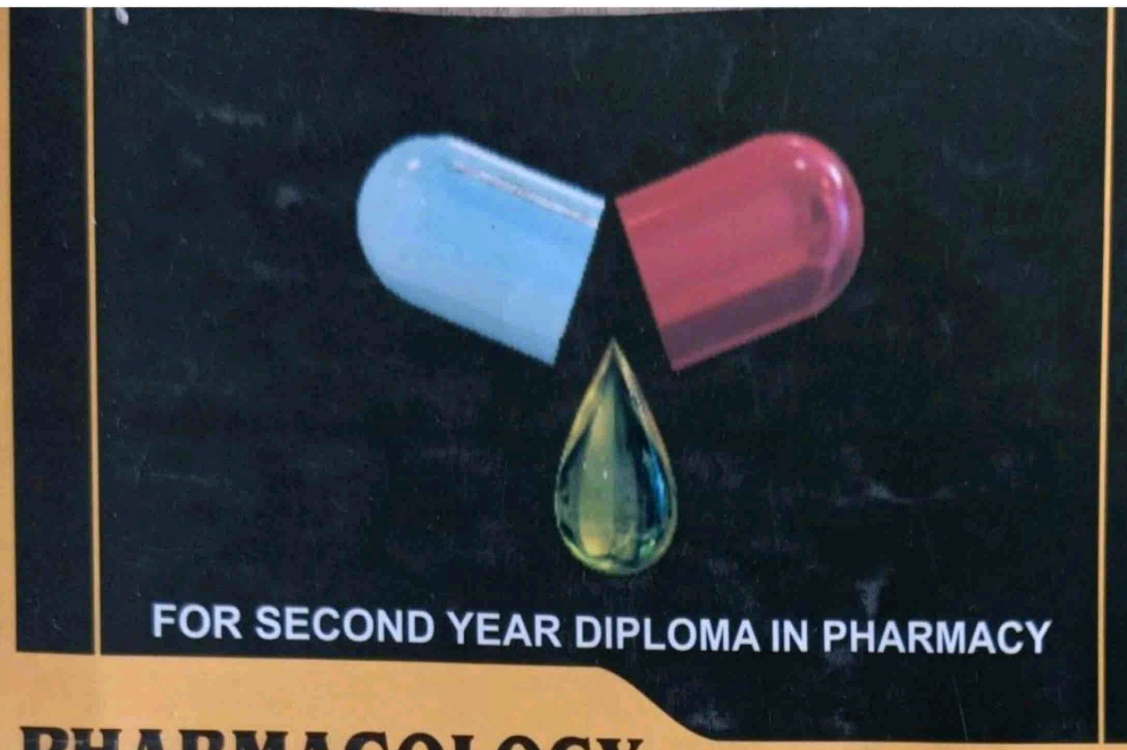

FOR SECOND YEAR DIPLOMA IN PHARMACY

PHARMACOLOGY & TOXICOLOGY

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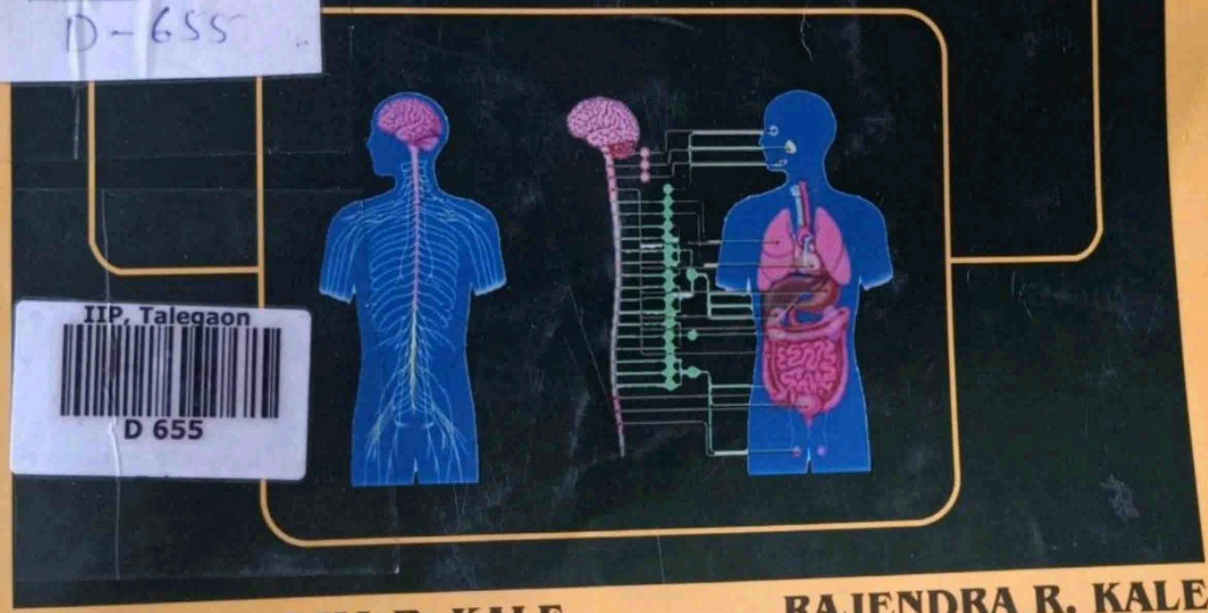

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Mrs. SHRADDHA R. KALE

RAJENDRA R. KALE

NIRALI PRAKASHAN
ADVANCEMENT OF KNOWLEDGE

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Chapter...1

GENERAL PHARMACOLOGY

SCOPE AND INTRODUCTION TO PHARMACOLOGY

Pharmacology, the term is derived from the Greek word 'pharmakon' meaning drug and 'logos' meaning science.

Pharmacology, thus, is the science of drugs.

Word 'drug' is derived from French word 'drogue' meaning a dry herb. It is defined as any substance used for diagnosis. Prevention and relief of disease.

Pharmacology deals with study of sources of drugs, mechanism of action, toxicity, absorption, distribution and metabolism of drugs. Pharmacology has the following major divisions :

1. **Pharmacodynamics :**
   - ➢ It deals with interaction between the chemical components of the living system and drugs.
   - ➢ It co-relates mechanism of action of drug with their chemical structure.
   - ➢ It is a quantitative study of the biological and therapeutic effects of drugs.
2. **Pharmacokinetics :**
   - ➢ It is the branch of pharmacology that defines fate of drug and deals with absorption, distribution, metabolism and excretion of drugs.
3. **Therapeutics :**
   - ➢ It is the branch, that deals with the cure of diseases and is defined as "to take care of ".
4. **Toxicology :**
   - ➢ It deals with effects of poisons, methods for their detection, diagnosis and treatment. Hence, this branch is defined as science of poisons.
5. **Pharmacy :**
   - ➢ It is the branch that deals with preparation of drug and drug combinations in a suitable dosage form, suitable and convenient for administration.
6. **Chemotherapy :**
   - ➢ It is the branch of pharmacology that deals with drugs, capable of destroying the causative organism without destroying host cells.

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7. Pharmacopoeia :

- It is an official code containing a list of selected established drugs and medical preparations with information about their physical property, tests for their identity, purity and potency.

  e.g. Indian pharmacopoeia
  British pharmacopoeia
  United states pharmacopoeia

Sources of Drugs :

Sources of drug	Example of drugs
1. Mineral	Liquid paraffin Magnesium sulphate Magnesium trisillicate
2. Animal	Insulin Heparin Thyroid extract
3. Plant	Morphine Quinine Digoxin
4. Synthetic	Aspirin Sulfonamides
5. Microorganism	Penicillin Streptomycin

Nature of Drugs :

Nature of drug	Example of drugs
1. Alkaloid	Morphine Atropine
2. Glycosides	Digitalis
3. Fixes oils (food value)	Peanut oil Coconut oil
4. Volatile oils	Oil of eucalyptus Ginger oil Peppermint oil
5. Gums	Agar
6. Tannins	Tincture catachu

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ROUTES OF ADMINISTRATION OF DRUGS

(a) Topical / Local Route :

- It is simplest route.
- Drugs used for local application are dusting powders, lotions, paste, ointments and plasters.
- The sites where drugs are commonly applied are skin, eye, nose, ear, throat, rectum and vagina.
- In this technique, drug absorption through intact skin depends upon lipid solubility of drug.

(b) Oral / Enteral Route :

- This is the most commonly used route.
- Drugs are administered in simple dosage forms like tablets, capsules and liquids orally.

Advantages :

- It is safe.
- It is convenient.
- Self medication is possible.
- It is cheap.

Disadvantages :

- Onset of action is very slow.
- Irritant, unpalatable drugs cannot be given by this route.
- This route connot be used if patients are unconscious or unco-operative.
- In conditions like nausea and vomiting, this route cannot be used.
- 100% absorption is not possible as the drug is degraded and destroyed by digestive enzymes.
- It is not useful in emergency cases.
- High doses are effective.

(c) Sub-lingual Route of Administration :

- In this technique, the medicament has to be to chewed, not be swallowed.
- In this type of administration, the medicament is kept below the tongue, or chewed, which then mixes with saliva and directly enters the systemic circulation.

Advantages :

- Onset of action is very quick.
- Quick termination of action by spitting out the tablet.
- Overdoses can be avoided.
- 100% absorption is possible as degradation of drug by digestive enzymes is prevented.

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Applications :

- Tri-nitroglycerine in angina pectoris.
- Isoprenailine in bronchial asthma.

(d) Parenteral Routes of Administration :

- Routes of administration other than oral is known as "parenteral".
- Parenteral routes of administration can be discussed as,
  1. Injection
  2. Inhalation

Advantages :

- Onset of action is very quick.
- In unconscious or unco-operative patients, drugs can be administered by this route.
- In nausea and vomiting, drugs can be administered by this route.
- 100% absorption is possible as there is no degradation by gastric enzymes.
- Accuracy of dosage schedule is possible.
- Low doses are effective.
- Irritant, unpalatable drugs can be given.

Disadvantages :

- It is a costly route.
- It is inconvenient.
- Self medication is not possible.
- Once administered, action cannot be halted and hence risky route.

The various types of injections employed for parenteral administration of drugs are :

- Intradermal (I/D)
- Intramuscular (I/M)
- Subcutaneous (S/C)
- Intravenous (I/V)

[A] Intradermal Injection :

1. In this parenteral administration, drug is injected in the layers of the skin.
2. The drug is injected in a very small amount not more than 1 ml.
3. These injections are made for local rather than systemic effects.

Applications :

- This route is mainly utilized for diagnostic tests like Schick test for diphtheria.
- It is employed for diagnostic Dick test for scarlet fever.

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- Used for tuberculin test.
- This route is also used for introduction of vaccines like B.C.G. (Bacille Calmette Guerin)
- Allergic sensitization test may be carried out by this route.
- Local anaesthetics are sometimes injected by this route.

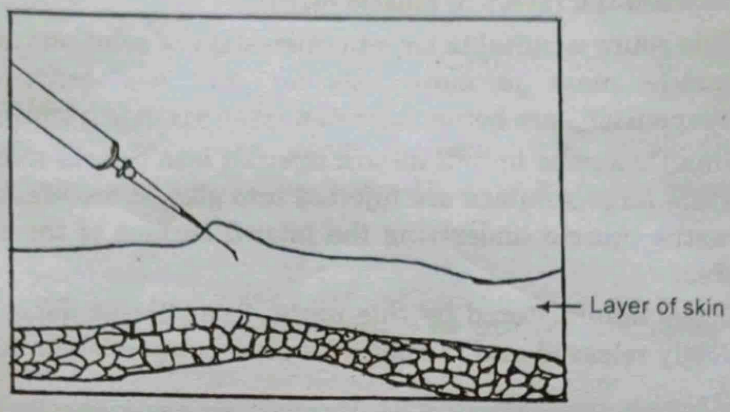

Fig. 1.1 : Intradermal Injection

[B] Subcutaneous :

1. In this type, drug is injected into the loose connective tissue - subcutaneous tissue under the skin.
2. Usually soluble drugs are injected by this route.
3. The site of injection usually is the outer surface of the upper arm or front of the thigh.
4. The drugs injected by this route are rapidly absorbed and their effect is prompt.
5. Only upto 2 ml quantity of drug can be injected by this route.
6. Drugs like adrenaline, morphine, insulin are administered by this route.

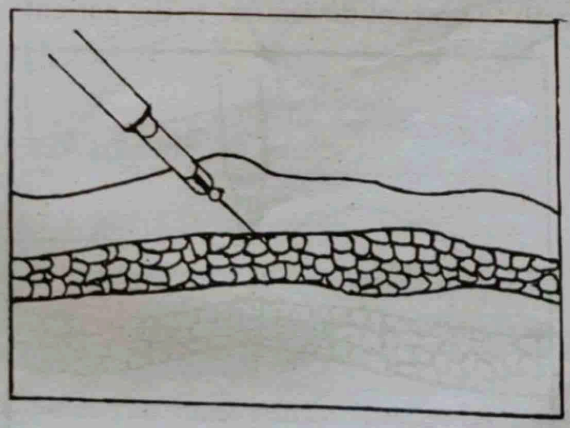

Fig. 1.2 : Cutaneous Injection

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[C] Intramuscular Administration :

1. In this type of administration, drug is injected in the layers of muscle tissue.
2. Intramuscular injections are made with a longer and heavier meedle, that penetrates the subcutaneous tissue. This permits the drug deposition deep between the layers of muscle mass.
3. This route is suitable for administration of solutions and suspensions. As the muscle mass is more vascular and less sensitive, irritant solutions /suspensions are better tolerated when given intramuscularly.
4. Small volumes upto 2 ml are injected into deltoid muscle (at shoulder joint) while large volumes are injected into gluteal muscle mass (at hip joint). The vastus muscle underlying the lateral surface of the thigh is an alternative area.
5. Drugs administered by this route, form "tissue depot" from where they are slowly released and thus provide slow but persistent action.

Applications :

- For administration of long action esters of sex hormones.
- For administration of steroids.
- For poorly soluble salts like benzanthine penicillin, or procaine penicillin G.

Precautions :

- Check that the needle is not in the blood vessel. The absence of blood in the barrel on pulling the plunger, after needle has been inserted in the muscle is a reliable assurance.
- Care should be taken to avoid injury to nerves.
- After selecting the appropriate site, cleanse the skin, stretch the skin between the thumb and forefinger to compress the subcutaneous tissue. The needle is held perpendicular to skin and the inserting movement should be quick and smooth to prevent discomfort to the patient.

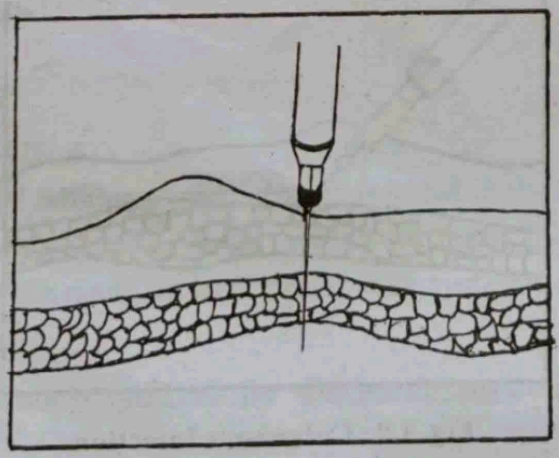

Fig. 1.3 : Intramuscular Injection

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[D] Intravenous Injection :

1. In this technique, the drug is introduced directly into the lumen of the vein.
2. Usually cubital vein at the bend of elbow is selected.
3. This route of injection bypasses all the barriers of drug absorption and hence 100% absorption is possible.
4. This route is usually reserved for emergency administration of potent drugs when a rapid action is desired.
5. Insoluble drugs, oily substance, drugs in suspension, markedly acid or alkaline salts incompatible with blood, should never be administered by this route.

Applications :

- Bolus doses of lidocaine are injected rapidly by intravenous route to control dangerous cardiac arrhythmia.
- Substances that would act as irritants on subcutaneous or intramuscular administration, may be given by slow intravenous injection.
- Infusions of large amounts of fluid are often made by venolysis of overcome dehydration. e.g. Normal saline.

This is also useful to supply nutrition to patients who cannot take fluids or food orally. e.g. DNS or dextrose normal saline.

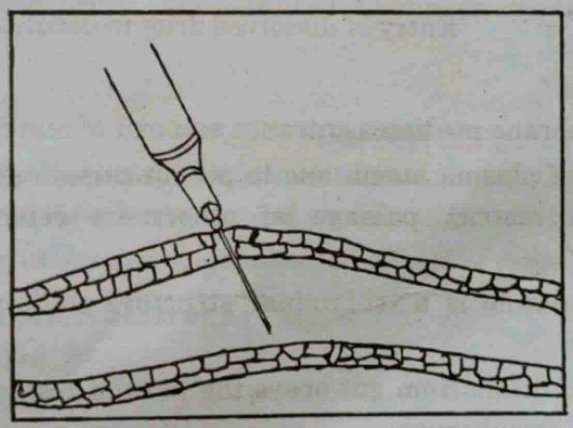

Fig. 1.4 : Intravenous Injection

General Precautions for Parenteral Administration :

- Aseptic technique must be employed whenever the drug is injected parenterally.
- Although skin cannot be made sterile, it must be made as clean as possible.
- A cotton pledget soaked in germicidal solution or rectified spirit is applied in a firm circular motion, moving from the centre outwards.

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- All equipments used in the preparation of injection must be sterile and handled in such a manner as to maintain sterility.
- Knowledge of the anatomy of the area in which injection is to be made is essential.

Note : All these above techniques have to be learnt and practiced.

Precautions :

- This is the most rapidly effective route, at the same time most dangerous route of administration. For once the drug is injected directly into the blood stream, it cannot be withdrawn or recalled, nor its action can be effectively slowed down.

  Thus, every effort must be made to avoid errors.
- Injections must be given very slowly.
- Care should be taken to avoid leakage of drug solution into surrounding tissue.
- Sloughing of tissue can occur if vasoconstrictors like nor-adrenaline extravaste.

ABSORPTION OF DRUGS AND FACTORS AFFECTING IT

- Disintegration : Breaking up of solid dosage form into granules.
- Dissolution : Entry of granules into the aqueous phase.
- Absorption : Entry of dissolved drug molecules into the blood flow.

Physiology :

- Plasma membrane mediates entrance and exit of material.
- This ability of plasma membrane to permit certain substances to enter and exit but to restrict passage of others, is referred to as "Selective permeability".
- Plasma membrane is a tri-laminar structure containing phospholipid and protein layer.
- Absorption of drugs from gut obeys the laws of transfer of molecules across the biological membranes.

Transport Mechanism :

- Most of the drugs are absorbed by **"passive diffusion"**.
- Few of the active agents are absorbed by **"active transport"** or **"carrier mediated transport"** mechanism.

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[A] Passive Transport Mechanism :

This is the most commonest mechanism by which most of drugs are transported across cell membrane.

- Passive process is referred to as "diffusion" and occurs when there is greater movement of molecules or ions from a region of their higher concentration to a region of their lower concentration.
- Thus "passive process" is dependent on "concentration gradient".
- Drugs which are lipid soluble (unionised) are transferred across the cell membrane by passive diffusion.
- In this process, bi-directional movement of the concerned molecules depend on the concentration gradient without involvement of energy.
- This process is not dependent on pH of medium, provided the drug dissolves in intestinal fluid and reaches the absorptive surface.

[B] Active Transport Mechanism :

- This is a well defined and specialized process in which drug is transported against a concentration gradient with the involvement of energy.
- The drug attaches to a special carrier in the membrane which facilitates diffusion across membrane and releases the drug.
- Inorganic ions like sodium, potassium, chloride and calcium are absorbed by active transport.
- Drugs like synthetic drugs, steroids and hormones are absorbed by this transport.

Significance :

Knowledge regarding the rate of absorption is necessary :

1. To determine the frequency of administration.
2. To define duration of effective action.
3. For anticipation of desired and undesired effects of drug.

Factors Affecting Absorption of Drugs :

1. **Physical Properties**

(a) Physical state :

Liquids are better absorbed than solids.

Crystalloids are better absorbed than colloids.

Amorphous form is better absorbed than crystalline.

(b) Lipid and Water solubility :

Higher the lipids solubility, greater is the rate of absorption from gastro intestinal tract.

e.g. Fat soluble vitamins A, D, E and K are better absorbed.

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2. Dosage Form

(a) Particle size :

Large aggregates of an active compound do not disintegrate rapidly even though kept for a prolonged time in contact with gastric juices. Hence smaller the particle size greater is the rate of absorption.

e.g. Chloramphenicol, steroids etc.

(b) Formulation :

Substances like lactose, sucrose, starch, calcium phosphate, calcium lactate are used as inert diluents in formulating tablets and powders.

There are agents that may interfere with active drug and affect its absorption.

e.g. Calcium and magnesium ions reduce absorption of tetracyclines.

Calcium in calciferol may lead to calcium toxicity.

Absorption of drug can be delayed by formulating sustained released dosage form.

3. Physiological Factors

(a) pH :

pH of gastro-intestinal tract and blood may interfere with absorption of drug.

e.g. Acidic drugs are better absorbed in stomach – salicylates, barbiturates.

Basic drugs are well absorbed in alkaline environment of intestine-pethidine and ephedrine.

(b) Ionization :

Unionised drugs are lipid soluble while ionized are water soluble agents. Hence unionized drugs are better absorbed than ionized drugs.

(c) Presence of other agents :

Vitamin C enhances the absorption of iron from gastro-intestinal tract while phytates reduce it.

Liquid paraffin reduces absorption of fat soluble vitamins A, D, E, K.

Calcium by chelation reduces absorption of tetracycline.

(d) Presence of disease :

In presence of diseases, absorption of drugs is reduced.

In presence of liver cirrhosis, achlorhydria, rate of absorption is low.

In diarrhoea and dysentry increased intestinal motility reduces absorption.

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(e) Area of absorption :

Drugs are better absorbed in the intestine than in the stomach because of larger surface area of intestine.

(f) Gastro-intestinal transit time :

Absorption of drugs is influenced by presence of food, volume, viscosity, tone of gastric content.

Rapid absorption occurs if drugs are administered before meals.

METABOLISM, DISTRIBUTION, EXCRETION

Drugs after administration are distributed widely in the body. Distribution of drugs means transport of drugs to their target tissue, i.e. site of action.

For drug distribution body fluids act as solvent and vehicle.

Drugs are widely distributed in extracellular fluid, in blood, adipose tissue and body tissue.

Drugs are mainly metabolized in liver, kidney, lungs, skin and placenta.

The process of elimination of drugs from body is defined as excretion. Kidney, lungs, billiary system, intestine are organs involved in excretion. Some drugs are also excreted in saliva, milk and sweat.

Organs	Drug excreted
Kidney	Barbiturates, salicylates, amphetamine, penicillin, morphine, benzodiazepines.
Saliva	Iodides, metallic salts.
Lungs	Volatile general anaesthetics, paraldehyde.
Intestine	Purgatives like cascara, senna, sulfa like sulfaguanidine.
Bile	Tetracycline, chloramphenicol.
Skin	Metals like arsenic, mercury.
Milk	Barbiturate, diazepam, chloramphenicol .

Factor Affecting Drug Distribution :

- The pharmacological agents, when administered in a suitable dosage form, enter the blood stream, get uniformly distributed in the body and then reach the site of action.
- Distribution is defined as the delivery of drug molecules between the water, lipid and protein contents of the body. This involves transport of drug molecules across the membranes of gastro-intestinal epithelium, blood brain barriers, placental membrane, etc. This occurs by the following mechanism

(a) Pass e transfer includes (i) Simple diffusion (ii) Filtration.

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(b) Specialized transport includes (i) active transport (ii) facilitated diffusion (iii) pinocytosis.

- Drug, when enters the vascular system, gets distributed in various tissues and body fluids. The ways in which this process takes place are :.
  - The drug may largely stick to walls of the vascular system.
  - Low molecular weight agents get distributed via the body water.
  - Most of the pharmacological agents show un-uniform distribution.
  - Some agents are concentrated specifically in one/other tissue.
- These above processes are affected by following factors.
  (1) Plasma protein binding.
  (2) Physicochemical characteristics
  (3) Routes of administration
  (4) The presence of active transport system
  (5) Specific barriers.

Plasma Protein Binding :

- The pharmacological agents are transported bound to plasma proteins, albumin.
- Drug bound to plasma protein is in equilibrium with free drug in plasma and only unbound drug is available for distribution.

Physicochemical Characters :

Distribution of drugs depends upon lipid solubility of drug.

Higher the lipid solubility of pharmacological agent, more widely it is distributed in the body.

Route of Administration :

Drugs administration by parenteral route are better and widely distributed to organs and tissues, with rich blood supply, than the drugs administered by the oral route.

Regional Blood Flow :

Blood supply varies from one tissue to another. Distribution of drug is directly proportional to the blood flow in tissues.

Drug distribution is altered in presence of diseases.

- Presence of active transport system.

FACTORS MODIFYING THE DRUG ACTION

1. Age and Body Weight :

Age and body weight affects drug action. The drug response varies significantly at extremes of life. e.g. some drugs fail to respond in similar ways in new born

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infants and elderly. This is correlated with ability of an individual to detoxify drugs and convert them to inactive metabolites.

To avoid error it is essential to calculate dose for children with due comparison with standard adult dose, taking into consideration the age and weight factors.

a. Young's Rule : for children 2 to 12 years age.

$$\frac{\text{Age}}{\text{Age} + 12} \times \text{Adults dose} = \text{Child's dose}$$

b. Hamburger's Rule :

$$\frac{\text{Weight in kg}}{70} \times \text{Adults does} = \text{Child's dose}$$

c. $$\frac{\text{Body surface area } (m^2) \text{ of child}}{1.7} \times \text{Usual adult dose} = \text{Child's dose}$$

2. Sex Factor :

Drug responses differ according to sex. Females require smaller doses of drugs due to their lesser body weight. Drugs must be administered with due care in females as they have to pass through delicate periods of life like menstruation, pregnancy and lactation.

For example :

- Drugs producing pelvic congestion, like drastic purgatives, should be avoided during menstruation.
- Drugs which stimulate uterine musculatures, like drastic purgatives, antimalarial quinine and ergot alkaloids should be avoided in pregnancy.
- Many drugs are excreted in milk and either discourage breast feeding or enter foetal circulation and produce toxicity.
- Central nervous system depressants like morphine and barbiturate may produce excitement in females.

3. Time of Administration / Diet :

Most of drugs are advised to be taken after meal, so as to reduce risk of gastric irritation, nausea and vomiting.

e.g. Salicylates and derivatives.

Some drugs, on the other hand, are advised to be taken on an empty stomach :

- To get quick action.
- To avoid interference of food.
- To prevent destruction of drugs by digestive enzymes.

e.g. Antibiotics like penicillin, tetracycline.
Anthelmentics.
Anti-motion sickness agent.

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4. Environment :

During daytime central nervous system is highly active. Hence dose of barbiturates required to produce sleep during night is less than dose of barbiturate required to produce sleep during the day.

5. Route of Administration :

The onset of pharmacological action is quick when drugs are administered intravenously, eventhough doses are smaller, than when administered orally.

6. Emotional Factors :

The inert dosage forms, which resemble the actual medicament only in physical properties like colour, size, shape, smell is defined as "placebo".

Placebos are effective in conditions like angina pectoris, bronchial asthma and psychic disorder to avoid agrevation of condition due to emotional factors.

7. Metabolic Disturbances :

Changes in water, electrolyte balance, acid-base balance, body temperature, other physiological factors may affect drug response.

e.g. Salicylates reduce body temperature only in case of pyrexia.

Absorption of iron from gasto-intestinal tract is more in iron deficient anaemia.

8. Presence of Disease :

Drug responses are altered in presence of diseases.

e.g. In liver cirrhosis, drugs like barbiturate and chlorpromazine may produce prolonged effects.

Drugs which are excreted mainly by the kidney may prove toxic if administered during kidney impairment.

9. Cumulation :

Every drug has it's own half life i.e. time required for its absorption, distribution and excretion. If a drug is slowly excreted, its repeated administration may built up sufficient high concentrations in plasma, which is termed as cummulation and toxicity as cumulative toxicity.

e.g. Phenobarbitone in epilepsy, digitals in congestive cardiac failure.

10. Presence of Previous Drug Therapy :

Presence of previous drugs may stimulate or inhibit the pharmacological actions of other drugs.

e.g. Hypnosedative phenobarbitone and anti-epileptic phenytoin are potent inducers of microsomal enzyme system and thus have the effect of increasing dose requirements of other drugs.

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11. Addition, Additive Effect :

When two or more drugs administered, act on same physiological system, the total pharmacological action is equivalent to sum of their individual pharmacological actions.

This phenomenon is termed as "additive effect".

e.g. Ephidrine and aminophylline in asthma.

12. Synergism :

When two or more drugs administered together, act on different receptors, but produce same physiological action, which is greater than sum of their individual actions, the phenomenon is termed as "synergism".

Where 'syn' means with and 'ergo' means work.

e.g. Antihypertensive combination.

	Vasodilator	:	Hydralazine hydrochloride
+	β - blocker	:	Propranolol
+	Diuretic	:	Furosemide

13. Antagonism :

When two or more drugs administered together act on same physiological system, they try to oppose each other's pharmacological action. The agent is referred as antagonist and the phenomenon as antagonism.

The antagonism can be classified as follows :

(a) Chemical antagonism :

In this, biological activity of one drug can be reduced by a chemical reaction with another agent.

e.g. Acid and alkali.

Antacid therapy is best application of chemical antagonism.

e.g. $3HCl + Al(OH)_3 \rightarrow AlCl_3 + 3H_2O$

gastric — aluminium gel (weak alkali)

(b) Competitive or reversible antagonism :

In this an agonist and an antagonist compete for same physiological system. It is totally dependent on concentration of agonist and antagonist.

If a dose response curve is plotted, it shifts to right and maximum response is not affected.

e.g. Histamine × Anti-histaminics

Acetylcholine × Atropine.

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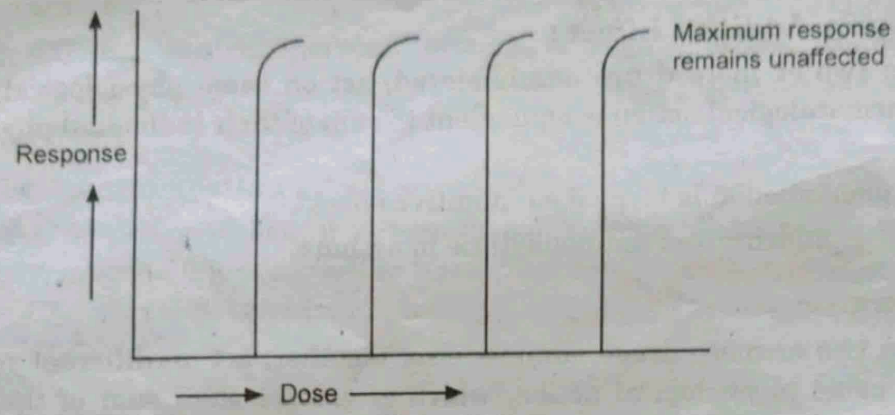

Fig. 1.5

(c) Non-competitive / irreversible antagonism :

In this type, antagonist interacts with receptor in such a way that effective concentration of agonist fails to combine with receptor and produce its own pharmacological action.

e.g. α-adrenergic blocker phenoxy benzamine combines with "α" receptors in such way that blockade cannot be overcome by increasing the concentration of "α" agonist nor-adrenaline.

