

(d) Lipid solubility: Lipid-soluble (non-ionized) drugs enter cells readily & are available everywhere. Distribution of such drugs is widespread unless plasma protein binding is extensive. Elimination of lipid-soluble drugs is usually slow because clearance from plasma via the kidneys removes only a small proportion of the drug in any given time. Water soluble drugs (ionized) can't cross the cell membrane, and so remains in mostly ECF. Similarly, low molecular weight drugs can cross easily and high molecular weight drugs (albumin) can't cross the capillary membrane & remains in plasma.

(e) Tissue sequestration: Considerable amounts of drug may be stored in certain tissues, particularly fat and muscle. Sequestration in this way gives an apparent large volume of distribution (see below) but also means that only a small proportion of total drug concentration will reach its site of action. This can create difficulties with the usage of certain drugs. For example, general aesthetics are highly lipid-soluble drugs. Sequestration into adipose tissue can make anaesthetizing obese people hazardous because it is difficult to control the amount of free drug in the circulation

Similarly, benzodiazepines (antianxiety drugs) can be difficult to clear from the body because they are stored in large amounts in adipose tissue. This can complicate withdrawal from their use. Apart from storage in lipid tissue, certain drugs can be preferentially taken up or sequestered into her tissues For example, griseofulvin has an affinity for keratin. Since this drug can be used to fungal infections of the skin and nails its sequestration into keratin is something of an advantage. The antibiotic tetracycline has an affinity for bones and teeth. It should never be used in children as its accumulation can damage teeth and stunt growth.

The **Volume of distribution (VD),** also known as Apparent volume of distribution, is used to quantify the distribution of a drug between plasma and the rest of the body after oral or parenteral dosing. It is called as Apparent Volume because all parts of the body equilibrated with the drug do not have equal concentration. It is defined as the volume in which the amount of drug would be uniformly distributed to produce the observed blood concentration.

Redistribution: Highly lipid soluble drugs when given by i.v. or by inhalation initially get distributed to organs with high blood flow, e.g., brain, heart, kidney etc. Later, less vascular but more bulky tissues (muscles, fat) take up the drug and plasma concentration fall and drug is withdrawn from these sites. If the site of action of the drug was in one of the highly perfused organs, redistribution results in termination of the drug action. The greater the lipid solubility of the drug, the faster is its redistribution.

Drugs which bind selectively to Plasma proteins e.g., Warfarin have Apparent volume of distribution smaller than their Real volume of distribution. The Vd of such drugs lies between blood volume and total body water i.e., between 6 to 42 litres. Drugs which bind selectively to Extra vascular Tissues e.g., Chloroquine have Apparent volume of distribution larger than their Real volume of distribution. The Vd of such drugs is always greater than 42 litres.

BIOTRANSFORMATION OF DRUGS

On entering the body, drugs are treated as if they are toxic substances, which need to be detoxified, if a mechanism exists and eliminated as soon as possible. This means that most drugs are subjected to some kind of metabolism and then excreted. Metabolism involves changes to the molecular structure of a substance and these changes are produced by the action of enzymes. This has two important effects on drug molecules:

1. The drug is made more water soluble and therefore more easily excreted by the kidneys.

2. The metabolites are usually less pharmacologically active than the parent drug This is not always the case. A drug metabolite may have a new and completely different pharmacological activity, or it may be as active as or more active than the original drug.

Prodrugs are drugs that have been designed to remain inactive until they have been metabolized by the body.

Some drugs are almost completely inactivated by first pass metabolism in the liver other tissues where significant metabolism of drugs can occur include the intestinal mucosa, the lungs and plasma.

Metabolic Reactions

There are two general types of metabolic reactions, which are known as Phase I and Phase 2 reactions

Phase 1 Reactions

Phase I reactions involve the bio-transformation of a drug by one or more of the following reactions to a more water-soluble metabolite, which is more likely to be excreted by the kidney or go on to Phase

2. This may increase the toxicity of some drugs.

Oxidation: Oxidation is the most important and commonest type of metabolic reaction, which involves the addition of oxygen to the drug molecule. In the liver, oxidation reactions are catalysed by a group of enzymes known as the microsomal mixed function oxidase system or the cytochrome P450 enzyme family. e.g., Barbiturates, phenothiazines, imipramine, ibuprofen, paracetamol, steroids, phenytoin, benzodiazepines, theophylline, and many other drugs are oxidized in this way.

Reduction: Reduction reactions involve the removal of oxygen or the addition of hydrogen to the drug molecule. Enzymes capable of catalysing reduction reactions are found in many body tissues, including the liver and in the intestinal bacteria. e.g. Drugs primarily reduced are chloralhydrate, chloramphenicol, halothane, warfarin.

Hydrolysis: Hydrolysis involves the splitting of a drug molecule by the addition of water. Enzymes capable of catalysing hydrolysis are found in many body tissues but particularly in the

small intestine. Examples are choline esters, procaine, lidocaine, procainamide, aspirin, carbamazepine-epoxide, pethidine, oxytocin.

Cyclization: This is formation of ring structure from a straight chain compound, eg, proguanil. Decyclization: This is opening up of ring structure of the cyclic drug molecule, eg barbiturates, phenytoin. This is generally a minor pathway.

Phase 2 Reactions

Phase 2 reactions make drugs or Phase I metabolites into more hydrophilic, less toxic substances by conjugation with endogenous compounds in the liver.

Glucuronide conjugation: This is the most important synthetic reaction carried out by a group of UDP-glucuronosyl transferases (UGTS). Examples are chloramphenicol, aspirin, paracetamol, lorazepam, morphine, metronidazole. Not only but endogenous substrates like bilirubin, steroidal hormones and thyroxine utilize this pathway.

Acetylation: Compounds having amino or hydrazine residues are conjugated with the help of acetyl coenzyme-A, e.g., sulfonamides, isoniazid, PAS, hydralazine, clonazepam, procainamide.

Methylation: The amines and phenols can be methylated; methionine and cysteine acting as methyl donors, e.g., adrenaline, histamine, nicotinic acid, methyldopa, captopril, mercaptopurine

Sulfate conjugation: The phenolic compounds and steroids are sulphated by sulfotransferases (SULTS), eg. chloramphenicol, methyldopa, adrenal and sex steroids.

Glycine conjugation: Salicylates and other drugs having carboxylic acid group as conjugated with glycine, but this is not a major pathway of metabolism.

Glutathione conjugation: Forming a mercapturate is normally a minor pathway. However, it serves to inactivate highly reactive quinone or epoxide intermediates formed during metabolism of certain drugs, e.g. paracetamol.

Microsomal enzymes: These are located on smooth endoplasmic reticulum (a system of microtubules inside the cell), primarily in liver, also in kidney, intestinal mucosa, and lungs. The monooxygenases, cytochrome P-450, glucuronyl transferase, etc. are microsomal enzymes. They catalyse most of the oxidations, reductions, hydrolysis, and glucuronide conjugation.

Non-microsomal enzymes: These are present in the cytoplasm and mitochondria of hepaticcells as well as in other tissues including plasma. The flavoprotein oxidases, esterases, amidases and conjugases are non-microsomal. Reactions catalysed are Some oxidations and reduction, many hydrolytic reactions, and all conjugations except glucuronidation.

Microsomal Enzyme Inhibition: One drug can competitively inhibit the metabolism of another if it utilizes the same enzyme or co-factors. However, such interactions are not as common as one would expect, because often different drugs are substrates for different cytochrome P-450 isoenzymes.

Microsomal Enzyme Induction: Many drugs, insecticides and carcinogens interact with DNA and increase the synthesis of microsomal enzyme protein, specially cytochrome P-450 and glucuronyl transferase. As a result, rate of metabolism of inducing drug itself and/or other drugs is increased.

First Pass (Pre-systemic) Metabolism: This refers to metabolism of a drug during its passage from the site of absorption into the systemic circulation. All orally administered drugs are exposed to drug metabolizing enzymes in the intestinal wall and liver (where they first reach through the portal vein).

Ques.3 Write in detailed about factors modifying drug action.

Ans- FACTORS MODIFYING DRUG ACTION

Variation in response to the same dose of a drug between patient on different occasions is a rule rather than exception. The factors modify drug action either:

(a) Quantitatively: The plasma concentration and/or the action of the drug is increased or decreased. Most of the factors introduce this type of change and can be dealt with by adjustment of drug dosage.

(b) Qualitatively: The type of response is altered. drug allergy or idiosyncrasy. This is less common but often precludes further use of that drug in the affected patient. Various factors are discussed below

1. Body Size: It influences the concentration of the drug attained at the site of action. The average adult dose refers to individuals of medium built. For exceptionally obese or lean individuals and for children dose may be calculated based on body weight (BW) or body surface area (BSA)

Individual dose BW (kg) 70x average adult dose

Individual dose = BSA(m^2) V1.7x average adult dose

The BSA of an individual can be calculated from Dubois formula:

$$BSA(m^2) = BW\ (kg)^{0.425} \times Height\ (cm)^{0.725} \times 0.007184$$

1. **Age:** The dose of a drug for children is often calculated from the adult dose;
   Child dose = [Age/(Age +12)] x adult dose (Young's formula)
   Child dose = Age/20 x adult dose (Dilling's formula)

Note: Infants & children are not small adults thus show physiological differences like

- Low g.fr and tubular transport-Gentamicin and Penicillin
- Low hepatic drug metabolizing systems in new born - gray baby syndrome
- Blood brain barrier (BBB) is more permeable – Kernicterus
- Faster transdermal absorption and faster rectal absorption - Diazepam After one-year faster metabolism than adults-phenytoin, carbamazepine

2. Sex:

- Females have smaller body size - required doses are lower
- Digoxin in Maintenance therapy of heart failure-mortality higher in women
- Beta blockers, methyldopa, diuretics-sexual function interference in males
- Gynaecomastia - Metoclopramide, chlorpromazine etc. in males
- Ketoconazole causes loss of libido in men but not in women.
- Pregnancy-particularly 3rd trimester marked and progressive physiological changes occur which can alter drug disposition.
- In women consideration must also be given to menstruation, pregnancy and lactation.

4. Species and Race: Species variation in drugs responses do exist. Some strains of rabbits are resistant to atropine; Rats and mice are resistant to digitalis. Similarly, racial differences have also been observed. e.g. Blacks require higher doses of atropine and ephedrine, while Mongols require lower doses; in Africans beta blockers are less effective.

5. Genetics: All key determinants of drug response, viz. transporters, metabolizing enzymes, ion channels, receptors with their couplers and effectors are controlled genetically Pharmacogenetics is the use of genetic information to guide the choice of drug and dose on an individual basis. It intends to identify individuals who are either more likely or less likely respond to a drug. There are some specific genetic defects which lead to discontinuous variation in drug responses, e.g.

- Atypical pseudocholinesterase results in prolonged succinylcholine apnoea.
- G-6-PD deficiency is responsible for haemolysis with primaquine, sulphonamide, dapsone, quinine, nalidixic acid, nitrofurantoin and menadione, etc.
- The low activity CYP2C9 variants metabolize warfarin at a slow rate and are at higher risk of bleeding. → Polymorphism of N-acetyl transferase 2 gene results in rapid and slow acetylator status with Isoniazid.

6. Route of Administration: Route determines the speed and intensity of drug response i.e., parenteral for speedy action. A drug may have different actions via different routes e.g., magnesium sulphate given orally causes purgation, applied on sprained joints-decreases swelling, while intravenously it produces CNS depression and hypotension.

7. Environmental Factors:

- ❖ Drug metabolism may get induced exposure to insecticides, carcinogens, tobacco smoke and charcoal broiled meat etc.
- ❖ Food interferes absorption of some drugs while enhances some drugs ampicillin gets reduced griseofulvin gets enhanced
- ❖ Hypnotics taken at night.

8. Psychological Factors: Efficacy of a drug can affect patient's beliefs, attitudes and expectations particularly CNS drugs eg., a nervous and anxious patient requires more general anaesthetic. Placebo is an inert substance which is given in the garb of medicine & works by psycho dynamic effects (not pharmacodynamics) where sometimes responses are equivalent to active drugs. Uses of placebo is like a control device in clinical trials and to treat a patient, e.g., Lactose tablet/capsules or water injections etc. Noceboes are negative psychodynamic effects of drugs.

9. Pathological States: Not only drugs modify disease processes, several diseases can influence drug disposition and drug action:

(a) GIT: Coeliac diseases (amoxicillin absorption decreased while Cephalexin and cotrimoxazole increased). Achlorhydria (Reduced aspirin absorption); NSAIDs aggravate peptic ulcer.

(b) Liver diseases:

- ❖ Increased bioavailability of drugs with high first pass metabolism
- ❖ Serum albumin reduced-protein bound drugs like Warfarin-more-free drug
- ❖ Metabolism and elimination of drugs may be reduced thus doses should be reduced-Morphine, Propranolol, lignocaine etc.
- ❖ Prodrugs are less effective (becampicillin)

(c) Kidney diseases:

- ❖ Clearance of drugs in unchanged form (aminoglycosides, digoxin, phenobarbitone) reduced-dose should be reduced
- ❖ Plasma protein, albumin reduced-binding of acidic drugs affected

(d) Permeability of BBB increased: Opiates etc. more CNS depression

(e) Thyroid diseases: Hypothyroid states (sensitive to digoxin, morphine and CNS depressants), Hyperthyroid states (resistant to inotropic action-prone to cause arrhythmia by digoxin).

10. Presence of other Drugs: Drugs can modify the response to each other by pharmacokinetic or pharmacodynamic interaction between them.

11. Cumulation: If Rate of administration > Rate of elimination, termed as cumulation. e.g. prolonged use of chloroquine causes retinal damage; Full loading dose of digoxin should not be given if patient has received it within the past week; A course of emetine should not be repeated within 6 weeks.

12. Tolerance: Requirement of higher dose of a drug to produce a given response.

- ❖ Natural: Species/individual inherently less sensitive - Rabbits to atropine and Blacks are tolerant to mydriatics.
- ❖ Acquired: Repeated use of a drug in an individual who was initially responsive become non-responsive (tolerant)- CNS depressants.

Tolerance may develop to one action of the drug but not to other action - Chlorpromazine. phenobarbitone, Morphine Cross tolerance is tolerance to pharmacologically related drugs like alcoholics to barbiturates and GA.

Tolerance Mechanism

- **Pharmacokinetic/drug disposition tolerance:** effective concentration of the drug at the site of action is decreased due to enhancement of elimination on chronic use - Barbiturates and Carbamazepine induce own metabolism.
- Pharmacodynamic tolerance: cells of target organs become less responsive – Morphine Barbiturates, Nitrates etc due to down regulation/desensitization of receptors

Tachyphylaxis (Tachy-fast' phylaxis-protection) Rapid development of tolerance when a drag is repeated in quick succession leads to reduction of responses. Usually occurs with indirectly acting drugs -- Ephedrine, tyramine, nicotine etc.

Ques.4 Explain in detail about adrenergic drugs.