In this type, when dose-response curve is plotted, it shifts to the right but maximum response is affected (Reduced).

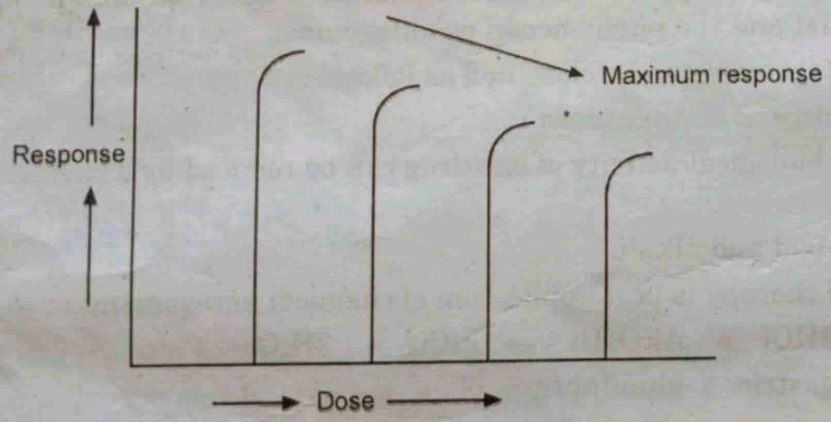

Fig. 1.6

(d) Physiological antagonism :

e.g. Adrenaline antagonizes bronchoconstriction produced by histamine.

Adrenaline antagonizes anaphylactic shock produced by penicillin.

14. Tolerance :

An unusual high dose of drug required to produce therapeutic response, produced by therapeutic dose of drug is known as "tolerance".

Tolerance can be discussed in two groups :

(a) Natural / Congenital

(b) Acquired / Pseudo

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(a) Natural / Congenital :

(i) *Species tolerance :*

- Rabbits can tolerate large amounts of belladonna due to the presence of atropine esterase in liver.

(ii) *In humans – Racial tolerance :*

- Negroes fail to produce dilation of pupils when ephedrine is instilled in conjunctival sac, as they are tolerant to sympathomimetic amines.
- Eskimos can tolerate high fat diet and carbohydrates.

(b) Acquired / Psuedo :

- Repeated administration or consumption of a drug results in slow development of resistance to its effect. Due to this, to achieve same therapeutic response, it is essential to increase the dose of drug. This phenomenon is termed as acquired tolerance.

  e.g. Morphine, cocaine, heroin, alcohol, nicotine, barbiturates etc.

Cross Tolerance :

In this phenomenon, if an individual initially develops tolerance to a drug belonging to a particular group, he shows tolerance to other drugs belonging to the same group.

e.g. Tolerance developed to alcohol and general anaesthetics.

Tolerance	Tachyphylaxis
• It means reduced responsiveness to drugs.	• It is defined as acute tolerance.
• It is an unusual resistance to respond to usual dose of drug.	• It is short lived, resistance to durg action, develops rapidly.
• When an unusual high dose of a drug is required to produce therapeutic response previously produced by therapeutic dose of a drug, "tolerance" is said to develop.	• Tachyphylaxis develops on repeated administration. When same pharmacological agent is administered in a same dose repeatedly, without a time interval inbetween, it fails to produce same pharmacological response. Declination in pharmacological response is referred to as 'Tachyphylaxis'.
• It develops slowly.	• It develops quickly.
• In this phenomenon original effect may be obtained by increasing the dose.	• Original effect may not be obtained by increasing the dose.
• E.g. Barbiturates, Vasodilators	• e.g. Ephedrine.

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DRUG INTERACTION

Definition :

It is defined as, an alteration in the duration or magnitude of pharmacological effect of one drug produced by another drug.

Thus, when more than one drug is administered at the same time the combined effect may be : (1) antagonism or (2) synergism.

Cause of Drug Interaction :

(i) Availability of potent drugs.

(ii) Multiprescription practice / poly pharmacy.

(iii) Irrational poly pharmacy.

(iv) Drug explosion.

Classification :

1. Drug interactions outside the body :
   - ➢ During formulation
   - ➢ During mixing
2. Drug interactions inside the body :
   - ➢ During pharmacokinetics
   - ➢ During pharmacodynamics

1. Drug interactions outside the body :

- ➢ During formulations
- ➢ During mixing

Alteration in the duration or magnitude of pharmacological effects of drugs can occur outside the body during formulation or mixing. These changes are correlated with changes in pH of solutions.

Many drugs are chemically or physically incompatiable in solution and cannot be safely mixed. For example :

[1] Dextrose and fructose are unsuitable vehicles for sodium or potassium salts of weakly acidic drugs like sulfonamide, barbiturate, methicillin etc.

[2] Pharmacological agents like barbiturates, phenytoin phenothiazines diuretics like furosemide should not be mixed with any other drug in solution.

These interactions, occuring outside the body during mixing or formulation, can be prevented :

- ➢ By avoiding direct addition of drugs to blood or amino acid solutions.
- ➢ Drugs should be mixed with infusion fluid just before use.

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2. Drug interactions inside the body :

➢ During pharmacokinetic :

Administration of two or more drugs may interact with each other and can affect each others pharmacokinetics, i.e. rate of absorption, absorption through gastro-intestinal tract, protein binding, etc.

The possible interactions are as follows :

No.	Drugs	Interactions
1.	Antacid like aluminium gel with antibiotics like tetracycline.	The cations like aluminium and calcium form insoluble complexes – "Chelates" with antibiotics.
2.	Liquid paraffin, emollient laxative with fat soluble vitamins like A, D, E, K.	Liquid paraffin, like mineral oil reduces absorption of fat soluble vitamins A, D, E, K.
3.	Phenylbutazone like analgesic if administered with anticoagulent warfarin	As phenylbutazone posseses higher binding capacity, it displaces warfarin from its receptor site.

➢ During pharmacodynamics :

Such type of drug interactions occur at the site of drug action at the receptor site. These interactions depend upon concentration of drug at receptor site. For example :

Drug 1	Drug 2	Receptor	Net interaction result
1. Nor-adrenaline (peripheral vaso constrictor)	Phentolamine (peripheral vessel blocker)	"α" receptors on peripheral vessels	No effect
2. Isoprenaline ("β" receptor stimulant)	Propranolol (β-blocker)	"β" receptors on heart and bronchii	No effect

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Drugs	If administered with drug / agent	Interaction effect
1. Mono–amino oxidase inhibitors like antipsychotics e.g. imipramine, desipramine	Tyramine cheese butter	Hypertensive crisis
2. Warfarin – anticoagulant	Phenyl butazone like analgesic	Bleeding / Haemorrhages
3. Ether- a liquid anaesthetic agent	Neomycin, an antibiotic	Respiratory paralysis

Role of Pharmacist to Avoid Drug Interactions :

- Pharmacists must keep in mind that, the more potent the drug, higher is the risk of toxicity.
- Pharmacists – Doctor – Patient's counselling is essential to make the physicians and patients aware about known interactions.
- Pharmacist and physician should maintain drug history and medical record of patients.

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Chapter...2

DRUGS ACTING ON CENTRAL NERVOUS SYSTEM

GENERAL ANAESTHETICS

Definition :

These are pharmacological agents which when administered externally, bring loss of all five modalities of sensation with reversible loss of consciousness.

Stages of General Anaesthesia :

The progress of general anaesthesia from the point of induction of anaesthetic is divided into four stages.

1. **Stage of analgesia and amnesia :**
   - This stage is inbetween induction of anaesthesia to the loss of consciousness.
   - It is characterized by loss of consciousness with feeling of floating, numbness and analegesia.
   - All reflexes are present.
   - This analgesia stage is suitable for dental surgery and obstetrical procedures.
2. **Stage of delirium or excitement :**
   - This stage is between the loss of consciousness to the first plane of surgical anaesthesia.
   - Neurones are released from the control of higher cerebral centers in this stage.
   - It is characterized by psychomotor excitement and hyperactivity of respiratory and cardiovascular reflexes.
   - This stage is not suitable for any surgical procedure.
3. **Stages of surgical anaesthesia :**
   - This stage starts when patient's excitement is stopped and breathing is regularized.
   - It is characterized by fixed eye ball (No wink response on touching the cornea) and shallow abdominal breathing.
   - All reflexes are completely abolished.
   - This stage is most suitable for major operations.
   - Anaesthesia should not pass beyond this stage.

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4. Stage of medullary paralysis :

- It is a stage of overdose beyond the stage of surgical anaesthesia in which medullary centres are completely paralysed.
- It is characterized by stoppage of breathing, fall of blood pressure to zero level and cardiovascular collapse. It leads to death.
- Vigorous and prompt measure only, can save the patient from this stage.

Properties of Ideal General Anaesthetic :

- Easy to administer.
- Should produce rapid and smooth induction and recovery.
- Should be non-inflammable and non-irritating.
- Should possess good analgesic effect.
- Should possess adequate muscle relaxation.
- Should possess sufficient margin of safety between stage of surgical anaesthesia and stage of medullary paralysis.
- Should not have any effect on liver, kidney and heart i.e. should not produce bronchospasm, laryngospasm, should not interfere with uterine contractility, should not affect blood pressure and cardiac contractility.
- Should be potent anaesthetic with adequate duration of action.
- Should not cause violent excitation, urinary retention, nausea and vomiting during induction, recovery and post anaesthesia period.
- Sings and stages of anaesthesia should be clear.

A single anaesthetic agent generally doesn't possess all ideal properties. So anaesthetic is associated with other agents like sedatives and hypnotics, muscle relaxants, anxiolytics, antiemetics, narcotic analgesics etc. and this concept is called as **"Basal Aanaesthesia"** .

Classification :

General anaesthetics are classified as follows :

(A) Volatile or Inhalatory Anaesthetics

1. Liquids :

- Ether
- Chloroform
- Halothane

2. Gases :

- Cyclopropane
- Nitrous oxide

(B) Non-volatile or Intravenous Anesthetics

1. Barbiturates :

- Thiopentone

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- Kemithal

2. **Non-barbiturates :**
   - Propanedid
   - Ketamine

(A) VOLATILE ANAESTHETICS

1. Pharmacology of Ether

Physical Properties :

- It is colourless, volatile liquid with a pungent odour.
- It boils at 35°C and vapours are irritant.
- When ether is exposed to air, moisture or light, it gets converted to ether peroxides and acetic aldehyde, which is irritant in nature.
- Ether is highly explosive.
- Hence it is stored in amber coloured bottles covered with black paper.

Advantages :

- It is the safest anaesthetic agent with wide margin of safety even in unexperienced hands.
  90 mg / 100 ml blood → induces anaesthesia
  190 mg / 100 ml blood → causes respiratory arrest.
- It is not only a safe anaesthetic but a good analgesic also.
- Ether possesses curarimimetic action i.e. produces good muscular relaxation.
- Ether does not modify blood pressure.
- It does not interfere with uterine contractility.
- It does not have any effect on liver, kidney and heart.
- No special or complicated apparatus is required.
- It is an economical agent.

Disadvantages :

- Induction is very slow and stormy.
- Ether vapours are irritant and may increase salivary, bronchial secretion. Accumulation of secretions may induce cough and laryngeal spasm.
- Ether is highly explosive, hence cannot be used for cauterisation.
- Recovery is slow and is associated with high incidences of nausea and vomiting.
- In children, it may produce convulsions.

Preparations :

- Anaesthetic ether, I.P.
- Spirit of ether, I.P.

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Dose :

- 1 – 4 ml

Therapeutic Uses :

- As general anaesthetic.
- As rubefacient.
- Used as solvent.
- As cleansing agent.

2. Halothane

Physical Properties :

- It is heavy, colourless liquid, anaesthetic agent.
- It is an inflammable, non-toxic fluorinated hydrocarbon.
- It has sweet, fruity odour and boils at 50°C.
- It affects most metals including stainless steel, brass and copper. It also affects rubber.

Advantages :

- Induction is very smooth as it has a sweet, fruity odour.
- Recovery is also fast, smooth with low incidences of nausea and vomiting.
- Being non-inflammable it does not cause irritation of respiratory passage. It inhibits salivary secretion hence endotracheal intubation is much easier.
- It does not produce bronchospasm and laryngospasm, hence can be used in patients with bronchial asthma.

Disadvantages :

- Muscular relaxation is inadequate.
- It causes respiratory, cardiovascular depression.
- Mental recovery is delayed.
- Shivering during recovery is very common.
- It is a poor analgesic.
- It is expensive, needs special apparatus for administration.

3. Chloroform

- It is no more used for therapy because of its :
- Hepato toxicity.
- Nephro toxicity.
- Cardio toxicity.

4. Cyclopropane

Physical Properties :

- It is a colourless gas with sweet odour and taste.
- It is available as liquid under pressure and administered in closed circuit.

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Advantages :

- It is a potent anaesthetic agent.
- Induction is pleasant and quicker.
- Recovery is rapid and smooth.
- Does not irritate respiratory passage.
- Incidences of nausea and vomiting are less.
- It produces adequate muscular relaxation.
- It does not affect blood pressure and cardiac contractility.

Disadvantages :

- The signs of anaesthesia are not clear.
- Rapid induction may produce laryngospasm, breath holding, tachypnoea, coughing.
- Cyclopropane may produce excitement and delirium.
- Stages of anaesthesia are not clear, as induction is very smooth.
- It increases capillary oozing.

5. Nitrous Oxide

Physical Properties :

- It is a colorless gas with sweet odour and taste.
- It is non-inflammable.

Advantages :

- It is non-inflammable and non-irritant.
- It produces rapid induction and recovery.
- It has good analgesic effects and hence can be used in dental practice.
- It is safest anaesthetic agent.
- Incidences of nausea and vomiting are rare.

Disadvantages :

- Pre-anesthetic medication is required as it is not a potent anaesthetic.
- Excitement may be violent.
- Special apparatus is required.

(B) NON-VOLATILE INTRAVENOUS ANAESTHETICS

Advantages :

- Easy to administer.
- Induction is rapid and smooth.
- Post-anaesthetic complications are rare.
- Recovery is very fast.
- Respiratory and myocardial functions remains unaffected.
- No irritation of respiratory passage.

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Disadvantages :

- Usual stages of anaesthesia are not clear.
- Coughing, apnea is common during induction.
- Muscular relaxation is very poor.
- Injection around nerve may produce palsy.

Preparations :

- Thiopenton sodium → 2.5% solution
- Methohexitone → 1 % solution
- Propanidid → 4 mg/kg
- Ketamine → 1.2 mg/kg

PREANAESTHETIC MEDICATION

Definition :

The pharmacological agent when administered externally with an important objective to make anaesthesia more smooth and agreeable for the patient, the phenomenon is termed as **"Preanaesthetic medication"**.

Aims and Objectives :

- For sedation – to reduce anxiety.
- To obtain an additive or synergestic effect.
- To minimize pre and post operative complications.
- To facilitate smooth and rapid induction.
- To overcome secretary effects of general anaesthetics.

Various agents preferred as preanaesthetic are as follows :

No.	Type	Drug	Trade name	Dose
1.	Opioid analgesic	Morphine Pethidine	– –	15 mg 15.30 mg
2.	Barbiturates	Pentobarbitone Secobarbitone	Nembutal Lipaton	30 mg –
3.	Anxiolytic	Diazepam	Valium	5 mg
4.	Anti-emetic	Promethazine	Avomine	30 mg
5.	Antisecretory	Atropine	–	0.6 mg
6.	Skeletal muscle relaxants	D-tubo curarine	Relaxyl	10 mg.

ANALGESICS

Physiology :

Pain is an unpleasant sensation which informs about structural and functional changes in the body and acts as a warning signal against disturbances in it.

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Pain is a sensation which is appreciated only by an individual and hence cannot be defined well.

Pain receptor organs are distributed throughout the body.

Clinically pain can be classified as follows :

1. **Superficial / Cutaneous pain :**
   This includes pain arising from skin, superficial mucous membranes and nerves.
2. **Deep, non-visceral pain from muscles, joints, ligaments, bones :**
   It is usually dull.
3. **Visceral pain :**
   It is diffuse, not easily localized, is associated with sweating, nausea, fall in blood pressure.
4. **Referred pain :**
   It is defined as deep pain, which may sometin s be misinterpreted as if it is coming from some part of the body other than actual site of stimulation.
   e.g. cardiac pain – commonly referred to left arm.
5. **Psychogenic / Functional pain :**
   It is defined as vague pain and is not related to any anatomical part of the body.

Broadly pain is classified as :

(a) Severe pains :

Associated with malignancy parturation, burns, fractures etc.

(b) Mild pains :

Associated with headache, bodyache, arthralgia, myalgia, neuralgia etc.

Neurophysiology of Pain (Pain Pathway)

Large diameter conducting nerve

↓

Reaches to spinal cord and activates
first transmission cell collateral cells
in substantia gelatinosa at the apex of dorsal
gray horn and gray matter of spinal cord

↓

Secondary axon from dorsal horn

↓

From spinothalamic tract

↓

Appears lateral to brain stem

↓

Finally terminates in thalamus

↓

Responsible for localization of pain sensation.

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Definition :

These are pharmacological agents which when administered externally relieves mild or moderate pains without affecting degree of consciousness.

Classification :

1. Narcotic analgesics / Opioid analgesics :

These are the pharmacological agents, which when administered externally, relieve severe degrees of pain associated with burns, parturitions, fractures, traumas, tumors, malignancy etc. by affecting degree of consciousness slightly – by producing narcosis (slight depression of central nervous system). Hence refered as 'narcotics'.

Opioid Analgesics :

(i) Phenanthrene derivatives → (a) Morphine
(b) Codeine
(c) Thebaine

(ii) Benzyl isoquinoline series → (a) Papaverine
(b) Noscapine
(c) Narcine

2. Non-opioid analgesics Or Non-narcotic analgesics, anti-pyretics :

These are the pharmacological agents, which when administered externally relieve mild, dull aching type of pain associated with myalgia (muscle pain), arthralgia (joint pain), neuralgia (nerve pain), toothache, bodyache, headache etc. without depressing central nervous system (without narcosis). Hence referred as non-narcotic.

e.g. Salicylates and derivatives.

[A] Pharmacology of 'Narcotic Analgesics' (e.g. Morphine)

(a) Mechanism of Action :

All narcotic analgesics acts on opiate receptors.

(b) Pharmacological Actions :

1. On central nervous system (C.N.S.)

(i) Analgesia :

Morphine when administered externally relieves severe degrees of pain associated with trauma, fractures, malignancy, burns, parturition, acute pericarditis, pleurisy etc.

Morphine relieves severe pains by following mechanism :

- It increase pain threshold.
- Thereby it decreases perception of pain sensation.

The net result of above mechanism is loss of pain sensation – i.e. analgesia.

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(ii) Euphoria, Sedation, Hypnosis :

In absence of disease when morphine is consumed even in therapeutic doses, it produces a sensation of emotional well-being called as 'euphoria'. In order to enjoy the euphoria, an individual is compelled to continue the drug which leads to 'addiction'.

As, in absence of disease when morphine is consumed, it produces euphoria – a pseudosensation of well-being, which leads to addiction. Morphine is the worst drug though it is a good, potent analgesic.

- Sedation induced by morphine is characterized by drowsiness, decreased physical activity, difficulty in concentration and is associated with lack of thoughts and ideas.
- Morphine when consumed produces sleep which is not related to natural sleep and is characterized by colourful vivid dreams.

2. On respiratory system :

Morphine produces respiratory depression by following mechanism :

(a) by its direct depressant action on brainstem and respiratory centre.

(b) by decreasing the sensitivity of the medullary respiratory centre to the increased plasma corbon-dioxide (CO_2) concentration. In toxic doses, morphine produces severe depression of respiratory centre.

3. On pupil :

Morphine acts on Edinger. Westphal nucleus of occulomotor nerve and produces pin-point miosis.

4. On cough centre :

Morphine depresses cough reflex by directly depressing medullary cough centre.

5. On Chemo Receptor Trigger Zone – "CTZ" :

Morphine acts on CTZ in the medulla, by stimulation and produces nausea and vomiting.

6. On gastro-intestinal tract :

Morphine reduces tone, motility, peristalsis of smooth muscles of gastro intestinal tract, reduces all digestive enzymes and leads to constipation.

Absorption, Fate, Excertion :

- When administered orally, absorption is slow and incomplete.
- Morphine exists in plasma, partly bound to plasma proteins and partly free.
- It is conjugated with glucouronic acid and is excreted though urine.

Side Effects :

- Euphoria followed by dysphoria.
- Constipation.
- Mental clouding.
- Nausea, vomiting
- Headache, fatigue.

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Therapeutic Uses / Applications :

1. Morphine is used as a good analgesic to relieve severe types of pains associated with myocardial infarction, fractures of long bones, burns, terminal stages of malignancy, pulmonary embolism, acute pericarditis etc.
2. It is used as pre-anesthetic agent.
3. It is a valuable agent in acute left ventricular failure.
   Tincture opium is used to produce constipation.

Preparations :

- Tincture opium, I.P. → 0.3 to 2.0 ml orally.
- Morphine sulphate injection, I.P. → 10 mg ampoule
  10 to 20 mg subcutenously

Contraindications :

Morphine should not be used in following conditions :

1. Head / Brain injury.
2. Undiagnosed abdominal pain.
3. With phenothiazines mono amino oxidase inhibitors.
4. Hypovlumic shock.
5. In old patients and infants.

Morphine / Opium Posioning

Causes :

- Clinical overdosage.
- Accidental or intentional overdosing during addiction by addicts.

Symptoms :

- Pin-point miosis.
- Respiratory depression – cyanosis.
- Nausea and vomiting.
- Clammy, pale skin.

Treatment :

(a) Symptomatic

- If intoxication is by mouth, gastric lavage is advised.
- If respiration is badly hampered, artificial respiration is advised.

(b) Drug treatment

- Pure antagonist → Naloxon
  Trade name → Narcan
  Dose → 0.4 mg I/V
- Partial antagonist → Nalorphine
  Trade name → Lethidrone
  Dose → 10 mg I/V

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[B] Non-narcotic – Analgesics, Antipyretics, Anti-inflammatory Agents

Definition :

These are the pharmacological agents, which when administered externally, relieve, dull, continuous aching type of pain associated with arthralgia (joint pain), myalgia (muscle pain), Neuralgia (nerve pain), bodyache, headache, toothache etc without inducing narcosis.

Classification :

Non-narcotics are classified as follows :

1. **Salicylic acid derivative :**
   - Acetyl salicylic acid.
   - Sodium salicylate.
2. **Para amino phenol derivatives :**
   - Paracetamol
   - Phenacitin.
3. **Pyrazolon derivatives :**
   - Oxyphenbutazone.
   - Phenylbutazone.
4. **Indole derivatives :**
   - Indomethacine.
5. **Propionic acid derivatives :**
   - Ibuprofen.
   - Ketoprofen.

Pharmacological Actions :

1. **Analgesia :**

   Salicylates and derivatives relieves dull pains related to joints, muscles, nerves, bodyache, headache, toothache by acting on thalamus and hypothalamus.

2. **Anti-pyrexia :**

   Pyrexia means rise in body temperature due to :
   - High prostaglandin levels.
   - Setting of thermostat at high levels.

   Salicylates and derivatives reduce body temperature by following mechanisms.
   - These agents reduce prostaglandin levels.
   - Thereby reset the thermostat to normal.
   - Promote heat loss by vasodilatation of small skin blood vessels as well as increasing sweating, thus acts as an antipyretic.

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3. **On respiration :**

Salicylates are respiratory stimulants. Salicylates stimulate respiration by :

- Direct action on medullary respiratory centre.
- Indirect action by increasing plasma carbon-dioxide concentration.

4. **On gastro-intestinal tract :**

Salicylates ingestion causes dyspepsia high incidences of nausea, vomiting, epigastric distress, belching, frank gastric bleeding and ulcers.

5. **On blood system :**

Salicylates reduce platelet aggregation, promotes fibrinolysis, prolongs bleeding time, interferes with the formation of endoperoxides thromboxanes, the chemical mediators essential for platelet aggregation.

6. **Anti-inflammatory action :**

Salicylates and derivatives have potent anti-inflammatory action and produce following effects :

- Decrease capillary permeability.
- Reduce exudation of fluid.
- Reduce development of inflammatory oedema.

7. **Uricosuric effect :**

- Salicylates in small doses 1 – 2 gm/day increase plasma-urate level by interfering urate secretion by distal tubule.
- Salicylates in large doses 5 gm/day inhibit reabsorption of urate by proximal tubule.
- This results in uricosuria.

8. **Hepatic and renal effect :**

- Salicylates increase secretion of bile by stimulation of hepatic parenchyma.

This is referred to as choleretic action.

- In large doses, salicylates may lead to acute hepatic necrosis.
- In high doses, salicylates cause transient increase in urine cell count, traces of albumin and tubular casts.

9. **Metabolic effect :**

- Salicylates cause conversion of large part of energy derived from oxidation, into heat, by uncoupling of oxidative phosphorylation. This is one of the causes of hyperpyrexia due to large dose of salicylates.

Absorption, Fate, Excretion :

1. Well absorbed from stomach and intact skin.
2. It remains bound to plasma proteins.
3. Mainly metabolized in liver.
4. Excreted in urine in the form of conjugates with glycine and glucouronic acid.

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Side Effects :

1. Dyspepsia, nausea, vomiting, epigastric distress, belching, frank gastric bleeding and ulcers.
2. Renal / Hepatic damage.

Therapeutic Uses :

1. Local application as keratolytic, fungistatic, antiseptic.
2. As analgesic to relative dull type of pains like arthralgia, myalgia, neuralgia, headache, toothache etc.
3. As an anti-pyretic.
4. Anti-inflammatory.
5. As anti-rheumatic
6. As anti-platelet agent.

Preparations :

1. Acetyl salicylic acid I.P. Aspirin → 0.3 to 1 gm orally
2. Soluble aspirin tablet I.P. → 300 mg orally

Salicylism

Cause :

- Prolonged administration of salicylates in the treatment of rheumatic fever or rheumatoid arthritis.

Symptoms :

- Headache.
- Dizziness.
- Vertigo.
- Tinnitus.
- Nausea and vomiting.
- Acid-base electrolyte imbalance.
- Restlessness, vertigo, tremors.
- Respiratory depression.

Treatment :

- Prompt hospitalization.
- Rehydration therapy to treat dehydration, hyperthermia and acid-base imbalance by administration of intravenous fluids.
- Gastric leavage to remove unabsorbed drug from stomach.
- To reduce body temperature external sponging with cold water or alcohol.
- Vitamin K and blood transfusion is advised to prevent or reat haemorrhagic complications.
- Hypokalemia can be prevented by intravenous administration of potassium.
- Ketosis is treated with intravenous administration of dextrose.
- Metabolic acidosis can be corrected by administration of sodium bicarbonate.
- Salicylate excretion can be enhanced by alkalinization of urine with 2% dextrose and 2% sodium-bicarbonate.

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[C] Rheumatism, Anti-Rheumatic

Definition :

It is an inflammatory disorder that affects musculoskeletal system i.e. joints, muscles, ligaments, tendons.

Anti-rheumatic agent :

No.	Drug	Trade name	Dose
1.	Phenylbutazone	Butazolidine	300 – 600 mg/day, oral
2.	Oxyphenbutazone	Suganril	300 – 600 mg/day, oral
3.	Indomethacin	Indicin	25 – 50 mg t.i.d., oral
4.	Ibuprofen	Brufen	200 – 400 mg
5.	Penicillamine	–	125 – 250 mg
6.	Chloroquin	–	150 – 300 mg

[D] Gout, Anti-Gout Agents

Gout is a disorder of purine metabolism and is characterized by hyperuricaemia with severe acute arthritis.

Anti-gout agents :

No.	Drug	Mechanism	Preparation
1.	Colchicine	It decreases synthesis or reduces inflammation and pain. It inhibits the migration of granulocytes to inflamed tissue. It reduces urate crystal deposition.	0.5 to 0.6 mg
2.	Probenecid (Benemid)	Blocks renal tubular reabsorption of uric acid and increases excretion in urine.	250 mg b.i.d. orally
3.	Sulphin phyrazone (Anturan)	Inhibits tubular reabsorption of uric acid.	100 – 200 mg b.i.d. orally.
4.	Ticrynafen (Salacryn)	Reduces serum uric acid level	125 mg/day orally
5.	Allopurinol (Zyloprim)	Enhances excretion of uric acid. Inhibits xanthene oxidase and reduces secretion of uric acid.	100 mg/day orally

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SEDATIVES AND HYPNOTICS

Sedatives :

These are pharmacological agents, which when administered relieve anxiety, stress and tension by inducing drowsiness.

Hypnotics :

These are pharmacological agents, which when administered induce sleep resembling natural sleep- Non-Rapid-Eye ball movement sleep (NREM).

Classification :

Hypno sedatives are classified according to group and their duration of action as follows :

[A] Barbiturates :

No.	Type	Duration of sleep	Examples
1.	Long acting	8 hours / more	Phenobarbitone
2.	Intermediate acting	4 – 8 hours	Amylobarbitone Butobarbitone
3.	Short acting	Less than 4 hours	Secobarbitone Hexobarbitone
4.	Ultra short acting	Very short duration	Thiopentone Kemithal

[B] Non-barbiturates :

Benzodiazepines :

- Chlordiazepoxide
- Diazepam
- Flurazepam
- Nitrazepam

(I) Pharmacology of Barbiturates

1. **Sedation :**
   Small dose of barbiturate is effective in reducing restlessness, irritability and nervousness.
2. **Hypnosis :**
   When administered, they depress the central nervous system, induce sleep resembling nautral sleep. Sleep induced by barbiturates is characterized by hangover.
3. **Anti-epileptic :**
   Barbiturates effectively control convulsions of epilepsy and tetanus.

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4. **Respiration :**
   Respiration is controlled by :
   Neurogenic drive → mediated through reticular system
   Hypoxic drive → mediated through carotid, aortic receptor
   Chemical drive → depends on plasma CO_2 concentration
   Barbiturates abolish all above three mechanisms and produce respiratory depression.
5. **Cardio vascular system :**
   Barbiturates produce fall in blood pressure and decrease in heart rate.
6. **On kidney :**
   Barbiturate therapy results in decrease in urinary output causing oliguria.

Side Effects :

- Megaloblastic anaemia
- Oliguria.
- Dependence.

Therapeutic Uses :

- As sedative, hypnotic.
- As anti-epileptic agent.
- Pre-anaesthetic agent.
- As general anaesthetic.
- In psychiatric disorders like anxiety and hysteria.

Preparations :

Phenobarbitone	Gardenal, Luminal	30 mg, 60 mg tab, oral
Butobarbitone	Soneryl	100 mg tab, oral
Amylobarbitone	Amytal	60 mg tab oral

Barbiturate Poisoning

Cause :

- Drug automatism
- Accidental overdoses by drug addicts.
- Suicidal intention

Symptoms :

- Marked excitement
- Renal failure
- Pulmonary edema
- Cardiac irregularities
- Respiratory failure.

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Treatment :

(a) Hospitalization and gastric lavage :

- If patient is conscious, and if within four hours after ingestion, patient is hospitalized, vomiting can be induced with syrup of ipecac or concentrated salt solution.
- If patient is unconscious, simple stomach wash and removal of gastric contents is fruitful.