Ans- ADRENERGIC DRUGS

Drugs that partially or completely mimic the actions of norepinephrine (NE) or epinephrine (E); also called catecholamines. Norepinephrine is released by sympathetic nerves upon nerve stimulation, while epinephrine is released by the adrenal medulla in response to a variety of stimuli such as stress. Biosynthesis of norepinephrine is as follows:

Adrenergic receptors are membrane bound G-protein coupled receptors classified as $\alpha(\alpha_1, \alpha_2)$ and $(\beta_1, \beta_2, \beta_3)$. Differences between α and β adrenergic receptors is as follows:

	α	β
1.Rnak order of potency of agonists	Adr > NA > Iso	Iso > Adn > NA
2.Antagonist	Phenoxybenzamine	Propranolol
3.Effector pathway	IP3/DAG↑, cAMP↓ K^+ channel	cAMP ↑, Ca^{2+} channel ↑

This classification was confirmed later by the discovery of selective α and β adrenergic antagonists. Important features of α and β receptors are given in table below:

	β_1	β_2	β_3
1.Location	Heat, JG cells in kidney	Bronchi, blood vessels uterus, liver, g.i.t., urinary tract, eye	Adipose tissue
2.Selective agonist	Dobutamine	Salbutamol, Terbutaline	BRL 37344
3.Selective antagonist	Metoprolol, Atenolol	ICI 118551 α-methyl propranolol	CGP 20712A (also β_1) ICI 118551 (also β_2)
4.Potency of NA as agonist	Moderate	Weak	Strong

	α_1	α_2
1.Location	Post junction on effector	Prejunctional on nerve ending (α_{2A}), also

	organs	post junctional in brain, pancreatice α cells and extra-junctional in certain blood vessels, platelets
2.Function sub-served	GU smooth muscle-contraction Vasoconstriction Gland-secretion Gut-relaxation Liver-glycogenolysis Heat-arrhythmia	Vasoconstriction Decreased central sympathetic flow Decreased insulin release Platelet aggregation Inhibition of transmitter release
3.Selective agonist	Phenylephrine, Methoxamine	Clonidine
4.Selective antagonist	Prazosin	Yohimbine, Rauwolscine

Classification is based on mechanism of action:

1. Direct-acting agonists e.g., epinephrine, norepinephrine

2. Indirect-acting agonists e.g., amphetamine, Cocaine

3. Mixed-action agonists e.g., Ephedrine, pseudo ephedrine

Direct-Acting Agonists

Epinephrine interacts with both α and β receptors. At low doses – β_2 effects (vasodilation) on the vascular system predominates and at high doses α_1 effects (vasoconstriction) are strongest.

Pharmacological Actions

1.Cardiovascular: Strengthens the contractility of the myocardium (positive inotropic: β_1 action) and increases its rate of contraction (positive chronotropic: β_1 action). Activates β_1 receptors on the kidney to cause renin release. Constricts arterioles in the skin, mucous membranes and viscera (α_1 effects), and it dilates vessels going to the liver and skeletal muscle (β_2 effects) Cumulative effect is an increase in systolic blood pressure & slight decrease in diastolic pressure Direct acting adrenergic agonist.

Dale's vasomotor reversal: Intravenous injection of adrenaline normally causes increase it blood pressure (α_1 effect) followed by prolonged fall (β_2 effect). If it is administered after giving a blockers, only fall in blood pressure is seen.

2. Respiratory: Powerful bronchodilation by acting directly on bronchial smooth muscle (β_2 action)

3. Hyperglycaemia: Significant hyperglycaemic effect because of increased glycogenolysis in the liver (β_2 effect), increased release of glucagon (β_2 effect), and decreased release of insulin (α_2 effect).

4. Lipolysis: Agonist activity on the β_3 receptors of adipose tissue.

Pharmacokinetics

Epinephrine has rapid onset; brief duration of action (due to rapid degradation). Oral administration is ineffective, because epinephrine and the other catecholamines are inactivated by intestinal enzymes. Only the metabolites are excreted in urine.

Therapeutic Uses

Anaphylactic shock, Bronchospasm; Cardiac arrest, greatly increase the duration of the local anaesthesia; To control epistaxis.

Adverse effects

- CNS disturbances anxiety, fear, tension, headache, and tremor.
- Haemorrhage cerebral haemorrhage, marked elevation of blood pressure.
- Cardiac arrhythmias trigger cardiac arrhythmias (in patients receiving digoxin).
- Pulmonary oedema can induce pulmonary oedema.
- Hyperthyroidism Increased production/up regulation of a receptors on the vasculature & β receptors in heart of the hyperthyroid individual; leading hypersensitive response.
- Diabetes Epinephrine increases the release of endogenous stores of glucose.

Nor Epinephrine/Nor Adrenaline

Agonist at α_1, α_2 and β_1 receptor with similar potency as epinephrine, but has relatively little effect on β_2 receptors. Increases peripheral resistance α_1 and both diastolic and systolic blood pressure β_1 Compensatory baroreflex activation tends to overcome the direct positive chronotropic effects of norepinephrine; however, the positive inotropic effects on the heart are maintained.

Therapeutic uses: carefully used to treat cardiogenic shock but dopamine is preferred as nor epinephrine is associated with renal shutdown.

Adverse effects: Excessive doses can cause severe hypertension. Not suitable for s.c... m. or undiluted i.v. injection danger of necrosis.

Dopamine

Immediate precursor of norepinephrine & epinephrine, have more important effects in regulating sodium excretion and renal function. Features distinguishing from norepinephrine & epinephrine

- 2-5 μg/kg/min-D, receptors- renal vasodilation
- 5-10 μg/kg/min-β_1 receptors - ↑ cardiac output
- >10 µg/kg/min-α_1 receptors-vasoconstriction

Its deficiency in the basal ganglia leads to Parkinson's disease, which is treated with its precursor levodopa Dopamine antagonists are antipsychotic drugs. Used in conditions with low cardiac output with compromised renal function.

Isoproterenol/isoprenaline

Very potent β_1 & β_2 receptor agonist and has negligible effect on a receptor. Positive chronotropic and inotropic actions (β_1). Activates β receptors almost exclusively, it is a potent vasodilator. These actions lead to marked increase in cardiac output and fall in diastolic and mean arterial pressure and lesser decrease or a slight increase in systolic pressure. Used in complete heart block to maintain sufficient idioventricular rate till external pacemaker can be implanted.

Dobutamine

It resembles dopamine, but its actions are mediated by activation of α and β receptors; racemic mixture of (levo) and (dextro) isomers. The dextro isomer is a potent β_1 agonist and an α_1 receptor antagonist. The levo isomer is a potent α_1 agonist. The resultant effects of dobutamine are α_1 stimulation. Dobutamine has a positive inotropic action caused by the isomer with predominantly α_1 receptor activity. It has relatively greater inotropic than chronotropic effect compared with isoproterenol. Used for patients of heart failure associated with myocardial infarction, cardiac surgery & for short term management of acute congestive heart failure.

Non Catecholamines-α_1 Agonist Drugs

Phenylephrine: Selective α_1 agonist. Not a catechol derivative - not inactivated by COMT and has a longer duration of action than the catecholamines. It is an effective mydriatic and nasal decongestant.

Methoxamine: A direct-acting α_1 receptor agonist. Causes a prolonged increase in BP due to vasoconstriction & a vagally mediated bradycardia. Clinical uses are rare and limited to hypotensive states.

Naphazoline & xylometazoline: Nasal decongestants in rhinorrhoea & to check epistaxis.

Oxymetazoline: Direct-acting α_1 agonist. Used as topical decongestants because of promoting constriction of the nasal mucosa; may cause hypotension, presumably because of a central clonidine -like effect.

Midodrine: A prodrug that is enzymatically hydrolysed to desglymidodrine, a selective α_1 receptor agonist Primary indication for midodrine is the treatment of orthostatic hypotension, due to impaired autonomic nervous system function.

Clonidine: Stimulates α_{2A} receptors at vasomotor centre, central sympathetic outflow reduced leads to in BP & HR Activates α_{2B} receptors present on sympathetic post ganglionic neurons α_2 agonists.

Therapeutic uses: Moderate hypertension. To control diarrhoea in diabetic patients with autonomic neuropathy, In prophylaxis of migraine, Menopausal hot flushes, Clonidine, methyldopa, guanficine are useful in the treatment of hypertension.

Adverse effects: Rebound hypertension (sudden removal of central sympathetic inhibition results in release of large quantities of stored catecholamines & due to super sensitivity of newly formed α_2 receptors); Dry mouth, Sedation.

β_2 Selective Agents

Salbutamol, terbutaline: Selective β_2 agonist smooth muscle relaxation of bronchi & uterus; Important in the treatment of asthma.

Salmeterol & formoterol: Selective β_2 agonist- longer duration of action (12 hrs); Formoterol has quicker onset of action while salmeterol has slow onset of action & used to prevent attacks of nocturnal asthma prophylaxis of exercise induced bronchospasm & COPD.

Ritodrine may cause uterine relaxation in premature labour.

BRL-37344 & AD-9677: β_2 receptors might prove potential target for new anti-obesity drugs. Main problem is they are short lived with transient action.

Indirect-Acting Sympathomimetics

First, they may enter the sympathetic nerve ending and displace stored catecholamine transmitter. Such drugs have been called amphetamine-like or displacers. Second, they may inhibit the reuptake of released transmitter by interfering with the action of the NE transporter, NET.

Amphetamine

Readily enters the CNS, where it has marked stimulant effects on mood and alertness and a depressant effect on appetite. Its D-isomer is more potent than the L-isomer. Amphetamine's actions are mediated through the release of NE and, to some extent, dopamine. Performance of simple mental tasks improved but number of errors increased due to over confidence. Drug of abuse & is capable of psychological

dependence but little or no physical dependence. Therapeutically used for narcolepsy and attention deficit hyperactive disorder.

Tyramine

High concentrations in some fermented foods like cheese. Readily metabolized by MAO in the liver and is normally inactive when taken orally because of a very high first-pass effect. If administered parenterally, it has an indirect sympathomimetic action caused by the release of stored techolamines. In patients treated with MAO inhibitors, tyramine may cause marked increases in blood pressure cheese reaction).

Mixed-Acting Sympathomimetics

Ephedrine: Ephedrine is a non-catechol; it has high bioavailability and a relatively long duration. It releases NE and activates β_2 receptors directly Crosses BBB and a powerful stimulant used to treat hypotension with spinal anaesthesia.

Picudoephedrine: Available over the counter is a component of many decongestant mixtures.

Phenylpropanolamine: A common component in over-the-counter appetite suppressants; removed from the market because associated with haemorrhagic strokes in young women.

Anorectic agents (Fenfluramine & dexfenfluramine): Reduce food seeking behaviour by enhancing serotonergic transmission in hypothalamus. Tolerance to anorectic action develops in 2 to 3 months.

Therapeutic Uses of Sympathomimetics

1. Treatment of Acute Hypotension in hypotensive emergency to preserve cerebral and coronary blood flow (NE, phenylephrine, and methoxamine have been used)

2. Cardiogenic shock and acute heart failure usually due to massive myocardial infarction (dopamine or dobutamine); Chronic Orthostatic Hypotension (Midodrine: orally active α_1, agonist).

3. Isoproterenol and epinephrine have been used in the temporary emergency management of **complete heart block and cardiac arrest.**

4. Dobutamine injection is used as pharmacologic **cardiac stress test.**

5. Bronchial asthma (β_2 -selective agents: Salbutamol, bambuterol, metaproterenol, terbutaline)

6. Anaphylaxis: Parenteral administration of epinephrine (β_1 increases cardiac output; β_2 relaxes constricted bronchioles and α_1, constricts capillaries).

7. Ophthalmic Applications: Phenylephrine is an effective mydriatic agent used to facilitate examination of the retina. Apraclonidine & brimonidine α_2 selective agonist lower intraocular pressure in glaucoma.

8. Genitourinary: Ritodrine, terbutaline (β_2 selective) and similar drugs have been used to suppress premature labor, Ephedrine or pseudoephedrine may be tried occasionally in the treatment of stress incontinence (loss of small amounts of urine associated with coughing. laughing, sneezing, exercising or other movements that increase intra-abdominal pressure and thus increase pressure on the bladder).

9. Treatment of narcolepsy: Modafinil with fewer disadvantages than amphetamine (excessive mood changes, insomnia, and abuse potential) is used.

10. Attention-deficit hyperactivity disorder (ADHD): Low doses of methylphenidate or clonidine. Modafinil may also be useful in ADHD.

Ques.5 Discuss anti-adrenergic drugs in detail.

Ans- ANTI-ADRENERGIC DRUGS

Drugs which antagonize the receptor action of Adrenaline and other related drugs at the receptor level (α and β) but do not produce signal transduction Le affinity is there but without intrinsic activity non-selective α-antagonists have been used in the treatment of pheochromocytoma (tumors that secrete catecholamines), and alpha-1 selective antagonists are used in primary hypertension and benign prostatic hyperplasia (BHP). β-receptor antagonists are used for hypertension, ischemic heart disease, arrhythmias, endocrinologic and neurologic disorders and many other conditions Blockade of peripheral dopamine receptors is of no recognized clinical importance but blockade of central dopamine receptors is utilized as antiemetic, antipsychotic and TCAs.

CLASSIFICATION

1. non-equilibrium type:

1. β- **halo alkylamines:** Phenoxybenzamine

II. Equilibrium:

1. non-selective:

(a) Ergot Ergotamine and Ergotoxine

(b) Hydrogenated ergot alkaloids: DHE. Dihydroergotoxine

(c) Imidazolines Tolazoline, Phentolamine

(d) Miscellaneous: Chlorpromazine, Histamine and Serotonin

2. Selective α_1: Prazosin, Terazosin, Doxazosin and Tamsulosin

3. Selective α_2: Yohimbine

General Effects of alpha Blockade

1 **CVS**: Blockade of α, (also α_1) receptor causes pooling of blood in capacitance vessels, reduced venous return and Cardiac output leads to fall in mean BP Postural Reflex is interfered causing dizziness and syncope on standing.

2. **Reflex tachycardia** due to fall in BP and increased NA release due to presynaptic blockade.

3. Nasal stuffiness and Miosis.

4. Increased Intestinal Motility-diarrhoea

5. **Reduced GFR**: Sodium retention and increase in blood volume; also, reflex renin release

6. Tone of the Bladder trigone, sphincter and prostate is maintained by α_1 A sympathetic blockade produces increased urine flow.

7. Inhibition of Ejaculation due to inhibition of contraction of vas deferens and others.

Phenoxybenzamine

Non-specific, long-acting irreversible alpha antagonist. Spontaneously cyclizes in the body to give ethylenimine intermediate - forms a strong covalent bond with a receptor i.e., blockade of alpha receptor (lasts for 3-4 days). Also blockade of 5-HT, histaminergic and cholinergic receptors clinically cause postural hypotension; blood flow to many organs increased due to reduction in peripheral resistance and increased venous return; CNS stimulation (nausea, vomiting on i.v. injection but oral doses cause depression, tiredness, and lethargy).

Erratic oral absorption and painful on IM or SC injections; excretes in urine in 24 Hrs leading to accumulation in adipose tissue. Used for Pheochromocytoma, Secondary shock and Peripheral vascular disease (Raynaud's disease). ADRs are postural hypotension, nasal stuffiness, miosis and inhibition of ejaculation.

Phentolamine: Non-specific, short acting reversible alpha antagonist at both 1 and 2 receptors: cardiac stimulation due to enhanced NA release (alpha-2 blockade) & inhibits serotonin release (muscarinic agonist). Uses are in pheochromocytoma, clonidine withdrawal, cheese reaction and in extravasations of NA and Adr injection.

Prazosin: Highly selective alpha-1 blocker (1 1000); Non-specific blockade of all subtypes α_{1A} ,

α_{1B} and α_{1D} blockade of sympathetic vasoconstriction causes fall in BP Effective orally (70%), metabolized in liver Used for Hypertension, Raynaud's disease.

Uses of α Blockers

1 Pheochromocytoma: Tumor of medullary cells of adrenals; VMA and normetanephrine estimation is diagnostic.

2. Hypertension: Not useful except Prazosin due to (compensated cardiac stimulation, postural

hypotension, impotence, nasal blockage etc.)