(b) Endotracheal intubation :

- If respiration is slightly affected, oxygen can be given by nasal catheter.
- Endotracheal intubation is adviced :
  (a) When spontaneous respiration is inadequate.
  (b) To remove secretion.
  (c) Patients showing depressed cough laryngeal reflexes.

(c) Forced diuresis :

- Diuretics like mannitol and furosemide are used to increase urinary excretion of barbiturates.
  Mannitol → 100 ml of 25% solution
  If urine volume collected after 24 hours is 10 – 12 litres, it is considered as satisfactory diuresis.
- For more potent diuresis :
  Furosemide – 20 mg with 500 ml of 1/2% sodium-bi-carbonate, 1 litre 5% dextrose intravenously.

(d) Alkalinisation of urine :

Allkalinisation of urine produces significant increase in excretion of barbiturates. Sodium-bi-carbonate 3.5 gm/50 ml added to one litre of fluid administered intravenously.

(e) Prophylactic antibiotics :

To prevent infection, antibiotics are used only in cases if tracheotomy or catheterisation is performed.

(f) Administration of intravenous fluids :

As during treatement, forced diuresis is adviced, that may result in dehydration. In order to rehydrate the patient, administration of fluids is adviced.

(g) Peritoneal dialysis :

For promoting excretion of barbiturates.

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(II) Benzodiazepines

- Benzodiazepines have a hypnotic action, and produces natural sleep without hangover.
- All benzodiazepines relieve anxiety.
- Benzodiazepines are anticonvulsants.
- These agents are relatively less toxic.

Preparations :

Diazepam	Valium, calmpose	5 – 10 mg
Flurazepam	-	15 – 30 mg
Nitrazepam	-	15 – 30 mg

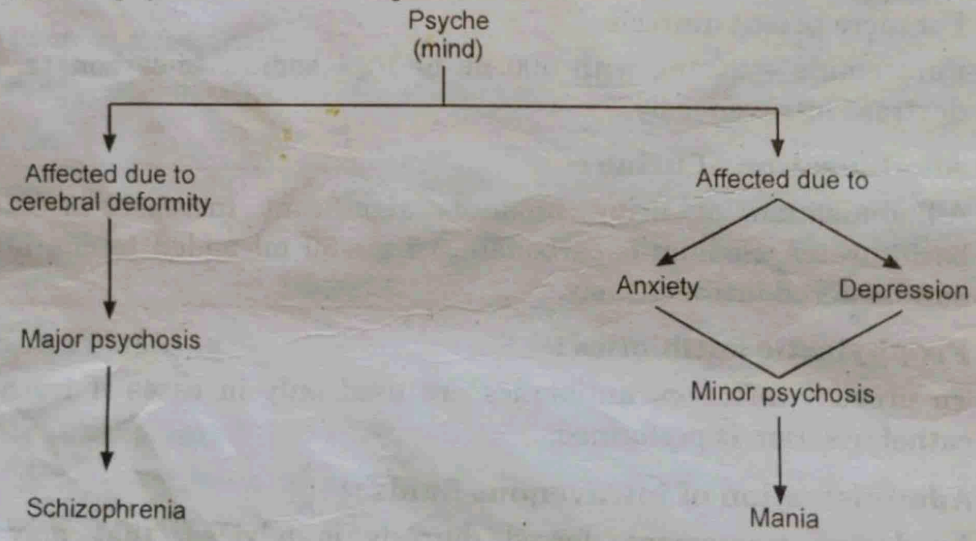
PSYCHOPHARMACOLOGICAL AGENTS

'Psyche' means mind which is an ill defined term. Psyche is affected by various stimuli, which induces behavioural changes in individuals. This is termed as *psychosis*.

Psychotics are pharmacological agents which induce psychosis.

e.g. morphine, LSD, Nicotine, Cannabis, alcohol.

The types of psychosis can be explained as follows :



Anti-psychotics :

These are mainly tranquilizers, which when administered, relieve symptoms associated with major or minor psychosis.

Tranquilizers :

These are anti-psychotics, which when administered, calm individuals without inducing sedation and hypnosis.

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Classification :

The anti-psychotics can be classified as follows :

(a) **Anti-psychotics / Neuroleptics / Major tranquilizers :** These are mainly used in schizophrenia.

- Phenothiazine → Chlorpromazine
- Rauwolfia akaloids → Reserpine

(b) **Anti-anxiety drugs / Anxiolytics / Minor tranquilizers :** These are used in anxiety states.

- Benzodiazepines → Diazepam, Oxazepam

(c) **Anti-depressants :** Mainly used to treat depression.

- Tricyclic- Anti-Depressant → Imipramine
- Mono-Amino-Oxidase inhibitors → Tranyl Cypromine

1. Phenothiazenes – Chlorpromazine

- It is the first anti-psychotic used in the management of schizophrenia.
- It produces following pharmacological actions.
- Chlorpromazine, when administered externally, reduces aggressiveness by inducing tranquilizing effect – calming effect.
- It reduces emotional outburst and causes psychomotor slowing.
- In schizophrenics, it induces interest in surroundings.
- When given chlorpromazine, person starts taking interest in food.
- Chlorpromazine thus changes reaction of individuals towards stimuli.
- Chlorpromazine in therapeuic doses posses atropine-like activity, i.e., causes dryness of mouth and intense thirst.
- It possesses anti-histaminic property.
- It acts on chemo-receptor-trigger zone and prevents nausea and vomiting.
- In females it induces psuedo-pregnancy and in males, it produces gynaecomastia.
- It promotes lactation and weight gain.
- Long term use of chlorpromazine may cause jaundice, blood dyscrasia, skin rash, photosensitivity.
- As it has large number of pharmacological action it is defined as Largactil.

Preparations :

Chlorpromazine	Largactil	200 – 800 mg oral
Trifluprомazine	Siquil	50 – 200 mg daily
Prochlorperazine	Stemetil	75 – 100 mg

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Rauwolfia Derivative :

- Reserpine an alkaloid belonging to group ruwolfia, a climbing shrub named so in honour of Dr. Leonard Rauwolf.
- It slows down motor activity when administered in psychic patients. It produces tranquilizing, relaxing effect.
- It has no anti-histaminic activity.
- It produces extrapyromidal side effects.

Preparation :

Reserpine	Serpasil	0.75 – 1.5 mg oral

2. Anti-anxiety / Anxiolytics :

- These agents when administered to maniac individuals, relieve tension and fear, remove nervousness and produce a sense of well-being.
- These agents have hypnosedative property.
- It is believed that these agents facilitate the effects of GABA (Gamma Amino Butyric Acid) receptor activation in the central nervous system.
- These agents have muscle relaxation property.
- Sedation lethargy, atoxia, weight gain are minor side effects.

Preparations :

Diazepam	Valium Calmpose	5 – 10 mg
Oxazepam	Serepax	10 mg
Chlordiazepoxide	Librium	10 mg
Lorazepam	Larpose	1 to 4 mg

3. Anti-depressants :

- These are also called as psychoanaleptic or mood elevators.
- Tri-cyclic, anti-depressant, block re-uptake of nor-epinephrine and thereby increases availability of the neuro-transmitter near the receptor.
- Mono-amino-oxidase inhibitors prevent oxidative deamination of catecholamines and serotonine and thereby increase functional availability of these monoamines in the brain.

Preparations :

Imipramine	Tofranil	50 - 100 mg oral
Tranylcypromine	Parnate	20 mg /day oral

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EPILEPSY AND ANTI-CONVULSANTS

Introduction :

Epilepsy is chronic convulsive disorder characterized by sudden loss or impairment of consciousness, usually but not always with characteristic body movements and sometimes with hyper autonomic activity.

Types of Epilepsy :

1. Grandmal epilepsy / Major epilepsy :
   - Characterized by sudden loss of consciousness and major convulsions with tonic spasm and clonic jerking of body.
   - Attacks can occur at any age.
2. Petitmal epilepsy :
   - Characterized by episodes of impairment of consciousness associated with bilateral clonic motor activity such as eye lid blinking.
3. Temporal lobe epilepsy.
4. Cortical focal epilepsy.
5. Hyps arrhythmia.

Causes of Epilepsy :

- Occassional, sudden, excessive, rapid, local discharging of grey matter.
- Epilepsy is co-related with impairment activity of inhibitory GABA (gamma – amino – butyric – acid)

Classification of Drugs :

No.	Types of epilepsy	Group name	Drugs
1.	Grandmal epilepsy	Barbiturate Hydantoin	Phenobarbitone Mephobarbitone Phynytoin Methoin
2.	Petitmal epilepsy	Oxazolidinedion derivatives Succinimides	Trimethadione Paramethadione Ethosuximide Methsuximide
3.	Status epilepsy	Miscellaneous	Diazepam Sodium valproate

Pharmacology :

1. **Di-phenyl-hydantoin :**
   - It is primary drug used in treatment of epilepsy.
   - It inhibits spread of seizure discharges in the brain and shortens the duration and amplification of synaptic potential after discharge.

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- It stabilizes the excitable neuronal membrane. It reduces post tetanic potentiation.
- Onset of action is very slow but action persists for sufficient time.
- Main drawback of drug is hyperplasia hypertrophy of gums.

Preparation :

Phenytoin	Dilantin	150 mg/day

- It is used in therapeutics to treat :
  - Grandmal epilepsy.
  - Psychomotor epilepsy.
  - Focal cortical epilepsy.

2. Barbiturates :

- Reduces spread of seizure activity.
- Raises seizure threshold.
- Barbiturates are sedatives and hence potentiates inhibitory pathway of GABA.
- Nystagmus, ataxia, megaloblastic anemia are common side effects.

Preparations :

Drug	Trade name	Dose
Phenobarbital	Luminal	50 mg, 100 mg orally
Mephobarbital	Mebaral	400 mg orally
Primidone	Mysolin	250 mg orally
Therapeutic uses : Used in ..... Grandmal epilepsy Petitmal epilepsy		

3. Oxazolidinedione derivatives :

- Oxazolidinedione derivatives like trimethadione paramethadione are specifically used in the treatment of petitmal epilepsy.
- Sedation and blurring of vision are common side effects.

Preparations :

Trimethadione	Traxidone	900 mg daily
Paramethadione	Paradione	300 mg/day

4. Benzodiazepines :

- These agents prevent polysynaptic activity in spinal cord.
- These agents thereby decrease neuronal activity in reticular system.

Preparations :

Diazepam	Valium	30 mg/day
Clonazepam	Clonopin	20 mg/day

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5. Suxinimides :

- These are less toxic than oxazolidindiones, hence preferably used in the treatment of petitmal epilepsy.
- Raises seizure threshold.

Preparations :

Ethosuximides	Zarontin	500 mg oral
Methsuximide	Celontin	500 mg oral

Status Epilepsy :

It is medical emergency characterized by repeated grandmal attacks without recovery of consciousness in between two attacks.

Drug therapy :

Diazepam	Intravenous 10 mg
Phenobarbital	Intravenous 250 mg
Phenytoin	Intravenous injection 250 mg
Chlormethiazole	Intravenous infusion 0.8% Solution 80 drops/minute
Paraldehyde	0.1 ml/kg Intramuscular

DRUG ABUSE

Definition :

Misuse of drugs for non-medical purpose which can lead to acute and chronic toxicity is defined as "Drug abuse".

Classification :

Drug abuse can be classified as follows :

(a) Permissive/present in common beverages / common practices.

- Caffeine present in tea, coffee, cold-drinks.
- Nicotine in different forms like smoking, chewing, intranasal administration.
- Alcoholic drinks.

(b) Prescription drugs :

Drugs which are used in therapeutics for their central effects may lead to abuse. e.g. opiate analgesics like morphine pethidine.

- Barbiturates.
- Tranquilisers
- Amphetamine.

These routinely prescribed agents can also be misused.

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(c) Prescription / Banned drugs :

e.g. ➢ Heroin
➢ Cocaine
➢ Ganja, Charas, Lysergic acid-di-ethyl amide.

CENTRAL NERVOUS STIMULANTS 'ANALEPTICS'

Definition :

These drugs when administered, overcome narcolepsy by simulating central nervous system.

Classification :

Analeptics are classified as follows :

1. **Cortical stimulants :**
   - ➢ Caffeine
   - ➢ Amphetamine
   - ➢ Methyl phenidate
2. **Medullary or respiratory stimulants :**
   - ➢ Picrotoxin
   - ➢ Pentylene tetrazole
   - ➢ Nikethamide
3. **Spinal stimulants :**
   - ➢ Strychnine

Preparations :

Pentylene tetrazole	Metrazole Leptazole	100 mg tablet
Bemegride	Megimide	0 ml I/V
Nikethemide	Coramine	1 – 4 ml
Doxapram	Dopram	0.5 – 1.5 mg/kg

Therapeutic uses :

- ➢ Caffeine is generally incorporated in analgesic preparation.
- ➢ Theophylline is widely used as bronchodilator in bronchial asthma.
- ➢ To treat paroxysmal dyspnoea.

PARKINSONISM AND ANTI-PARKINSONS DRUGS

Parkinsonism :

It is a chronic neurological, motor disorder characterized by progressive degeneration of dopaminergic neurons in brain stem. It is the result of

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neurohumoral imbalance between dopamine deficiency and domination of acetylcholine.

It is characterized by tremors, rigidity, bradykinesia. The tremors are repetitive and may appear during rest also. The rigidity is mild and characterized by several jerks.

The individual suffering from Parkinsonism can only perform slow sluggish movements called as bradykinesia or akinesia.

Aim :

Parkinsonism can be treated with two objectives :

1. To overcome the deficiency of dopamine.
2. To antagonize acetylcholine actions by using anti-cholinergics.

Classification :

1. **Drugs affecting "Brain Dopamine'**
   - Levodopa
   - Amontidine
   - Bromocryptine
2. **Centrally acting anti-cholinergic**
   - Benzotropin
   - Diphenhydramine

Pharmacology of Levodopa :

- Levodopa is a precursor of dopamine.
- The dopamine deficiency in Parkinsonism cannot be satisfied by administration of direct dopamine because -
  1. When administered orally it is inactivated by mono-amino-oxidase inhibitors present in gut mucosa.
  2. When administered parenterally, being a poor lipid soluble agent, it cannot cross blood-brain barrier.
- Hence its precursor levodopa is used. Levodopa is pharmacologically inert, but when administered, can penetrate blood-brain barrier to produce its pharmacological effect. It is converted to dopamine.
- Levodopa improves akinesia and rigidity in Parkinsonism.
- It also improves speech, facial expression, posture, gait, handwriting etc.
- It is used in idiopathic Parkinsonism.
- Anorexia, nausea, vomiting, insomnia, psychological disturbances are very common.

Preparation :

Kevidioa	Levodopa	125 – 500 mg

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Other drugs	Trade Name	Dose
Amantidine	Amantrel	100 mg/day oral
Bromocryptine	Proctinal	40 – 100 mg/day oral
Benzhexol	Artane	5 –15 mg/day
Orphenadrine	Disipal	15 mg/day oral
Benzotropine	Cogentin	4 mg / oral
Procylidine	Kamadrin	2.5 mg t.i.d. oral

LOCAL ANAESTHETICS

Local anaesthetics are the pharmacological agents which, when applied or injected, block conduction as well as generation of impulses in localized area and bring loss of sensation without affecting degree of consciousness. They cause reversible blockage of nerve conduction and so they cause loss of sensation in localized area of administration for restricted interval of time.

Classification :

1. **Naturally occurring :** e.g. cocaine.
2. **Synthetic compounds :**
   (a) Nitrogen containing :
   e.g. Procaine, Lignocaine, Benzocaine, Amethocaine.
   (b) Non-nitrogenous :
   e.g. Benzyl alcohol, propanediol.
3. **Miscellaneous :** e.g. Clove oil.

Ideal Characteristics of Local Anaesthetics :

- It should be free from systemic toxicity.
- It should be non-irritant to the muscular tissue.
- It should not cause damage to the nerves.
- It should be freely soluble in lipids, as their local anaesthetic property is directly proportional to lipid solubility.
- It should be effective on topical as well as parenteral administration.
- It should possess quick onset and a sufficient duration of action, required to complete surgical procedures.

Mechanism of Action of Local Anaesthetics :

- Local anaesthetics act on outer part of cell membrane.
- Local anaesthetics are known to reduce the membrane permeability changes to Na^+ - chief extracellular cation and to K^+ - chief intracellular cation.
- It is believed that Ca^{++} ions control passage of Na^+ across the cell membrane. Local anaesthetics, competitively prevent binding of Ca^{++} to membrane and thus interferes with transport of Na^+ across the cell membrane.

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- Thus by decreasing Na^+ transport, local anaesthetic reduces threshold potential, thus propagation of action potential across nerve is blocked.
- The net result of all above series of action of agent results in anaesthesia.

Techniques of Applications of Local Anaesthetics :

1. **Topical / surface anaesthesia :**
   - In this technique local anaesthetic is used in the form of ointment, cream, or powder and is directly applied to the site which is to be anesthetized.
   - It is strictly contraindicated for application to mucous surfaces, damaged skin surfaces, wounds and burns.

Applications :

- To reduce pain and itching of ulcers, fissures and haemorrhoids.
- To anaesthetize corneal surface, mucosa of mouth, nose, pharynx, larynx, urethra etc.

Drugs used – Lignocaine, Amethocaine.

2. **Infiltration anaesthesia :**
   - In this technique, anaesthesia is produced by injecting anaesthetic agent throughout the area to be anaesthetized. In this, nerve endings are anaesthetized by their direct exposure to drugs.

Application :

Used for minor operation like removal of cyst.

Drugs used – Procaine, lignocaine.

3. **Nerve block anaesthesia :**
   - In this technique either the anaesthetic agent is injected in surrounding area of that part which is to be operated, or deposited close to the mixed nerves like radial ulnar, palantine etc.
   - Accordingly it is defined as field block or nerve block anaesthesia.

Drugs used – Procaine, lignocaine.

4. **Spinal anaesthesia :**
   - In this technique the drug is injected into the subarachnoid space.
   - After administration, agent reaches to the roots of spinal nerves and dorsal root of ganglia.
   - The drug is injected at the site to block roots of those nerves which innervate the area to be operated.
   - During administration position of the patient plays a vital role in restricting the anaesthesia to desired level.
   - Duration of spinal anaesthesia can be increased by addition of 0.2 ml of 1 : 1000 solution.

Applications :

In obstetrics.

In gynaecological surgery.

Drug used – Lignocaine

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Pharmacology :

1. Lignocaine :

- It is a commonly used local anaesthetic and most stable.
- It has quick onset of action and high degree of penetration.
- It is widely used for :
  - (a) Infiltration anaesthesia.
  - (b) Intravenous.
  - (c) Nerve block.
  - (d) Epidural anaesthesia.
  - (e) Sub-archnoid anaesthesia.
- The common side effects are bradycardia, hypotension and some others.

Preparations :

- 0.25 to 5% solution → Infiltration anaesthesia.
- 1 to 2% solution → Nerve block anaesthesia.
- 2% topical ointment.

Addition of adrenaline, 1 in 200,000 concentration prolongs actions of local anaesthetics.

2. Procaine :

- it is a nonirritant local anaesthetic.
- It is effective rapidly when administered parenterally.
- It is not effective as a topical anaesthetic.
- It's duration of action is very short and can be prolonged by administration of adrenaline.
- It is relatively less toxic, but has a vasodilator property and can cause hypotension and bradycardia.

Preparations :

- 1 – 2 % → Central block anaesthesia.
- 50 – 20 mg intrathecally → For spinal anaesthesia.
- 2% solution → For infiltration anaesthesia.

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Chapter...3

DRUGS ACTING ON AUTONOMIC NERVOUS SYSTEM

INTRODUCTION

Human nervous system is mainly divided into two broad divisions :

1. Central nervous system.
2. Peripheral nervous system.

The peripheral nervous system is further divided into two branches :

(a) Autonomic nervous system.

(b) Somatic nervous system.

Autonomic nervous system was named by Langley in 1898. Autonomic means independent of voluntary control – 'self regulating' where Autos – self and nomos – regulating.

The autonomic nervous system is broadly divided into two divisions :

(a) Parasympathetic (Inhibitory).

(b) Sympathetic (Stimulatory).

These two divisions are in a state of dynamic equilibrium. The parasympathetic nervous system mainly plays a role in tissue building reactions.

The sympathetic nervous system prepares the individual to adjust to stress and prepares the body for flight or fight.

Anatomy :

The autonomic nervous system including both the branches, consists of a non-mylinated pre ganglionic fibre, which forms a synapse with the cell body of a non-mylinated, second neurone termed as post ganglionic fibre. The post ganglionic fibre in turn terminates in a synapse with the receptor of organ supplied by it. (Fig. 3.1)

The synapse between pre and post ganglionic fibre is termed as "ganglion".

While synapse between post ganglionic fibre and receptor is termed as neuron-effector junction.

The pre ganglionic neurons of sympathetic system have their origins – cell bodies – in the thoracic and lumbar vertebrae of the spinal cord. The pre ganglionic neurons of the parasympathetic system have their origin (cell bodies) in the lower brain – cranium and in the sacral portion of the spinal cord (cranio – sacral flow).

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Neuro-humoral transmitter :

- The main neuro-humoral transmitter of parasympathetic system is acetylcholine, hence the system is also referred to as cholinergic system.
- The main neuro-humoral transmitter of sympathetic system is adrenaline, hence also called as adrenergic system.

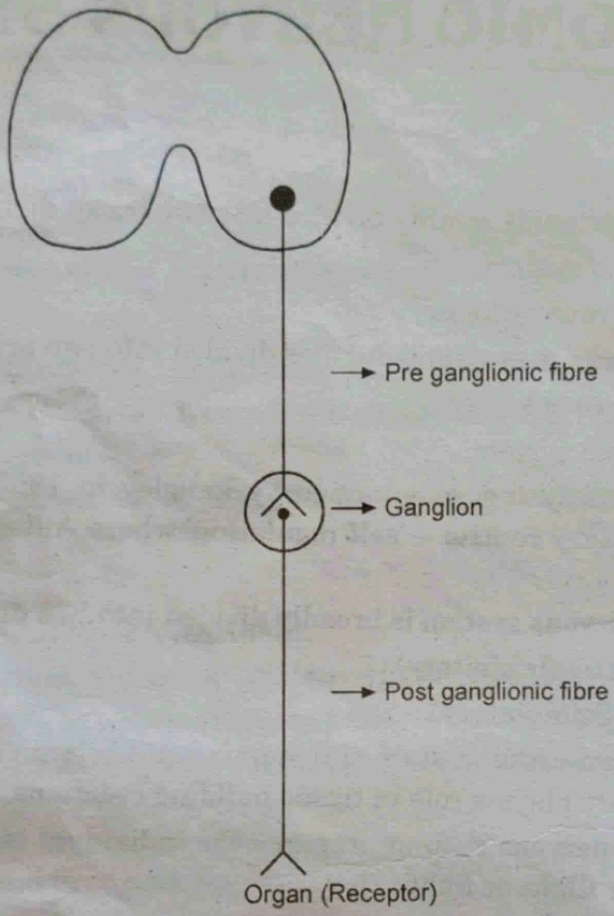

Fig. 3.1

CHOLINERGIC DRUGS

Parasympathomimetic / Cholinomimetics :

These pharmacological agents, when administered externally, mimic the response elicited by parasympathetic nerve fibre.

Classification :

(a) Esters of choline :

- Acetylcholine
- Methacholine
- Carbacol
- Bethanecol

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(b) Cholinomimetic alkoloids :

- Pilocarpine
- Muscarine
- Arecholine

(c) Choline esterase inhibitors / anti-choline esterase :

- Reversible synthetic : Neostigmine
- Reversible natural : Physostigmine
- Irreversible : Organo-Phosphorous compounds

Receptors :

Parasympathetic nerve fibres go to the following organs :

Heart, blood vessels, smooth muscles of eye ball, smooth muscles of intestine and exocrine gland, which are referred to as muscarine receptors, and adrenal medulla and skeletal muscles, which are referred to as nicotinic receptors.

1. ACETYLCHOLINE

Mechanism of Action :

Acetylcholine combines with muscarinic as well as nicotinic receptors and produces pharmacological actions.

Pharmocological Actions :

[A] Muscarnic actions :

(i) **Heart :** Acetyl choline depresses sinoauricular node, S.A. node, reduce conductivity, contractility, automaticity, rhythmicity, depresses A – V node conduction and leads to stopping of the heart.

(ii) **Blood vessels and blood pressure :** Acetylcholine vasodilates blood vessels, thereby causing decrease in peripheral resistance and output and leads to hypotension.

(iii) **Eye ball :** Acetylcholine contracts the circular fibres of sphincter pupillae and cilliary muscles, which results in relaxation of suspensory ligament of the lens. This reduces the tension on the lens. The net result is reduction in the size of pupil called as **miosis**.

As the size of pupil reduces, focal length reduces. Person can see the objects which are near to him but is unable to observe those which are far away. The vision is thus fixed for short distance. This is termed as **spasm of accommodation**.

By this miotic effect, acetylcholine tends to reduce intraoccular tension, by facilitating drainage of occular fluid through the canal of schlemm.

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(iv) **Smooth muscles of gastro-intestinal-tract :** Acetylcholine increases tone, rhythmic activity of smooth muscles of gastro-intestinal tract and increases peristalsis.

It contracts smooth muscles of gall bladder and urinary bladder.

It relaxes smooth muscles of trigonal sphincter.

(v) **Exocrine glands and secretions :** Acetlycholine increases the gastric, intestinal, pancreatic, bronchial, salivary, lacrimal, nasopharyngeal, secretions. It also enhances sweating.

[B] Nicotinic actions :

(i) Acetylcholine stimulates adrenal medulla to release adrenaline and noradrenaline.

(ii) Acetylcholine induces contraction of skeletal muscles.

Therapeutic Uses :

- Acetylcholine is destroyed by pseudo choline esterase present in blood serum, intestines, skin and many other tissues.
- It is destroyed by true choline esterase present in nervous tissue, human placenta and erythrocytes. Hence it is not effective orally.
- It has extremely transient action. Hence cannot be used for any therapeutic purpose.

Preparation :

- Acetylcholine

  Trade name : Miochol

  Ophthalmic : 1 :100 (10 mg / ml) intra ocular solution.

2. METHA CHOLINE

- It is parasympathomimetic agent.
- It belongs to the group 'esters of choline'.
- It acts only on muscarinic receptors and produces its pharmacological actions on heart, blood vessels, eyeball, intestine and exocrine glands similar to acetyl choline.
- It is resistant to the psuedo and true choline esterase.
- Metha choline can be administered orally, but it is poorly and irregularly absorbed.

Applications :

- Metha choline in a dose 10 mg – 40 mg subcutaneously is used to treat paroxysmal atrial tachycardia.
- Metha choline is used to treat glaucoma.

Preparations :

- Metha choline

  Trade name : Mecholyl 10 – 40 mg subcutaneous.

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3. CARBACOL

- It is parasympathomimetic agent.
- It belongs to the group "esters of choline".
- It has potent muscarinic actions.
- It is not readily hydrolysed by true and psuedo choline esterase.

Applications :

- It is used to treat post operative intestinal atony and retention of urine.
- It is used to treat glaucoma.
- It is used to treat paroxysmal atrial tachycardia.

Preparation :

- Carbachol

Trade name	: Isopto carbachol
Opthalmic	: 0.1 – 3 % eye drops.
Parenteral	: 0.01% for intramuscular injection.

4. BATHANECHOL

- It is a parasympathomimetic agent and belongs to the group "choline esters".
- It has more selective muscarine action on gastro-intestinal tract and the urinary bladder.
- It has negligible nicotinic actions.
- It is resistant to true and psuedo choline esterase.

Applications :

- It is used to treat abdominal distention.
- It is used to treat paralytic ileus.
- It is used for post operative urinary retention.

Preparation :

- Bethanechol

Trade name	: Urecholine
Oral dose	: 30 – 120 mg daily.
Subcutaneous	: 2.5 mg – 30 mg daily.

5. PILOCARPINE

- It is a cholinomimetic alkaloid obtained from leaves of pilocarpus microphyllus.
- It is a potent stimulant of glandular tissue such as sweat gland and salivary gland.
- It has marked diaphoretic effect and produces profuse sweating.
- It acts as a saliagogue and increases salivary secretion.
- In eye, it produces miosis and spasm of accommodation which lasts for 2 to 3 days.

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Application :

- It is mainly used in glaucoma.

Preparation :

- Pilocarpine

  Trade name : Pilocar.

  Ophthalmic : 0.25% to 0.5% in 1 to 10% solution.

CHOLINE ESTERASE INHIBITORS OR ANTI-CHOLINE ESTERASE

Definition :

These pharmacological agents when administered externally block psuedo and true choline esterase enzyme, prevent destruction of acetyl choline and set free acetyl caholine.

Classification :

1. Reversible choline esterase inhibitors :
   (a) Natural : Physostigmine.
   (b) Synthetic : Neostigmine.
2. Irreversible choline esterase inhibitor :
   Organo phosphorous compounds.

1. Reversible, Natural, Anti-choline Esterase

(a) Physostigmine :

- It is an alkaloid obtained from dried ripe seed of physostigma venenosum.
- It blocks true and psuedo choline esterase enzyme reversibly.
- It is rarely used for systemic purpose.

Applications :

- It is used in ophthalmology for the treatment of glaucoma.
- It is used in the treatment of atropine poisoning.

Preparation :

- Physostigmine

  Trade name : Eserine

  Ophthalmic : 0.1% to 1% solution.

(b) Synthetic-Neostigmine :

- It is the synthetic quaternary ammonium compound.
- It inhibits both psuedo and true choline esterase enzyme.
- Its action on gastrointestinal tract is that it increases tone, motility of gut and promotes propulsion of intestinal contents.

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- Neostigmine improves power of skeletal muscles by following mechanisms :
  (a) by its anti-choline esterase activity causing greater accumulation of acetyl choline at motor end plates.
  (b) by increasing amount of acetylcholine released during each nerve impulse.
  (c) as it structurally resembles acetylcholine it directly stimulates cholinergic receptor on motor end plate.

Application :

- It is the drug of choice in treatment of myasthenia gravis.

Preparation :

- Neostigmine

  Trade name : Pro stigmin

  Preparation : Neostigmine bromide tablet I.P. 15 mg. dose b.i.d.

2. Organo-Phosphorous Compound Poisoning

Cause :

- Occupational : person engaged in spraying insecticide.
- Accidental : by consumption of agriculture products sprayed with insecticide.
- Suicidal : due to intentional ingestion.

Symptoms :

Miosis, headache, bronchospasm, hypotension, respiratory depression, convulsions, nausea, vomiting, abdominal cramps.

Diagnosis :

If on administration of 0.6 mg of atropine the symptoms improve, case belongs to O.P.C. poisoning.

Treatment :

Symptomatic :

- If ingested by mouth, rapid gastric lavage is advisable.
- For removal of secretions and maintenance of patient's airways, place the patient in a prone position.
- Clear the mouth and pharynx, with finger or suction.
- If airway obstruction persists, then endotracheal intubation has to be done.
- If the patients' body is soiled with insecticides, remove clothes and a medicated bath is recommended.

Drug Treatment :

- Atropine sulphate : 2 – 4 mg initially upto 50 mg parenterally.
- Enzyme reactivators : Obidoxime : 250 mg

  Pralidoxime : 1 to 2 gms by slow I/V injection.

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CHOLINERGIC BLOCKING AGENTS (ANTI-CHOLINERGICS)

BELLADONA ALKALOIDS

Definition :

These pharmacological agents when administered externally, antagonize (blocks) the muscarinic actions of acetylcholine.

Source :

Belladonna alkaloids are mainly obtained from atropa belladonna and also from hyoscymus niger, datura stramonium.

Pharmacological Actions :

1. **Exocrine glands and secretions :** Atropine reduces all exocrine secretions including lacrimal, salivary, gastric, intestinal, sweat, laryngeal, pharyngeal and causes dryness of mouth and intense thirst.
2. **On gastro-intestinal tract :** Atropine reduces tone, motility, peristalsis and causes constipation.
3. **Urinary tract :** It produces reduction in uretral peristalsis.
4. **Eye ball :** Atropine when instilled in the eye, it relaxes constrictor pupillae - circular muscles of the iris and tightening of suspensory ligament.

   This results in dilation of pupil called as mydriasis.

   Because of mydriasis, focal length is increased, person can see the objects which are far away but fails to observe the objects which are near. This is termed as 'cycloplegia'.

   Because of mydriasis and cycloplegia, person becomes more sensitive to bright light, this is termed as 'Photophobia'.

   Cycloplegia produced by atropine lasts for 7 to 11 days.

Absorption, Fate, Excretion :

- It is well absorbed orally.
- In blood it is bound to plasma protein.
- It is eliminated by kidney.

Applications / Therapeutic Uses :

- As an anti-spasmodic, to relax the spasm of smooth muscles of intestine, urinary and billiary tract.
- As an anti-secretory :
  (i) To reduce gastric secretions in peptic ulcer.
  (ii) To reduce night sweats in patients with tuberculosis.
- As a pre-anesthetic medication : to reduce salivary, bronchial secretion.
- Opthalamic uses : in fundoscopic examination of the eye.

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- In myasthenia gravis along with neostigmine to block muscarinic actions of neostigmine.
- In the treatment of organo phosphorous compound poisoning.
- May be used in nocturnal enuresis.
- In the treatment of Parkinsonism.

Preparation :

- Atropine

Oral	:	0.4 – 0.6 mg tablets
Parenteral	:	0.05, 0.1, 1 mg / ml
Ophthalmic	:	0.5% to 1 %

Contraindication :

- Narrow angle glaucoma.
- Angina pectoris.
- Congestive heart failure.

Side Effects :

- Dryness of mouth and intense thirst.
- Blurring of vision.
- Urinary retention.
- Palpitation, tachycardia
- Constipation.
- Hyper-pyrexia.

BELLADONA POISONING

Causes :

- Overdosing during treatment of nocturnal enuresis.
- Application of belladona plaster over large denuded surfaces may produce systemic absorption leading to introxication.
- Ingestion of leaves or seeds.

Lethal Dose :

Children	:	10 – 20 mg
Adults	:	80 – 130 mg

Symptoms :

- Dryness of mouth.
- Mydriasis / blurring of vision / photophobia.
- Urinary retention.
- Hyper pyrexia.
- Mania and delirium

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Diagnosis :

Add a drop of patient's urine in cat's eye, dilation of pupil confirms belladonna poisoning.

Treatment :

Symptomatic :

- If poisoning is by mouth, to remove the poison, gastric lavage is advised.
- Keep the patients' room dark to alleviate photophobia.
- Catheterisation is advised as remedy for urinary retention.
- To treat pyrexia : ice cold bag sponging is advised.
- If respiration is severely hampered, artifical respiration is advised.
- To treat delirium and restlessness diazepam is advised.

Drug Treatment :

Physostigmine – 1 to 4 mg by slow I/V route.

Atropine Substitutes Mainly Used in Eye :

1. Atropine is rarely used in eye examination as :
   - It is not specific in action.
   - Possesses long duration of action.
   - May prove to be allergic.
2. Hence atropine substitutes are used :
   - For selective mydriatic and cycloplegic action.
   - For their shorter duration of action.
   - In case of atropine tolerance.

Agents :

No.	Drug	Ophthalmic dose	Duration
1.	Homatropine	1 – 2 % solution	1 – 3 days
2.	Eucatropine	2 – 5 % solution	12 – 24 hours
3.	Cyclopentolate	0.5 – 1 % solution	12 – 24 hours

SPASMOLYTICS – ANTI-SPASMODICS

Definition :

These pharmacological agents when administered, relieve spasm.

Agents :

1. Atropine Methonitrate : 0.2 mg - 0.4 mg
2. Methscopolamine Bromide : 2 mg - 5 mg orally.

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3. Methantheline : 50 mg - 100 mg orally
4. Propanthelline : 30 – 40 mg orally
5. Oxyphenonium : 10 mg oral
6. Di-cyclomine : 10 mg / 5 ml

ADRENERGIC DRUGS

SYMPATHOMIMETICS / ADRENOMIMETICS

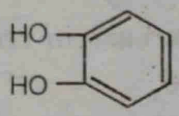
Definition :

These pharmacological agents when administered externally mimic the responses elicited by sympathetic nerve fibres.

Classification :

Sympathomimetics are classified in two main groups :

(a) Catechol amines : containing catechol nucleus



- Adrenaline
- Nor-adrenaline
- Isoprenaline

(b) Non-catecholamines : without catechol nucleus

- Ephedrine
- Amphetamine

Receptors :

Sympathetic nerve fibre innervates following organ :

Heart, blood vessels, smooth muscles of eye, smooth muscles of intestine, glands.

They are referred to as : α, β_1, β_2, receptor organs as follows :

Organs	Receptor
Heart	β_1
Peripheral blood vessels	α
Deep skeletal blood vessels	β_2
Bronchii	β_2
Eye and other smooth muscles	α

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(a) Catechol Amines : Adrenaline

Pharmacological action :

1. **On heart :** Adrenaline acts on β_1 receptors of heart and increases heart rate, conductivity, contractility, automaticity, rhythmicity and leads to stimulation of myocardium.
2. **On blood vessels and blood pressure :**
   (i) *In low doses* : Adrenaline in low therapeutic doses causes peripheral vasoconstriction (due to its α action), increase in resistance, increase in output and thereby rise in peripheral – systolic blood pressure.
   (ii) *In high doses* : In high doses adrenaline activates both receptors α - peripheral blood vessels as well as β_2 skeletal muscle blood vessels.
   It causes peripheral vasoconstriction and leads to rise in systolic blood pressure.
   This is followed by skeletal muscle vasodilation, decrease in resistance, decrease in output and fall in diastolic blood pressure.
   This blood pressure response in moderate doses of adrenaline is termed as **'bi-phasic response'**.
   (iii) Sir Dale working on this response, postulated that, if ergot extract is administered prior to adrenaline dose, then this biphasic response can be converted into depressor response.
   Ergot extract blocks 'α response'. This is termed as **'Dale's Reversal'**.

Bi-phasic Response and Dale's Vasomotor Reversal :

(i) Adrenaline – low dose response on blood pressure.

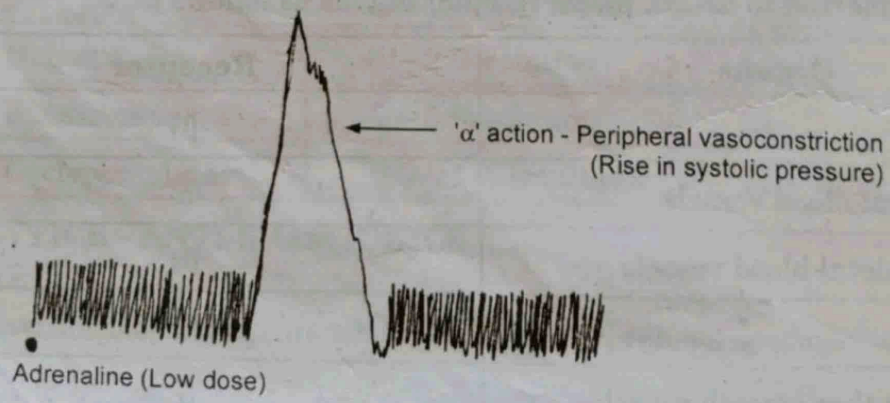

Fig. 3.2

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(ii) Adrenaline – high dose response on blood pressure. **Bi-phasic Response**

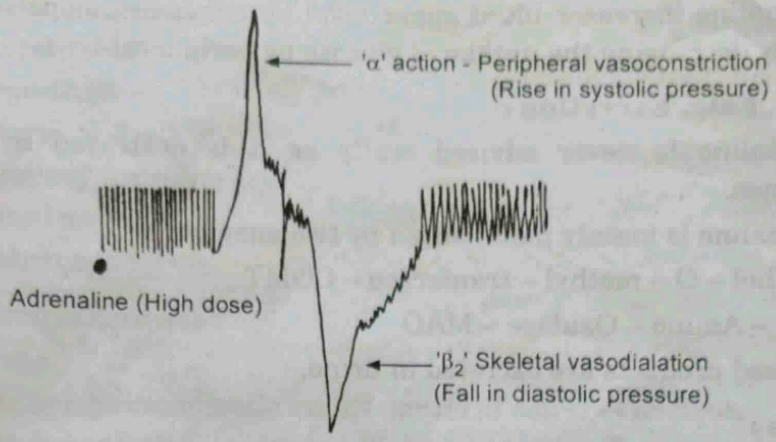

Fig. 3.3

(iii) Dale's reversal – high dose adrenaline + ergot extract.

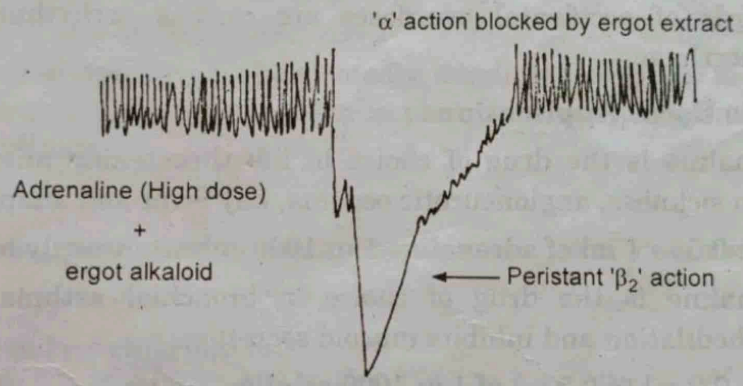

Fig. 3.4

3. On smooth muscles :

Adrenaline is a powerful relaxant of bronchial muscles.

Adrenaline relaxes the smooth muscles of gut and reduces motility.

4. On eye ball :

Adrenaline produces mydriasis with exopthalmus due to contraction of orbital muscles.

5. On respiration :

Adrenaline is a weak stimulant of respiration when administered by I/V route produces apnoea.

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6. Metabolic effect :

Adrenaline increases blood sugar level by enhancing hepatic glycogenolysis and by decreasing the uptake of glucose by peripheral tissue.

Absorption, Fate, Excretion :

- Adrenaline is never advised orally as it is destroyed by gut and liver enzymes.
- Adrenaline is mainly metabolized by two enzymes :

  Catechol – O – methyl – tranferase – COMT

  Mono – Amino – Oxidase – MAO
- Oxidised products are excreted in urine.

Side Effects :

- If given intravenously, may cause a sudden marked increase in blood pressure, precipitating sub-arachnoid haemorrhage and hemiplegia.
- Fear, anxiety, restlessness, pallor, throbbing headache, tremor, palpitation.
- Hazards of accidental overdoses are cardiac arrhythmias, hypertension, haemorrhage.

Therapeutic Uses / Applications :

- Adrenaline is the drug of choice in life threatening allergic reactions like serum sickness, angioneurotic oedema, hay fever and anaphylactic shock.

  Dose : 0.5 to 1 ml of adrenaline 1 in 1000 subcutaneously or intramuscularly.
- Adrenaline is the drug of choice in bronchial asthma. It induces good bronchodilation and inhibits mucoid secretion.

  Dose : 0.2 ml to 0.5 ml of 1 in 1000 solution.
- It is used in treatment of heart block and cardiac arrest.

  Dose : 0.3 ml to 0.6 ml subcutaneously.
- It is used as topical haemostatic to produce peripheral vasoconstriction which stops nasal and gum bleeding.

  Packs soaked in adrenaline of 1 : 1000, 1 : 20,000 solution are used in dental practice to control bleeding after tooth extraction.
- It is added in local anesthetic injection. Adrenaline in the concentration of 1 : 20,000 when used with local anesthetic, produces vasoconstriction and reduces the systemic absorption of local anesthetic agent.

  Thereby, it prolongs duration of action as well as systemic toxicity of local anaesthetics.

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Contraindications :

Adrenaline is contraindicated in following conditions :

- Thyrotoxicosis
- Hypertension
- Arteriosclerosis
- Coronary insufficiency
- Spinal anaesthesia
- Diabetes

(b) Non-catechol Amines :

1. Ephedrine :

- It is the sympathomimetic amine devoid of catechol nucleus.
- It is the naturally occuring alkaloid obtained from plants of the genus ephedra.
- It is an indirect acting sympathomimetic, acts by releasing nor-adrenaline.
- It has potent central nervous system activity.
- It acts on 'α' and 'β' receptors.
- Same dose of ephedrine, if repeatedly administered, fails to produce same pressor response. This declination in pharmacological response is defined as **tachyphyllaxis**.

Side Effects :

- Tachycardia, premature systoles, insomnia, emotional disturbances.

Applications :

- It is used in bronchial asthma.
- It is used as mydriatic in elderly persons.
- It is also used as nasal decongestant.

Preparations :

- Ophthalmic : 2 – 5 % solution.
- Decongestant : 0.5 % solution.

2. Amphetamine :

- It is an indirect acting sympathomimetic amine devoid of catechol nucleus.
- It has a potent central nervous system stimulant action.
- It has an anorexiant effect i.e. depresses appetite.
- It is mainly used :
  (i) As an analeptic to overcome narcolepsy.
  (ii) As an anorexiant in management of obesity.
- It is available as 5 – 10 mg tablet for oral administration.

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SYMPATHOLYTICS / ADRENERGIC BLOCKERS

Definition :

These pharmacological agents when administered externally, competitively block adrenergic alpha, beta, ganglionic receptor and thereby the actions of catecholamines mediated through receptor.

Classification :

Sympatholytics are classified as :

1. **α – alpha receptor blockers :**
   - Phentolamine
   - Phenoxybenzamine
   - Ergot alkaloids.
2. **β – beta receptor blockers :**
   - Propranolol
   - Atenolol
   - Timolol
3. **Ganglion blockers :**
   - Pempidine
   - Pentolinium
   - Macamylamine

1. α - alpha receptor blocking agents

Definition :

These pharmacological agents when administered externally, competitively block adrenergic alpha receptors and thereby actions of adrenaline and nor-adrenaline mediated through receptor.

Agents :

Drug	Trade name	Preparations
Doxazocin	Cardura	1, 2, 4, 8 mg tablets – oral
Phenoxybenzamine	Dibenzyline	10 mg capsules – oral.
Phentolamine	Rigitine	5 mg / ml for injection
Prazocin	Minipress	1, 2, 5 gm capsule – oral
Terazocin	Hytrin	2, 5 mg capsule – oral
Tolazoline	Priscoline	25 mg / ml for injection

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Therapeutic Uses :

1. Alpha receptor blockers are used in the management of pheochromocytoma.
2. These are used in hypertension.
3. These are used in the treatment of peripheral vascular diseases.
4. Phentolamine is used to reverse the intense local vasoconstriction caused by excess infiltration of alpha agonist in subcutaneous tissue during intravenous administration.

2. β- Beta receptor blocking agents

Definition :

These pharmacological agents when administered externally, competitively block beta adrenergic receptors and thereby actions of catecholamines mediated through beta-adrenergic receptor.

Agents :

Drug	Trade name	Preparation
Acebutolol	Sectrol	200, 400 mg capsule, oral
Atenolol	Tenormin	50, 100 mg tablets, oral
Betaxolol	Kerlone, Betoptic	10,20 mg tablets, oral 0.25 % ophthalmic drops
Carteolol	Cartrol	2.5 mg, 5 mg tablet, oral
Esmolol	Breviblock	10 mg / ml for I/V injection 250 mg / ml for I/V infusion
Propranolol	Inderal	10 mg, 20, 40, 60, 80 mg tablet 80 mg, 120, 160 mg sustained released capsule 4, 8, 80 mg / ml solution 1 mg / ml for injection
Pindolol	Visken	5, 10 mg tablet, oral
Metoprolol	Lopressor	1 mg / ml for injection
Lebetelol	Tarndate	100, 200, 300 mg tablet, oral 5 mg / ml for injection
Timolol	Blocardren	5, 10, 20 mg tablets, oral 0.5% ophthalmic drops

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Therapeutic Uses :

- Beta blockers like propranolol is preferred in angina pectoris. It reduces cardiac work and oxygen consumption and improves exercise tolerance in angina.
- Beta blockers are used in the treatment of cardiac arrhythmia.
- These are used to treat pheochromocytoma.
- These play a vital role in management of essential hypertension.
- Idiopatheic, hypertrophic, subaortic, stenosis is the condition characterized by hypertrophy of left ventricular muscle, marked by palpitation, dyspnoea and angina. In this condition propranolol is the drug of choice.
- Propranolol is the drug of choice in thyrotoxicosis.
- Propranolol is useful in Parkinsonism.
- Propranolol is preferred in case of anxiety.

Contraindications :

Beta blockers are strictly contraindicated in following conditions :

- Congestive heart failure.
- Hypotension .
- Bronchial asthma.
- Diabetes mellitus.

Side Effects :

Dizziness, tiredness, depression, increased dreaming, gastro-intestinal upset, mental depression, postural hypotension.

3. Ganglion blockers

Definition :

These pharmacological agents when administered externally, competitively block cholinergic ganglion. These agents, by occupying nicotinic cholinergic receptor on the postsynaptic membrane which does not permit the released acetyl choline to occup these receptors.

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Agents :

Drug	Trade name	Preparation
Macamylamine	Inversin	2.5 mg table, oral
Trimethaphan	Arfonad	500 mg / 10 ml ampule for injection
Prempidine	Perolysen	2.5 mg tablet, oral
Pentolinium	Ansolysen	10, 20 mg tablet, oral

Application :

- Mainly used in the treatment of hypertension.

NEURO MUSCULAR BLOCKING AGENTS

Definition :

The pharmacological agents that block transmission of nerve impulses at the skeletal neuromuscular junction and causes skeletal muscle relaxation are called as neuromuscular blocking agents.

Agents :

Drug	Trade name	Preparations
d.tubocurarine	Curare	15 mg / ml injection 0.2 to 0.7 mg/kg by I/V route
Pancuronium	Pavulon	60 – 100 mg/kg by I/V route
Gallamine	Flixidil	80 – 120 mg I/V
Alcuronoium	Alloferin	10 – 15 mg I/V
Succinylcholine	Midarine	30 – 100 mg I/V
Hexafluo renium	Mylaxen	Supporting agent

Therapeutic Uses / Applications :

- These agents are preferred as adjuvant to anesthesia to promote skeletal muscle relaxation during abdominal surgery, orthopaedic work, laryngoscopy, bronchoscopy etc.
- These are used in electro-convulsive therapy.
- The skeletal muscle relaxants are used to relieve the spasm of tetanus, athetosis, status epilepticus.

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MYASTHENIA GRAVIS

Definition :

It is the disease of uncertain etiology, characterized by profound weakness of skeletal muscle, easy fatiguability and intermittent periods of exacerbation.

Causes :

It is considered to be an autoimmune disease caused by the deficiency of the postsynaptic neuromuscular acetyl choline receptor complex.

Diagnosis :

Administration of edrophonium causes marked improvement in muscle power.

Treatment :

- Neostigmine : 15 mg 4 hrly. + 0.6 mg atropine.
- Ephedrine sulphate : 25 mg - 50 mg t.i.d.
- Potassium chloride : 1 – 2 mg t.i.d.
- Prednisolone : 100 mg once a day.

Contraindications :

Streptomycin, Kanamycin, Lignocaine, Procainamide, Quinidine, Barbiturates are strictly avoided.

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Chapter...4

DRUGS ACTING ON EYE

MYDRIATICS AND MIOTICS

[1] Mydriatics :

Definition : These pharmacological agents, when instilled topically or administered externally, dilate the pupil i.e. produces mydriasis.

Mechanism :

Pupil is supplied by parasympathetic as well as sympathetic nerve fibre.

The parasympathetic supply is through occulomotor nerve and supplies to constrictor pupillae. The sympathetic supply is through superior cervical ganglion and supplies to dilator pupillae.

When mydriatics are instilled in eye, it causes relaxation of constrictor pupillae, i.e. circular muscle fibres and causes tightening of radial muscle fibres, i.e. dilator pupillae.

This causes flattening of lens known as mydriasis.

Because of mydriasis, the focal length is also increased which fixes the sight for far vision, i.e. a person can see the objects which are far away but fails to see the objects which are too near. This is termed as **cycloplegia**.

[2] Miotics :

Definition : These pharmacological agents when instilled in the eye, cause reduction in size of pupil – miosis (constriction of pupils).

Mechanism :

Pupil is supplied by parasympathetic as well as sympathetic nerve fibre.

The parasympathetic supply is through occulomotor nerve and supplies constrictor pupilae i.e. circular muscle fibres.

When miotics are instilled in eye, they cause contraction of circular muscle fibres, i.e. constrictor pupilae and relaxation of radial muscle fibres, i.e. dilator pupilae.

This causes marked reduction in size of pupil which is referred to as miosis.

Because of miosis, focal length of pupil is also reduced, person can see the objects which are near but fails to observe those that are far away, this is termed as **spasm of accommodation**. Drugs acting on eyeball are classified as follows :

[A] Mydriatics and Cycloplegics

1. **Parasympatholytics :**
   - Atropin
   - Homatropin
   - Cyclopentolate
   - Tropicamide
   - Scopalamine

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2. **Sympathomimetics :**
   - Adrenaline
   - Phenylephrine
   - Cocaine
   - Ephedrine

[B] Miotics and Agents causing Spasm of Accommodation

1. **Parasympathomimetics :**
   - Acetylcholine
   - Methacholine
   - Carbachol
   - Pilocarpine
   - Physostigmine
   - Edrophonium
2. **Sympatholytics :**
   - Guanethedine
   - Tolazoline
   - Dibenamine

DRUGS USED IN GLAUCOMA

Glaucoma is an occular disease characterized by elevated intraoccular pressure, which causes damage to optic nerve head producing visual loss.

The damage to optic nerve head and visual loss is probably due to ischaemia and may be attributed to direct pressure on nerve.

The main objective in the management of glaucoma is to reduce the elevated intraoccular pressure.

The various agents used are as follows :

1 **Miotics :**

These are parasympathomimetics, when instilled topically in the eye, cause constriction of pupil, contraction of cilliary muscle and causes fall in intraoccular pressure. The decreased resistance to the outflow of aqueous humour causes fall in intraoccular pressure.

e.g.
- Pilocarpine
- Carbachol
- Physostigmine

2. **Adrenergic agents :**

Adrenaline and pilocarpine mixture for open angle glaucoma.

3. **β - adrenoreceptor blocker :**
   - Timolol.
4. **Carbonic anhydrase inhibitors :**
   - Acetazolomide.
   - Dichlorphenamide.
5. **Osmotic agents :**
   - Hypertonic solution of glycerine.
   - Mannitol.

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Chapter...5

DRUGS ACTING ON RESPIRATORY SYSTEM

BRONCHODILATORS

Bronchial asthma is clinical entity characterized by airway obstruction, narrowing of bronchii, which leads to paroxysmal dyspnea and wheeze.

Factors like allergens, drugs, dust, cold air, exercise, chemicals, histamine precipitates asthmatic attack.

Bronchial narrowing leads to hypoxemia, hypercapnia. Prolonged hypoxemia may cause pulmonary hypertension, right ventricular failure while hypercapnia (increase in arterial CO_2 tension) causes cerebral vasodilation, rise in intracranial tension, mental confusion and coma.

Clinically bronchial asthma can be discussed in three groups :

Types

1. Episodic form :

- In this type cause is known as either allergy, or respiratory tract infection or psychological trauma.
- Individual suffers from acute spasm attacks and responds nicely to bronchodilators.

2. Status Asthmaticus :

- It is severe and persistant attack, and is associated with respiratory failure or insufficiency.
- Do not respond to bronchodilators.

3. Chronic Asthma :

- It is characterized by persistant dyspnoea and wheeze. It is due to inflammation and thickening of bronchial mucosa. It is correlated with excessive secretion of mucus, decreased elastic recoil of lung tissue and bronchospasm.

Anti-asthmatics :

These pharmacological agents, known as "bronchodilators", when administered prevent and relieve symptoms of asthma.

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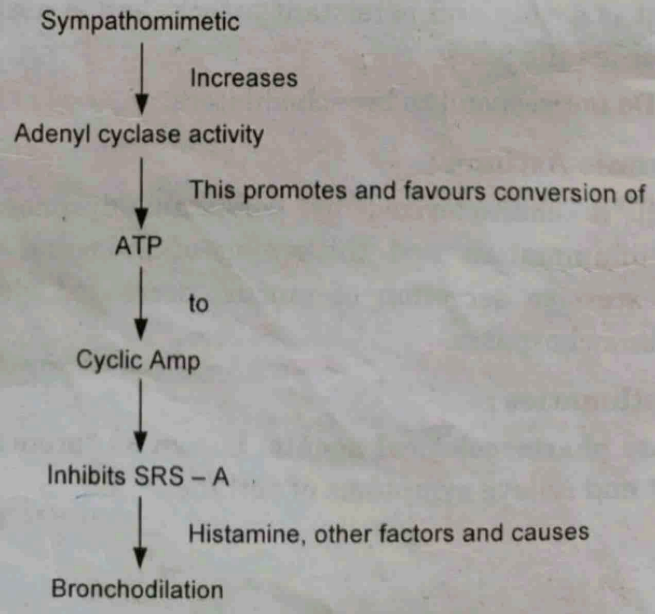
Classification :

Bronchodilators are classified as follows :

1. **Sympathomimetic Amines**
   - **(a) Drug with α and β effects :**
     - Adrenaline
     - Ephedrine
   - **(b) Drugs with β_1 and β_2 effects :**
     - Isoprenaline
     - Orciprenaline
   - **(c) Drugs with β_2 receptor effects :**
     - Salbutamol
     - Terbutaline
2. **Anticholinergic Drugs**
   - Atropine
   - Ipratropine
3. **Phosphodiestarase Inhibitors**
   - Theophylline
   - Aminophylline

Pharmacology :

1. **Sympathomimetic Amines :**
   - It is believed that Slow Reacting Substance – A (SRS – A), histamine, eosinophil, chemotactic factor released from mast cells causes broncho-constriction.
   - Sympathomimetic amines acting on β receptor acts through cyclic Amp mechanism as follows :



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Preparations :

- Adrenaline - 0.2 to 0.5 ml in 1 : 1000 aqueous solution, subcutaneously.
- Isoprenaline - 10-20 mg sublingually 0.1 to 0.5 ml mg of 1 : 200 solution by inhalation.
- Orciprinalline - 0.5 mg/ml injection, 0.5 to 1 mg intramuscular.
- Salbutamol - 0.5 mg subcutaneous.
- Terbutaline - 2.5 to 5 mg orally.

2. Anti-cholinergics :

- It is believed that cellular cyclic guanosin monophosphate causes brancho-constriction.
- It is known that drugs like carbacol, methacholine increases its concentration.
- Anti-cholinergics when administered, reduce the concentration of cyclic guanosin-monophosphate in bronchial muscle and restores balance between Cyclic AMP and c GMP.

Preparation :

- Ipratropium - Atrovent – 40-80 μg inhalation.

3. Phospho-diesterase Inhibitors :

- It is known that enzyme phospho-diesterase reduces levels of cyclic AMP which is a bronchodilator.
- These agents block activity of phospho-diesterase and thereby increase levels of cyclic AMP.

Preparations :

- Aminophylline - 250 mg slow I/V
- Choline theophyllinate - 400 mg oral

Treatment of Status Asthamaticus :

- Hospitalization of patient.
- Initially Aminophylline by I/V route.
- Followed by hydrocortisone sodium succinate 100 mg I/V
- Followed by beta 2 receptor stimulant.
- Bronchial leverage to remove mucus plugs.

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- Broad spectrum antibiotics.
- Rehydration therapy orally.

NASAL DECONGESTANT

Definition :

These are the pharmaceutical agents which when administered externally relieve nasal congestion.

Agents :

Drug	Trade name	Preparation / dose
Cyclopentamine-hydrochloride	Clopane	0.5 – 1 % topical
Mephentermine sulphate	Wyamine	0.5 % topical
Naphazoline-hydrochloride	Privine	0.5 % topical
Oxymetazoline – HCl	Afrin	0.5 % topical
Xylometazoline – HCl	Otrivin	0.05 – 0.1 % topical
Propylhexidrin – HCl	Benzedrex	by inhaler topical
Tetrahydrozolin – HCl	Tyzin	0.05 - 0.1 % topical
Ephedrine sulphate	-	0.5 – 3 % topical
Psuedo ephedrine hydrochloride	Sudafed	30 – 60 mg orally

ANTI-TUSSIVES

Definition of Cough :

Irritation in the pharynx or in the deepest level of respiratory tract initiates a protective reflex known as cough.

Cough may be associated with large amount of sputum, referred to as productive, or dry without much sputum.

Cause :

1. Environmental irritants may cause cough by irritation of bronchial tree.
2. Inhalation of allergens like dust, chemical, pollens.
3. Due to common cold.
4. Due to upper respiratory tract infection.
5. Pulmonary diseases.
6. Lung infection.

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Anti-tussive :

These are pharmacological agents used for symptomatic relief of cough. Anti-tussives are classified as follows :

Classification :

1. Pharyngeal demulscents, local silogogues :
   - Syrups
   - Linctuses
2. Expectorants :
   - Saline expectorants
3. Centrally acting cough suppressants :
   - Codeine
   - Morphine

Pharmacology :

1. **Demulscents :**
   - These agents when administered increase the flow of saliva and produce a protective soothing effect.
   - These are administered in the form of lozenges troches, cough drops, linctuses.
   - These are mainly used in cough due to irritation of pharyngeal mucosa above epiglottis.
   - Lemon drops, glycerrhiza increases saliva.
2. **Expectorants :**
   - Expectorant means 'to drive from chest'.
   - These preparations increase demulscent respiratory tract fluid which covers and protects respiratory mucosa.
   - These preparations are fruitful in the treatment of cough due to irritation of respiratory mucosa below epiglottis.
   - Ammonium chloride, ipecacuanha, potassium iodide, squill are used as expectorants.
3. **Centrally acting cough suppressants :**
   - These agents when administered suppress the cough centre located in the medulla.

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- These preparations are mainly used in symptomatic relief of dry irritant type of cough.
- Codeine, noscapine, antihistaminics like diphenhydramine are used as central suppressants.

4. Mucolytic agent :

- These pharmacological agents when administered, make sputum thin and less viscid, so that it can be easily expectorated.
- Following mucolytics are preferred in the therapy :

1.	Acetyl cysteine	-	2.5 ml of 20% solution
2.	Bromhexine	-	8 –16 mg t.i.d.
3.	Pancreatic dornase	-	-----

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Chapter...6

AUTOCOIDS

PHYSIOLOGICAL ROLE OF HISTAMINE

Definition :

Histamine is tissue amine or biogenic amine. It is an imidazoline compound widely distributed in the body. It is present in various biological fluids. In platelets, leucocytes, basophils and mast cell. The highest concentration is present in lungs and skin.