3. BHP (Benign prostatic hyperplasia): Effects of α blocking causes relaxation of neck and prostate structures; reduction in obstruction. 5-α reductase inhibitors like Finasteride decreases size of the prostate, thus, better voiding.

1 Secondary Shock-Phenoxybenzamine

2. Peripheral vascular disease-beneficial in Raynaud's disease

3. Congestive Heart Failure

4. Short term Papaverine /Phentolamine induced penile erection (PIPE) for impotence

β-Adrenergic Blockers Classification

1. Cardio selective: Metoprolol, atenolol, acebutolol, bisoprolol, esmolol, nebivolol

2. non-selective (β_1 and β_2):

(a) Without intrinsic sympathomimetic activity: Propranolol, Sotalol and Timolol

(b) With intrinsic sympathomimetic activity (ISA): Pindolol and Oxprenolol

(c) Additional alpha blocking property: Labetalol and Carvedilol

PROPRANOLOL

Pharmacological Actions

1. Heart: Decrease in Heart rate, decrease in cardiac output, decrease in force of contraction; cardiac work and oxygen consumption is reduced; at high doses membrane stabilizing and direct depressant action.

2. Blood Pressure: It blocks catecholamines induced vasodilation and cause increase in TPR and decrease in cardiac output- but negligible change in blood pressure.

3. Respiratory: Bronchoconstriction due to blockade of dilator beta-2 receptors thus beta-1 selective drugs are preferred.

4. Eye: Decreases IOP by reducing production of aqueous humor (glaucoma)

5. CNS: Behavioural, forgetfulness and nightmare etc. and suppresses anxiety

6. Skeletal Muscle: Reduction of Tremor, Reduction of exercise capacity: reduction in blood flow, glycogenolysis and lipolysis.

7. Metabolic:

- Lipid: Inhibits sympathetic stimulation of lipolysis and consequent increase in free fatty acid level-triglyceride level increased.
- Carbohydrate: Inhibition of glycogenolysis in heart, muscle and liver- β_2 mediated (recovery from its action delayed & warning signs are masked): β_1, selective are much safer.

Pharmacokinetics

Most drugs are well absorbed after oral administration; propranolol undergoes extensive hepatic (fine-pass) metabolism dependent on hepatic blood flow, higher bioavailability if taken with food.

ADRS: Precipitation of CCF Oedema, bradycardia; life threatening asthma; risk of coronary heart disease, tiredness and reduced exercise capacity, cold bands and feet, withdrawal effects.

OTHER β BLOCKERS

i. Cardioselectivity: More selective in blocking β_1 receptor than β_2

Advantages: Lower propensity to cause bronchoconstriction lesser interference with carbohydrate metabolism - safer in diabetics: lower incidence of cold hand and feet-no/less β_2 block; lesser suppression of essential tremor, lesser impairment of exercise capacity

II. Intrinsic sympathomimetic activity: Pindolol, cicloprolol

Advantages: (Partial agonist action) Lesser bradycardia and depression of contractility thus preferred in elderly, sick sinus syndrome etc. withdrawal, less/no interference with lipid profile

iii. Membrane stabilizing effect: Lidocaine, local anaesthetic action; typically blocks Na^+ channel (antiarrhythmic action).

iv. Lipid insolubility: Atenolol, cicloprolol, bisoprolol etc. Less likely to produce sleep disturbances, longer acting as incompletely absorbed, no first pass metabolism, excreted unchanged in urine.

Metoprolol: Prototype of cardio-selective blockers Le β_1, selective (also inverse agonist), safer patients with bronchoconstriction and preferred in patients with insulin; less first pass metabolism. Used indiabetics and patients in OHs

Atencial: Selective β_1 and low lipid solubility, longer duration of action with once daily dong, no lipid profile adverse effects - Hypertension and angina.

Partial beta-agonist: Pindolol, acebutalol, celiprolol, carteolol, bopindolol, oxprenolol, and pesbutolol. They show major CVS applications i.e., less plasma lipid action and bradycardia. Also have intrinsic sympathomimetic activity. However, doubtful clinical benefit.

Esmolol: Partial agonist and MSA; Ultra short acting (less than 10 minutes) & inactivated by esterases in blood

Cellprolol: Selective beta-1 with additional beta-2 agonistic activity, Safe in asthmatics; Causes vasodilation by NO production (NA receptor mediated) - additional benefit as antihypertensive.

Nebivolol: Highly selective beta-1 blocker, Acts as NO donor Le improves endothelial function and delay of atherosclerosis; no deleterious effects on carbohydrate, lipid metabolism.

Uses of Beta Blockers

- Hypertension: 1st line of agent
- Angina pectoris - not in vasospastic
- Myocardial infarction Prevent reinfarction, ventricular fibrillation & reduces infarct size.
- Cardiac arrhythmias: Class II type of agent – Propranolol
- Congestive Heart failure
- Pheochromocytoma
- Hyperthyroidism: T4-T3+ sympathetic symptoms + Migraine Anxiety: social phobia
- Essential Tremor
- Glaucoma

$\alpha + \beta$ BLOCKERS

Labetalol: Alpha + beta blocker ($\alpha_1 + \beta_1 + \beta_2$ block + β_2 agonistic); Moderately potent and used in Pheochromocytoma and clonidine withdrawal.

Carvedilol: $\beta_1 + \beta_2$ and $\alpha_1$blocker and Ca^+ channel blocker, Used in Hypertension and especially preferred in CHF as cardioprotective.

Ques.6 Explain drugs acting on the eye.

Ans- MIOTICS AND MYDRIATICS

IN GLAUCOMA

Miotics increase the tone of ciliary muscle (attached to scleral spur) and sphincter pupillae which pull on and somehow improve alignment of the trabeculae so that outflow facility is increased, Lot falls in open angle glaucoma. Pilocarpine is the preferred miotic. The action is rapid and short lasting (4-6 hr), 6-8 hourly instillation is required and even then i.o.t. may fluctuate in-between. Diminution of vision, especially in dim light (due to constricted pupil), spasm of accommodation and brow pain are frequent side effects. Systemic effects-nausea, diarrhoea, sweating and bronchospasm may occur with higher concentration eye drops.

(a) Pilocarpine (along with other drugs) is used in angle closure glaucoma as well.

(b) To reverse the effect of mydriatics after refraction testing.

(c) To prevent formation of adhesions between iris and lens or iris and cornea, and even to break those which have formed due to iritis, corneal ulcer, etc. a miotic is alternated with a mydriatic

3.2 DRUGS USED IN GLAUCOMA

Glaucoma is a group of diseases characterized by a progressive form of optic nerve damage, associated with raised (>21 mmHg) intraocular tension (i.o.t.). The chief therapeutic measure is to lower Lot to target level, either by reducing secretion of aqueous humor or by promoting its drainage. Major amount of aqueous (~90%) drains through the trabecular route, while ~10% fluid passes into the connective tissues paces within the ciliary muscle-then via supra-choroid into spieleral vessels (uveoscleral outflow). Illustration of aqueous humor dynamics and the sites of action of ocular hypotensive drugs is given below in the figure:

1. Miotics in angle closure glaucoma

2. Miotics in open angle glaucoma

3. β blockers; α_1 agonist;α_2 agonists, carbonic anhydrase inhibitors

4. Prostaglandins and possibly adrenaline

5. Adrenaline

A. OPEN ANGLE (WIDE ANGLE, CHRONIC SIMPLE) GLAUCOMA

It is probably a genetically predisposed degenerative disease affecting patency of the trabecular mesh work which is gradually lost past middle age. The i.o.t. rises insidiously and progressively. Ocular hypotensive drugs are used on a long-term basis and constitute the definitive treatment in majority of cases.

1. **β Adrenergic blockers:** Timolol, Betaxolol, Levobunolol, Carteolol and Metipranolol Topical β blockers are one of the first line drugs, but PGF2α analogues are increasingly used now. In contrast to miotics, the β blockers do not affect pupil size, tone of ciliary muscle or outflow facility, but lower i.o.t. by reducing aqueous formation. This probably results from down regulation of adenylyl cyclase due to β_2 receptor blockade in the ciliary epithelium and a secondary effect due to reduction in ocular blood flow. They are as effective as miotics and produce less ocular side effects.

2. α Adrenergic agonists: Adrenaline, Dipivefrine, Apraclonidine, Brimonidine. The i.o.t. reduction is due to increased uveoscleral outflow and β_2 receptor mediated increased hydraulic conductivity of trabecular filtering cells. Reduction in aqueous formation can result from α_2 and α_1 receptor activation in ciliary body. Adrenaline frequently produces ocular smarting and vasoconstriction followed by reactive hyperaemia. It is not used now because of ocular intolerance and possible systemic effects.

3. Prostaglandin analogues: Latanoprost Low concentration of PGF2α was found to lower i.o.t. without inducing ocular inflammation. It acts by increasing uveoscleral outflow, possibly by increasing permeability of tissues in ciliary muscle or by an action on episcleral vessels. An effect on trabecular outflow is also possible. Ciliary body COX-2 is down regulated in wide angle glaucoma indicating a physiological role of PG in aqueous humor dynamics,

4. Carbonic anhydrase inhibitors: Acetazolamide, Dorzolamide.

It reduces aqueous formation by limiting generation of bicarbonate ion in the ciliary epithelium. It is used to supplement ocular hypotensive drugs for short term indications like angle closure, before and after

ocular surgery/laser therapy Systemic side effects-paraesthesia, anorexia, hypokalaemia, acidosis, malaise and depression restrict long term use to few cases in which target i.o.t. is not achieved even by concurrent use of 2-3 topical drugs.

5. Miotics: Topical pilocarpine and/ or anti ChE.

Because of several drawbacks, they are now used only as the last option. In open angle glaucoma, they lower Lot by increasing ciliary muscle tone thereby improving patency of trabeculae.

B. ANGLE CLOSURE (NARROW ANGLE, ACUTE CONGESTIVE) GLAUCOMA

It occurs in individuals with a narrow iridocorneal angle and shallow anterior chamber. The i.o.t remains normal until an attack is precipitated, usually by mydriasis. The i.o.t. rises rapidly to very high values (40-60 mmHg). It is an emergent condition; failure to lower i.o.t. quickly may result in loss of sight. Vigorous therapy employing various measures to reduce i.o.t. is instituted.

1. Hypertonic mannitol (20%) 1.5-2 g/kg or glycerol (10%): infused i.v. decongests the eye by osmotic action. A retention enema of 50% glycerine is also sometimes used.

2. Acetazolamide: 0.5 g i.v. followed by oral twice daily is started concurrently.

3. Miotic: Once the i.o.t. starts falling due to the above i.v. therapy, pilocarpine 1-4% is instilled every 10 min initially and then at longer intervals. Contraction of sphincter pupillac changes the direction of forces in the iris to lessen its contact with the lens and spreads the iris mass centrally causes pupillary block is removed and iridocorneal angle is freed.

4. Topical β blocker: Timolol 0.5% is instilled 12 hours in addition.

5. Apraclonidine (1%)/latanoprost 0.005% instillation may be added. Drugs are used only to terminate the attack of angle closure glaucoma. Definitive treatment is surgical or laser iridotomy. Few cases, who have chronic narrow angle glaucoma, may be treated with a miotic/other ocular hypotensive drug for long periods, but often surgery /laser therapy is ultimately required.

Ques.7 Write in detailed about general anaesthetics.

Ans- GENERAL ANAESTHETICS

Assesiberia is a reversible condition of comfort and quiescence for a patient within the physiological limit before, during and after performance of a procedure.

General anaesthesia: for surgical procedure to render the patient unaware/unresponsive to the painful stimuli. Drugs producing General Anaesthesia are called General Anaesthetics.

Local anaesthesia: reversible inhibition of impulse generation and propagation in nerves. In sensory nerves, such an effect is desired when painful procedures must be performed, e.g., surgical or operations. Drugs producing Local Anaesthesia are called Local Anaesthetics e.g. Procaine, Lidocaine and Bupivacaine etc

General Anaesthetics are the drugs which produce reversible loss of all modalities of sensation and consciousness, or simply, a drug that brings about a reversible loss of consciousness.

Essential components of GA

- Loss of all modalities of sensations

- Sleep and Amnesia
- Immobility or Muscle relaxation
- Abolition of reflexes-somatic and autonomic

Anaesthesia event follows:

- **Induction:** It is the period which begins with the administration of an anaesthetic upto the development of Surgical anaesthesia. Done by inducing agents – Thiopentone sodium.
- **Maintenance:** Sustaining the state of anaesthesia. Done by Inhalation agents - Nitrous oxide and halogenated hydrocarbons.
- **Recovery:** Antiaesthetic stopped at the end of surgical procedure and consciousness regains An ideal anaesthetic possesses:

An ideal anaesthetic possesses:

- A smooth and rapid loss of consciousness
- A prompt recovery after its administration is discontinued
- A wide margin of safety and be administration is discontinued

Form observations of safety and be devoid of adverse effects of inhaled diethyl ether, anaesthetic effects on the brain can be divided into four stages :

I. Stage of analgesic: The patient initially experiences analgesia without amnesia. Later in stage I both analgesia and analgesia are produced.

II. Stage of excitement: The patient often appears to be delirious and may vocalize but is amnesic. Respiration is irregular both in volume and rate and retching and vomiting may occur.

III. Stage of surgical anaesthesia: This stage begins with the recurrence of regular respiration and extends to complete cessation of spontaneous respiration (apnoca). Four planes of stage III have been described in terms of changes in ocular movements, eye reflexes, and pupil size, which may represent signs of increasing depth of anaesthesia.

IV. Stage of medullary depression: This deep stage of anaesthesia includes severe depression of the CNS, including the vasomotor centre in the medulla, as well as the respiratory centre in the brain stem. Without circulatory and respiratory support, death rapidly happens.

CLASSIFICATION

1. Intravenous Anaesthetics

- Barbiturates (e.g., thiopental, methohexital)
- Benzodiazepines (e.g., midazolam, diazepam)
- Propofol
- Ketamine (Dissociative anaesthesia)
- Opioid analgesics: morphine, fentanyl (Neurolept analgesia), remifentanil
- Miscellaneous sedative-hypnotics (e.g., etomidate, dexmedetomidine)

2. Inhaled Anaesthetics: isoflurane, desflurane and sevoflurane, as well as nitrous oxide. These compounds are volatile liquids that are aerosolized in specialized vaporizer delivery systems.

3. Balanced Anaesthesia: modern anaesthesia typically involves a combination of intravenous (e.g. for induction of anaesthesia) and inhaled (e.g. for maintenance of anaesthesia) drugs. However, volatile

anaesthetics (e.g., sevoflurane) can also be used for induction of anaesthesia and intravenous anaesthetics (e.g. propofol) can be infused for maintenance of anaesthesia.

MECHANISM OF ACTION

I. Meyer-Overton rule: Lipid water partition coefficient- GA (gases) are highly lipid soluble and therefore can easily enter in neurones. After entry causes disturbances in physical chemistry of neuronal membranes fluidization. Finally, obliteration of Na^+ channel and refusal of depolarization.

II. For inhalation anaesthetics: MAC is defined as the minimum alveolar concentration that prevents movement in response to surgical stimulation in 50% of subjects. Correlates with oil/gas partition coefficient. For Intravenous agent's potency of i.v. agent is defined as the free plasma concentration (at equilibrium) that produces loss of response to surgical incision in 50% of subjects:

III. Modern theory:

1. To activate $GABA_A$ receptor-chloride channel

2. To activate glycine receptor

3. To inhibit NMDA channel receptor

4. To inhibit nicotinic acetylcholine receptor isoforms

Diethyl Ether: Colourless, highly volatile liquid with a pungent odour. Produces irritating vapours and are inflammable and explosive. 85 to 90 percent is eliminated through lung and remainder through skin, urine, milk and sweat & can cross the placental barrier

Advantages: Can be used without complicated apparatus; Potent anaesthetic and good analgesic; Muscle relaxation; Wide safety of margin; Respiratory stimulation and bronchodilation, does not sensitize the heart to adrenaline; No cardiac arrythmias; Can be used in delivery: Less likely hepatic or nephrotoxicity.