Pharmacodynamics of Histamine :

Histamine acts on H_1 and H_2 receptors.

- Histamine H_1 receptor activity causes smooth muscle contraction, increased vascular permeability and increased mucus secretion.
- Histamine H_2 receptor activity increases gastric acid secretion.

Pharmacology of Histamine :

- Histamine produces contractions of large blood vessels and arterioles.
- It causes throbbing headache, palpable temporal pulsation and transient increase in cerebrospinal fluid pressure.
- It produces triple response characterized by flush, flare, wheel when administered intradermally, 10 – 20 micrograms.
- It increases heart rate and contractility.
- It is a powerful stimulant of hydrochloric acid secretion by oxyntic cells of stomach.

Preparation :

Histamine acid phosphate I.P. 1 mg/ml. 0.5 to 0.1 mg subcutaneously.

Therapeutic uses :

- To study gastric secretion.
- Diagnosis of pheochromocytoma.

ANTI-HISTAMINICS

Anti-histaminics are pharmacological agents which when administered externally antagonize effects of histamine on H_1 and H_2 receptor.

[A] H_1 – Receptor Antagonist

These agents competitively block effects of histamine mediated through H_1 receptor.

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Classification :

1. Potent and sedative :
   - Diphenhydramine
   - Promethazine
2. Potent but less sedative :
   - Chlorcyclizine
   - Chlorpheniramine
3. Less potent less sedative :
   - Mepyramine
   - Chlorpheniramine

Pharmacology :

- Anti-histaminics block triple response of histamine.
- These agents antagonize stimulant action of histamine on smooth muscle of gastro-intestinal tract.
- These agents inhibit histamine induced salivary secretion.
- They antagonize histamine induced bronchospasm.
- Anti-histaminics by acting on vestibular apparatus, prevent vomiting arising due to motion sickness. These agents also prevent vomiting caused by labryrinth disturbances.
- Anti-histaminics possess local anaesthetic effect.
- Anti-histaminic shows pharmacological activity resembling atropine.

Pharmacokinetics :

- Anti-histaminics are well absorbed orally as well as parenterally.
- These are metabolized in the liver.
- Degradation products are eliminated in urine.

Side Effects :

- Sedation
- Fatigue
- Dryness of mouth
- Blurring of vision
- Sense of tightness in chest

Therapeutic Uses :

- To treat allergic disorders like urticaria, rhinitis, cough.
- As local anaesthetics.
- To produce hypothermia during surgery.
- To treat motion sickness.

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Preparations :

➢ Diphenhydramine	Benadryl	50 mg oral
➢ Mepyramine maleate	Antisan	50 mg oral
➢ Pheniramine maleate	Avil	25 mg oral
➢ Chlorpheniramine maleate	Zeet	5 –20 mg oral

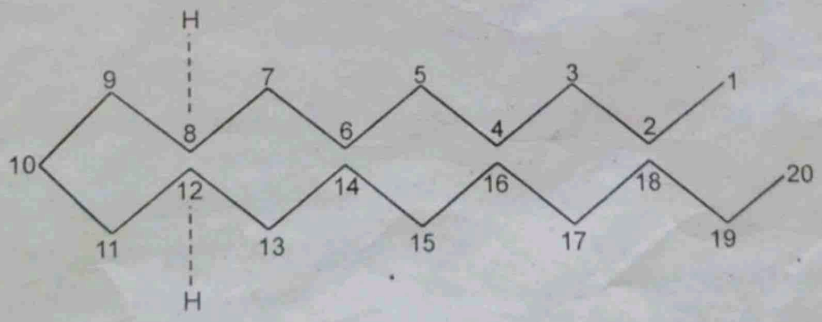
[B] Histamine H_2 Receptor Antagonist

- These agents, when administered competitively block action of histamine on H_2 receptor.
- These agents block histamine induced gastric hydrochloric acid secretion.

  e.g. Cemetidine (tagamet) 400 mg
  Burimamide
  Ranitidine 25 mg / ml I/V slow infusion.
- These are used in the treatment of peptic ulcer.

PROSTAGLANDINS

- Von Euler in 1935 discovered and isolated prostaglandins from human seminal fluid. This substance extracted from seminal fluid is known as prostaglandin because of its origin from prostate gland.
- Derivatives of prostaglandin are closely related to cyclic, 20 carbon unsaturated fatty acids named as prostanoic acid.
- Prostaglandins are synthesized from arachidonic acid by the action of prostaglandin synthetase which is widely distributed in the body in prostate, seminal vesicles, livers, kidney, pancreas etc.
- On the basis of their chemical structure the prostaglandins are classified into six groups – A, B, C, D, E, F. Out of the list, PGE_2 and $PGF_{2\alpha}$ are used in therapeutics.



Prostanoic acid

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Physiological Role of Prostaglandins :

- Prostaglandins play a vital role in reproductive physiology.
- In males, prostaglandins are involved in erection, ejaculation, sperm motility and steroidogenesis.
- In females, it is responsible for uterine and fallopian tube contractility.
- Prostaglandin plays a vital role in gastric secretions.
- Prostaglandin maintains spontaneous smooth muscle tone.

Pharmacology :

1. **On cardiovascular system :**
   - PGE_2 and $PGF_{2\alpha}$ produces peripheral vasodilation and fall in blood pressure.
2. **Gastro-intestinal tract :**
   - PGE_2 is known to inhibit gastric acid secretion and protects gastric and duodenal mucosa.
   - PGE_2, $PGF_{2\alpha}$ causes contraction of gut muscles.
   - Prostaglandins by increasing intestinal fluid secretion causes diarrhoea.
3. **Platelet aggregation :**
   - Prostaglandins cause platelet aggregation.
4. **Central nervous system :**
   - It acts as transmitter.

Therapeutic Uses :

(i) For induction of labour.

(ii) For termination of pregnancy in second trimester.

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Chapter...7

CARDIO VASCULAR DRUGS

CARDIOTONICS

Cardiac Glycosides :

These are defined as group of steroid compounds that can increase cardiac output and affect electrical function of heart.

Pathophysiology of Congestive Cardiac Failure (C.C.F.) :

Cardiac membrane is lipoproteinous in nature. Normally Na^+ ions are concentrated extracellularly and K^+ ions are concentrated intracellularly.

When Na^+ levels fall
↓
Sarcoplasmic reticulum remains inactive
↓
Causes low levels of Ca^{++}
↓
Leads to weak myocardial systole
↓
This causes accumulation of blood in ventricles
↓
Leads to ventricular distension
↓
Heart tries to expel this accumulated blood volume
↓
Gets exhausted and fails to work
↓
This failure due to accumulation of blood volume is defined as
↓
Congestive cardiac failure

Aims :

The drugs used in the treatment of congestive cardiac failure should act in the following ways :

1. by reducing cardiac work load.
2. by relieving the pulmonary congestion.
3. by increasing force of contractility should increase cardiac output.

Cardiac glycosides are used in management of congestive cardiac failure.

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Source / Chemistry :

Cardiac glycosides are obtained from dried leaves of plant digitalis purpurea or foxgloves. The other's are white foxglove, digitalis lanata, stropanthus gratus, stropanthus kmobe etc.

Mechanism :

"Effect on cardio vascular function in congestive cardiac failure".

1. Digitalis derivatives when administered to individuals suffering from congestive cardiac failure :

(i) Acts directly on the myocardium and increases conductivity, automaticity, rhythmicity and causes forceful contraction of heart.

Because of powerful contractions, ventricular blood is forced from right side into artery and from left ventricles to aorta.

This causes complete emptying of heart.

(ii) Digitalis derivatives blocks Na^{++} – K^{+} ATPase enzymes and improves levels of Na^{+} and acts as represented below :

Digitalis
↓
Blocks Na^{+} – K^{+} ATPase enzyme
↓
Increase Na^{+} plasma level
↓
Activates sarcoplasmic reticulum
↓
Releases Ca^{++}
↓
Combines with cardiac muscles
↓
Causes forceful contraction
↓
Leads to complete emptying of heart (ventricles)
↓
Thus relieves congestion
↓
Restores myocardial function

Thus digitalis derivatives, by their direct and indirect action, improve the force of contractility and thereby assure complete emptying of heart.

Thus, digitalized heart can do work with less energy expenditure or more work with some energy expenditure.

Hence digitalis is defined as "Cardiotonic".

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2. Effect on automaticity, conductivity, contractility, blood pressure, heart rate :

(i) Automaticity :

Digitalis increases the ability of purkinje cells and ventricular muscles to initiate impulses.

(ii) Conduction velocity :

The conduction velocity is slightly increased in the atria and ventricles by small doses of digitalis.

(iii) Blood pressure :

Digitalis increases mean arterial pressure in normal individuals only.

(iv) Heart rate :

Digitalis does not affect heart rate in normal individuals, but reduces it in congestive cardiac failure patients.

Extra Cardiac Actions :

1. On Kidney :

Digitalis increases rate of excretion of Na^+ and water by kidney and thus exerts diuresis.

2. On Gastro-intestinal Tract :

High doses of digitalis produces diarrhoea, nausea, vomiting.

Side Effects :

1. Anorexia, nausea, vomiting, diarrhoea.
2. Headache, fatigue, insomnia.
3. Yellow/green vision, blurred vision.
4. Cardiac arrhythmia.

Therapeutic Uses :

1. To treat heart failure.
2. To treat atrial fibrillation.
3. To treat atrial flutter.
4. To treat paroxysmal atrial tachycardia.

Contraindication :

Digitalis is strictly contraindicated in following clinical conditions :

1. Myocardial infarction.
2. Ventricular tachycardia.
3. Partial heart block.
4. Previous digitalis therapy.
5. Calcium administration.

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Digitalis Interactions :

1. **Digitalis, Calcium :**

   It is known that calcium ions increase the force of contraction of heart. High plasma – Ca^{++} levels stimulates the myocardium so much, that it leads to cardiac arrest during systole. Digitalis is also known to increase the force of contraction of heart.

   Thus digitalis and calcium act synergetically and may prove to be toxic.

   Hence during digitalis therapy Ca^{++} ion administration must be avoided.

2. **Digitalis, Quinidine :**

   Quinidine, when administered in individuals taking digitalis, increase serum digoxin levels.

   This may cause adverse effects of digitalis and other clinical complexities.

   Hence must by avoided.

Preparations :

- Digoxin tablet I.P. - 0.25 mg
- Digoxin injection I.P - 0.5 mg / 2 ml ampoule I/V
- Ouabaine injection - 0.5 mg / 2 ml ampoule I/V

Note on Digitalisation :

Digitalis toxicity is referred as overdigitalisation.

Therapeutic levels of digoxin – 0.5 to 2.5 mg / ml.

The plasma value above normal range is taken as overdigitalisation.

Treatment of Overdigitalisation :

1. Immediately stop the administration of digitalis.
2. Stop if any diuretic administration is in continuation.
3. Mild tachycardia can be treated with atropine.
4. Mild toxicity can be treated by administration of potassium salts – 5 to 7.5 g of potassium chloride orally daily.

   A solution of 40 m equvi. of potassium chloride in 500 ml of 5% glucose can be administered intravenously.
5. Ventricular tachycardia can be treated with phenytoin (250 mg well diluted).

ANTI-ARRYTHMIC DRUGS

Pathophysiology :

Disorders of impulse generation and impulse conduction are the two common causes of arrhythmias. This is cor-related with re-entry disturbances theory.

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According to this theory, affected myocardium shows areas of depressed function with prolonged refractory period (rest period).

Thus, an impulse arising in the myocardium, will be diverted to normal excitable tissue and will reach again (by taking circuitous route) to the depressed area.

Repetition of this cycle may lead to arrhythmia.

Factors which precipitate arrhythmias include :

- Myocardial ischaemia with hypoxia.
- Electrolyte abnormalities
- Excessive stress
- Excessive discharge of endogenous catecholamines

According to disorders of impulse generation arrhythmia can be classified as

- Ectopic
- Paroxysmal supraventricular tachycardia
- Atrial flutter
- Atrial fibrillation
- Ventricular tachycardia.

In atrial flutter, the heart rate is 250 – 300/min.

In atrial fibrillation, the heart rate is 500 /min.

In ventricular fibrillation heart is incapable of expelling blood.

Classification :

Anti-arrhythmic agents are classified as follows :

1. **Complete depressants of myocardium**
   - Quinidine
   - Procainamide
2. **Partial depressants of myocardium**
   - Lignocaine
3. **Sympatholytic / Beta blocker**
   - Propranolol
4. **Calcium channel blocker**
   - Nifedepine
   - Verapamil

Pharmacolgy :

1. (a) **Complete depressant – 'Quinidine' :**

Quinidine is isomer of the anti-malarial drug quinine.

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Cardiac actions : Quinidine acts as an anti-arrhythmic and restores rhythm to its normal range in the following way :

- **Automaticity :**

  Quinidine depresses the re-entry of sodium into the cell during depolarization, and thereby depresses diastolic depolarization.

  By this action quinidine depresses automaticity in all cardiac tissues.

- **Excitability :**

  Quinidine depresses excitability of cardiac tissue and thus makes weak ectopic impulse ineffective.

- **Conduction velocity :**

  Quinidine reduces conduction velocity in all cardiac tissues. It increases refractory period and reduces excitability. This decreases cardiac rate and rhythm restores to normal.

- **Refractory period :**

  Quinidine depresses potassium efflux during repolarization and thus prolongs refractory period.

- **A. V. node conduction :**

  Quinidine depresses conduction within atria and purkinje system

- **Contractility :**

  Quinidine depresses entry of calcium ions into cardiac muscle cells.

  Thus it reduces contractility, i.e. exerts negative ionotropic action.

Pharmakokinetics of Quinidine :

- It is completely absorbed from the gut.
- It is excreted by the kidney.

Side Effects :

- Cinchonism characterized by tinitus, vertigo, blurring of vision.
- **Embolism :**

  Sudden restoration of normal rhythm, may dislodge the mural thrombi attached to auricular appendages. This may occlude the blood vessels causing embolism.

Therapeutic Uses :

Quinidine is used to treat :

- Atrial fibrillation
- Atrial flutter
- Paroxysmal supraventricular tachycardia
- Ventricular arrhythmias.

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Preparations :

- Quinidine suplhate - 200 mg t.i.d. oral.
- Quinidine gluconate - 200 mg oral

(b) Complete depressant – 'Procainamide' :

- Procainamide has a definite depressant effect on S A node.
- It reduces excitability.
- It reduces conduction velocity.
- It prolongs refractory period.
- It is less potent than quinidine.
- It is rapidly and completely absorbed from gut when administered orally.
- Nausea, bitter taste, anorexia are common side effects.
- It is used in ventricular arrhythmias.

Preparation :

- Procainamide - Pronestyl - 250 mg oral.

2. Partial depressant – 'Lignocaine' :

- Lignocaine is a local anaesthetic.
- It decreases the duration of action potential.
- It enhances conduction velocity.
- It increases membrane responsiveness.
- It shortens duration of action potential.
- It reduces re-entry type of circuitous transmission.
- It is always administered intravenously.
- It is excreted unchanged in urine.
- It is useful to treat ventricular arrhythmias.

Preparation :

- Lignocaine - Xylocard - 50 –100 mg I/V

3. Sympatholytic / Beta blocker – 'Propranolol' :

- Propranolol is a potent sympatholytic i.e. adrenoreceptor blocker.
- It blocks cardiac beta-receptor.
- In addition, it has membrane stabilizing activity.
- It blocks effects of adrenaline and nor-adrenaline on A – V nodal tissue.
- It prolongs nodal refractory period.
- It slows down firing rate of S A node and atrial pacemaker.
- It is completely absorbed when administered orally. It is metabolized in liver and metabolites are excreted in urine.

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Preparation :

- Propranolol - Inderal - 30 – 60 mg oral

4. Calcium Channel Blocker :

- These agents, when administered, inhibit influx of calcium through cardiac cell membrane into cardiac cell.
- These agents slows down AV conduction.
- These agents also cause peripheral vasodilation.

Preparation :

- Verapamil - Isoptin - 40 mg oral.

ANTI-ANGINAL DRUGS

Angina Pectoris – Pathophysiology

- Angina pectoris is a symptom of myocardial ischemia and occurs due to imbalance between oxygen demand and oxygen supply of myocardium.
- It is characterized by sudden severe chest (substernal) pain, which is referred at left shoulder.

  Anginal attacks may be due to :

  (a) Temporary ischemia : lack of oxygen.

  (b) Atherosclerosis : hardening of arterial vessels.

  (c) Vasospasm.
- Oxygen consumption of myocardium rises when :
  1. heart size increases.
  2. heart rate increases.
  3. systemic blood pressure and myocardial contractility increases.
- Emotions and exercise may precipitate attack.
- Angina index is an index of the myocardial oxygen consumption.

  Angina Index = Heart rate × Blood pressure.

Anti-anginal Drugs :

These are pharmacological agents which when administered either prevent anginal attack or relieve the symptoms.

Classification :

Anti-anginal drugs are classified as follows :

1. Organic nitrates :
   - Nitroglycerine
   - Amyl nitrite
   - Isosorbide dinitrate.

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2. Beta adrenergic blocking agents :
   - Propranolol
3. Calcium channel blocker :
   - Nifedepine
   - Verapamil.

Pharmacology of Anti-anginal Drugs :

1. Organic nitrates :

- Nitrites when administered, directly relax smooth muscles.
- These agents dilate all types of blood vessels.
- As it relaxes vascular smooth muscles, it lowers resting blood pressure. Blood pressure, being an important determinant of myocardial oxygen requirement, when lowered by nitrites, relieves anginal attack.
- Nitrites shorten duration of cardiac systole and also reduce cardiac size.
- Thus nitrites reduce cardiac work.
- These agents decrease venous return, reduce end diastolic pressure and volume and reduce ventricular size and wall tension.

This improves ventricular efficiency and reduces oxygen demand.

Side Effects :

- Hypotension
- Nitrite syncope
- Tolerance
- Methhaemoglobinaemia.

Therapeutic Uses :

- To treat angina pectoris.
- For bronchial asthma.
- In abdominal cramps of lead colic.
- In trigeminal neuralgia.
- In Raynaud's disease.

Preparation :

- Sodium nitrite : 0.3-0.5 g dissolved in 15 ml water is injected intravenously.
- Nitro glycerine : 0.15 to 0.6 mg sublingually.
- Iso-sorbide (Sorbitrate) : 5 – 10 mg sublingually.

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2. Beta Blockers : Propranolol

- Propranolol - Beta adrenergic receptor blocker produces protective action.
- It blocks activity of heart mediated through beta receptor.
- Thereby it reduces cardiac oxygen demand.
- Propranolol is combined with nitrate to obtain a synergestic effect.
- Hypoxia and precipitation of congestive cardiac failure are common side effects.

Preparation :

- Propranolol - Inderal - 10 – 40 mg t.i.d.

3. Calcium Channel Blockers :

- Calcium is chief excitatory cation for skeletal and smooth muscle. Calcium blockers when administered, interfere with entry of calcium in myocardial and vascular smooth muscles and thus decrease availability of intracellular calcium.
- These agents block entry of extracellular calcium ions.
- These drugs depress contractility of myocardium, reduces cardiac work and myocardial oxygen consumption.
- When given orally, it is effectively and completely absorbed.
- Constipation, leg cramps and heart block are the major side effects.

Preparation :

- Verapamil - Cordilox Isoptin - 40 mg tab, oral.
- Nifedepine - Calcigard - 5 mg oral.

HYPERTENSION – ANTI-HYPERTENSIVE

Increase in blood pressure both in systolic and diastolic pressure above normal values (Systolic : 110-120 mm Hg and Diastolic : 60-80 mm Hg) is defined as **hypertension**. ~~To define~~ the drugs used to decrease the BP is anti-hypertensive agents.

Etiologically hypertension can be grouped into two types as follows :

1. Primary hypertension where the cause which leads to rise in blood pressure is not known.
2. Secondary hypertension where rise in blood pressure is secondary to renal disorders like glomerulonephriltis, pyelonephriltis, Cushings syndrome, pheochromocytoma etc.

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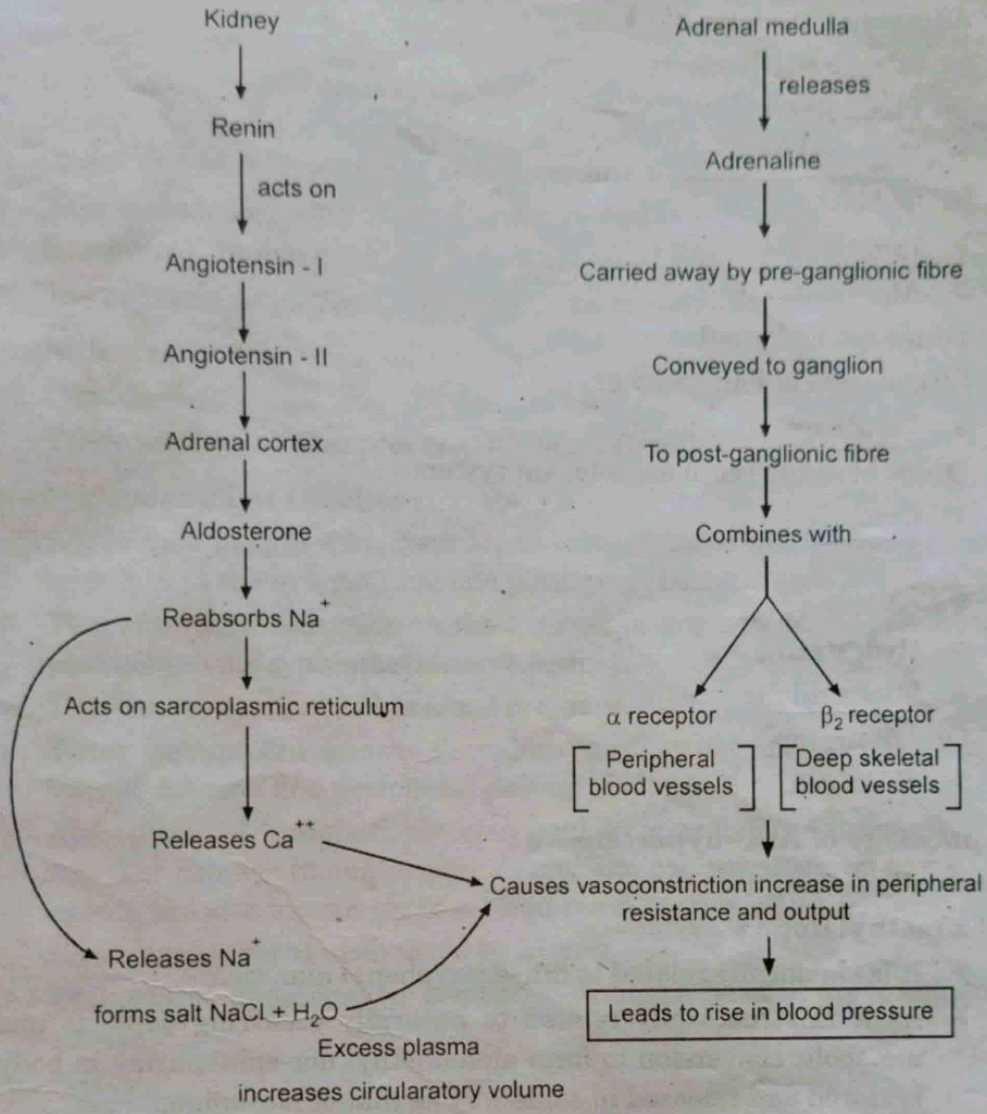

Etiological Pathway

Classification of Antihypertensive According to Site of Action :

1. Centrally acting :
   - α methyl dopa
   - Clonidine
2. Adrenergic ganglion blocker :
   - Hexamethonium
   - Pentolinium
   - Mecamylamine
3. Adrenergic neurone blocker :
   - Guanethedine
   - Reserpine

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4. Adrenergic receptor blockers :
   (i) 'α' receptor blockers :
   - Phentolamine
   - Phenoxybenzamine

   (ii) 'β' blockers :
   - Propranolol
   - Alprenolol

5. Drugs acting by reflex :
   Stimulation of baroreceptor.
   - Veratrum

6. Drugs blocking renin angiotensin system :
   - Catopril
   - Sarlasin

7. Vasodilators :
   - Hydralazine
   - Minoxidil

8. Oral di-uretics :
   - Thiazides.

Pharmacology of Anti-hypertensive :

1. Centrally Acting :

(a) α methyl dopa :

- It is chemically related to dihydroxyphenyl alanine.
- As it is structurally related to naturally occurring dopa, it undergoes metabolic conversion to form alphamethyl nor-epinephrine in body which is stored and released in same way as that of nor-epinephrine.
- Thus 'α methyl dopa' acts as a psuedo neurohumoral transmitter, it reduces sympathetic activity.
- It is believed that 'α methyl dopa', by blocking enzyme dopa decarboxylase, prevents conversion of dopa to dopamine.
- With all above possible actions it acts as an anti-hypertensive and normalizes blood pressure.
- It is well absorbed orally and is excreted in urine.
- Sedation, orthostatic hypotension are common side effects.

Preparation :

- Methyldopa

  Trade name - Aldomet - 250 mg t.i.d.

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(b) Clonidine :

- Clonidine is potent antihypertensive.
- When administered stimulates 'α' adrenergic receptors in the vasomotor centre and blocks release of nor-adrenaline from nerve terminals.
- This leads to lowering of blood pressure and bradycardia.
- It is a lipid soluble drug and is well absorbed when administered orally.
- The common side effects are drowsiness, constipation.

Preparation :

- Clonidine

  Trade name - Catapres - 0.1 mg tablet.

2. Adrenergic Ganglion Blocker :

- Adrenergic ganglion blockers when administered blocks transmission of impulses in the sympathetic and parasympathetic autonomic ganglia.
- This results in reduction in the amount of nor-adrenaline released from post ganglionic sympathetic nerve ending.
- This causes marked fall in blood pressure.
- These agents are known to reduce cardiac output, venous return by venous dilation and peripheral pooling of blood.
- Absorption of ganglion blockers varies according to their nature i.e. whether belongs to quaternary ammonium compound group or not. These agents are also known to cross blood-brain barrier.

  These are excreted unchanged by kidney.
- Orthostatic hypotension, confusion, tremors, mania are common side effects.

Preparation :

- Trimethaphan

  Trade name - Arfonad

  Ampoule contains 0.25 g of sterile.

  Powder - 1 mg/ml.

3. Adrenergic Neurone Blockers :

(a) Guanethedine :

- These agents when administered prevent release of norepinephrine from peripheral adrenergic nerves.
- This reduces contraction of vascular smooth muscle due to sympathetic nerve stimulation.
- This results in lowering of blood pressure.

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- Guanethedine is commonly used agent. When administered, incompletely absorbed from gastro-intestinal tract and is excreted through urine in 24 hours.
- Postural hypotension is common side effect.

Preparation :

- Guanethedine
  Trade name - Ismelin - 10-20 mg / day

(b) Reserpine :

- It is an adrenergic neurone blocker.
- Reserpine is known to deplete catecholamines from storage sites (adrenaline, nor-adrenaline)
- It also depletes 5-hydroxy-tryptamine, i.e. serotonin.
- Reserpine acts on 'granular uptake' and granular amine storage.
- It also inhibits release of renin.
- When administered, it is readily absorbed from gastro-intestinal tract.
- Weight gain, sedation, mental depression, nasal congestion are common side effects.

Preparation :

- Reserpine
  Trade name - Serpasil - 0.25 mg tablet.

4. Adrenergic Receptor Blocker :

(a) Alpha receptor blockers :

- These pharmacological agents when administered competitively, block peripheral alpha receptor.
- This results in vasodilation, reduction in resistance, output and fall in blood pressure.
- The drugs belonging to this group are rarely used as an antihypertensive because of their side effects and erratic oral absorbtion.

Preparations :

- Phentolamine - Regitine - 2.5 mg I/V
- Prazocin - Minipress - 1 mg t.i.d.

(b) Beta receptor blockers :

- These agents competitively block the response of catecholamines mediated through beta adrenergic receptors.
- By blocking cardiac beta receptor, these agents reduces heart rate, cardiac output.
- These are also known to reduce plasma renin activity.
- Bradycardia, bronchospasm, peripheral vasoconstriction are common side effects.

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Preparations :

- Propranolol - Inderal - 120 mg – 400 mg.
- Oxprenolol - Trasicor - 100 mg.
- Atenolol - Atilol - 50 – 100 mg.

5. Drugs Acting on Renin Angiotensin System :

- Saralasin, competitively inhibits activity of angiotensin II at vascular smooth muscle receptor site.
- Catopril inhibits conversion of angiotensin I to angiotensin II by blocking angiotensin convertase enzyme.
- Catopril lowers systemic arterial resistance and thereby systolic and diastolic pressure.
- Catopril is rapidly absorbed from gut.
- Loss of sense of taste, vertigo and headache are common side effects.

Preparation :

- Catopril - 25 mg – 50 mg tablet.

6. Vasodilators :

- These agents act by causing direct relaxation of arterial wall.
- These agents, thereby produce vasodilation, decrease in resistance, cardiac output and thereby blood pressure.
- Tachycardia nasal de-congestion, palpitation are common side effects.

Preparation :

- Hydralazine - Nepresol - 50 mg.
- Minoxidil - Loniten - 0.5 mg.

7. Oral Diuretics :

- Diuretics plays an important role in management of hypertension.
- When administered, these agents produce diuresis, thereby reducing the intracellular fluid volume and in turn cardiac output.
- By their direct vasodilating property, these agents cause decrease in peripheral vascular resistance.
- Thiazides, furosemide are commonly used diuretics.
- Muscle weakness, cramps, hypokalemia are common side effects.

Preparation :

- Chlorothiazide - Esidrex - 500 mg.
- Furosemide - Lasix - 20 mg.

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Management of Hypertension :

1. **Mild hypertension :**
   - Initially hydrochlorothiazide - 2 5 mg t.i.d.
   - Sedative like benzadiazepine - Diazepam.
   - Centrally acting reserpine / Beta blocker.
2. **Moderate hypertension :**
   - Clonidine - 0.1 mg t.i.d.

   Or α methyl dopa - 1.5 gms.
3. **Severe hypertension :**
   - Initially hydralazine - 10 mg t.i.d.
   - Calcium channel blockers - Verapamil / nifedepine.
   - Guanethedine - 10 mg.

DRUGS USED IN ATHEROSCLEROSIS

Atherosclerosis means hardening of blood vessels due to hyperlipidaemia, hyperlipropeinemia and deposition of lipid material in the intimal walls of the arteries. This may lead to coronary thrombosis and myocardial infarction.

During atherosclerosis, mainly the cerebral, coronary, vertebral and renal arteries are affected.

Atherosclerosis may lead to coronary heart diseases, cerebro-vascular disease and peripheral vascular disease.

Cholesterol level 200 mg/ 100 ml or higher and triglyceride levels 150 mg / 100 ml or above, are taken as 'lethal levels'.