Disadvantages: Inflammable and explosive; Slow induction and unpleasant, Struggling, breath holding, salivation and secretions (drowning); Slow recovery; nausea & vomiting.

Enflurane: Non-inflammable, with mild sweet odour like halothane in action, except better muscular relaxation. Depresses myocardial force of contraction and sensitize heart to adrenaline; Induces seizure in deep anaesthesia and therefore not used now.

Isoflurane: Isomer of enflurane and have similar properties but slightly more potent.

Advantages: Rapid induction and recovery, good muscle relaxation, coronary, Less Myocardial depression; No renal or hepatotoxicity; low nausea and vomiting. No dilatation of pupil and no loss of light reflex in deep anaesthesia; no seizure and preferred in neurosurgery.

Disadvantages: Pungent and respiratory irritant, Maintenance only, no induction: Hypotension, Costly.

Intravenous Anaesthetics

Rapid induction (one arm-brain circulation time); supplemented with analgesic and muscle relaxants.

Thiopentone sodium: Ultra short acting Barbiturate, Water soluble, Alkaline & Dose-dependent suppression of CNS activity.

Pharmacokinetics: Redistribution (Blood Brain Muscle Body fat concentration of thiopentone Hepatic metabolism (elimination half-life 7-12 hrs); CNS depression persists for long (>12 hr)

Side effects: Laryngospasm (Atropine and succinylcholine), shivering and delirium during recovery, tissue necrosis-gangrene.

Advantages: Rapid induction - does not sensitize myocardium to adrenaline, no nausea and vomiting, non-explosive and non-irritant.

Disadvantages: Depth of anaesthesia difficult to judge Pharyngeal and laryngeal reflexes persists; Respiratory depression; Hypotension (rapid) - shock and hypovolemia; CVS collapse.

Propofol: Replacing thiopentone now for induction and maintenance. Rapid induction & distribution. Propofol is extensively metabolized & 88% of an administered dose appears in the urine.

Ketamine: (Phencyclidine derivative - Dissociative anaesthesia); a state characterized by immobility, amnesia and analgesia with light sleep and feeling of dissociation from one's own body and mind and the surroundings. Site of action is cortex and subcortical areas NMDA receptors.

Fentanyl: (Neurolept analgesia) supplement in Balanced anaesthesia in combination with diazepam used in diagnostic, endoscopic and angiographic procedures; adjunct to spinal and nerve block anaesthesia.

COMPLICATIONS OF ANAESTHESIA

During anaesthesia: Respiratory depression, Salivation, respiratory secretions, cardiac arrhythmias, Fall in BP. Aspiration, Laryngospasm and asphyxia, Delirium and convulsion, Fair and explosion

After anaesthesia: Nausea and vomiting. Persisting sedation, Pneumonia, liver, kidney damage. Nerve palsies, Emergence delirium, Cognitive defects

Preanesthetic Medication

It is the term applied to the use of drugs prior to the administration of an anaesthetic agent to make anaesthesia safer and more agreeable to the patient. Its aim is to:

- Relief of anxiety diazepam or lorazepam, midazolam, promethazine
- Amnesia for pre- and post-operative events: diazepam or lorazepam, midazolam promethazine
- Analgesia Morphine and its congeners
- Decrease secretions: Atropine
- Antiemetic effects: Metoclopramide, domperidone
- Decrease acidity and volume of gastric juice: ranitidine, famotidine

Ques.8 Discuss sedatives and hypnotics.

Ans- SEDATIVES AND HYPNOTICS

Sedatives: A drug that reduces excitement, calms the patient (without inducing sleep) Sedatives in therapeutic doses are anxiolytic agents; most sedatives in larger doses produce hypnosis (trans like state in which subject becomes passive and highly suggestible). Site of action is on the limbic system which regulates thought and mental function.

Hypnotics: A drug which produces sleep resembling natural sleep. They are used for initiation and or maintenance of sleep. Hypnotics in higher doses produce general anaesthesia. Site of action is on the midbrain and ascending RAS which maintain wakefulness.

CLASSIFICATION

PHARMACOLOGY

1. Benzodiazepines

(a) Short acting: Triazolam, Oxazepam, Midazolam

(b) Intermediate acting: Alprazolam, Estazolam, Temazepam, Lorazepam, Nitrazepam

(c) Long acting: Diazepam, Flurazepam, Clonazepam, Chlordiazepoxide

OR

(a) Hypnotic: Diazepam, Flurazepam, Nitrazepam, Alprazolam, Temazepam, Triazolam

(b) Antianxiety: Diazepam, Chlordiazepoxide, Oxazepam, Lorazepam, Alprazolam

(c) Anticonvulsant: Diazepam, Lorazepam, Clonazepam, Clobazam

II. Barbiturates

(a) Long Acting: Phenobarbiton

(b) Short Acting: Butobarbitone, Pentobarbitone

(c) Ultra-short Acting: Thiopentone, Methohexitume

III. Miscellaneous Agents

(a) Z. Drugs: Zolpidem, Zopiclone, Zalepion

(b) Melatonin receptor agonist: Ramelteon

(c) Others: Antidepressants, Antihistaminics

Mechanism of Action

Barbiturates/Benzodiazepines bind to $GABA_A$ receptor at different allosteric sites facilitating GABA action. Barbiturates increase duration & Benzodiazepines increase frequency of opening of a C1 channel which leads to membrane hyperpolarization and ultimately CNS depression.

Benzodiazepines: increase frequency of opening of C1 channels induced by GABA (GABA facilitatory action); also increase binding of GABA to $GABA_A$ receptor.

Barbiturates: increase duration of opening of CI channels induced by GABA (GABA facilitatory action). At high conc. it can directly increase C1 conductance through CI channels (GABA mimetic action); inhibit Ca dependent release of neurotransmitters; depress glutamate induced neuronal depolarization through AMPA receptor. At very high conc. (anaesthetic doses) it depresses voltage sensitive Na^+ & K^+ channels.

BARBITURATES

Pharmacokinetics: well absorbed after oral administration and distribute throughout the body (more lipid soluble= fast onset & short duration of action, rapid drop in blood level as drug is redistributed); metabolized in the liver, and inactive metabolites are excreted in urine.

Pharmacological Actions

- At low doses, produce sedation (have a calming effect and reduce excitement); higher doses cause hypnosis, followed by anaesthesia (loss of feeling or sensation), and, finally, coma and death.
- Barbiturates do not raise the pain threshold and have no analgesic properties

- Barbiturates suppress the hypoxic and chemoreceptor response to CO_2 and overdosage is followed by respiratory depression and death.
- Large dose causes circulatory collapse due to medullary vasomotor depression & direct vasodilation.

Therapeutic Uses

- Anaesthesia: The ultra-short-acting barbiturates, such as thiopental.
- Anticonvulsant: Phenobarbital (tonic-clonic seizures/refractory status epilepticus).
- Sedative hypnotise: Mild sedatives to relieve anxiety, nervous tension, and insomnia.
- Hyperbilirubinemia and kernicterus in the neonates (increase glucouronyl transferase activity).

Adverse effects: drowsiness, impaired concentration, and mental and physical sluggishness; drug "hangover" & chronic use results in development of tolerance. Abrupt withdrawal from barbiturates may cause tremors, anxiety, weakness, restlessness, nausea and vomiting, seizures, delirium, and cardiac depression. Death may also result from overdose.

Acute Barbiturate Poisoning: Mostly suicidal causing excessive CNS depression, flabby and comatose with shallow and failing respiration, CVS collapse, renal shut down, pulmonary complications

Treatment

- Gastric lavage (activated charcoal)
- Supportive patent airway, assisted respiration, oxygen, IV fluid and vasopressors like Dopamine
- Alkaline diuresis : Sodium bicarbonate I meq/kg IV with or without mannitol - for long acting one
- Haemodialysis: highly effective in long as well as short acting ones
- No specific antidote

BENZODIAZEPINES

Pharmacokinetics: Lipophilic, rapidly, and completely absorbed after oral administration; distribute throughout the body and penetrate into the CNS. Redistribution occurs from CNS to skeletal muscles & adipose tissue (termination of action). All benzodiazepines are metabolized in the liver-Phase I : (liver microsomal system)- Phase II: glucuronide conjugation and excreted in the urine.

Pharmacological Actions

- Reduction of anxiety- At low doses, the benzodiazepines are anxiolytic
- Sedative hypnotic - All have sedative and calming properties; some can produce hypnosis (artificially produced sleep) at higher doses.
- Anterograde amnesia - Temporary impairment of memory with use of the benzodiazepines.
- Anticonvulsant
- Dependence - Psychological and physical dependence can develop if high doses are given for a prolonged period. Abrupt discontinuation results in withdrawal symptoms- confusion, anxiety, agitation, restlessness, insomnia, tension and (rarely) seizures

Adverse Effects: Drowsiness and confusion; ataxia occurs at high doses, cognitive impairment.

Therapeutic Uses

- Anxiety disorders: The longer-acting agents, such as clonazepam, lorazepam, and diazepam, are often preferred in panic disorder, generalized anxiety disorder (GAD), social anxiety disorder,

performance anxiety, post-traumatic stress disorder, obsessive-compulsive disorder, and extreme anxiety associated with phobias and anxiety related to depression and schizophrenia.

- For panic disorders, alprazolam is effective for short and long-term treatment
- To control Alcohol withdrawal symptoms chlordiazepoxide, diazepam & oxazepam
- Sleep disorders
- Amnesia: Often employed as pre-medication for anxiety-provoking and unpleasant procedures, such as endoscopy, dental procedures, and angioplasty
- Seizures: Lorazepam and diazepam are the drugs of choice in terminating status epilepticus.
- Useful in the acute treatment of alcohol withdrawal and reduce the risk of withdrawal-related seizures.
- Muscular disorders: Diazepam for skeletal muscle spasms, spasticity from degenerative disorders such as multiple sclerosis and cerebral palsy.

Advantages of Benzodiazepines over Barbiturates

Benzodiazepines	**Barbiturates**
1. Less neuronal depression & high TI	More neuronal depression
2. No anesthesia even at high dose; patient can be aroused	Loss of consciousness & low margin of safety
3. No effect on respiration or cardiovascular functions at hypnotic dose	Cause respiratory and cardiac depression
4. No effect on REM sleep	++ suppression of REM sleep; Withdrawal rebound ↑ in sleep & hangover
5. Abuse liability very low	Tolerance & Dependence
6. No hyperalgesia	Hyperalgesia (↑ sensitivity to pain)
7. Amnesia without automatism	Amnesia with automatism; Loss of short-term memory
8. Not enzyme inducer - Less drug interactions	Potent enzyme inducers- More drug interactions
9. Specific antagonist - Flumazenil	No antagonist available

Flumazenil (Benzodiazepine antagonist): FDA approval selective competitive antagonist of BZD receptors (BZ-1); blocks action of Benzodiazepines and Z-drugs but not other sedative /hypnotics. Used in acute BZD toxicity (reversal of BZD sedation e.g., after endoscopy).

NON-BENZODIAZEPINES

Z-drugs: Zolpidem, Zaleplone, Zopiclone: Not structurally related to benzodiazepines, but selectively bind to the benzodiazepine receptor sub-type BZ, do not significantly alter the various sleep stages and hence, are often the preferred hypnotics. No anticonvulsant or muscle-relaxing properties. Shows few withdrawal effects, exhibits minimal rebound insomnia, and little tolerance occurs with prolonged use.

Ramelteon: Selective agonist at the MT_1 and MT_2 subtypes of melatonin receptors. Melatonin is a hormone secreted by the pineal gland that helps to maintain the circadian rhythm underlying the normal sleep wake cycle. Indicated for the treatment of insomnia characterized by difficulty falling sleep (increased sleep latency) Advantage is no effects on sleep architecture, no rebound insomnia or significant withdrawal symptoms, minimal potential for abuse.

PHARMACOLOGY

Short Answers

Ques.1 Write a short note on pharmacology.

Ans- **Pharmacology** (an amalgam of the Greek pharmakos, medicine or drug and logos, study) is a broad discipline describing the use of chemicals to treat and cure disease. Pharmacology as a science encompasses the following

- the action of natural chemicals in the body,
- the origins and sources of drugs;
- their chemical structure and physical characteristics;
- their mechanisms of action;
- their metabolism and excretion;
- studies of their action on whole animals, isolated organs, tissues and cells, enzymes, DNA and other components of cells;
- ultimately studies of their actions in humans and their therapeutic uses.

There are subdisciplines within pharmacology representing specialty areas. Pharmacokinetics deals with the disposition of drugs in the human body. To be useful, drugs must be absorbed and transported to their site of therapeutic action. Drugs will be ineffective in therapy if they do not reach the organs(s) to exert their activity. Pharmacodynamics is the study of the interaction of the drug molecule with the biological target (referred to generically as the "receptor," vide infra). This discipline lays the foundation of pharmacology since all therapeutic application of drugs has a common root in pharmacodynamics (i.e., as a prerequisite to exerting an effect, all drug molecules must bind to and interact with receptors).

Pharmacology is also the study of the toxic effects of drugs and chemicals in the environment. All drugs are capable of being toxic and all drugs can produce unwanted effects at high doses, or if used incorrectly. The difference between a medicine and a poison is often merely a matter of concentration. In therapeutics, the treatment of disease is intended to have a beneficial effect with adverse effects kept to an acceptable minimum. Development of new drugs can happen in many ways. Drugs have been developed following observation of side effects when being used for other purposes. It is now known that the site of action of many drugs is a cellular receptor. As knowledge of receptor structures has developed, this has allowed drugs to be designed to fit with receptors. The human genome project and mapping of genes has led to work on the development of drugs to alter genes.

Ques.2 What are the scopes of pharmacology?

Ans- **SCOPE OF PHARMACOLOGY**

It provides the rational basis for the therapeutic use of the drug. Before the establishment of the discipline, even though many remedies were used, but doctors were reluctant to apply scientific imply to therapeutics. In 1920s, many synthetic chemicals were first introduced and the modem balconies began to develop Scientific understanding of drugs enables us to Prodo logical effect of a new chemical that will produce a specified therapeutic effect. The logy has expanded greatly over the last decade to incorporate many new therapists drug design, genetic screens, protein engineering and use of approaches novel drug delivery vehicles including viruses and artificial cells. Our society needs pharmacology who understand the basis of modern therapeutics for careers within academic, pharmaceutical and governmental laboratories to shady and develop tomorrow's drugs

PHARMACOLOGY

The importance of pharmacology to health care professionals cannot be overestimated. Patients gly likely to be receiving at least one drug: many older patients are likely to be on them drug, and prescription of eight or nine drugs at the same time is not uncommon. This poly Macy and it increases the chance of patients experiencing adverse effects or the drug-drug interactions. Depending on the nature of their work, health care professionals considerable time with individual patients who might have questions about their drug therapy As professionals, they should be able to advise patients or know when to refer them to other experts in the health care team. Drug therapy of disease is ever expanding, new drugs exist for effective treatment or cure of more diseases than ever before. It is therefore important for health care professionals to have an understanding of therapeutic uses of medicines, normal doses, adverse effects, interactions with other drugs, precautions and contraindications.

Prescribing can be described in the following three ways:
1. to order in writing the supply of prescription-only medicine for a named patient;

2. authorize by means of an NHS (National Health Service) prescription the supply of any medicine (prescription-only, pharmacy or general sales list item) at public expense;

3. to advise a patient on suitable care or medication, including over-the-counter drugs, and therefore with no written prescription.

All health care professionals who are involved in prescribing, and/or administration of medicines must abide by standards set out by their respective professional bodies.

Ques.3 Write a short note on local routes of administration.

Ans- LOCAL ROUTES

It is the simplest mode of administration of a drug at the site where the desired action is required. side effects are minimal.

1. **Topical:** Drug is applied to the skin or mucous membrane at various sites for local action.

(a) Oral cavity: As a suspension, e.g. nystatin; as a troche, e.g. clotrimazole (for oral candidiasis), as a cream, e.g. acyclovir (for herpes labialis); as ointment and jelly, e.g. 5% lignocaine hydrochloride (for topical anaesthesia); as a spray, e.g. 10% lignocaine hydrochloride (for topical anaesthesia).

(b) GI tract: As tablet that is not absorbed, e.g., neomycin (for sterilization of gut before surgery).

(c) Rectum and anal canal:

(i) As an enema (administration of drug into the rectum in liquid form):

- Evacuant enema (for evacuation of bowel): For example, soap water enema- soap acts as a lubricant and water stimulates the rectum.
- Retention enema: For example, methylprednisolone in ulcerative colitis.

(ii) As a suppository (administration of the drug in solid form into the rectum), e.g., bisacodyl-for evacuation of bowels.

(d) Eye, ear, and nose: As drops, ointments and sprays (for infection, allergic conditions, etc.),

e.g., gentamicin eye/ear drops.

(e) Bronchi: As inhalation, e.g., salbutamol, ipratropium bromide, etc. (for bronchial asthma and

chronic obstructive pulmonary disease).

(f) Skin: As ointment, cream, lotion, or powder, e.g., clotrimazole (antifungal) for cutaneous candidiasis.

Intra-arterial route: This route is rarely employed. It is mainly used during diagnostic studies such as coronary angiography and for the administration of some anticancer drugs, e.g., for treatment of malignancy involving limbs.

3. Administration of the drug into some deep tissues by injection, e.g., administration of triamcinolone directly into the joint space in rheumatoid arthritis.

Ques.4 What are physio-chemical properties of drug substance.

Ans- Physio-chemical properties of drug substances

Drug solubility & dissolution rate: The rate determining steps in absorption of orally administered drugs are:

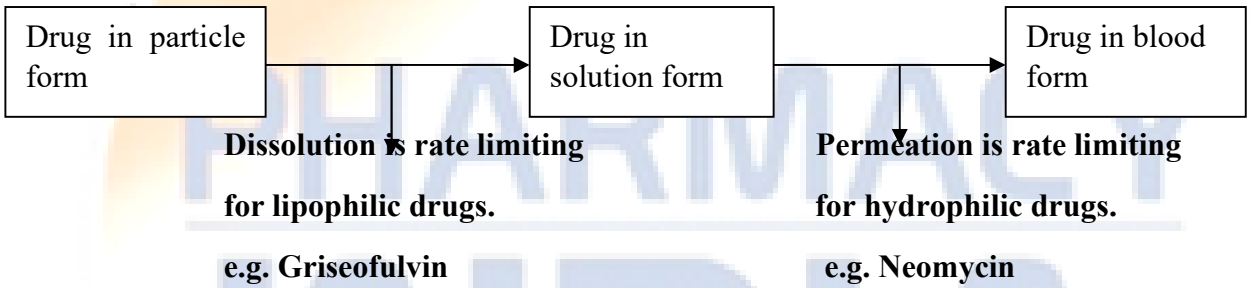

Fig. 1.2: Rate determining steps

- **Particles size & effective surface area:** The smaller the particle size (by micronization), the greater is the effective surface area, more intimate contact between solid surface and aqueous solvent, the higher is the dissolution rate and increase in absorption efficiency, e.g., soluble non-hydrophobic drugs like Griseofulvin, chloramphenicol whose dissolution is rate limited.
- **Polymorphism & amorphism:** Many compounds form crystals with different molecular arrangements, or polymorphs. These polymorphs may have different physical properties, such as dissolution rate and solubility. Amorphous form has greater aqueous solubility than the crystalline forms because the energy required to transfer a molecule from crystal lattice is greater than that required for non-crystalline solid.
- **Solvates & hydrates:** The stoichiometric type of adducts where the solvent molecule is incorporated with the crystal lattice of the solid are called as solvates. The solvates can exist in different crystalline forms called as pseudomorphs and the phenomenon is pseudo polymorphism. When the solvent in association with drug is water, the solvate is known as hydrate. e.g., anhydrous form of theophylline and ampicillin are more bioavailability than their monohydrate & trihydrate forms.
- **Salt form of drug:** At given pH, the solubility of drug, whether acidic/basic or its salt, is a constant. While considering the salt form of drug, pH of the diffusion layer is important not the pH of the bulk of the solution. e.g. salt of weak acid, which increases the pH of the diffusion layer, promotes the solubility and dissolution of a weak acid and absorption is bound to be rapid.

- **Ionization state:** Unionized state is important for passive diffusion through membrane so important for absorption. Ionized state is important for solubility.
- **Drug pK, & lipophilicity & GI pH** (pH partition hypothesis)

(B) Formulation Factors

- **Disintegration time (D.T):** Rapid disintegration is important to have a rapid absorption so lower D.T. is required. D.T. of tablet is directly proportional to amount of binder and compression force. Also, if the disintegrated drug particles do not dissolve then absorption and ultimately bioavailability is not achieved.
- **Manufacturing variables:**

(1) Method of granulation depending on the method wet/dry granulation can be used to produce tablets that dissolve at a faster rate.

(2) Compression force influence the hardness, density, porosity, disintegration & dissolution of tablet.

- **Nature & type of dosage form:** Drug formulations are designed to provide an attractive, stable, and convenient method to use products Conventional dosage forms may be broadly characterized in order of decreasing dissolution rate as solutions, solid solutions, suspensions, capsules and tablets, coated capsules and tablets, and controlled release formulations
- **Pharmaceutical excipients:** The more the number of excipients in the dosage form, the more complex it is & the greater the potential for absorption and bioavailability problems Commonly used excipients in various dosage forms are vehicle, diluents, binders & granulating agent, disintegrants, lubricants, suspending/viscosity agents, surfactants, and colorants.
- **Product age & storage conditions:** Product aging and storage conditions can adversely affect the bio-availability by change in especially the physio-chemical properties of the dosage forms. For example: precipitation of the drug in solution, hardening of tablet & change in particle size of suspension

Ques.5 What are patient related factors?

Ans- Patient Related Factors

(A) Physiological Factors

1. Membrane physiology: Nature of cell membrane & Transport processes (discussed earlier in the chapter)

2. Gastro-Intestinal motility:

(a) Gastric emptying rate: Gastric emptying is a first order process by which food leaves the stomach and enters the duodenum. Rapid gastric emptying is required when the drug is best absorbed from distal part of the small intestine. Delayed gastric emptying is required when drugs are absorbed from proximal part of the small intestine and prolonged drug absorption site contact is desired. Factors that influence gastric emptying rate are

- Volume of meal (bulky material tends to empty more slowly than liquids)
- Composition of meal (carbohydrates> proteins > fats)

- ❖ Physical state and viscosity of meal (Solutions or suspensions of small particles empty more rapidly than do chunks of material that must be reduced in size prior to emptying)
- ❖ Body posture (Lying on the left side decreases emptying rate and right side promotes it)
- ❖ Emotional state (Anxiety promotes whereas depression retards it)
- ❖ Disease state (gastric ulcer, hypothyroidism retards it, while duodenal ulcer, hyperthyroidism promotes it)

(b) Intestinal motility: Normal peristaltic movements mix the contents of the duodenum, bringing the drug particles into intimate contact with the intestinal mucosal cells. The drug must have a sufficient time (residence time) at the absorption site for optimum absorption. In the case of high motility in the intestinal tract, as in diarrhoea, the drug has a very brief residence time and less opportunity for adequate absorption

(c) Drug stability in GIT: Metabolism or degradation by enzymes or chemical hydrolysis may adversely affect the drug absorption and thus reduces bioavailability Generally, a problem with orally administered drugs which can be destructed by gastric acid

(d) Intestinal transit: Long intestinal transit time is desirable for complete absorption of drug e.g for enteric coated formulation & for drugs absorbed from specific sites in the intestine, Peristaltic contraction promotes drug absorption by increasing the drug membrane contact and by enhancing dissolution especially of poorly soluble drugs.

(e) Blood flow to GIT: It continuously maintains the concentration gradient across the epithelial membrane. The GIT is extensively supplied by blood capillary network. Absorption of polar molecules doesn't depend on the blood flow but lipid soluble molecules highly depend on the blood flow. Food influences blood flow i.e. perfusion increases after meals & persist for few hours but absorption is not affected.

3. Age: In infants, the gastric pH is high and intestinal surface and blood flow to the GIT is low resulting in altered absorption pattern in comparison to adults. In elderly persons, altered gastric emptying, decreased intestinal surface area and GI blood flow impairs drug absorption.

Ques.6 Give the factors influencing drug metabolism.

Ans- FACTORS INFLUENCING DRUG METABOLISM

Drugs and xenobiotics often are metabolized by several different phase I and phase II pathways to give several metabolites. The relative amount of any metabolite is determined by the concentration and activity of the enzymes responsible for the biotransformation. The rate of metabolism of a drug is particularly important for its pharmacological action as well as its toxicity.

1. Age Differences: Age-related differences in drug metabolism are generally quite apparent in the new-born. In most foetal and new-born animals, undeveloped or deficient oxidative and conjugative enzymes are chiefly responsible for the reduced metabolic capability seen. In general, the ability to carry out metabolic reactions increases rapidly after birth and approaches adult levels in about 1 to 2 months eg. caffeine has half-life of 4 days in neonates in comparison to 4 hrs in adult.

2. Diet: The enzyme content and activity are altered by several dietary components. Low protein diet decreases and high protein increases the drug metabolism. As enzyme synthesis is promoted by protein diet. Grape fruit juice inhibits metabolism of many drugs and improve their oral bioavailability.

3. Gender difference: Drug metabolism rate in men and women is different may be due to sex hormone. In human studies have shown that women metabolize benzodiazepines slowly than men.

4. Species and strain differences: Species difference is observed in phase I and phase II reactions, both qualitative and quantitative variations in the enzyme and their activity have been observed. Human liver contains less cytochrome P-450/gm of tissue than do the liver of other species. Just as difference in drug metabolizing ability between different species is attributed to genetics, the differences are observed between strains of same species also. It may be studies under two headings:

(i) Pharmacogenetics: A study "of inter-subject variability in drug response is called as pharmacogenetics Polygenetic control is observed in twins in identical twins (monozygotic) is very little or no difference in metabolism in various drug but large variation was observed in fraternal (dizygotic).

(ii) Ethic Variations: Difference observed in the metabolism of drug among difference races are called as ethic variations. Such variation may be monomorphic or polymorphic g Approximately equal percent of slow and rapid acetylators are found among whites and black whereas the slow acetylators dominate Japanese.

Ques.7 Give the general mechanism of drug action.

Ans- GENERAL MECHANISM OF DRUGS ACTION

Drug-Receptor Interaction: Drugs can produce their actions by

1. Binding with biomolecules (Receptor-mediated mechanisms) (protein target). Biomolecules - Targets = Receptors

2 non-receptor mediated mechanisms i.e., Physiochemical properties of drugs.

Receptor: It is a membrane bound or intracellular macromolecular protein which is capable of binding the specific functional groups of the drug or endogenous substance. Binding of a drug with its receptor results in the formation of drug receptor complex (DR) which is responsible for triggering the biological response.

D+R>>>> D-R complex >>>> Effect

Affinity: Ability of a drug to combine with the receptor**.**

Efficacy (Intrinsic Activity): Capacity of a drug receptor complex (D-R) to produce an action. It is the maximal response produced by a drug (E max).

Agonist is a drug that combines with receptor and elicit a response (has affinity and Full efficacy)

Agonist: A drug that combines with its specific receptor to produce maximal effect by increasing its concentration (affinity & high efficacy), eg. acetylcholine (Ach).

Partial Agonist combines with its receptor & evokes a response as a full agonist but produces sub-maximal effect regardless of concentration (affinity & partial efficacy), e.g., pindolol.

Antagonist is a drug that combines with a receptor without producing responses. It blocks the action of the agonist (has affinity but no or zero efficacy), e.g., atropine. Drugs can produce their actions by binding with biomolecules (Receptor-mediated mechanisms). The protein targets for drug binding can be some physiological receptors, Enzymes, ion channels, Carriers and Structural proteins.

Ques.8 What is the effect of combination of drugs?

Ans- EFFECT OF COMBINATION OF DRUGS

Combinations of two or more drugs, simultaneously or in quick succession produces:

1. No interference with each other's effects.

2. May oppose each other's actions (antagonism)

3. May produce similar actions on the same organ (synergism)

1. Drug Synergism

This is facilitation of the effects of one drug by another when given together. Its types are

(a) Additive (summation)

(b) Supra-additive (Potentiation)

(a) Summation/Addition Effect of drugs: Final effect is same as the algebraic sum of the magnitude of individuals drugs and side effects do not add up.

A+B Effect of drug A+ Effect of drug B

e.g., (Summation): Aspirin: (-) PG synthesis + Codeine: Opioid agonist analgesia

e.g., Addition: Ibuprofen: (-) PG synthesis + Paracetamol. (-) PG synthesis→→→ analgesia ++

(b) Supraadditive (Potentiation): When two drugs are given together the final effect is much more than the simple algebraic sum of the magnitude of individual drugs.

Effect of drug A+B> Effect of drug A+ Effect of drug B

e.g., Sulphamethoxazole & Trimethoprim→ sequential blockade of two steps in synthesis of folic acid in micro-organisms; Levodopa + Carbidopa (Synergism by altering Pharmacokinetics of the other).

II. Drug Antagonism

Combined effect of two drugs is less than the sum of the effects of the individual drugs. Onedrug decreases/opposes / reverses/counters the effect of other drug by different mechanisms.

Effect of drugs A+ B< Effect of drug A+ Effect of drug B

Ques.9 Write a short note on pharmacological actions of cholinergic agonists.

Ans- PHARMACOLOGICAL ACTIONS

A. Muscarinic

1. Heart: ACh hyperpolarizes the SA nodal cells and decreases the rate of diastolic depolarization. As a result, rate of impulse generation is reduced, bradycardia or even cardiac arrest may occur (M_2, subtype).

2. Blood vessels: All are dilated, though only few (skin of face, neck, salivary glands) receive cholinergic innervation (M_3,). Fall in BP and flushing, especially in the blush area occurs.

vasodilatation is mediated through the release of an endothelium dependent relaxing factor (EDRF) which is nitric oxide (NO).

3. Smooth muscle: Smooth muscle is contracted (mainly through M3 receptors). Tone and peristalsis in the gastrointestinal tract is increased and sphincters relax causing abdominal cramps and evacuation of bowel. The detrusor muscle contracts while the bladder trigone and sphincter relax leads to voiding of bladder. Bronchial muscles constrict, dyspnoea, precipitation of an attack of bronchial asthma.

4. Glands: Secretion from all parasympathetically innervated glands is increased via M_3, and some My receptors: sweating, salivation, lacrimation, tracheobronchial and gastric secretion.