Hypolipidaemic drugs used in the treatment :

Drug	Trade name (dose)	Side effect
1. Clofibrate	Atromid – S (2 gm divided dose)	Nausea, gastro-intestinal upset, headache, alopecia.
2. Nicotinic acid	Niacin (1.5 gm – 8 gm /day)	Dizziness, liver dysfunction.
3. Cholestyramine	Questran (4 gm t.i.d.)	Constipation, heart burn, impaired Ca^{++} absorbtion.
4. Dextrothyroxine	Choloxin	Rarely used as it causes angina and arrhythmia.
5. Probucol	Loreleo (500 mg)	Headache paraesthesias.
6. Sitosterols	Cytellin (9 – 20 g)	Bad taste.
7. Safflower oil	Polyunsaturated fatty acid (75 ml of emulsion)	----

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Chapter...8

DRUGS ACTING ON BLOOD SYSTEM

HAEMATINICS

Introduction :

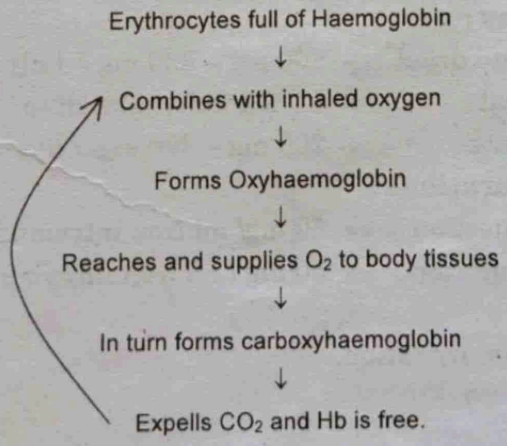
Haematinics are pharmacological agents, which when admimistered, favour erythropoeics, i.e. synthesis of red blood cells and also oxygen carrying capacity of cells.

Anaemia is a physical state of body characterized by profound weakness, low count of erythrocytes and low concentration of haemoglobin in each red cell.

Haemoglobin is a complex blood protein synthesized as follows :

Iron + porphyrin
↓
heam + globin → Haemoglobin

The red cells with this conjugated protein Haemoglobin plays a vital role in Respiration i.e. oxygenation of tissues as follows :



Thus, lack of erythrocytes or low concentration leads to low oxygen carrying capacity causing profound weakness known as *anaemia*.

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Causes of Anaemia

1. **Excessive blood loss :**
   - During accidents.
   - During surgery.

   For this whole blood administration is advised.
2. **Defective Erythropoiecis :**
   - Iron deficiency.
   - Vitamin B_{12} deficiency.
   - Folic acid deficiency.

   For such types of anaemias haematinics are advised.

(a) Haematinics in iron deficiency anaemia (Hypochromic – microcytic anaemia)

Iron :

- Iron is essential for synthesis of haemoglobin and tissue oxidation.
- Iron available from dietary sources provides 1 mg to 2 mg iron per day.
- During menstruation, pregnancy and lactation iron requirement is increased upto 2.5 mg to 3 mg.
- Sources – It is found in meat, leafy vegetables, milk, eggs etc.
- Ferrous (Fe^{++}) form of iron is better absorbed than ferric (Fe^{+++}) form.
- When administered orally, transferrin favours its transport. It is stored as ferritin and haemosiderin.
- Iron is excreted through faecal matter, skin, bile, urine and sweat.

Preparations :

1. **Oral preparations :**
   - Ferrous sulphate dried → 200 mg – 300 mg / daily
   - Ferrous gluconate → 1 – 2 g individual dose
   - Ferrous fumarate → 200 mg – 400 mg / day
2. **Parenteral preparations :**
   - Iron dextran injection → 50 mg/ ml iron intramuscular
   - Iron sorbitex injection → 50 mg / ml iron intramuscular

Side Effects :

- Gastro-intestinal irritation.
- Nausea.
- Vomiting
- Constipation.

(b) Haematinics in vitamin deficiency anaemia

- Vitamin B_{12} - Cyanocobalamine is mainly used.
- It is prepared by microorganisms in lumen of the intestine.

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- Intrinsic factor favours gastro-intestinal absorption of vitamin B_{12}.
- Daily requirement is 3 – 5 μg.
- Egg yolk, milk and liver are rich sources of vitamin.

Preparations :

- Cyanocobalamine - 30 μg (intramuscular)
- Hydroxy cobalamine - 1 μg (intramuscular)

(c) Folic acid as haematinic

- It is a water soluble vitamin.
- It is present abundantly in yeast, liver and vegetables.
- Daily requirement of folic acid is 50 μg.

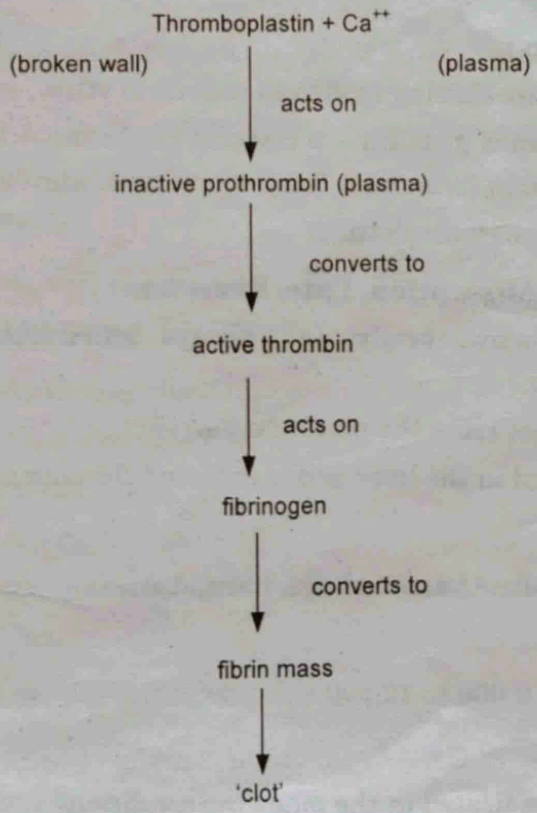
Preparation :

- 10 – 20 mg / day
- It is mainly used for megaloblastic anaemia.

COAGULANTS – ANTICOAGULANTS

When a blood vessel ruptures, bleeding occurs and within a short period blood looses its fluidity and sets into semisolid mass, known as clot. This mechanism is known as **clotting**.

The steps involved in clotting are as follows :



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Anticoagulants are pharmacological agents which when administered, inhibit the mechanism of clot formation.

These are classified as follows :

1. 'Directly acting – intravenous anticoagulants'
   - Heparin
2. "Indirectly acting – oral anticoagulants"
   - Warfarin
   - Phenindione

Pharmacology :

1. Directly acting intravenous anticoagulants

Heparin :

- Naturally it occurs in mast cells of liver and hence the name heparin.
- Commercial heparin is obtained from the lung, intestinal mucosa of cattles and pigs.
- It is mucopoly saccharide with molecular weight of 20,000.

Mechanism of action :

- Heparin prevents clotting in vivo as well as in vitro.
- Heparin with an α globulin – a cofactor in plasma – forms a complex which prevents thrombin formation. It interferes with aggregation of platelets.
- Thus, it interferes with clotting.

Pharmacokinetics (Absorption, Fate, Excretion) :

- It is not effective orally and always administered intravenously or subcutaneously.
- Heparin does not cross the placental barrier.
- It is metabolized in the liver and is excreted through urine.

Side Effects :

- Heparin may cause haemorrhage, haematuria.

Preparation :

- Heparin - 10,000 to 12,500 U.V., 800 U/kg I/V or S/C

Contraindication :

Heparin is contraindicated in the following conditions :

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- Peptic ulcer.
- Haemophilia.
- Threatened abortion.

2. Indirectly acting - slow anticoagulants – coumarin derivatives

- Coumarins are effective only in vivo.
- Coumarins act as anti-coagulants in the following way :
  1. coumarin competitively inhibits vitamin K in liver.
  2. coumarin suppresses the synthesis of prothrombin and factors essential for clotting like VII – proconvertin. IX Christmas factor, X – Stuart – Prower factor.
  3. Thus, it prolongs time taken for prothrombin action.

Pharmacokinetics :

- When administered, they are readily and completely absorbed. These agents cross placental barrier and may be secreted in mother's milk.
- It is metabolized in liver and is excreted through urine.

Side Effects :

- Haemorrhages is main drawback.

Preparation :

- Warfarin sodium

Trade name
- Uniwarfin

Dose
- 10 mg daily orally
- Pendion – 50 – 150 mg/daily

Therapeutic Uses of Anticoagulants :

- To treat venous thromboembolism.
- To treat arterial thrombosis.
- To treat pulmonary embolism.
- In acute myocardial infarction.
- In atrial fibrillation.
- In cerebro vascular disorders.
- During vascular surgery.

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HAEMOSTATICS

Definition :

These pharmacological agents when administered, stop capillary oozing.

- Pack soaked in adrenalin.
- Cellulose.

Haemostatics are pharmacological agents which when administered stop / arrest bleeding. These are the agents used to control oozing from capillary vessels.

Mechanism :

These agents prevent oozing by formation of an artificial clot. They form a ferrous matrix, which hastens clotting.

When applied on the affected surface, these agents are absorbed from site of application.

Limitations :

They are not used to arrest bleeding from large arteries and veins.

Mechanism of Action :

- These agents are directly applied on the affected bleeding surface.
- They are absorbed from site of application.
- Hence they are known as absorbable haemostatics.

Agents Used :

1. **Gelatin sponge :**
   - It is a surgical sponge used during operations.
   - It is kept in place after the closure of operative surface.
   - It is moistened with thrombin or thromboplastin solution.
   - It is completely absorbed in 4 – 6 weeks.
2. **Oxidised cellulose :**
   - It is the surface haemostatics.
   - When used, it catalyses reaction between haemoglobin and celluloic acid.
   - It is poorly absorbed.
   - It is defined as surgical cotton / gauze.
3. **Human fibrinogen :**
   - It is the solution containing fibrinogen with thrombin.

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- Therapeutically it is preferred for restoring normal plasma fibrinogen levels.

4. Fibrin foam :

- It is absorbable haemostatic when applied directly to bleeding area and favoures blood clotting.

5. Russel's viper venom :

- It is mainly preferred in cases of haemophilia.
- It is applied locally. It has a strong thromboplastin activity.

6. Thrombin

BLOOD SUBSTITUTES AND PLASMA EXPANDER

Introduction :

Reduced blood volumes, i.e. hypovolemia, mainly leads to shock. In such critical conditions it is essential to restore the intravascular blood volume and oxygen carrying capacity by administration of fluids intravenously.

To satisfy blood volume, the agents used are :

1. Blood and its elements.
2. Plasma volume expanders.

1. Blood and Its Elements

(a) Citrated whole human blood :

- Whole human blood is collected from a healthy donor by following aseptic technique and is preserved with acid citrate dextrose solution.
- Haemorrhagic shock, or blood loss, during surgical procedure can be replaced by administration of whole blood.
- The net quantity to be administered is 540 ml.
- Before administration it is essential to check and confirm the blood groups of donor and recipient, to avoid blood transfusion complications.

(b) Red cells (packed) stored at temperature 10° C :

In severe anaemia, it is essential to improve the oxygen carrying capacity of blood, hence it is not essential to administer whole blood. Whole blood administration can affect the circulatory load, hence packed red cells administration is advised.

(c) Dried human plasma.

(d) Human serum albumin.

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2. Plasma Volume Expanders

Definition :

These are pharmacological agents with high molecular weight, which when administered parenterally remain in the blood stream and increase the circulatory fluid volume by exerting an osmotic pressure.

e.g.

- Dextran 40 – Low molecular weight dextran 10% solution in dextrose or sodium chloride injection.
- Dextran 70 – High molecular weight 6% solution. 50 ml intravenously.
- Gelatin solution : 6 % solution.

Applications :

- In the management of burns.
- Shock.
- Haemorrhage.

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Chapter...9

DRUGS AFFECTING RENAL FUNCTION

DIURETICS

Physiology :

Kidney is a responsible organ, not only for excretion, but also for regulation of volume and composition of body fluids.

The main factors which assist the separation of excess fluid are :

1. Renal blood flow (RBF) → 1.2 litre / minute
2. Glomerular filtration rate (GFR) → 125 cc / minute

Formation of urine occurs in nephron in three stages as follows :

(a) Active Na^+ reabsorption :

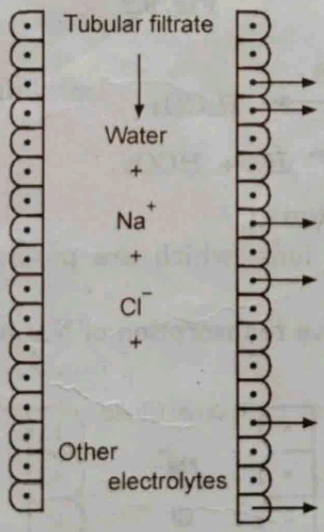

Fig. 9.1

Sodium ions are actively reabsorbed by tubular cells and in extracellular fluid and establish electro-chemical gradient. To neutralize this positive charge, reabsorption of chloride occurs.

Due to osmotic gradient, equiosmatic volume of water is reabsorbed.

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(b) Exchange of Na^+ - H^+ ions :

Tubular cell contains an enzyme carbonic anhydrase, which forms the carbonic acid in the cell, which dissociates into bicarbonate ion leaving free hydrogen ion.

This free hydrogen ion is exchanged with sodium ion in filtrate.

This leads to active reabsorption of sodium chloride, equiosmotic volume of water.

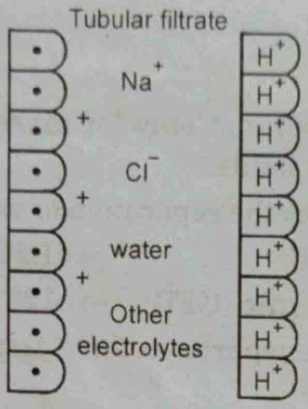

Fig. 9.2

$$H_2O + CO_2 \xrightarrow{C.A} H_2CO_3$$

$$H_2CO_3 \longrightarrow H^+ + HCO_3^-$$

(c) Exchange of K^+ and Na^+ ions :

Tubular cells contains K^+ ions, which are passively transferred in lumen of tubule.

In exchange of K^+ ions, active reabsorption of Na^+, Cl^- and equiosmotic volume of water occurs.

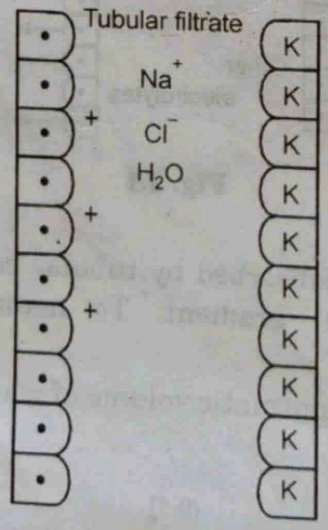

Fig. 9.3

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Diuretics :

These are pharmacological agents which when administered, increase rate of formation of urine as well as excretion of urine.

Classification :

Diuretics are classified as follows :

1. Water and osmotic diuretics :
   - Mannitol.
   - Urea.
   - Glycerol.
2. Xanthine diuretics :
   - Caffeine.
   - Theophylline.
3. Mercurial diuretics :
   - Mersalyl.
   - Mercaptomerin.
4. Carbonic anhydrase inhibitors :
   - Acetazolamide.
5. Thiazide diuretics :
   - Chlorothiazide.
6. Loop / high celling diuretics :
   - Frusemide.
7. Potassium sparing diuretics :
   - Spironolactone.
   - Triamterene.
8. Acid forming salt :
   - Ammonium chloride.

Pharmacology of Diuretics :

1. Osmotic diuretics :

- Osmotic diuretics are pharmacologically inert.
- These are non-metabolisable.
- They are freely filtered by the glomerulus.
- They are not significantly absorbed by renal tubules.

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- In presence of osmotic diuretics, active reabsorption of sodium is reduced and thereby reabsorption of equiosmotic volume of water. Thus, osmotic diuretics by acting on proximal tube brings net loss of water and electrolytes i.e. enhances diuresis (urinary flow).

Preparations :

- Mannitol → 25% solution in 50 ml ampoules intravenously.
- Isosorbide → 1 – 2 gm/kg body weight as 50% solution.
- Glycerol → 120 g /day orally.

2. Xanthine diuretics :

- Xanthine diuretics act by increasing renal blood flow (RBF) as well as by inhibiting tubular reabsorption of sodium.
- This produces a net loss of water and electrolytes, i.e. diuresis.
- Xanthine diuretic action is not much affected by changes in acid base balance.
- Theophylline is the most effective xanthine diuretic than aminophylline which is a weak diuretic.

Preparation :

- Theophylline
- Aminophylline

  By slow I/V route in a dose 0.25 to 0.50 g diluted in 10 to 20 ml of 5% glucose solution.

3. Mercurial diuretics :

- Mercurial diuretics are ineffective orally and may cause renal impairment.
- Use of mercurial diuretics is hazardous and hence rarely preferred.

4. Carbonic anhydrase inhibitors : diuretics :

- The hydration of carbon dioxide takes place under the influence of carbonic anhydrase to form carbonic acid. carbonic acid in turn dissociates and breaks to give hydrogen and bicarbonate ions.
- In relation to the tubular cells, this carbonic anhydrase enzyme helps to produce free H^+ ions which are secreted in tubules in exchange for sodium ion which in turn results in reabsorption of equiosmotic volume of water.

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- When diuretics like acetazolamide, are administered, they inhibit enzyme carbonic anhydrase and thus interfere with the ability of the renal tubular cells to produce free H^+ ions.
- As fewer / less / no free hydrogen ions are available for exchange with sodium, the sodium ion along with bicarbonate ion along with equiosmotic volume of water is excreted ---- i.e. diuresis occurs.
- The mechanism of carbonic anhydrase inhibitor can be explained as follows :

(a) $CO_2 + H_2O \xrightarrow{\text{Carbonic anhydrase}} H_2CO_3$ (Carbonic acid)

H_2CO_3 (Carbonic acid) → Dissociates in tubules → $H^+ + HCO_3^-$

$H^+ + HCO_3^-$ ← Exchanged with Na → Tubular sodium ← Causes reabsorption of equiosmotic volume of water

(b) In presence of carbonic anhydrase inhibitor :

$CO_2 + H_2O \xrightarrow[\text{anhydrase inhibitor}]{\text{Carbonic}}$ No formation of carbonic acid → No availability of free H^+ ion ← No exchange with Na^+ ion ← No reabsorption ← Brings net loss of water and electrolytes → Diuresis occures

Preparations :

- Acetazolamide.
- Diamox (Trade name).
- 0.25 gm tablet.
- 1 / 2 tablets.

5. Thiazide diuretics :

- Thiazide diuretics mainly act on the first part of the tubule on the proximal tubule.
- Thiazide exhibits pharmacological action by inhibiting sodium reabsroption.

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- Thus, Thiazide administration results in total loss of water and electrolytes : ... i.e. diuresis occurs.
- The main drawbacks of thiazide diuretics are hypopotasaemia, hyperuricaemia, aggrevation of diabetes mellitus.

Preparations :

Chlorothiazide	diuril	250 mg daily
Hydrochlorothiazide	hydreodiuril (Esidrex)	25 mg daily

6. Loop/high celling diuretics :

- It is a potent , oral, non-mercurial diuretic.
- On oral administration, it acts mainly on Loop of Henle and prevents active tubular reabsorption of sodium and chloride. Thus these agents reduce tubular diffusion and reabsorption of equiosmotic volume of water.
- Thus administration of these agents results in net loss of water and electrolytes : diuresis.
- Because of high potency, loop diuretics must be used cautiously as rapid reduction in extra cellular fluid volume, can result in a cardio vascular collapse with associated hypokalaemia, hypochloraemic alkalosis.

Preparations :

Furosemide	Lasix	20 – 80 mg
Bumetanide	Burine	20 – 40 mg I/V

7. Potassium sparing diuretics :

- Aldosterone is an adrenal mineral corticoid which plays an important role in the maintenance of electrolyte balance in the body. It stimulates the sodium pump at the distal tubular ion exchange site, causes sodium reabsorption and loss of potassium.
- Potassium sparing diuretics are chiefly aldosterone antagonist, antagonizes this tubular effect of aldosterone, leading to sodium and water loss in the urine. Thus these agents spare, i.e. protect potassium ion. Hence, known as 'potassium sparing diuretics'.

Preparations :

Spironolactone	Aldactone	25 mg b.i.d.
Triamterene	Dytac	100 mg oral

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8. Acidifying salts :

- Acidifying salts, like ammonium chloride, when administered orally, after absorption ammonia is converted by the liver to urea and during the process free H^+ ions are released.

$$NH_4Cl \longrightarrow NH_3 + H^+ + Cl^-$$

- The hydrogen ions in turn reacts with bicarbonate and other buffers in ECF. Reduction in bicarbonate changes the $\frac{H.HCO_3}{B.HCO_3}$ ratio.
- This causes acidosis and a fall in intracellular pH of tubular cell. This causes diuresis.
- Ammonium chloride has a nauseating taste and causes gastric irritation. As better agents are available, this agent is rarely used as a diuretic.

Preparation :

- Ammonium chloride → 8 to 12 gm in divided dose daily.

Therapeutic Applications :

To treat

1. Congestive heart failure.
2. Essential hypertension.
3. Hepatic cirrhosis with ascites.
4. Nephrotic syndrome.
5. Chronic renal failure.
6. Acute oliguric renal failure.
7. Acute glomerular nephrittis.
8. Oedema of pregnancy.
9. Cerebral oedema.
10. Glaucoma.
11. Intraoccular surgery.
12. Diabetes insipidus.
13. Salicylate barbiturate poisoning.

Side Effects of Diuretics :

1. Metabolic acidosis.
2. Alkalosis.
3. Hypokalaemia.
4. Dilutional hyponatraemia.

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Contraindications :

1. Diuretics are strictly contraindicated in liver cirrhosis, as it induces electrolyte imbalance causing hepatic coma.
2. Diuretics are contraindicated in diabetes patient which may develop hyperglycaemis.
3. In patients with gout, diuretics may cause hyperuricaemia.
4. Patient on lithium therapy should not be administered diuretics as they decrease renal excretion of lithium causing lithium intoxication.

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Chapter...10

HORMONES AND HORMONE ANTAGONISTS

HYPOGLYCEMIC AGENTS

Physiology :

Pancreas is partly endocrine in nature. It is composed of Islets of Langerhans with 'alpha α' and 'beta β' cells, which secrete hormones. These hormones regulate blood sugar level as follows :

[A] α cells secrete

Glucagons
↓ which converts
Glycogen (stored)
↓ to
Glucose
(glycogenolysis)

[B] β cells secrete

Insulin
↓ which converts
Excess glucose
↓ to
Glycogen
(glyconeogenesis)

The chief carbohydrates consumed by human are starch : a polysaccharide and sugar : a disaccharide. The ingested carbohydrates are digested by enzymes as :

(a) Salivary amylase ptyline which converts starch to maltose.

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(b) Acid hydrolyses in stomach.

(c) Pancreatic amylase, maltase and lactase. Maltase invertase in intestinal juice converts disaccharides maltose, lactose, sucrose into monosaccharide glucose.

Thus, most of the consumed polysaccharides are converted to monosaccharides such as glucose, galactose and fructose, which are absorbed in small intestine.

The glucose thus available is utilized by tissues for their energy as per the requirement.

It is postulated that in healthy individuals, utilization of glucose, which is derived from the daily ingested food stuffs, occurs as follows :

1. 3% is stored in liver and muscle as glycogen.
2. 30 % is converted to fatty acids.
3. Rest enters Krebs cycle and is utilized partly for energy production and partly for synthesis of aminoacids.

Pathophysiology of Dibetes Mellitus :

Diabetes mellitus is hereditary disorder with metabolic and vascular dearrangements. The word diabetes (means to flow through) was introduced by Greek physician "Aeretaeus", in the first century A.D. 'Mellitus' means sweet, the presence of sugar in the urine of diabetics was demonstrated by Dobson, in 1755.

It is stated that disfunctioning of β cells of pancreas, or lack of total insulin, or deficiency of insulin, leads to total reduction in the transfer of glucose in cells, synthesis of glycogen from glucose diminishes, protein is converted abnormally to glucose at a high rate.

Clinical Symptoms :

1. Hyperglycemia.
2. Hyperlipemia.
3. Ketonemia
4. Azoturia.

Clinical Types of Diabetes Mellitus :

1. **Maturity onset type :** It occurs in obese (overweight), elderly persons. It starts in adult life and it is a stable form.
2. **Juvenile type :** It occurs in younger overweight persons, starts during the time of maturation. It is characterized by absolute deficiency of insulin and hence it is a serious type of diabetes.

Aims of Treatment :

1. To control symptoms adequately with diet, exercise and drugs.
2. To maintain optimum body weight.
3. To correct metabolic disturbances.

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4. To prevent or delay degenerative vascular complications.

Ideal Properties of Anti-diabetic Agents :

1. Should be effective by mouth.
2. Should be non-toxic.
3. Should correct basic metabolic defects in diabetics.

Insulin :

Theory :

Insulin is a polypeptide hormone secreted by β cells of Islets of Langerhans in pancreas. It was discovered in 1922 by Banting, and is derived form the Latin word "insula" which means an island.

Insulin has a molecular weight of about 6000, consisting of two amino acid chains A and B linked by two disulfide bridges. Each A and B chain contains 21 to 30 amino acids respectively.

It is obtained from the pancreas of cattle and pigs.

Human insulin which can be biosynthesized by cultures of bacteria, of *E. coli*, is available for clinical use.

Storage, Release :

In human pancreas, there are two million islets, most of them concentrated in the tail of pancreas. Insulin is stored in the form of granules. The storage of insulin is facilitated by Zinc which makes insulin less soluble. In normal humans 200 units of insulin is present and a normal individual secretes insulin of about 50 units daily.

Insulin is synthesized within the β cells as a single chain polypeptide precursor called pro-insulin. High circulating levels of glucose stimulate the release of insulin. Under fasting conditions, the pancreas secretes 20 μg of insulin per hour. Insulin is released by exocytosis. Aminoacids, fatty acids, ketones and non-glucose also stimulate insulin release.

Transport, Fate, Excretion :

Insulin disappears rapidly from the plasma. (Half life 5-6 minutes). It circulates in the plasma in a free non-protein bound form.

It is completely degraded by most of the tissues, especially by liver, kidneys, pancreas etc. It appears in urine.

Pharmacological Actions :

When administered in diabetes mellitus, "Insulin" re-corrects the disturbances in carbohydrate, fat, protein, electrolytes and water as follows :

1. In diabetes mellitus, carbohydrate metabolism is totally disturbed. When insulin is administered :
   (a) It facilitates entry of glucose and other sugars into the cell.

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(b) It facilitates phosphorylation of glucose and promotes glycogen synthesis.

(c) Insulin inhibits glycogenolysis and gluconeogenesis and thus increases utilization of glucose. The net result of insulin action on carbohydrate metabolism is the use of glucose as fuel and storage of some glucose as glycogen. This reduces blood glucose level.

2. In diabetes mellitus, insulin deficiency causes mobilization of fat from adipose tissue into blood stream. The availability of free fatty acids to the liver, leads to an increased production of acetoacetic acid-ketone bodies causing metabolic ketoacidosis.

   Insulin administration stimulates the synthesis of fatty acids and triglycerides. Thus, it antagonizes the metabolic ketoacidosis.

3. Insulin deficiency in diabetes mellitus, impairs protein synthesis and favours protein breakdown in muscle.

   Insulin administration enhances the transfer of aminoacids into cells and promotes their conversion into protein.

4. Insulin enhances entry of potassium into cells and its involvement in gluconeogenesis. Insulin antagonizes the excess of body water loss.

Preparations :

[A] Commercial insulin is a mixture of the hormone extracted from the pancreas of cattle (bovine) or pigs (porcine). The potency of insulin is assayed by comparing the new sample with an international standard for its hypoglycemic effect.

Preparations are adjusted to contain 40, 80, 100, 500 units/ml according to need.

[B] Newer Insulins :

1. **Actrapid :** It is a clear, neutral solution – (pH – 7) of recrystallised monocomponent of porcine insulin.
2. **Rapitard :** It is a cloudy mixture of actrapid and large insoluble crystals of bovine insulin.
3. **Monotard :** It is a monocomponent of insulin-zinc suspension and contains purified porcine insulin.

Note :

- All insulin preparations are usually administered subcutaneously.
- Regular insulin can be administered intravenously.
- The insulin preparations are marketed in 10 ml vials.

Side Effects, Precautions :

1. **Hypoglycaemia :**

   It is a common adverse effect and may result due to :

   (i) too large a dose of insulin injected.

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(ii) failure to eat a properly balanced diet.
(iii) violent unaccustomed physical exercise.
(iv) consumption of alcohol.

2. **Insulin allergy :**
   It is characterized by local itching, redness, swelling and pain at the site of injection.
3. **Insulin lipodystrophy :**
   It is characterized by atrophy of subcutaneous fat at the site of frequent insulin injections.
4. **Insulin presbyopia :**
   It is loss of visual accommodation due to alterations in the physical properties of the lens occurring due to rapidly controlled diabetes with insulin.
5. **Insulin neuropathy :**
6. **Insulin resistance :**
   Due to repeated administration, the daily requirement gradually increases due to formation of insulin antibodies. When requirement exceeds 200 units/day it is belived that insulin resistance has developed.
7. **Obesity :**

Therapeutic Applications :

1. In diabetes mellitus.
2. Schizophrenia.
3. In anorexia nervosa where insulin improves the appetite.
4. In burns : in which insulin with glucose administration reduces nitrogen and potassium losses in burn patients.

Oraly Hypoglycaemic Agents

Definition :

These pharmacological agents, when administered orally are highly effective in diabetics.

Theory :

- These agents act essentially by causing the release of insulin from the pancreas.
- Hence these agents are of little use in total diabetic or insulin dependent type of diabetes.
- They are most effective in mild cases of diabetes like maturity onset type in which residual insulin is present in the pancreatic β cells.

Classification :

Oral hypoglycaemic agents are classified in two groups :

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[A] Sulfonyl urea derivatives :

- Tolbutamide
- Chlorpropamide
- Acetohexamide.
- Glibenclamide.

[B] Biguanides :

- Phenformin.
- Metformin.

[A] Sulfonyl Urea Derivatives

- These compounds are chemically related to sulfonamides devoid of antibacterial activity.
- These derivatives stimulate the beta cells of islets to secrete insulin.
- When administered, these derivatives cause degranulation of beta cells.
- These agents are in effective in insulin dependent diabetic patients and only effective in patients who have residual insulin in pancreatic β cells.
- When administered, these are readily absorbed from gastro-intestinal tract.
- Their biological half-lives vary from 6 hours to 36 hour.
- Sulphonyl ureas, when administered in therapeutic doses during diabetes treatment, produce common side effects like nausea, vomiting, epigastria, discomfort, weakness etc.
- Drugs like salicylates, phenylbutazone, propranolol chloramphenicol and alcohol may potentiate the hypoglycaemic effect of sulfonyl urea.
- Oral hypoglycaemics like sulfonyl ureas are strictly contraindicated in pregnancy, severe infection and hepatic impairment.

Preparations :

➢ Tolbutamide	Rastinon	0.5 to 1.0 gm tablet / 1.5 g daily.
➢ Chlorpropamide	Diabenese	0.1 to 0.25 g tablet / 0.25 gm daily
➢ Glibenclamide	Daonil	5 mg tablet / 0.005 gm daily
➢ Glipizide	Glynase	5 mg tablet.

[B]Biguanides :

- These pharmacological agents when administered orally, are highly effective.
- They are effective in the absence of functioning pancreatic beta cells or residual insulin.
- They inhibit glucose absorption from the gut and hepatic gluconeogenesis.
- When administered, they accelerate the peripheral utilization of glucose.
- These agents may cause gastro-intestinal upset, vomiting, diarrhoea, anorexia.

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Preparations :

- Phenformin 25 mg twice daily
- Metformin 0.5 g to 1.5 g daily.

ANTI-THYROID DRUGS

Pharmacology of Thyroid Hormones :

The thyroid gland is situated at the base of the throat having two symmetrical lateral lobes, one on either side of trachea, joined by a thin portion of thyroid tissue known as **isthmus**.

The thyroid glands synthesize two important hormones thyroxin and tri-iodo thyronin. About 90% of the body iodine is present in the thyroid gland, mainly as organic iodine.

Thyroid hormones are essential :

1. As substitution therapy in cretinism.
2. To treat non-toxic giotre.
3. As a serum cholesterol lowering agent.
4. Thyroid suppression test.

Thyroid hormones are essential physiologically for :

1. Calorigenic action.
2. Growth.
3. Metabolic action.
4. It stimulates rate as well as force of contraction of myocardium.
5. It is essential for mylination of nerve fibre.

Inadequate or excessive secretion of these hormones results in the clinical condition known as hypothyroidism and hyperthyroidism respectively.

Management of Hyperthyroidism and Antithyroid Agents

Hyperthyroidism (Thyrotoxicosis) :

Excessive secretion of thyroid hormones results in the clinical condition known as hyperthyroidism. Hyperthyroidism can be discussed in two major forms :

1. Graves disease with exophthalmos goitre.
2. Toxic goitre.

Symptoms :

Hyperthyroidism is characterized by fatigue, irritability, agitation, hyperkinetic behaviour voracious appetite, loss in weight, excessive sweating, tremors, tachycardia, palpitation, hypertension. This may be associated with exophthalmus and thyroid enlargement.

Treatment :

The management of hyperthyroidism mainly depends on antithyroid drugs.

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Antithyroid Drugs :

Definition : These pharmacological agents when administered externally manage the symptoms of thyrotoxicosis effectively.

Classification : Anti-thyroid drugs are classified as follows :

[A] Goitrogens

1. *Ion inhibitors :*
   - Potassium perchlorate.
   - Thiocynate.
2. *Organic anti-thyroid drugs :*
   - Thiomides such as propylthiouracil, methimazole, carbimazole.

[B] Iodides, lithium

[C] Radioactive iodine

Pharmacology :

[A] Goitrogens : These are the pharmacological agents, which when administered, interfere with thyroid hormonal synthesis and decrease hormonal level in blood.

1. Ion inhibitors :

- Ion inhibitors like potassium thiocynate and perchlorate when administered, competitively inhibit the trapping of iodides by thyroid gland.
- It effectively controls the symptoms of hyperthyroidism.
- It is very cheap and less toxic.
- In therapeutic doses it may cause gastric irritation, fever, skin, rash, aplastic anaemia.

Preparation :

- Potassium perchlorate : 600- 800 mg /day in divided dose.
  The maintenance dose is 200 –400 mg/day

2. Thiomides :

- These agents when administered, block thyroid hormone synthesis by inhibiting coupling of iodotyrosines, conversion of MIT to DIT and formation of MIT.
- These agents are rapidly absorbed after oral administration. They are partly metabolized in the liver and excreted in urine unchanged.
- These agents may produce effects like fever, skin rashes, edema of the feet, arthralgia etc.

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- It is essential to prepare endometrium for progesteron action.
- It is known to prepare the uterus for spermatozoal transport.

(b) Synthetic Oestrogen :

- When synthetic oestrogen is administered, it is released into the circulation, binds strongly to proteins and reaches to their site of actions, i.e. organs like uterus, vagina, breast, antirior pituitary, hypothalamus.

Therapeutic Applications :

- Menopausal syndrome.
- Ovarian dysgenesis.
- Primary amenorrhoea.
- Carcinoma of prostate in male.
- To treat breast cancers in postmenopausal women.
- To treat functional uterine bleeding and endometriosis.
- To treat dysmenorrhoea.
- As an oral contraceptive with progesterone.

Contraindications :

Oestrogens are contraindicated in following clinical conditions :

- Pre-menopausal carcinomas of breast and uterus.
- Hypertension and thromboembolic diseases.
- Undiagnosed genital bleeding.
- Renal and hepatic diseases.

Side Effects :

- Nausea and vomiting.
- Breast tenderness.
- Salt and water retension causes weight gain, oedema and cardiac failure.

Preparations :

- Naturally occurring oestrogen – Oestradiol 17 - β
  0.22 to 1.5 mg I / M.
- Semi-synthetic steroidal oestrogen :

Ethynyl estradiole	0.05 to 0.1 mg orally.
Mestranol	0.1 to 0.2 mg orally.
Quinestrol	0.05 to 0.1 mg orally.

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- Synthetic non-steroidal oestrogens :

Benzoestrol	0.2 mg to 1 mg orally
Hexoestrol	03 mg to 06 mg orally.

Progesterone

1. Natural progesterone :

Definition, Synthesis :

- Progesterone is steroid derivative. 'Pregnane' is the natural progesterone.
- It is synthesized in ovary, testis, placenta and adrenals.
- The progesterone synthesis mainly occurs in corpus luteum.
- It has very short plasma half-life of 05 minutes.
- It is rapidly metabolized by liver and is excreted through urine as sulphate and glucuronide conjugates.

Pharmacological Action :

- Progesterone induces secretory phase in the endometrium.
- If ovum is not fertilized the secretion of progesterone is inhibited, which is responsible for onset of menstruation.
- If ovum is fertilized, progesterone prepares the endometrium for implantation.
- Progesterone develops breast for lactation.
- It makes uterus less sensitive to oxytocin.

2. Synthetic Progesterone :

Synthetic progesterone are classified in three groups mainly :

- Progesterone derivatives.
- Testosterone derivatives.
- 19 - non-testosterone derivatives.

Therapeutic Uses :

- Mainly used as oral contraceptive.
- As a diagnostic to test oestrogen secretion.

Contraindications :

- May increase blood pressure in females receiving progestins.
- May cause atherosclerosis.

Preparations :

- Nor-ethindrone : 0.5 mg
- Nor-gestrel : 0.05 mg

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Male Sex Hormones – Testosterone

Definition :

The most important androgen secreted by testes is testosterone. It is secreted by interstitial cells of Leydig.

1. Natural Testosterone :

Synthesis :

- Testes, ovary, adrenal cortex and placenta secrete enzymes, which play an important role in synthesis of testosterone.
- It occurs in the interstitial cells of Leydig and also in subtentacular sertoli cells.
- Secreted testosterone enters into systemic circulation, attaches to specific "sex hormone binding protein" and reaches the target cells.

Metabolism and Excretion :

- Testosterone is inactivated in liver and as conjugate with sulphate or glucuronic acid, is excreted in urine.

Properties of Natural Testosterone :

- It induces secondary sex characters in males like body hair, deep voice, penile growth.
- Supports spermatogenesis.
- Induces protein anabolism.

2. Synthetic Testosterone :

Therapeutic Uses :

- It is used to treat cryptochildism.
- As replacement therapy in hypogonadism.
- In females it is used to treat breast cancer.
- As it is capable to stimulating haemopoeisis, it may be used in aplastic anaemia or leukaemias.

Side Effects :

- Sodium water retention causing weight gain and hypotension.
- Hypercalcaemia, premature closure of epiphysis and linear growth is affected.
- Hepatic disfunction and cholestatic jaundice.

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Contraindications :

Testosterone is strictly contraindicated in following clinical conditions :

- Carcinoma of prostate.
- Hypertension.
- Liver disease.

Preparations :

- Testosterone injection : 50 mg I/V three times weekly.
- Testosterone propionate : 5 to 25 mg oil I/M four times weekly.
- Methyltestosterone : 25 mg to 50 mg sublingually / orally.

Oral Contraceptives

Definition :

These pharmacological agents when administered internally prevent conception (pregnancy).

Mechanism of Action :

The combination of estrogen and progestins produce their contraceptive effect by following mechanism :

1. The combination selectively inhibits the pituitary function. The hypothalamic gonadotropin releasing hormone (GRH) is inhibited which leads to inhibition of Follicle Stimulating Hormone (FSH) and Leutenising Hormone (LH) from pituitary. This results in inhibition of ovulation.
2. The combination produces change in the cervical mucus, in uterine endometrium, change in the motility and secretion in fallopian tubes. All these changes decrease possibility of conception and implantation.
3. It is postulated that oestrogen brings out all above changes while progesterone only causes endometrial shedding. Thus, it is belived that inhibition of ovulation is mainly due to oestrogen and progesterone only causes withdrawal bleeding.

Classification :

Oral contraceptives are classified into three groups :

1. Oestrogen, progesterone – combination pill.
2. Sequential estrogen, progesterone – sequential pill.
2. Continuous low dose progesterone – mini pill.

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Accordingly the various pharmacological agents are :

Type	Oestrogen	Progesterone	Trade name
1. Combination pill	a. Ethynylo estradiole (0.05 mg)	Ethynodiole diacetate (1 mg)	Hemovulen
	b. Ethynylo estradiole (0.05 mg)	Ethynodiole diacetate (1 mg)	Ovulen 50
	c. Ethinyl estradiole (0.05 mg)	Lynstrenol (1 mg)	Lyndiol (1mg)
	d. Ethinyl estradiole (0.05 mg)	Norethisterone acetate (1 mg)	Minovlar ED.
	e. Ethinyl estradiole (0.05 mg)	Norgestrel (0.5 mg)	Ovral
2. Sequential pill	a. Ethynyl estradiole (0.1 mg)	Dimethisterone (25 mg)	Oracon
	b. Mestranol (0.08 mg)	Nor-ethindrone (2 mg)	Norquen
3. The mini pills (only progesterone)	a. --------	Norestrel (0.075 mg)	Orvette
	b. ---------	nor-ethindrone (0.35 mg)	Micronor

Mode of Administration :

- Combination pill : Administered as a single daily dose from 5th day of cycle to 25th day of cycle, counting first day of cycle as day '1'.
- Sequential pill : Administered from 5th day to 25th day of cycle. First '5'→ 20th day of cycle along Oestrogen single daily dose. Remaining '5' days only Oestrogen progesterone combination.
- Mini pills : Daily in continuation.

Therapeutic Uses :

- As oral contraceptives. These agents offer safe, reversible contraception.
- These preparations are used in endometriosis, characterized by severe days menorrhoea.

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- These preparations are used to treat premenstrual tension and menstrual irregularities.

Side Effects :

- Nausea, vomiting, headache, lethargy, breast discomfort, breakthrough bleeding, oedema, mild depression are the mild side effects.
- Serious adverse effects include, amenorrhoea, weight gain, increased skin pigmentation, vaginal infection.
- Moderate side effects includes, thromboembolism, myocardial infarction, gastro intestinal disorder etc.

Contraindications :

Oral contraceptives are strictly contraindicated in following clinical conditions :

- Thromboembolic diseases.
- Liver diseases.
- Breast and uterine carcinoma.
- Vaginal bleeding.
- Migraine.
- Hypertension.
- Epilepsy.

Precautions :

- It is better to follow advice and examination by gynaecologists before the person is subjected to oral contraceptive therapy.
- Great care must be taken in cases with previous history of asthma / diabetes/ endocrine disorder.
- Oral contraceptives must be discontinued if the person reports headaches, acute visual disturbances etc.

Drug Interactions :

- Antibiotics like Rifampicin antitubercular drug, increases the incidences of breakthrough bleeding in women during oral contraceptive therapy.
- Antibiotics like ampicillin and tetracycline, have been known for failure of oral contraception.
- Drugs like phenytoin (anti-epileptic), phenobarbiton (hypnosedatives) are potent inducers of hepatic microsomal enzymes and hence are expected to increase rate of metabolism of contraceptive.

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CORTICOSTEROIDS

Definition :

Corticosteroids are adrenocortical hormones produced and released by adrenal cortex.

The secretion of adrenocortical steroids is controlled by the pituitary release of corticotrophin i.e. ACTH → adreno-cortico-trophic hormone.

Classification :

The classification of corticosteroids, according to zones that form adrenal cortex can be explained as follows :

1. Gluco-corticosteroids : Cortisol, hydrocortisone released from middle and inner zones of adrenal cortex – zona fasciculate and zona reticularis.
2. Mineral corticosteroid : Aldosterone released from zona glomerulosa, the outer zone of adrenal cortex.
3. Sex hormones.

1. Gluco-corticoids :

The chief glucocorticoid secreted in humans is hydrocortisone cortisol.

Actions :

[A] Metabolic effects :

(a) Glucocorticoids inhibit amino acid – protein synthesis and stimulates their conversion into glucose in liver. Glucocorticosteroids inhibit peripheral glucose utilization.

(b) Glucocorticosteroids cause redistribution of fat in the body with loss from extremity and a deposition in neck and supra clavicle area giving "moon like face" appearance.

[B] Cardio vascular system :

Absence of glucocorticoids causes increase in capillary permeability, reduction in cardiac output and exerts positive ionotropic action.

[C] Central nervous system :

Glucocorticoids stimulate slight changes in mood, a false sensation of well being, nervousness and restlessness.

[D] Anti-inflammatory action :

Glucocorticoids prevent inflammatory reactions such as local heat, redness, swelling, tenderness etc.

[E] Gastro-intestinal system :

Glucocorticoids increase the secretion of gastric hydrochloric acid, pepsinogen and pancreatic tripsinogen.

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Side Effects :

Weight gain, osteoporosis, diabetes, peptic ulcers, psychosis, cataract, glaucoma.

Therapeutic Uses :

- To treat allergic disorders :
  Like odema, asthma, serum sickness etc.
- To treat eye diseases :
  Like allergic conjunctivitis, optic neuritis.
- To treat skin diseases :
  Like atopic dermatitis, xerosis.
- To treat haemotological disorder :
  Like blood dyscrasias, purpurea etc.

Absorption, Fate, Excretion :

- Exists in plasma protein bound form.
- Cortisol is taken up by liver, where it is metabolized and conjugated to form water soluble compounds which are excreted in urine.
- Synthetic corticosteroid are well, rapidly and completely absorbed from gut.

Contraindications :

- Peptic ulcer.
- Hypertension.
- Psychosis.
- Diabetes mellitus.
- Osteoporosis.
- Glaucoma.
- Pregnancy.

Preparations :

- Cortisone acetate I.P.
  25 mg tablet, twice a day upto 400 mg daily.
- Cortisone injection I.P.
  Suspension of 25 mg / ml cortisone acetate.
  Single dose 'intra muscularly'. (I/M).
- Prednisolon tablet I.P
  10 to 100 mg / day

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2. Mineral Corticoid :

Definition :

These are corticosteroids which regulate water and electrolyte balance and hence are referred to as mineral corticoids.

The chief mineral corticosteroids are :

(i) aldosterone and (ii) deoxycorticosterone.

Pharmacological Actions :

Aldosterone and other steroids cause reabsorption of sodium from urine by the distal renal tubules.

It also increases sodium reabsorption in sweat, salivary glands and gastro intestinal mucosa.

Side Effects :

Weight gain, hypertension, hypokalemia.

Therapeutic Uses :

Mineral corticosteroids are used in management of Addisons' disease.

Preparations :

- Desoxycorticosterone acetate injection I.P.
  5 mg / ml.

Dose : 2 – 5 mg /day I/M.

- Desoxycorticosterone trimethyl acetate injection I.P.
  25 to 100 mg once a month I/M.

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Chapter...11

DRUGS ACTING ON DIGESTIVE SYSTEM

CARMINATIVES

These are the pharmacological agents, which when administered externally, expel gas from the stomach or intestine during the treatment for flatulence and colics.

Mechanism of Action :

- These are pharmacological agents, which are aromatic volatile oils in nature
- These agents cause mild irritation, thereby increasing gastro-intestinal motility and cause relaxation of sphincters.
- These agents produce a feeling of warmth in the stomach.

Preparations :

The various food spices and condiments, like cardamom fruits, ginger, fennel fruits, asafoetida, cinnamon bark, cloves, cariander and anise, posses carminative properties.

With sodium bicarbonate, these agents form important constituents of various grips.

Therapeutically these volatile oils are used in the form of tinctures.

e.g. Tincure cardamom
Tincture zingiberis

Side Effect :

In individuals, suffering from peptic ulcer, biliary tract diseases, irritable colon syndrome it may cause flattent dyspepsial.

DIGESTANTS

Definition :

These are pharmacological agents which when administered promote the process of digestion in the gastro-intestinal tract.

Digestants

1. Hydrochloric acid (Dilute) :

Dilute hydrochloric acid I.P. 10% w/v hydrochloric acid. The preparation is usually diluted with 25 to 50 volumes of water and 4 to 6 ml of diluted solution are administered by mouth through a straw to prevent its effect on teeth.

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2. Pepsin :

This is a proteolytic enzyme obtained from the glandular layer of the fresh stomach of the hog.

It is administered orally in 0.5 to 1 g. doses.

3. Renin :

This is partially purified milk curdling enzyme, obtained from glandular layer of calf's stomach.

4. Pancreatin :

This contains the enzymes amylase, lipase and trypsin obtained from hog or ox pancreas.

It is administered in enteric coated capsule.

5. Bile, Bile salts, Bile acids :

Bile salts increase the flow as well as the concentration of bile.

The preparations available are :

(a) Ox bile extract tablet → 300 mg orally

(b) Dehydrocholic acid → 250 mg twice a day oral.

6. Chenodeoxycholic acid → 10 – 15 mg/kg/day

ANTACIDS, DRUGS USED IN ULCER

Gastric Antacids

These are the pharmacological agents defined as weak bases, which when administered, neutralize the gastric acid secretion by raising the gastric pH above 4.0 to 4.5.

Classification :

Antacids are classified in two groups :

1. Systemic antacids :

These are the gastric antacids when administered get absorbed into systemic circulation, and may cause systemic alkalosis.

Example : Sodium bicarbonate.

2. Non-systemic antacids :

These are gastric antacids, which when administered, form insoluble complexes in the small intestine. These are usually water insoluble preparations.

Example : Aluminium hydroxide gel.

Calcium carbonate

Magnesium trisilicate.

Magnesium hydroxide.

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Mechanism of Action :

The antacids act as weak bases and reduce the quantity of free hydrochloric acid in the stomach by the following mechanisms :

1. direct neutralisation of pre-formed acid.
2. buffering of pre-formed acid.
3. adsorption of hydrogen ions as well as adsorption and inactivation of pepsin.

Ideal Properties of Antacids :

1. Ideal antacids should act quickly.
2. It should have prolonged action.
3. It should not interfere with digestion of food.
4. It should be non-toxic, palatable, cheap and easily available.

Pharmacology of Antacids :

1. Systemic antacid – 'sodium bicarbonate' :

- It is white, water soluble and completely absorbable antacid.
- It reacts with gastric acid as follows :

$$\underset{\text{antacid}}{NaHCO_3} + \underset{\text{gastric acid}}{HCl} \longrightarrow NaCl + H_2O^- + CO_2\uparrow$$

- It is an effective and rapidly acting antacid. One gram of drug neutralizes 12 m equivalent of acid.
- (1 gram neutralizes 120 ml of 0.1 N HCl)
- During the neuralization process, carbon dioxide is liberated, which gives the patient a sense of relief from abdominal discomfort.
- It is not recommended for long term use as it produces systemic alkalosis.
- It makes the pH totally neutral or alkaline and thus interferes with the peptic digestion of food. Due to gastrin release there is compensatory increased secretion of acid gastric juice – which is termed as rebound acidity.

Contraindications :

- Hypertension.
- Congestive cardiac failure.
- Renal disorders.

Preparation :

- 1 – 5 gm in water and repeated as required.

2. Non-systemic antacid :

(a) Aluminium hydroxide gel :

- It is a commonly used antacid.

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- In the gel form, it is a nonabsorbable buffer antacid.
- It has slow onset of action and low neutralizing capacity.

  (1 gm neutralizes 12.5 to 25 ml of 0.1 N HCl)

  $Al(OH)_3 + 3HCl \rightarrow AlCl_3 + 3H_2O$
- In addition to anti-acid property, aluminium hydroxide gel possesses astringent and demulscent properties, by which it provides a protective covering over the ulcerative area.
- Aluminium hydroxide gel is relatively palatable and is devoid of major serious toxicity.
- The most common side effect of aluminium hydroxide gel is, constipation. To relieve constipation, it is always combined with magnesium salts like magnesium hydroxide or tri-silicate.
- Aluminium hyroxide gel is strictly contraindicated in combination with tetracycline, barbiturates, warfarin, quinidine and chlorpromazine, as it reduces absorption of these agents by chelation, i.e. by forming insoluble complexes – chelates.

Preparations :

- Aluminium hydroxide tablets - gelusil - 2 tablets to be chewed.
- Aluminium hydroxide gel - divol - 4-8 ml every two hour.

(b) Magnesium tri-silicate :

- It is available as a fine white tasteless powder.
- In the stomach, it acts as both antacid and adsorbent.
- When administered, it reacts with gastric acid to from hydrated silicon dioxide as follows :

  $Mg_2Si_3O_8 \cdot nH_2O + 4HCl \rightarrow 2MgCl_2 + 3SiO_2 + (n + 2)\ H_2O$

  As it is gelatinous in consistency, it provides protective coating to ulcer area.

  One gram of magnesium trisilicate neuralizes about 9 -11 M equiv., of gastric acid.
- It may cause mild diarrhoea.

Preparation :

- Magnesium tri-silicate.

  2.4 mg every 1 – 4 hour.

  Tablet should be chewed before being swallowed, as it does not disintegrate rapidly in the stomach.

(c) Calcium carbonate :

- It is a non-systemic antacid and occurs as a white, odourless powder with a chalky taste.

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- In the stomach it reacts with gastric acid to form calcium carbonate as follows :

  $CaCO_3 + 2HCl \rightarrow CaCl_2 + H_2O + CO_2 \uparrow$

  1 gram of drug neutralizes 21 M equiv. of acid.
- It acts quickly, producing prolonged duration of action.
- The main drawback of calcium carbonate is, its chalky taste can be unpalatable and it can cause constipation.

Preparation :

- Calcium carbonate : 1 gm table

  Dose : 2 – 4 gm

Ulcer Healing Agents :

Antacids are weak bases. When administered, neutralizes gastric hydrochloric acid. These agents however do not possess any ulcer healing property.

Agents that heal ulcers are :

1. Milk :

Milk drip containing aluminium hydroxide gel administered through a Ryle's tube into the stomach may produce rapid healing of ulcers.

2. Cemetidine :

- It is Histamine H_2 receptor antagonist.
- It is known to inhibit the basal and meal stimulated gastric secretion.
- It is very effective in promoting healing of gastric and peptic ulcer and is valuable in the treatment of duodenal ulcer.
- When administered orally, it is absorbed effectively.

  It is excreted through the urine. Crosses the placental barrier and is secreted in milk.

Preparations :

- Cemetidine

  (Tagamet)

  200 mg tablet.
- Cemetidine

  (Tagamet)

  100 mg/ml injection – by I/M route.

3. Ranitidine :

- Ranitidine, an ulcer healing agent, is more selective and long lasting in its actions.
- It is considered as safe antacid.

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Preparations :

- Ranitidine tablet 150 mg oral
- Ranitidine injection 25 mg/ml by slow i/v administration.

4. Carbenoxolon sodium :

- It is a derivative of glycyrrhizinic acid, a constituent of liquorice root.
- It enhances healing of ulcer by increasing production of gastric mucus and prolongs life of epithelial cells.
- In addition it has local anti-inflammatory action.

Preparation :

- Carbenoxolone sodium
  (Biogastron)
  100 mg twice/thrice daily for four weeks.

5. Anticholinergics :

- Antispasmodic, anticholinergics are used in the management of peptic ulcer as they reduce intestinal spasm.
- They inhibit acid and pepsin secretion and relieve pain.
- As anticholinergics cause dryness to mouth, blurring of vision, retention of urine, they should not be given continuously to ulcer patients.

Preparations :

- Atropine → 0.3 to 04 mg
- Tincture belladona → 1 mg
- Propantheline → 15 mg

PURGATIVES, LAXATIVES

Physiology of Constipation :

Persons vary considerably in the frequency with which their bowels are evacuated. In some individuals bowel movement occurs twice or thrice, while in others it may occur after every two days. Because of this variability, it is difficult to define constipation. However, when the interval between bowel movements is greater than 24 hours and the subject as a result, suffers distress or discomfort characterized by headaches, digestive disturbances or if feces are abnormally dry and hard and the evacuation of the bowels difficult, the phase is defined as 'constipation'.

Causes of Constipation :

1. A diet which leaves too little unabsorbed residue or one which contains too little fluid.
2. A colon which absorbs too readily and thus causes drying of feces.
3. Hypertonic state of the muscle of the colon.

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Pharmacology of Constipation :

Constipation can be treated by using the group of pharmacological agents known as 'cathartics'.

'Cathartics' : It can be defined as a pharmacological agent, which when administered, increases tone, moility, peristalsis and relieves constipation.

'Purgatives' : These are drastic cathartics which when administered relieve constipation, by causing gripping pain in abdomen and loss of water.

'Laxatives' : These are mild cathartics which when administered, relieve constipation without gripping pain and loss of water.

Classification :

Cathartics can be classified as follows :

(a) Stimulant or irritant laxatives :

- Castor oil.
- Cascara sagrada.
- Senna.

(b) Bulk forming laxatives :

- Bran.
- Methyl cellulose.
- Isapgol husk.

(c) Osmotic laxative (Saline purgatives) :

- Magnesium sulphate.

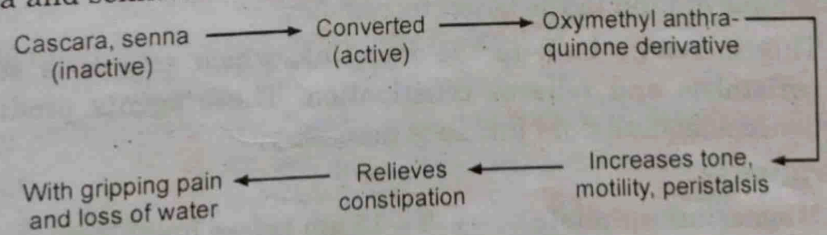
(d) Emolient laxatives (Fecal softners) :

- Liquid paraffin.
- Dioctyl sodium sulphosuccinate.

(a) Stimulant or Irritant Laxative

1. Cascara and senna :

- These are anthraquinone derivatives.
- These are drastic cathartics, i.e. simulant, irritant laxatives.
- Cascara and senna act as irritant cathartics as follows :



Preparations :

- Senna Glaxenna – 0.6 – 2 gm at bed time
- Cascara sagrada – 1 to 2 tablets at bed time.

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2. Castor oil :

- It is an irritant laxative.
- It is fixed oil obtained from the seeds of Ricinus communis linn.
- Castor oil itself is non-irritant, but when ingested, it is hydrolysed in the intestine by pancreatic lipase, to glycerol and ricinoleic acid. Ricinoleic acid acts as an irritant and causes purgation.
- Castor oil acts on the small intestine and produces copious liquid stool with fluid loss.
- Castor oil is strictly contraindicated in pregnant women as it stimulates uterine contractions.

Preparation :

- Castor oil, I.P. → 5 ml to 15 ml

(b) Bulk Forming Laxatives :

- These are mild cathartics.
- These are natural or semisynthetic polysaccharides and cellulose derivatives.
- When administered orally, these agents are not absorbed and thus increase the indigestible residue. These agents thus absorb water and swell up and thus relieve constipation by increasing fecal mass, which stimulates, peristalsis. Along with these agents, adequate fluid intake must be taken to avoid intestinal obstruction.

Preparations :

- Bran → 12 – 24 gm in divided dose.
- Isapgol husk → 5 to 15 gm
- Methyl cellulose → 1 g four times / day

(c) Osmotic Cathartics / Laxatives :

- Osmotic laxatives are mainly salts which when administered orally, are not absorbed much and remain in gastro-intestinal-tract.
- Such pharmacological agents exert on osmotic effect and maintain the volume of fluid in the bowel by osmosis.
- This increases bulk in the intestine, which acts as a stimulant, initiates peristalsis and relieves constipation. These agents produce watery stools, hence adequate fluid intake is necessary.

Preparations :

- Magnesium sulphate → 5 – 15 gm before breakfast.
- Magnesium carbonate → 2 – 5 gm as per requirement.
- Magnesium hydroxide → 2 – 4 gm as per requirement.

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(d) Emolient laxatives :

- Liquid paraffin is most widely used as an efficient laxative.
- Liquid paraffin is mineral oil consisting of a mixture of hydrocarbons obtained from petroleum.
- Liquid paraffin exerts a softening and lubricating effect on feces.
- It is mild in action.
- It is usually administered at bedtime.
- It interferes with the absorption of essential fat soluble substances and may cause deficiency of vitamins A, D and K.

Preparation :

- Liquid paraffin, I.P. → 8 to 30 ml.

Clinical Applications of Cathartics :

- To relieve constipation.
- Before radiological examination of gastro-intestinal tract.
- In haemorrhoides.
- In gynaecological practice.
- In case with anal fissures.

ANTI-DIARRHOEALS

Diarrhoea is defined as rapid passage of fecal matter through gastro-intestinal tract and a frequent passage of semisolid or liquid feces.

Antidiarrhoeals are pharmacological agents, which when administered, alter the tone and motility of bowels, or act as adsorbents, which adsorb the irritants.

Anti-diarrhoeals :

1. **The opiates :**
   - Opiates are used for symptomatic relief of diarrhoea.
   - When administered, these agents reduce the propulsive movements of the colonic muscle and thereby allow the feces to remain for a longer time in the lumen so that water is re-absorbed.
   - The main drawback of opiates as antidiarrhoeals is, these agents may cause addiction and tolerance, if taken frequently.

   Preparations :
   - Paregoric - Camphorated preparation of opium - 4 ml
   - Laudanum - Tincture of opium – 0.3 to 0.6 ml
   - Codeine phosphate - – 16 to 30 mg
2. **Diphenoxylate hydrochloride** - Lomotil - 5 mg three times daily
3. **Antispasmoidc** - Atropine sulphate - 0.25 to 1 mg
   - Belladona tincture - 0.6 to 2 ml

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4. Hydrophillic agents :

These agents when administered, absorb water in the lumen and form gelatinous mass. This reduces free water content of stool.

➢ Methyl cellulose	Celevac	1 to 3 gm
➢ Psyllium seeds	-	5 to 15 gm
➢ Isapgula husk	Isogel	3 to 5 gm

5. Demulscent :

These agents when administered, provide soothing effect to the irritated intestinal mucosa.

➢ Bismuth carbonate	2 g orally
➢ Magnesium oxide	1 g orally

6. Adsorbents :

These are pharmacological agents which when administered, adsorb noxious substances such as bacteria, gases and bacterial toxins.

➢ Activated charcoal	1 to 6 mg orally
➢ Kaolin	3 gm orally
➢ Mixture of kaolin Pectin (Keopectate)	15 ml orally

7. Miscellaneous drugs :

➢ Chenodeoxycholic acid	Chenodol	10 to 15 mg / kg body weight per 24 hour orally.
➢ Lactulose		50 % w /v solution in a dose 50 ml orally
➢ Cholestyramine	Questran	Orally

EMETICS, ANTIEMETICS

Emesis is a complex reflex co-ordinated by the vomiting centre in the medulla.