5. Eye: Contraction of circular muscle of iris causes miosis. Contraction of ciliary muscle causes spasm of accommodation, increased outflow facility, reduction in intraocular tension (especially in glaucomatous patients).

Ques.10 Define anti-cholinergic drugs. Give the classification of anti-cholinergic drugs.

Ans- ANTI-CHOLINERGIC DRUGS

Conventionally, anti-cholinergic drugs are those which block actions of ACh on autonomic effector sand in the CNS exerted through muscarinic receptors. Though nicotinic antagonists also neuromuscular blockers." block certain actions of ACh, they are generally referred to as 'ganglion blockers' and

Classification

1. Natural alkaloids: Atropine, Hyoscine (Scopolamine)

2. Semisynthetic derivatives: Homatropine, Atropine methonitrate, Hyoscine butyl bromide, ipratropium bromide, Tiotropium bromide

3. Synthetic compounds:

(a) Mydriatics: Cyclopentolate, Tropicamide.

(b) Antisecretory-antispasmodics:

- **Quaternary compounds:** Propantheline, Oxyphenonium, Chdinium, Pipenzolate methyl bromide, Isopropamide, Glycopyrrolate
- **Tertiary amines:** Dicyclomine, Valethamate, Pirenzepine

(c) Vasicoselective: Oxybutynin, Flavoxate, Tolterodine

(d) Antiparkinsonian: Trihexyphenidyl (Benzhexol), Procyclidine, Biperiden

Ques.11 What is anti-cholinesterase poisoning?

Ans- ANTI-CHOLINESTERASE POISONING

Anti-cholinesterase's are easily available and extensively used as agricultural and household insecticides, accidental as well as suicidal and homicidal poisoning is common.

- Irritation of eye, lacrimation, salivation, sweating, copious trachea-bronchial secretions, miosis, blurring of vision, breathlessness, colic, involuntary defecation, and urination.
- Fall in BP, bradycardia or tachycardia, cardiac arrhythmias, vascular collapse.

- ❖ Muscular fasciculations, weakness, respiratory paralysis (central as well as peripheral).
- ❖ Excitement, tremor, ataxia, convulsions, coma, and death.
- ❖ Death is generally due to respiratory failure.

Treatment

1. Termination of further exposure to the poison, fresh air, wash the skin and mucous membranes with soap and water, gastric lavage according to need.

2. Maintain patent airway, positive pressure respiration if it is failing.

3. Supportive measures- maintain BP, hydration, control of convulsions with judicious use of diazepam.

4. Specific antidotes

(a) Atropine is highly effective in counteracting the muscarinic symptoms, but higher doses are required to antagonize the central effects.

(b) Cholinesterase reactivators: Oximes are used to restore neuromuscular transmission in case of organophosphate anti-ChE poisoning. Pralidoxime (PAM), obidoxime (more potent than pralidoxime) and diacetyl-monoxime (DAM), which is lipophilic.

Ques.12 What are the pharmacological actions of anti-cholinergic drugs?

Ans- Pharmacological Actions

1. CNS: Atropine has an overall CNS stimulant action. However, hyoscine produces effects (depressant) even at low doses.

- ❖ Atropine stimulates many medullary centres -vagal, respiratory, vasomotor.
- ❖ It depresses vestibular excitation and has anti-motion sickness property.
- ❖ By blocking the relative cholinergic over activity in basal ganglia, it suppresses tremor and rigidity of parkinsonism.
- ❖ High doses cause cortical excitation, restlessness, disorientation, hallucinations and delirium followed by respiratory depression and coma

2. CVS:

Heart: The most prominent effect of atropine is to cause tachycardia; due to blockade of M receptors on SA node through which vagal tone decreases HR.

BP: Tachycardia and vasomotor centre stimulation tend to raise BP, while histamine release and direct vasodilator action (at high doses) tend to lower BP

3. Eye: Atropine causes mydriasis, abolition of light reflex and cycloplegia lasting 7-10 days; results in photophobia and blurring of near vision. The intraocular tension tends to rise, especially in narrow angle glaucoma.

4. Smooth muscles: All visceral smooth muscles that receive parasympathetic motor innervation are relaxed by atropine (M, blockade).

- ❖ Tone and amplitude of contractions of stomach and intestine are reduced, constipation occur, spasm may be relieved.
- ❖ Bronchodilation and reduces airway resistance, especially in COPD and asthma patients.
- ❖ Relaxant action on ureter and urinary bladder, urinary retention can occur in older males with prostatic hypertrophy.

5. Glands: Atropine markedly decreases sweat, salivary, tracheobronchial, and lacrimal secretion (M, blockade); skin and eyes become dry, talking and swallowing may be difficult.

Atropine decreases secretion of acid, pepsin, and mucus in the stomach.

6. Body temperature: Rise in body temperature occurs due to both inhibition of sweating as well as stimulation of temperature regulating centre in the hypothalamus.

7. Local anaesthetic: Atropine has a mild anaesthetic action on the cornea.

Ques.13 Give the classification of non-steroidal anti-inflammatory drugs (NSAIDS).

Ans- Classification

A. Non-selective COX inhibitors (traditional NSAIDs)

1. Salicylates: Aspirin

2. Propionic acid derivatives: Ibuprofen, Naproxen, Ketoprofen.

3. Anthranilic acid derivative: Mephenamic acid

4. Aryl-acetic acid derivatives: Diclofenac, Aceclofenac.

5. Oxicam derivatives: Piroxicam, Tenoxicam.

6. Pyrrolo-pyrrole derivative: Ketorolac

7. Indole derivative: Indomethacin.

8. Pyrazolone derivative: Phenylbutazone, Oxyphenbutazone

B. Preferential COX-2 inhibitors: Nimesulide, Meloxicam, Nabumeton.

C. Selective COX-2 inhibitors: Celecoxib, Etoricoxib, Parecoxib.

D. Analgesic-antipyretics with poor anti-inflammatory action:

1. Para aminophenol derivatives: Paracetamol

2. Pyrazolone derivative: Metamizol, Propiphenazone.

3. Benzoxazocine derivative: Nefopam

Ques.14 Give the pharmacological actions of aspirin.

Ans- Pharmacological Actions

1. Analgesic, antipyretic, anti-inflammatory actions: Aspirin is a weaker analgesic than morphine type drugs. It effectively relieves inflammation, tissue injury, connective tissue and integumental pain, but is relatively ineffective in severe visceral and ischaemic pain.

2. Metabolic effects: significant only at anti-inflammatory doses especially in skeletal muscles. due to uncoupling of oxidative phosphorylation increased heat production. Chronic use of large doses causes negative N_2 balance by increased conversion of protein to carbohydrate.

3. Respiration: stimulated by peripheral (increased CO_2 production) and central (increased sensitivity of respiratory centre to CO_2) actions.

4. Acid-base and electrolyte balance: Initially, respiratory stimulation predominates and tends to wash out CO_2 despite increased production, respiratory alkalosis, which is compensated by increased renal excretion of HCO_3; (with accompanying $N a^+$, K^+ and water).

5. GIT: Aspirin and released salicylic acid irritate gastric mucosa, cause epigastric distress, nausea and vomiting. It also stimulates CTZ.

6. Urate excretion: Aspirin in high dose reduces renal tubular excretion of urate.

7. Blood: Aspin, even in small doses, irreversibly inhibits TXA2 synthesis by platelets. Thus, it interferes with platelet aggregation and bleeding time is prolonged to nearly twice the normal value.

Ques.15 Write a short note on angle closure glaucoma.

Ans- ANGLE CLOSURE (NARROW ANGLE, ACUTE CONGESTIVE) GLAUCOMA

It occurs in individuals with a narrow iridocorneal angle and shallow anterior chamber. The i.o.t remains normal until an attack is precipitated, usually by mydriasis. The i.o.t. rises rapidly to very high values (40-60 mmHg). It is an emergent condition; failure to lower i.o.t. quickly may result in loss of sight. Vigorous therapy employing various measures to reduce i.o.t. is instituted.

1. Hypertonic mannitol (20%) 1.5-2 g/kg or glycerol (10%): infused i.v. decongests the eye by osmotic action. A retention enema of 50% glycerine is also sometimes used.

2. Acetazolamide: 0.5 g i.v. followed by oral twice daily is started concurrently.

3. Miotic: Once the i.o.t. starts falling due to the above i.v. therapy, pilocarpine 1-4% is instilled every 10 min initially and then at longer intervals. Contraction of sphincter pupillac changes the direction of forces in the iris to lessen its contact with the lens and spreads the iris mass centrally causes pupillary block is removed and iridocorneal angle is freed.

4. Topical β blocker: Timolol 0.5% is instilled 12 hourly in addition.

5. Apraclonidine (1%)/latanoprost 0.005% instillation may be added. Drugs are used only to terminate the attack of angle closure glaucoma. Definitive treatment is surgical or laser iridotomy. Few cases, who have chronic narrow angle glaucoma, may be treated with a miotic/other ocular hypotensive drug for long periods, but often surgery /laser therapy is ultimately required.

Ques.16 What are intravenous anaesthetics?

Ans- Intravenous Anaesthetics

Rapid induction (one arm-brain circulation time); supplemented with analgesic and muscle relaxants.

Thiopentone sodium: Ultra short acting Barbiturate, Water soluble, Alkaline & Dose-dependent suppression of CNS activity.

Pharmacokinetics: Redistribution (Blood Brain Muscle Body fat concentration of thiopentone Hepatic metabolism (elimination half-life 7-12 hrs); CNS depression persists for long (>12 hr)

Side effects: Laryngospasm (Atropine and succinylcholine), shivering and delirium during recovery, tissue necrosis-gangrene.

Advantages: Rapid induction - does not sensitize myocardium to adrenaline, no nausea and vomiting, non-explosive and non-irritant.

Disadvantages: Depth of anaesthesia difficult to judge Pharyngeal and laryngeal reflexes persists; Respiratory depression; Hypotension (rapid) - shock and hypovolemia; CVS collapse.

Propofol: Replacing thiopentone now for induction and maintenance. Rapid induction & distribution. Propofol is extensively metabolized & 88% of an administered dose appears in the urine.

Ketamine: (Phencyclidine derivative - Dissociative anaesthesia); a state characterized by immobility, amnesia and analgesia with light sleep and feeling of dissociation from one's own body and mind and the surroundings. Site of action is cortex and subcortical areas NMDA receptors.

Fentanyl: (Neurolept analgesia) supplement in Balanced anaesthesia in combination with diazepam used in diagnostic, endoscopic and angiographic procedures; adjunct to spinal and nerve block anaesthesia.

Ques.17 What are the complications of anaesthetics?

Ans- COMPLICATIONS OF ANAESTHESIA

During anaesthesia: Respiratory depression, Salivation, respiratory secretions, cardiac arrhythmias, Fall in BP. Aspiration, Laryngospasm and asphyxia, Delirium, and convulsion, Fair and explosion

After anaesthesia: Nausea and vomiting. Persisting sedation, Pneumonia, liver, kidney damage. Nerve palsies, Emergence delirium, Cognitive defects

Preanesthetic Medication

It is the term applied to the use of drugs prior to the administration of an anaesthetic agent to make anaesthesia safer and more agreeable to the patient. Its aim is to:

- Relief of anxiety diazepam or lorazepam, midazolam, promethazine
- Amnesia for pre- and post-operative events: diazepam or lorazepam, midazolam promethazine
- Analgesia Morphine and its congeners
- Decrease secretions: Atropine
- Antiemetic effects: Metoclopramide, domperidone
- Decrease acidity and volume of gastric juice: ranitidine, famotidine

Ques.18 Give the therapeutic uses & treatment of barbiturates.

Ans- Therapeutic Uses

- Anaesthesia: The ultra-short-acting barbiturates, such as thiopental.

- Anticonvulsant: Phenobarbital (tonic-clonic seizures/refractory status epilepticus).
- Sedative hypnotise: Mild sedatives to relieve anxiety, nervous tension, and insomnia.
- Hyperbilirubinemia and kernicterus in the neonates (increase glucouronyl transferase activity).

Treatment

- Gastric lavage (activated charcoal)
- Supportive patent airway, assisted respiration, oxygen, IV fluid and vasopressors like Dopamine
- Alkaline diuresis: Sodium bicarbonate I meq/kg IV with or without mannitol - for long acting one
- Haemodialysis: highly effective in long as well as short acting ones
- No specific antidote

Ques.19 Give the mechanism of action of general anaesthetics.

Ans- MECHANISM OF ACTION

I. Meyer-Overton rule: Lipid water partition coefficient- GA (gases) are highly lipid soluble and therefore can easily enter in neurones. After entry causes disturbances in physical chemistry of neuronal membranes fluidization. Finally, obliteration of Na^+ channel and refusal of depolarization.

II. For inhalation anaesthetics: MAC is defined as the minimum alveolar concentration that prevents movement in response to surgical stimulation in 50% of subjects. Correlates with oil/gas partition coefficient. For Intravenous agent's potency of IV agent is defined as the free plasma concentration (at equilibrium) that produces loss of response to surgical incision in 50% of subjects:

III. Modern theory:

1. To activate $GABA_A$ receptor-chloride channel

2. To activate glycine receptor

3. To inhibit NMDA channel receptor

4. To inhibit nicotinic acetylcholine receptor isoforms

Diethyl Ether: Colourless, highly volatile liquid with a pungent odour. Produces irritating vapours and are inflammable and explosive. 85 to 90 percent is eliminated through lung and remainder through skin, urine, milk and sweat & can cross the placental barrier

Advantages: Can be used without complicated apparatus; Potent anaesthetic and good analgesic; Muscle relaxation; Wide safety of margin; Respiratory stimulation and bronchodilation, does not sensitize the heart to adrenaline; No cardiac arrythmias; Can be used in delivery: Less likely hepatic or nephrotoxicity.

Disadvantages: Inflammable and explosive; Slow induction and unpleasant, Struggling, breath holding, salivation and secretions (drowning); Slow recovery; nausea & vomiting.

Enflurane: Non-inflammable, with mild sweet odour like halothane in action, except better muscular relaxation. Depresses myocardial force of contraction and sensitize heart to adrenaline; Induces seizure in deep anaesthesia and therefore not used now.

Isoflurane: Isomer of enflurane and have similar properties but slightly more potent.

Advantages: Rapid induction and recovery, good muscle relaxation, coronary, Less Myocardial depression; No renal or hepatotoxicity; low nausea and vomiting. No dilatation of pupil and no loss of light reflex in deep anaesthesia; no seizure and preferred in neurosurgery.

Disadvantages: Pungent and respiratory irritant, Maintenance only, no induction: Hypotension, Costly.

Ques.20 Give the classification of epileptic seizures.

Ans- CLASSIFICATION OF EPILEPTIC SEIZURES

I. Partial (Focal) Seizures:

A. Simple Partial Seizures: (SPS, cortical focal epilepsy) lasts 1/2-1 min. Confined to a group of muscles or localized sensory disturbance depending on the area of cortex involved in the seizure, without loss of consciousness.

B. Complex Partial Seizures: (CPS, temporal lobe epilepsy, psychomotor) attacks of bizarre and confused behaviour and purposeless movements, emotional changes lasting 1-2 min along with impairment of consciousness

C. Partial with secondary generalized tonic classic seizure: The partial seizure occurs first and evolves into generalized tonic-clonic seizures with loss of consciousness.

II. Generalized Seizures:

A. Generalized Tonic- Clonic Seizures: major epilepsy, grand mal, commonest, lasts 1-2 min. Sequence is aura cry unconsciousness tonic spasm of all body muscles → cry → clonic jerking followed by prolonged sleep and depression.

B. Absence Seizures: minor epilepsy, petit ma, prevalent in children, lasts about 1/2 min. Momentary loss of consciousness, patient apparently freezes and stares in one direction, no muscular component or little bilateral jerking.

C. Myoclonic Seizures: shock-like momentary contraction of muscles of a limb or the whole body.

Ques.21 What are the advantages of benzodiazepines over barbiturates?

Ans- Advantages of Benzodiazepines over Barbiturates

Benzodiazepines	Barbiturates
1. Less neuronal depression & high TI	More neuronal depression
2. No anesthesia even at high dose; patient can be aroused	Loss of consciousness & low margin of safety
3. No effect on respiration or cardiovascular functions at hypnotic dose	Cause respiratory and cardiac depression
4. No effect on REM sleep	++ suppression of REM sleep; Withdrawal rebound ↑ in sleep & hangover
5. Abuse liability very low	Tolerance & Dependence
6. No hyperalgesia	Hyperalgesia (↑ sensitivity to pain)
7. Amnesia without automatism	Amnesia with automatism; Loss of short-term

	memory
8. Not enzyme inducer - Less drug interactions	Potent enzyme inducers- More drug interactions
9. Specific antagonist - Flumazenil	No antagonist available

Ques.22 Write a short note on anti-anxiety drugs?

Ans- ANTI-ANXIETY DRUGS

Anxiety is a state which occurs in all human beings at some time or the other. It is also a cardinal symptom of many psychiatric conditions. The drugs used to relieve anxiety are called antianxiety of anxiolytic agents. Anti-anxiety drugs relieve moderate-to-severe anxiety & tension. They are prescribed for a number of illnesses:

- Generalized Anxiety (GAD)
- Post-Traumatic Stress Disorder (PTSD)
- Phobias
- Obsessive Compulsive Disorder (OCD)
- Panic Disorder Insomnia related to Anxiety

CLASSIFICATION

1. Benzodiazepines: Diazepam, Chlordiazepoxide, Oxazepam, Lorazepam, Alprazolam

2. Azapirones: Buspirone, Gepirone, Ispapirone

3. Sedative antihistaminic: Hydroxyzine

4. β blocker: Propranolol

These drugs increase or help the inhibitory neurotransmitter action of gamma-aminobutyric inhibitor in all areas of CNS. So, there is inhibition or control on the cortical & limbic system of the brain, which is responsible for emotions such as rage & anxiety. Because anxiety is a common complaint and is a part of most physical and mental illness, and because the BZDs:

- have little effect on other body systems,
- have lower dependence producing liability: withdrawal syndrome is milder and delayed due to their long half-lives,
- are relatively safe even in gross over dosage, they are presently one of the most widely used class of drugs

Side effects: that occur in their use to relieve anxiety are sedation, light-headedness, psychomotor and cognitive impairment, vertigo, confessional state (especially in the elderly), increased appetite and weight gain, alterations in sexual function. At anti-anxiety doses, cardiovascular and respiratory depression is minor.

Chlordiazepoxide: It was the first BZD to be used clinically Oral absorption is slow produces a smooth long-lasting effect, preferred in chronic anxiety states, often combined with other drugs in psychosomatic diseases.

Diazepam: It is quickly absorbed, produces a brief initial phase of strong action followed by prolonged milder effect due to a two-phase plasma concentration decay curve (distributive phase 1hr, elimination phase $t_{1\backslash 2}$ 20-30 hours). It is preferred in acute panic states and anxiety associated with organic disease.

Lorazepam: Has slow oral absorption. Being less lipid-soluble than diazepam, its rate of entry in brain is slower. It has been preferred for short lasting anxiety states, panic, obsessive-compulsive neurosis, and tension syndromes, as well as psychosomatic diseases.

Alprazolam: A high potency anxiolytic BZD which in addition has some mood elevating action in mild depression: is particularly useful in anxiety associated with depression.

Ques.23 What are mood stabilizing agents?

Ans- **MOOD STABILIZING AGENTS**

Lithium Carbonate is a small monovalent cation which exert beneficial effects in manic patients. The probable mechanisms of action can be:

- It accelerates pre-synaptic re-uptake & destruction of catecholamines, like NE.
- It inhibits the release of catecholamines at the synapse.
- It decreases postsynaptic serotonin receptor sensitivity.

All these actions result in decreased catecholamine activity, thus ameliorating mania.

Pharmacokinetics

Lithium is readily absorbed with peak plasma levels occurring 2-4 hours after a single oral dose of lithium carbonate. It is distributed rapidly in liver & kidney & more slowly in muscle, brain & bone. Elimination is predominately via tubules & is influenced by sodium balance Depletion of sodium can precipitate lithium toxicity.

Adverse Effects

The margin between the therapeutic and toxic levels of lithium carbonate is very narrow Toxicity occurs at levels only marginally higher than therapeutic levels: Nausea, vomiting and mild dinocap (minimized by starting at lower doses): Thirst and polyuria, Fine tremors and rarely seizures are seen even at therapeutic concentrations; CNS toxicity-coarse tremors, giddiness, ataxia, or in-coordination, nystagmus, mental confusion, slurred speech.

Uses

Lithium is used as its carbonate salt because this is less hygroscopic and less gastric irritant than other salts Used for acute mania; prophylaxis in bipolar disorder, inappropriate ADH secretion Syndrome.

Ques.24 Give the mechanism of action and adverse drug reactions of anti-psychotics.

Ans- **Mechanism of Action**

All antipsychotics (except clozapine-like atypical) have potent dopamine (increased production of dopamine transmits the nerve impulses to the brainstem faster than normal. This results in strange thoughts, hallucination & bizarre behaviour) D receptor blocking action; antipsychotic potency has shown good correlation with their capacity to bind to D, receptor. Phenothiazines and thioxanthene's also block D_1, D_3, and D_4, receptors. Blockade of dopaminergic projections to the temporal and prefrontal areas constituting the "limbic system' and in meso-cortical areas is probably responsible for the antipsychotic

action. Other atypical antipsychotics which have weak D_2 blocking action However, they have significant 5-HT_2, and al blocking action, and some are relatively selective for D, receptors.

ADVERSE DRUG REACTIONS

- Nausea, Gl upset, Skin rashes; Sedation; Photosensitivity: Orthostatic hypotension
- **Anticholinergic effects:** Dry mouth, Blurred vision, Constipation, Urinary retention
- **Hormonal effects:** Decreased libido, gynecomastia, Amenorrhea; Infertility. Weight gain
- **ECG changes:** Q-T prolongation and T wave suppression
- Decreased threshold level, Agranulocytosis: Hypersalivation
- **Extrapyramidal symptoms:** Pseudo-parkinsonism (tremor, shuffling gait, drooling. rigidity), Akinesia (muscular weakness); Akathisia (continuous restlessness and fidgeting); Dystonia (involuntary muscular movements [spasms] of face, arms, legs, and neck); Oculogyric crisis (uncontrolled rolling back of the eyes).
- **Tardive dyskinesia** (bizarre facial and tongue movements, stiff neck, and difficulty swallowing)
- **Neuroleptic malignant syndrome (NMS):** Severe parkinsonian muscle rigidity. Hyperpyrexia, Tachycardia, Tachypnoea, Fluctuations in blood pressure, Diaphoresis, Rapid deterioration of mental status & Stupor and coma.

Ques.25 What are the pharmacological actions of morphine?

Ans- PHARMACOLOGICAL ACTIONS OF MORPHINE

1. CNS:

Analgesia: Strong analgesic; visceral pain is relieved better than somatic pain. Inhibits release of excitatory transmitters from primary afferents at **substantia gelatinase** of dorsal horn in spinal cord. At supraspinal level in cortex, midbrain and medulla alter processing and interpretation and send inhibitory impulses through descending pathway.

Sedation: Drowsiness and indifference to surroundings, inability to concentrate and extravagant imagination, colourful day dream, larger doses produce sleep

Mood effects: In Normal persons calming effect, mental clouding, feeling of detachment, lack of initiative etc. unpleasant in absence of pain (DYSHORIA). But in persons with pain & addicts" sense of wellbeing, pleasurable floating feelings -kick (EUPHORIA)

Depression: Both rate and depth of respiration are diminished, Cough Centre depressed; Temperature regulating centre depressed.

Stimulation: sensitize CTZ to vestibular and other impulses; vagal centre (bradycardia)

2. GIT: Constipation due to direct action on intestine reducing propulsive movement, spasm of sphincters, decrease in all GIT secretions

3. Smooth Muscles: Biliary colic due to closure of sphincter of Oddi; urinary urgency but difficulty: Bronchospasm.

4. Miosis is a pharmacologic action to which little or no tolerance develops.

Ques.26 Write a short note on opioid analgesics.

Ans- OPIOID ANALGESICS

Algesia (pain) is an ill-defined, unpleasant sensation, usually evoked by an external or internal noxious stimulus.

Analgesic is a drug that selectively relieves pain by acting in the CNS or on peripheral pain mechanisms, without significantly altering consciousness.

Opium is a dark brown, resinous material obtained from poppy (Papaver somniferum) capsule. It contains two types of alkaloids.

I. Phenanthrene Derivatives

Morphine (10% in opium); Codeine (0.5% in opium); The Baine (0.2% in opium/non-analgesic)

II. Benzoisoquinoline Derivatives (Non-analgesic)

Papaverine (1%); Noscapine (6%)

Opioid alkaloids (e.g., morphine) produce analgesia through actions at regions in the central nervous system (CNS) that contain peptides with opioid-like pharmacologic properties. The general term currently used for these endogenous substances is **endogenous opioid peptides.** Three families of endogenous opioid peptides have been described in detail: the **endorphins,** the pentapeptide methionine - enkephalin **(met-enkephalin)** and leucine-enkephalin **(leu-enkephalin),** and the **dynorphins.** The three families of opioid receptors have overlapping affinities for these endogenous peptides is as follows:

Receptor Subtype	Functions	Endogenous Opioid Peptide Affinity
μ **(mu)**	Supraspinal and spinal analgesia; sedation; inhibition of respiration; slowed GI transit; modulation of hormone and neurotransmitter release	Endorphins>enkephalins> dynorphins
δ **(delta)**	Supraspinal and spinal analgesia; modulation of hormone and neurotransmitter release	Enkephalins > endorphins and dynorphins
κ **(kappa)**	Supraspinal and spinal analgesia; psychotomimetic effects; slowed GI transit	Dynorphins >> endorphins and enkephalins

CLASSIFICATION

1. Natural Opium Alkaloids: Morphine and Codeine

2. Semi-synthetic: Diacetylmorphine (Heroin) and Pholcodeine

3. Synthetic Opioids:

(a) Phenylpiperidines:

- Pethidine (Mepiridine) and its congeners - Diphenoxylate and Loperamid
- Fentanyl and its congeners - Sufentanil, remifentanil and alfentanil

(b) Phenyl-heptylmines: Methadone, Propoxyphene and Dextropropoxyphene

(c) Benzomorphans: Pentazocine

(d) Morphinan compounds and congeners: Levorphanol and Butorphanol

4. Agonist-antagonists (k analgesics): Nalorphine. Pentazocine, Butorphanol

5. Partial/weak μ agonist +κ antagonist: Buprenorphine

6. Pure antagonists: Naloxone, Naltrexone, Nalmefene

Ques.27 Explain centrally acting muscle relaxants.

Ans- CENTRALLY ACTING MUSCLE RELAXANTS

Muscle relaxant is a drug which affects skeletal muscle function and decreases the muscle tone. It may be used to alleviate symptoms such as muscle spasms, sprains & pain. Muscle relaxants are of two major therapeutic groups' neuromuscular blockers and spasmolytic.

Spasmolytics are used to alleviate musculoskeletal pain, spasms and to reduce spasticity in a variety of neurological conditions. They are of three types

- Centrally acting
- Directly acting
- Miscellaneous

Centrally acting drugs reduce skeletal muscle tone by a selective action in the cerebrospinal axis, without altering consciousness. They selectively depress spinal and supra spinal poly-synaptic reflexes involved in the regulation of muscle tone, Polysynaptic pathways in the ascending reticular formation which are involved in wakefulness are also depressed, though to a smaller extent. All centrally acting muscle relaxants cause sedation. They have no effect on neuro muscular transmission and on muscle fibres but reduce decerebrate rigidity, upper motor neuron spasticity and hyperreflexia.

Classification

1. Mephenesin congeners: Mephenesin, Cansoprodol, Chlorzoxazone, Chlormezanne Methocarbamol

2. Benzodiazepines: Diazepam and others

3. GABA mimetics: Baclofen

4. Central α2 agonist: Tizanidine

MEPHENESIN CONGENERS

Mephenesin: First drug to be discovered as a muscle relaxant. Modulates reflexes maintaining muscle tone. It is not used clinically because it causes gastric irritation, and when administered IV it causes thrombophlebitis, haemolysis and marked fall in BP.

Carisoprodol: Has favourable muscle relaxant, sedative, analgesic antipyretic, and anticholinergic properties. It is used in musculoskeletal disorders associated with muscle spasm.

Chlorzoxazone: Pharmacologically like mephenesin, has a longer duration of action and is better tolerated orally.

Chlormezanone: Has anti-anxiety and hypnotic actions and is used for tension states associated with increased muscle tone. Methocarbamol: Less sedative and longer acting than mephenesin. Orally used in

reflex muscle spasm and chronic neurological diseases. It can be given IV without producing thrombophlebitis and haemolysis-used for orthopedic procedures and tetanus.

Diazepam: A benzodiazepine (BDZ) which acts in the brain on specific receptors, enhancing transmission by the inhibitory amino acid neurotransmitter GABA responsible for the regulation of muscle tone. Muscle tone is reduced by supra spinal rather than spinal action. It has more sedative activity than muscle relaxation and sedation limit the dose that can be used for muscle relaxation. Diazepam is particularly valuable in tetanus and spinal injuries. When combined with analgesics, it is useful for rheumatic disorders associated with muscle spasm.

Very Short Answers

1. Hospital provides special facilities
(a) Nursing
(b) Dietary
(c) Blood banking
(d) All of these

2. Function of hospital except
(a) Patient care
(b) Research
(c) Clinical support
(d) Rehabilitation

3. Concept of District hospital
(a) Clinical service
(b) Clinical support
(c) Only (a)
(d) Both (a) & (b)

4. Based on types of medicine the hospital is
(a) Allopathic hospital
(b) ENT hospital
(c) Kidney hospital
(d) Cancer hospital

5. Patient care service include
(a) Diagnosis
(b) Prophylaxis
(c) Both (a) & (b)
(d) Only (a)

6. Immunization
(a) Helps to prevent disease
(b) Treatment of disease
(c) Play a vital role of hospital
(d) Educational training

7. The district hospital provide
(a) Clinical service
(b) Clinical support
(c) Administrative service
(d) All of these

8. Public limited company hospitals are at
(a) Chennai
(b) Mumbai
(c) Ahmedabad
(d) Vellore

9. Following are the hospitals on the basis of types of patient except
(a) Diabetes hospital
(b) Pediatric hospitals
(c) Accident hospital
(d) General hospitals

10. Which is the clinical service except
(a) Gynecology
(b) Pediatric
(c) Radiology
(d) Cardiac

11. Based on working the medical staff is
(a) Consultants
(b) Visiting specialist
(c) Administrator
(d) Both (a) & (b)

12. Minister of state for Health include except
(a) Secretary
(b) Deputy secretary

(c) Commissioner
(d) Joint commissioner

13. Clinical support include
(a) Pathology
(b) Radiology
(c) Blood bank
(d) All of these

14. Administrative service include.
(a) Finance
(b) Personnel
(c) Both (a) & (b)
(d) None of these

15. Educational training facility is specially for except
(a) Medical student
(b) Pharmacist
(c) Nursing
(d) Patients

16. Objective of hospital pharmacy
(a) To educate patient, nurse, interns and pharmacy trainers on various aspects of drug
(b) To participate in research work
(c) Both (a) and (b)
(d) None of the above

17. Hospital pharmacy is defined as
(a) Actual practice of pharmacy in medical
(b) Actual practice of pharmacy in hospital
(c) Actual practice of pharmacy in industry
(d) Both (a) and (b)

18. Function of hospital pharmacy
(a) To estimate the requirements of facilities, supplies and equipment
(b) To co-ordinate financial plan operation for all hospital
(c) To write prescriptions for patients
(d) Both (a) and (b)

19. Pharmacist requirement in small hospitals
(a) 15
(b) 08
(c) 03
(d) 10

20. In general hospital with less than 200 bed, the pharmacy should be located in
(a) Ground floor
(b) First floor
(c) Second floor
(d) Both (a) and (c)

21. An hospital with 100 beds is

(a) Small hospital
(b) Large hospital
(c) Medium hospital
(d) Very small hospital

22. Inventory consist of
(a) Raw material
(b) In progress goods
(c) Finished goods
(d) All of these

23. How munch floor space is required for hospital pharmacy in 50 bed hospital ?
(a) 250 sq. feet
(b) 320 sq. feet
(c) 435 sq. feet
(d) None of these

24. Procurement of drug included in
(a) Pharmacy activity
(b) Supportive activity
(c) Educational activity
(d) None of these

25. Educational activity arranges seminar, workshop on
(a) Patient care
(b) Sterilization
(c) Pharmacy activity
(d) Medicines

26. How many pharmacists required for 300 bed hospital ?
(a) 10
(b) 5
(c) 1
(d) 3

27. Hospital pharmacist has
(a) Technical abilities
(b) Administrative ability
(c) Academic ability
(d) All of these

28. Manufacturing ability comes under
(a) Technical abilities
(b) Administrative ability
(c) Academic ability
(d) None of these

29. GPP stands for
(a) Good pharmacy practice
(b) Good manufacturing practice
(c) Great pharmacy practice
(d) None of these

30. Hospital pharmacist should have the following abilities
(a) Technical
(b) Administrative
(c) Research
(d) All of these

31. PTC include
(a) Physician
(b) Pharmacist
(c) Patient
(d) Only (a) & (b).

32. A chairperson is appointed from
(a) Physician
(b) Nurses
(c) Patient
(d) Administrator

33. Purpose of PTC
(a) Educational
(b) Advisory
(c) Both (a) & (b)
(d) Only (a)

34. Programs, seminars, workshops are included in
(a) Educational
(b) Advisory
(c) Both (a) & (b)
(d) Administrator

35. The success of meeting depends upon
(a) Agenda
(b) Functions
(c) Objectives
(d) All of these

36. The agenda of the committee is
(a) Minutes of previous meeting
(b) Drug safety in a hospital
(c) Hospital formulary sections
(d) All of these

37. To review adverse drug reactions to the drug is
(a) Agenda
(b) Purpose
(c) Objective
(d) All of these

38. Sometimes the drug may produce unwanted or unexpected effects are called
(a) Overdosage
(b) Adverse drug reaction

(c) Hypersensitivity
(d) Allergic condition.

39. The committee acts by
(a) To treat such patients
(b) To prevent such happenings in the future
(c) Both (a) & (b)
(d) None of these

40…….. is a prime responsibility of the hospital pharmacist.
(a) Drug safety
(b) Adverse drug reaction
(c) Objective
(d) Patients care

41. Guidelines of PTC is
(a) Library and documentation facility shall be provided.
(b) Dispensing of medicine shall be done only by the registered pharmacist.
(c) Adequate number of pharmacists must be appointed to fulfill the 24hr working requirements, in different shifts.
(d) All of the above

42. PTC stands for:
(a) Pharmacy and treatment community
(b) Pharmacy and therapeutic committee
(c) Pharmacy and therapeutic composition
(d) None of the above

43. In the composition of PTC, the pharmacist works as
(a) Chairperson
(b) Secretary
(c) Administrator
(d) Anesthetist

44. Guidelines to achieve drug safety is as follows
(a) Dispensing of the medicine
(b) Adequate facilities shall be provided for the storage and handling medicine in the pharmacy
(c) Both (a) and (b)
(d) None of the above

45. …….. is the prime responsibility of the hospital pharmacist.
(a) Proper medication
(b) Drug safety
(c) Treating to the patient
(d) Caring of the disease 16.

46. …….. plays a vital role in drug safety in hospital.
(a) PTC
(b) GMP
(c) ADR
(d) P&T committee

47. Member of the pharmacy therapeutic committee
(a) Pharmacist
(b) Doctor
(c) Nurse
(d) Patient

48. A list of drugs stocked at the hospital which have been selected based on therapeutic factors as well as cost
(a) Closed formulary
(b) Open formulary
(c) Formulary
(d) None of these

49. A type of formulary that requires physicians to order only the medications on the formulary list
(a) Closed formulary
(b) Open formulary
(c) Formulary
(d) None of these

50. The hospital formulary consist of list of in the hospital:
(a) Instruments
(b) Drugs
(c) Staff
(d) Patients

51. Which of the following is the part of hospital formulary ?
(a) Information on hospital policies
(b) Drug product listing
(c) Special information
(d) All of these

52. While prescribing the medicine the Physician must write name of drug.
(a) Proprietary
(b) Non-Proprietary
(c) Both (a) & (b)
(d) Other than above

53. The needs of hospital formulary system is increasing nowadays because of
(a) Increase in the no. of drugs in the market
(b) Increased influence of advertising practice
(c) Competition in marketing
(d) All of the above

54. Substantial patient care & financial benefits can be greatly increased by using
(a) Generic drugs
(b) Branded drugs
(c) Both (a) & (b)
(c) None

55. Which of the following criteria should be taken in to and deletion of drug in formulary?
(a) Drug must be recognized by pharmacopoeia
(b) The manufacturer should be licensee under D&C act

(c) Drug should not have secret component
(d) All of the above

56. The drug list consist of list of therapeutic agents by their generic names followed by information on:
(a) Pharmacokinetics
(b) Directions of use
(c) Strength and dosage form
(d) Toxicity

57. The number of pharmacist in P.H.C.
(a) 1
(b) 2
(c) 3
(d) None of these

58.In ….. type of formulary, the information given under each monograph is subject to local needs:
(a) Private formulary
(b) National formulary
(c) Both (a) & (b)
(d) None

59. In ……type of formulary drugs are added or deleted with less frequency while in…….. type of formulary drugs are added or deleted with greater frequency.
(a) National, private
(b) Private, national
(c) Both can possible (d) None

60. Type of formulary can be kept up to date easily then the type of formulary.
(a) Leaflet, bound
(b) Bound, leaflet
(c) Both can be possible
(d) None

61. While writing the prescription, the strength of the medicine prescribed in the……..
(a) Matrix system
(b) Imperial system
(c) Both can be possible
(d) None

62. EOQ stands for
(a) Economic Open Quality
(b) Equipment Order Quantity
(c) Essential Order Quantity
(d) Economic Order Quantity

63. In ABC analysis A items are
(a) 10% quantity of drug with low cost, 70% consumption
(b) 10% quantity of drug with high cost, 70% consumption
(c) 70% quantity of drug with high cost, 10% consumption
(d) 10% quantity of drug with neither high cost nor cheap, 10% consumption

64. Full form of VED analysis
(a) Vital, Efficient, Desirable
(b) Vital, Essential, Desirable
(c) Viable, Essential, Desirable
(d) Vital, Efficient, Desirable

65. Following are the essential narcotic drugs except
(a) Codeine
(b) Dihydrocodeinone
(c) Fentanyl
(d) Clobazam

66. Select the correct reserved antibiotic
(a) Cefixime
(b) Tigecycline
(c) Tetracycline
(d) Amphotericin

67……..number of copies of purchase order are prepared
(a) 6
(b) 9
(c) 7
(d) 8

68. Cold storage temperatures is
(a) 5 to 2°C
(b) 2 to 8°C
(c) 8°C to 25°C
(d) 25°C to 10°C

69. Vitamins stored in
(a) Freezer
(b) Cold temperature
(c) Cool temperature
(d) Room temperature

70. ILR is
(a) Integrated light refrigerator
(b) Intensive lined refrigerator
(c) Ice light refrigerator
(d) Ice-lined refrigerators

71. Following which disposal method used for cytotoxic drugs
(a) low and medium temperature incineration
(b) High temperature incineration
(c) disposal to sewers and water courses
(d) directly to landfill

72. Patient who occupy the space in the hospital are called
(a) Ambulatory patients
(b) In-patients
(c) Operating patients

(d) None of these

73. Area in sq. ft. for compounding and dispensing laboratory in hospital should be atleast 100 bed
(a) 320(b) 300
(c) 185
(d) 312

74. Ambulatory patients are
(a) Required to admit in the ward for treatment
(b) Required to go home after taking treatment in O.P.A.
(c) Required emergency treatment
(d) None of these

75. Services are provided for immediate medical attention or in case of an accident.
(a) Primary care
(b) Referral care
(c) Emergency care
(d) None

76. 24 hour services are given to patients who require immediate care for the survival,
(a) Emergency out-patient
(b) Referred out-patient
(c) Special out-patient
(d) General out-patient

77. ..... Deals with majority care for daily personal health needs.
(a) Primary care
(b) Tertiary care
(c) Emergency care
(d) All

78. Following is the reason behind the growth of out-patient service.
(a) The deficiency of medical practitioners in some areas.
(b) The need of health community.
(c) To conduct teaching programmers as per the needs of the hospital.
(d) All

79. Emergency service is for
(a) 12 hrs
(b) 24 hrs
(c) 20 hrs
(d) 8 hr

80. .....Patients are referred to the hospital for a specific purpose due to lack of facilities available with the clinic.
(a) Emergency out-patient
(b) Referred out-patient
(c) Specific out-patient
(d) General out-patient

81. After completion of general checkup, the patients are asked to go for for accurate diagnosis.
(a) Clinical

(b) Pathological
(c) Both (a) & (b)
(d) None

82. A combined in-patient and out-patient unit with service provided from same window for out-patient dispensary.
(a) True
(b) False
(c) Sometime
(d) None

83. .....Patients are one who decide the image of the hospital as per the service received by them.
(a) Out-patient
(b) In-patient
(c) Both
(d) None

84. Prescription is dispensed by the.....
(a) Pharmacist
(b) Physician
(c) Doctor
(d) Patient

85. For the waiting patient the prescriptions is identified by.
(a) Name
(b) Number
(c) Address
(d) Medicine is directly dispensed

86. The patients those get hospitalized for treatment are called
(a) Ambulatory patient
(b) In-patient
(c) General patient
(d) None

87. To In-patient in hospital medicine is distributed to patient by which method.
(a) Floor stock system
(b) Numerical method
(c) Arrange in a container
(d) All of these

88. Unit dose dispensing system is used for
(a) In-patient
(b) Out-patients
(c) Both
(d) None

89. Individual prescription order system is adopted by..... hospital.
(a) Large hospital
(b) Medium hospital
(c) Small hospital
(d) Very big hospital

90. For In-patients the dispensed medicine is labelled by
(a) Patients name
(b) Number
(c) Given randomly
(d) Directly given to the patients

91. Give the advantage of individual prescription order system.
(a) Reduced man power
(b) Close control on inventory is possible
(c) Both (d)
(d) None

92. Dispensing of medicine is difficult in absence of pharmacist is in which system. (a) Floor stock system
(b) Unit dose system
(c) Combination system
(d) Individual prescription order system

93. In.....System both pharmacy and nursing station are responsible for drug distribution.
(a) Floor stock system
(b) Unit dose system
(c) Combination system
(d) Individual prescription order system

94. Those medicines which are stocked at the nursing station all the times and are charged to the patients account after their administration is called

(a) Unit dose dispensing
(b) Charged floor stock
(c) Non-Charged floor stock
(d) None

95. Penicillin G 3 lac units/ml is included in
(a) Antibiotics
(b) Antallergic
(c) Anti-coagulant
(d) Miscellaneous

96. Procaine is
(a) Cardiovascular drug
(b) Antallergic drug
(c) Anti-epileptic drug
(d) Anticoagulant

97. Envelop method is used for
(a) Charged floor stock
(b) Non-Charged floor stock
(c) Both
(d) None

98. For envelop method who fills prefilled envelops of medicines.

(a) Physician
(b) Nurses
(c) Pharmacist
(d) Patient

99. The stock of non-charge floor stock drugs is maintained by
(a) Category of drug
(b) Frequency of drug use
(c) Cost of drug
(d) All of these

100. Drug basket method is adopted for
(a) Non-charge floor stock
(b) Charge floor stock
(c) Both
(d) None

101. Stainless steel designed cupboard is design for which system.
(a) Drug basket method
(b) Mobile dispensing unit
(c) Unit dose dispensing
(d) Centralized unit dose dispensing

102. Advantages of complete floor stock system are
(a) Required drugs are especially available
(b) Minimizes return of medicine to pharmacy
(c) Reduction in patient prescription orders
(d) All of the above

103. CUDDS stands for
(a) Centralized unit dose drug distribution system
(b) Central utility dose drug distribution system
(c) Centralized unit dose drug dispensing system
(d) Central unit dose drug dispensing system

104. Avoids losses and drug wastage during handling is under.
(a) Drug basket method
(b) Mobile dispensing unit
(c) Unit dose dispensing
(d) All of these

105. In..... system, more staff is needed to prepare dosage.
(a) Drug basket method
(b) Mobile dispensing unit
(c) Unit dose dispensing
(d) All of these

106. Satellite pharmacy is adopted for
(a) Large hospital
(b) Medium hospital
(c) Small hospital
(d) Very big hospital

PHARMACOLOGY

107. Satellite pharmacy is adopted at
(a) Each floor
(b) For 2 floor one pharmacy
(c) Only one in a hospital
(d) Depends on hospital type

108 For pre-packaging, which factors are taken into consideration
(a) Call cycle of the out-patients
(b) Stability of the product
(c) Availability of the medicine
(d) All of these

109. The Disadvantage of satellite pharmacy is
(a) Effect on the budget of hospital
(b) Efficiently drugs can be distributed
(c) Time of drug distribution could be reduced
(d) None

110. Which is the policy and fact that considered by hospital authorities while pre-packaging
(a) The call-cycle of the out-patient
(b) Stability of the product
(c) Both (a) & (b)
(d) None of these

111. Advantage of pre-packaging is
(a) Inventory technique
(b) It reduce over all cost of medicine
(c) Required more man power
(d) All of these

112. Role of pharmacist at bedside pharmacy:
(a) Ward visit
(b) Detailing
(c) Interaction and alloying anxiety affright
(d) All above

114. required in the area of.....
(a) Operation theater
(b) Medical
(c) Ward
(d) Bed side area

115. Management of staff having the following types
(a) Pharmacist control
(b) Part of nursing control
(c) Dual controlled
(d) All of these

116. The person who is working in CSS should have the knowledge of the following:
(a) Principal of sterilization
(b) Good laboratory

(c) Both (d)
(d) None

117. A branch of the in-patient pharmacy responsible for preparing, dispensing, and monitoring medications for specific patient areas
(a) Pharmacy satellite
(b) Central pharmacy
(c) Out-patient pharmacy
(d) None of these

118. A prescription for schedule II and schedule III-controlled drug is valid for
(a) 10 days
(b) 12 days
(c) 14 days
(d) None