The afferent and efferent pathways which cause vomiting are carried by vagus and sympathetic nerves.

Chemo-receptor trigger zone, is a major sensory relay station, present in the lateral border of the area postrema of medulla oblongata.

Afferent stimulations like tactile pharyngeal impulses, labyrinthine disturbances, pain, distension of viscera, psychological factors, increased intracranial pressure, emetic drugs, radiation therapy, electrolyte disturbances, endocrine disturbances, pregnancy etc., cause 'Emesis' i.e. vomiting.

Emetics :

These are pharmacological agents which are used for induction of vomiting.

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Classification :

(a) Centrally acting emetics :

- Apomorphine.

(b) Peripherally acting emetics :

- Mustard.
- Sodium chloride.

(c) Peripherally as well as centrally acting :

- Inpecauanha
- Cardiac glycoside.

Preparations :

- Apomorphine injection, I.P. :
  3 mg of salt / ml.
  Dose - 2 to 8 mg subcutaneously. (S/C)
- Mustard - 1 teaspoonful in water.
- Ipecacuanha – 15 ml by mouth.

Therapeutic Application :

Emetics are advised in certain cases of poisoning where gastric lavage facilities are not available.

e.g. Bellandona poisoning.
Barbiturate poisoning

Precautions, Side Effects, Contraindications :

1. Emetics must be used continuously because aspiration of the gastric contents into respiratory passage may occur during emesis.
2. Emesis may cause perforation of the stomach if ingested poison is caustic.
3. Severe emesis may cause collapse and may worsen the existing state of the sufferer.
4. Emetics should be administered with caution to children and the elderly.
5. Emetics are contraindicated in pregnant women, in individuals with cardiac decompensation, hypertension, hernia, peptic ulcer and pulmonary tuberculosis.

Antiemetics :

Antiemetics are pharmacological agents used specifically to prevent or relieve nausea and vomiting.

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Classification :

1. Anticholinergics → Scopolamine
2. Antihistaminics → Diphenhydramine, Cyclizine
3. Antidopaminergics → Chlorpromazine
4. Miscellaneous → Haloperidol
   Trimehobenzamide
   Benzquinamide.

Mechanism of Action :

Antiemetics produce antiemesis action by acting on either of the receptor sites as follows :

1. directly on vomiting centre.
2. by acting on CTZ (chemo receptor trigger zone)
3. acting peripherially.

Preparations :

- Scopolamine hydrobromide → 0.6 mg to 1 mg Subcutaneously
- Prochlorperazine → 2 to 5 mg
- Chlorpromazine → 10 to 25 mg

Therapeutic Applications :

- As an antiemetic especially in post-operative vomiting.
- To control vomiting during cancer therapy.
- To treat reflex esophagitis.
- To treat vomiting due to motion sickness.
- To treat vomiting during pregnancy. (Alongwith Pyridoxin)
- To treat vomiting during G.I.T. disturbances
- To treat vomiting due to psychological reasons.

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Chapter...12

CHEMOTHERAPY OF MICROBIAL DISEASES

CHEMOTHERAPY – INTRODUCTION

General Introduction :

Chemotherapy can be defined as "the use of chemical compounds in the treatment of infectious diseases, so as to destroy offending parasites or organisms without damaging the host tissues".

The history of chemotherapy can be discussed in three periods as :

- Pre-Ehrlich era before 1891.
- Paul-Ehrlich era.
- Period after 1935 – well known by discovery of sulfonamides and antibiotics.

The various events, developments, major contribution to chemotherapy are as listed below :

- Domagk Mietsch, in 1938, introduced a dye 'Prontosil' inhibiting streptococci.
- Pasteur and Joubret, in 1877 – 1885, postulated that one bacterium could produce a substance that would stop the growth of another.
- Emmerich and Low, in 1889 (1899), discovered that extracts of Pseudomonas aeruginosa in high dilutions could destroy a variety of pathogenic cocci as well as diptheria, cholera, plague organism.
- Sir Alexander Fleming, in 1928, observed that one of his bacterial culture plates was contaminated by a fungus, which prevented growth of surrounding bacterial colonies.

  The fungus was later discovered as Penicillin notatum.

  Schataz, Bugie and Waksman, in 1944, reported the isolation of antibiotic streptomycin from Streptomyces griseus.

Significance of Various Terms Used in Chemotherapy :

Chemotherapeutic index : According to Ehrlich, substances used as anti-infectives, should produce greater effects on parasites (maximum parasitotropic) and minimum effects on host cells and tissues (minimum organotropic). Such anti-

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infective agents are defined as 'desirable' and posses a favourable chemotherapeutic index, which can be represented as :

$$\text{Chemotherapeutic index (C.I)} = \frac{\text{Maximum tolerated dose}}{\text{Minimum curative dose}}$$

Taking into consideration the various routes of administration, different hosts, the above formula is modified as :

$$\text{Chemotherapeutic index (C.I)} = \frac{\text{L.D. 0.1}}{\text{C.D. 99.9}}$$

where,

L D. 0.1. = a dose which will kill all animlas except 0.1%.

C D. 99.9 = dose which cures all animals except 0.1%.

This index indicates margin of safety of anti-infective agents.

General Mechanism of Action of Anti-infective Agents :

The various chemotherapeutic, anti-bacterial agents, used in therapy, act by either of following mechanism :

- Inhibition of bacterial cell-wall synthesis.
- Inhibition of cytoplasmic membrane function.
- Inhibition of nucleic acid synthesis.
- Inhibition of protein synthesis.
- Control of microbial enzymes.
- By competing for an essential metabolite in a substrate.

URINARY ANTISEPTICS

Introduction / Pathophysiology :

Urinary tract infection is defined as a condition characterized by presence of actively multiplying bacteria in the urinary bladder.

When 100,000 or more organisms are present in 1 ml of urine in two separately tested samples, then it is the condition referred to as urinary tract infection. Usually during infection, along with bacteria, white cells also appear.

The clinical conditions informing urinary tract infection are :

- Acute pyelonephritis – it is characterized by pain in the loins, fever, rigors and frequency of micturation.
- Chronic pyelonephritis – characterized by asymptomatic bacteria.
- Cystitis – it is characterized by frequency of micturation, fever, tenderness over supra pubic region.

The causative organism of urinary tract infections is *Escherichia Coli*.

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URINARY TRACT ANTISEPTICS

Definition :

These are pharmacological agents, which when administered, inhibit the growth of causative organisms of urinary tract infection. Because these agents act locally on kidneys, urinary bladder and uterus. They are called as urinary tract antiseptics.

Classification :

(a) Urinary tract antiseptics

- Methenamine mandelate
- Nalidixic acid
- Oxalinic acid
- Nitrofurantoin

(b) Antibiotics

- Ampicillin
- Carbenecillin
- Cephalosporins
- Ciprofloxacin

Mechanism of Action :

The pharmacological agents, which are used as urinary antiseptics, when administered get concentrated in the renal tubules and effectively inhibit the growth of the infection causing organisms.

Adverse / Side Effect :

Gastro-intestinal tract upset is very common.

Preparation / Dose :

Drug	Trade name	Dose
1. Nitrofurantoin	Furadantin	100 mg / 6 hr. with food
2. Nalidixic acid	Gramoneg	1 gm four times / day
3. Nitrofurazone	Furacin	0.2% concentration available as ointment, cream
4. Methenamine	Mandelamine	1 gm four times / day
5. Oxolinic acid	-	750 mg two times / day oral
6. Furazolidone	Furoxone	100 mg 3 times/day for 5 days

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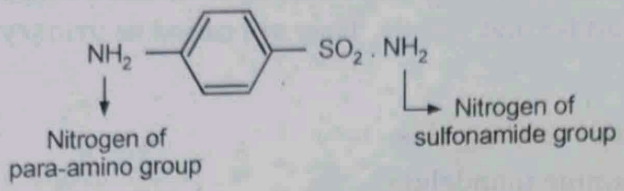
SULFONAMIDES

Definition :

The antimicrobial compounds containing a sulfonamide – SO_2NH_2 group are called as sulfonamides.



Classification :

Sulfonamides are classified as follows :

(a) Used for the treatment of systemic infection :

- Short acting sulfonamides :
  Sulfadiazine, sulfadimidine, sulfacetamide.
- Intermediate acting sulfonamides :
  Sulfamethoxazole
- Long acting sulfonamides :
  Sulfamethoxypyridazine

(b) Used for local gastro intestinal infection. Sulfagaunidine, succinyl sulfathiazole.

Anti-bacterial Spectrum :

Sulfonamides are effective against Gram positive and Gram negative organisms like :

- Streptococci, staphylococci, gonococci, pneumococci etc.
- Clostridia
- Haemophilus influenzae, vibrio, *E. coli* etc.
- Chlamydia

Mechanism of Action :

Folic acid derived from Para-amino-benzoic acid is essential for growth and multiplication of microorganism.

Sulfonamides inhibit folic acid synthetase enzyme; and because of its structural resemblance to para-amino-benzoic acid, removes PABA from the site and inhibits conversion of Para-amino-benzoic acid to folic acid, by attaching to the site.

Because of deficiency of folic acid, microorganism cannot multiply and grow. Thus, growth and multiplication of microorganism stops.

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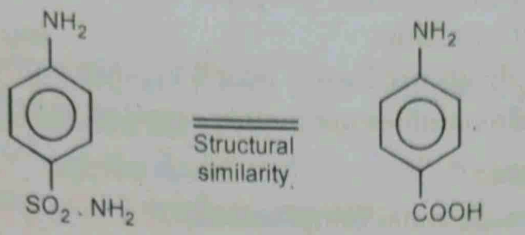
This is termed as **'bacteriostatic'** action of sulfonamide. Schematically it can be represented as follows :



Sulfonamide — Para-amino benzoic acid

1. Normally when

Mycobacteria
↓
Attacks human body
↓
Releases Para-amino-benezoic acid
↓ by folic acid synthatase
Converted to folic acid
↓
Utilized by microorganisms for their growth and multiplication

2. When

Sulfonamides administered
↓
Because of structural similarity With PABA
↓
Removes PABA from site
↓
Prevents synthesis of folic acid
↓
Causes deficiency of folic acid
↓
Results in bacteriostasis

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Absorption, Fate, Excretion :

Sulfonamides used for systemic purposes are well absorbed. The main site of absorption is the small intestine.

In the blood, these drugs are loosely bound to plasma proteins.

Free, acetylated sulfonamides are mainly excreted in urine.

Adverse / Side Effects :

(a) Sulfonamides cause renal complications.

In the presence of acidic urine, the acetylated form of sulfonamide is precipitated in collecting tubules and calyces. This causes renal irritation, obstruction to urinary flow, crystaluria, albuminuria, haematuria, oliguria and anuria.

These renal complications can be minimized by

- Advising high fluid intake to ensure adequate output of urine.
- By alkalinisation of urine, to increase solubility of conjugated products.
- By using sulfa combination.

(b) On blood system sulfonamides causes agranulocytosis thrombocytopenia.

Drug	Trade names	Oral dose
Sulfadiazine	Gantrisin	2 – 4 gm orally / 6 hr.
Sulfisoxazole	Gentanol	2 – 4 gm orally / 6 hr.
Sulfamethoxy pyridazine	Lederkyn medicil	Initially 1 gm followed by 0.5 g daily.
Succynyl sulfathiazole	Sulfasuxidine	10 – 20 g daily divided dose.
Pthalyl sulfathiazole	Sulfathalidine	10 g daily divided dose.
Sulfacetamide	Albucid	10 to 30%, 1 or 2 drops in both eyes every four hours.

Clinical Application / Therapeutic Uses :

- To treat urinary tract infections –

  Urinary tract infection is caused by the microorganism *E.Coli*, which is highly sensitive to sulfonamides.
- To treat acute bacillary dysentery.
- In the prophylaxis of meningocaccal meningitis.
- In the treatment of trachoma and inclusion conjunctivitis.
- To treat nocardiasis.
- In the management of burns and skin disorder.

Contraindications :

Sulfonamides should be not used (contraindicated) in patients :

- With a history of sulpha hypersensitivity.

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- Advanced kidney diseases with an elevated blood urea nitrogen.
- Pregnant women in last trimester.

Sulfonamide Interaction :

- Sulfonamides, if administered with oral anti-coagulents or methotrexate, increase their pharmacological effect.
- Sulfonamides, if administered with oral hypoglycemic agent like sulfonylurea, potentiates hypoglycaemic action.
- Analgesics like indomethacin and probenecid salicylates, reduce efficacy of sulfonamide by displacing it from the binding site.

Sulfa Combination :

- Sulfa combination is preferred instead of only sulfa in practice, for following reasons :
  (i) Combination therapy overcomes each others drawbacks (side effects).
  (ii) In combination low doses are effective.
  (iii) Combinations acts synergistically.
- In sulfa combination, sulfamethoxazole is combined with trimethoprim.
- Trimethoprim is a pyrimidine derivative and is effective against pathogenic bacteria.
- In this combination these agents are preferred because.
  (i) Trimethoprim and sulfamethoxazole act synergestically.
  (ii) Trimethoprim is a structural anologue of dihydrofolic acid and hence inhibits the enzyme dihydrofolate reductase, which is involved in conversion of dihydrofolic acid to tetrahydrofolic acid.
  (iii) Sulfonamides inhibit conversion of Para-amino-benzoic acid to folic acid and thus inhibits synthesis of folic acid.
  (iv) Thus, together these drugs prevent growth of microorganisms by producing folic acid deficiency.
  (v) Pharmacokinetic studies make it clear, that the half lives of these two agents are identical and approximately similar.
  Half life of trimethoprim : 16 hrs
  Half life of sulfamethoxazole : 10 –12 hrs.
- Schematically, the mechanism of action of sulfa combination, can be represented as follows :

Para-Amino-Benezolic Acid
| ⟶ inhibited by sulfamethoxazone
Folic acid
| ⟶ inhibited by trimethoprim
Folinic acid

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Clinical Application / Therapeutic Uses :

- As a preparation of choice in the urinary tract infection, caused by *E. Coli.*
- In the treatment of respiratory tract infections including acute and chronic bronchitis.
- To treat gastro-intestinal infections, specifically in the treatment of shigellosis.
- Combination is useful for the treatment of septicaemias and serious infections caused by gram –ve bacilli.
- In the treatment of plague.
- In the treatment of veneral, i.e. sexually transmitted diseases, like syphilis and gonorrhoea.
- Combination is successfully suggested in cases of neonatal meningitis.

Adverse / Side Effect :

It is postulated that trimethoprim may increase the gastro-intestinal and haematological toxicity of sulphamethoxazole.

Interactions :

- Combination increases pharmacological action of anti-coagulant warfarin and of anti-epileptic phenytoin sodium.
- It should not be administered to pregnant women, especially during the first trimester and to children below 12 years of age.

Preparation / Dose :

Trimethoprim, sulfamethoxazole are combined with each other in a ratio 1 : 5. Accordingly the various preparations available are :

Combination	Trade names	Dose
Trimethoprim 80 mg + Sulfamethoxazole 400 mg	Septran Bactrim, supristol	1 / 2 tablets for 14 days.
Paediatric tablets – Trimethoprim – 20 mg + Sulfamethoxazole – 100 mg	–	1 / 2 tablets
Trimethoprim 90 mg + Sulfadiazene 410 mg	Aubril	1 tablet twice / day

ANTIBIOTICS

These are chemical compounds produced by living microorganisms like bacteria, fungi and actinomycetes, which at high dilutions, are capable of inhibiting or killing bacteria and other microorganisms.

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Potency :

It is defined as activity per milligram of a chemotherapeutic agent and is expressed on the basis of "minimum inhibitory concentration, which is capable of inhibiting the multiplication of one of the susceptible microorganisms".

Bacteriostatic Activity :

It is defined as "ability of a compound to inhibit growth and multiplication of micro-organisms" e.g. chloramphenicol, erythromycin, tetracycline, sulphonamides etc.

Bactericidal Activity :

It is defined as ability of a compound to kill microorganism.

e.g. penicillins, cephalosporins, vancomycin etc.

Antibacterial Spectrum :

This refers to the range of activity of a compound.

Usually activity of a compound is expressed either as broad-spectrum or narrow - spectrum.

PENICILLIN

Definition :

Antibiotics are chemical substances derived from various species of microorganisms, such as fungi, actinomycetes, bacteria and in higher concentrations suppress growth of other microorganism.

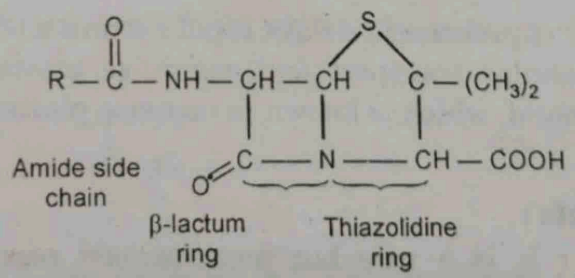
Penicillin is one of the most important antibiotics.

Source :

It is extracted from the mould penicillium notatum.

Structure :

Penicillins represent a large group of antimicrobial agents, consisting of a fundamental nucleus, 6 – Amino – Penicillanic – acid (6 – APA) having a Beta lactum ring.



Classification :

(a) Natural penicillins

- Benzly penicillin (penicillin G)
- Phenoxy methyl penicillin (penicillin V)

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(b) Penicillinase resistant penicillins

- Methicillin
- Nafcillin
- Oxacillin

(c) Broad-spectrum penicillin

- Ampicillin
- Amoxicillin

(d) Penicillins active against pseudomonas

- Carbenicillin

Mechanism of Action :

Penicillins act by interfering with the synthesis of the cell wall mucopeptide of gram-postive cocci. This makes the cell membrane of the organism vulnerable to damage by solutes in the surrounding medium (plasma).

Thus, penicillins are bactericidal drugs and are effective mainly against multiplying organisms.

Antibacterial Spectrum :

Penicillins are mainly effective against Gram-positive and Gram-negative cocci. Streptococci, staphylococci, Gonococci, pneumococci, meningococci are sensitive to penicillin.

Absorption, Fate, Excretion :

Penicillin G, i.e. benzyl penicillin, is inactivated by gastric acid, when orally administered.

Hence, as its absorption is inadequate and irregular, benzyl penicillin is administered by intramuscular route.

Penicillin is widely distributed in the body. It crosses the placental barrier.

Penicillin is eliminated by the kidneys while small amounts appear in bile, milk and saliva.

Co-administration of probenecid delays rapid excretion of penicillin. It competes with penicillin for tubular transport and can raise plasma-penicillin level. The normal dose of probenecid, which is known to increase plasma penicillin level, is 0.5 g six hourly.

Adverse / Side Effects :

- **Anaphylaxis :** It is a rare but most serious reaction. Anaphylaxis can develop even with a minute quantity of penicillin and is irrespective of the route of administration. It is characterized by an acute cardio-vascular collapse, bronchospasm and edema of larynx.
- Serum sickness like syndrome with skin rash, fever, eosinophilia, asthma, etc.

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- Renal complications like haematuria, albuminuria.
- Hyper Kalemia.

Preparation / Dose :

1. Benzyl penicillin	Penicillin G, I.P., injection	500,000 units per ml intramuscular
2. Phenoxy methyl penicillin	Penicillin V	250 mg orally six hourly

Clinical Application / Therapeutic Uses :

- To treat pneumococcal infection.
- To treat streptococcal infection.
- To treat staphylococcal infection.
- To treat meningococcal infection.
- To treat infections with anaerobes.
- Penicillin is the choice of antibiotic in the treatment of sexually transmitted diseases like syphilis and gonorrhoea.
- As a prophylactic, penicillin is used in dental procedures, bronchoscopy, tonsillectomy, surgical procedures.
- Penicillin is effective in the management of tetanus, diptheria, gangrene.

Test for Detection of Penicillin Allergy :

Skin test :

- Scratch the skin through a drop of solution containing 10,000 units of benzyl penicillin per ml.
- If a central wheel due to local edema occurs after 15 minutes, it is considered a positive reaction.

Treatment for Anaphyplactic Shock :

The hypersensitivity reaction produced by penicillin, referred to as anaphylactic shock, can be treated by using following pharmacological agents :

(i) Adrenaline : 0.2 to 0.5 ml I/M
(ii) Prednisolon : 100 mg
(ii) Promethazine : 50 mg

STREPTOMYCIN

AMINOGLYCOSIDE ANTIBIOTIC – STREPTOMYCIN

Definition :

These are the antibiotics composed of aminosugars, connected by glycosidic linkage. Streptomycin is obtained from streptomyces griseus.

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Antibacterial Spectrum :

Streptomycin is effective against M.tuberculosis, Shigella species, Brucella, H. Influenzae, H.ducreyii, Nocardia etc. Streptomycin is more effective in alkaline pH (7 – 8) than acidic pH.

Mechanism of Action :

Ribosomes prepare enzymes under messenger RNA.

It is believed that streptomycin combines with bacterial ribosome, interferes with messenger – RNA combination and compels ribosomes to prepare wrong amino acids sequence, which results in destruction of bacterial cell.

Streptomycin may be bactericidal or bacteriostatic.

Absorption, Fate, Excretion :

- Streptomycin is poorly absorbed from gastro-intestinal tract.
- Streptomycin is usually injected intramuscularly.
- Streptomycin is excreted by glomerular filtration in urine.

Adverse / Side Effects :

- Streptomycin, on oral administration, may cause nausea and vomiting.
- Intramuscular administration of streptomycin may cause abscess and fever.
- Streptomycin causes damage to 8th cranial nerve and impairs auditory and vestibular function.

  Streptomycin may cause deafness in babies born to mothers receiving streptomycin during pregnancy, as it crosses the placental barrier.

Preparation / Dose :

Drug	Trade name	Dose
1. Streptomycin	-	0.5 – 2.0 g / I/M / day
2. Kanamycin	Kantres	1 gm I/M / day
3. Gentamicin	Garamycin	3 – 5 mg / kg / day / I/M
4. Tobramycin	Nebcin	3 – 4 mg / kg/ day / I/M
5. Amikacin	Amikin	15 mg / kg / day / I/M

Clinical Application / Therapeutic Uses :

- It is a drug of choice in the treatment of tuberculosis.
- It is useful in treatment of urinary tract injection due to *E. Coli*.
- It is useful in treatment of meningitis.
- Streptomycin is advised in bacteremia and bacterial endocarditis.
- It is the preferred drug in infections like tularemia.
- In the treatment of brucellosis, streptomycin is effective.

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Contraindication / Interactions :

- Frusemide and ethacrynic acid, like diuretics, are potentially ototoxic and must be avoided being taken with streptomycin.
- As streptomycin causes neuromuscular blockade, it must be avoided being taken in combination with neuromuscular blocking agents.

TETRACYCLINES AND OTHER ANTIBIOTICS

BROAD SPECTRUM ANTI-BIOTICS

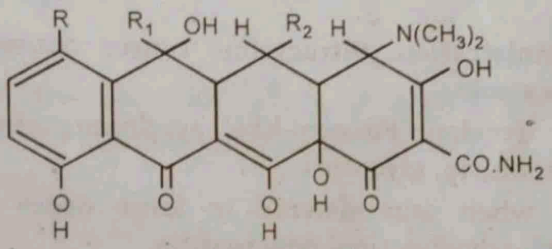
Definition :

These antibiotics are not only effective against gm–positive and gram–negative organisms, but also rickettsiae, mycoplasmae, chalmydia and brucella. Hence, they are called Broad Spectrum Antibiotics.

TETRACYCLINE

Definition :

Tetracyclines are broad-spectrum antibiotics and are naphthalene derivative.



Antibacterial Spectrum :

Tetracyclines are effective against Gram-positive and Gram-negative organisms, including pneumococci, gonococci, clostridia, H.indluenzae, H.pertusis. H.ducreyi, Brucella, vibrio comma etc.

Mechanism of Action :

Tetracyclines act by inhibiting certain essential enzyme systems of bacterial cell. Tetracyclines are known to inhibit protein synthesis in bacterial ribosomes.

Tetracyclines bind with magnesium, manganese and calcium to form insoluble complexes 'chelates', and by removing these divalent metallic cations from sites, they inhibit enzyme activation.

Thus, tetracyclines are bacteriostatic in action.

However, in higher concentrations or parenteral administration, they may exert a bactericidal effect.

Absorption, Fate, Excretion :

- Tetracyclines form insoluble complexes on chelation with calcium, magnesium and aluminium.
- Hence absorption of tetracycline on oral administration, is variable and incomplete.

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- It is also advised to avoid tetracyclines with food or milk as it forms chelates, which are insoluble complexes, with divalent ions present in milk and food.
- Therefore, tetracyclines must be administered by intravenous, intramuscular, or by local application.
- Tetracyclines, administered intramuscularly, produce peak plasma level within one hour and sufficient levels are maintained for 12 hours.
- Tetracyclines are widely distributed in the body and are excreted mainly in the urine by glomerular filtration.

Adverse / Side Effects :

- Tetracyclines chelate with calcium, forming a tetracycline orthophosphate complex. This is deposited in areas of calcification in bones and teeth. This affects bone and teeth development. Tetracyclines, if administered to pregnant women, may lead to yellow staining of the teeth of infant and defective formation of enamel.

  Hence, they should not be administered to infants and children upto the age of 12 years.
- On oral administration, tetracycline causes nausea, vomiting, epigastric distress, loose stools.
- Tetracyclines develop 'Fanconi-like' syndrome, characterized by nausea, vomiting, proteinuria, glycosuria.
- Tetracyclines when administered in large doses intravenously, develop jaundice, hepatic dysfunction, pancreatitis.
- In infants, tetracycline administration results in Benign – intracranial hypertension, characterized by headache, photophobia.

Preparation / Dose :

Drug	Trade name	Dose / route
Chlortetracycline	Aureomycin	
Oxytetracycline	Terramycin	250 mg 6 hourly oral
Tetracycline	Achromycin	
Demethyl-chlortetracycline	Ledermycin	
Methacycline	Rondomycin	150 mg to 300 mg 6 hourly oral
Doxycycline	Vibramycin	
Minocycline	Minocin	150 mg to 300 mg 6 hourly oral
Rollitetracycline	Reverin	

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Clinical Applications / Therapeutic Uses :

- Tetracyclines are very effective in rickettsial infections like murine, epidemic, scrub typhus, rickettsial pox, Q fever, Rocky mountain spotted fever.
- To treat granuloma inguinale.
- In the treatment of plague.
- In the treatment of primary atypical pneumonia.
- To treat cholera.
- To treat chalmydia infections.
- To treat bacillary infections.
- In the treatment of urinary tract infection.
- Tetracyclines are useful in acne vulgaris.
- To treat veneral diseases.

Contraindication :

- Tetracyclines are strictly contraindicated in pregnant women and children upto 12 years of age.

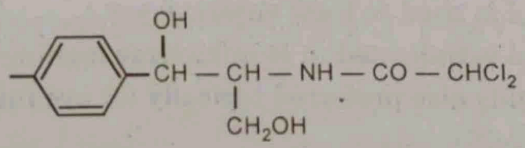
Interaction :

- Tetracyclines interact with milk, food by forming insoluble complexes with calcium, magnesium, manganese and aluminium.

CHLORAMPHENICOL

Definition :

It is a broad-spectrum antibiotic derived from streptomyces venezuelae.



Antibacterial Spectrum :

Chloramphenicol is a broad-spectrum antibiotic, effective against Gram-positive and Gram-negative bacteria, chlamydia, rickettsiae, salmonella typhie etc.

Mechanism of Action :

Chlorampenicol acts by inhibiting bacterial protein synthesis. It is a bacteriostatic agent.

Absorption, Fate, Excretion :

- When administered orally, it is completely absorbed in the gut.
- It can also be administered by the intramuscular and intravenous route.
- Chloramphenicol is 60% bound to plasma protein.
- It is mainly excreted in urine.

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Adverse Effects :

- Chloramphenicol, due to its nitrobenzene radical, produces bone marrow toxicity, characterized by bone marrow depression, anaemia, leukopenia, thrombo-cytopenia, agranulocytosis, aplastic anemia.

  To prevent this risk of bone marrow depression – aplastic anaemia, prolonged or repeated use of chloramphenicol should be avoided.

  During treatment, blood cell count should be monitored, and if total leucocyte count drops below 4000 / cu mm blood, then treatment should be stopped.
- Neonates and premature infants, if administered by chloramphenicol in large doses, may develop 'grey baby syndrome' characterized by progressive abdominal distension, vomiting, refusal to feed, loose greenish stools and irregular respiration.
- During chloramphenicol theraphy, gastro-intestinal disturbances like nausea, vomiting, glossitis, stomatitis, enterocolitis may occur.

Preparation / Doses :

1. Chloramphenicol (tablet)	250 mg capsule / oral 1.5 to 3.0 gm dose.
2. Chloramphenicol palmitate (suspension)	125 mg / ml for paediatric use 50 mg / kg (body wt.) / day dose
3. Chloramphenicol sodium succinate (injection)	1 gm vial 50 mg / kg (body wt.) / day dose

Clinical Application / Therapeutic Uses :

- Chloramphenicol is used to treat enteric fever.
- Chloramphenicol is indicated in H.influenzae meningitis.
- Chloramphenicol is also preferred topically for eye infections.

Note :

- Chloramphenicol therapy should not be prolonged unduly.
- Repeated therapy with chloramphenicol should be avoided.
- During chloramphenicol therapy, frequent blood cell counting should be done.
- Chloramphenicol therapy is supplemented with haematinics i.e. iron preparations.

Contraindications :

- Chloramphenicol should be avoided during pregnancy.
- It should be avoided in neonates and premature infants.

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Chapter...13

DISEASES AND TREATMENT

ANTI-TUBERCULAR DRUGS

Introduction :

Tuberculosis is a chronic infectious disease. It is caused by tubercle bacilli (mycobacterium tuberculosis)

Robert Koch, in 1882, discovered tubercle bacillus, thus the disease was referred to as tuberculosis. It is a systemic disease, commonly involves respiratory system, but can affect other organs.

Difficulties in the Treatment of Tuberculosis :

1. Tubercle bacilli grow very slowly.
2. The caseation also tends to block the blood vessels, supplying the necrotic area, making penetration by anti-tubercular drugs difficult.
3. Tubercle bacilli remain viable, and multiply even when ingested by macrophages.
4. Organism develops resistance to chemotherapeutic agent.

Classification :

Classification of anti-tubercular drugs is based on their efficiency and low toxicity (safety). The agents are classified into two major groups :

(a) Primary or standard drugs or first line

1. Bacteriostatic :

- Ethambutol (E)
- Paraminosalicylic (PAS)
- Thiacetazone (T)

2. Bactericidal :

- Isonicotinic acid hydrazide (INH)
- Rifampicin (R)
- Streptomycin (S)
- Pyrazinamide (Z)

(b) Secondary or reserve drugs or second line

1. Bacteriostatic :

- Ethionomide (Eth)
- Cycloserine (C)

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2. **Bactericidal :**
   - Copremycin (A)
   - Kanamycin(K)

Primary / Standard / First line drugs are highly effective, while Secondary / Reserve drugs are used occasionally, because of bacterial resistance and low efficiency. Secondary drugs are indicated when the organisms are resistant to first-line drugs.

Steps Involved in Treatment of Tuberculosis :

Drug resistance is the main difficulty in management of tuberculosis. Hence to avoid it, anti-tuberculour agents are always used in combination.

The various therapies advised are as follows :

(a) Optimum anti-tubercular therapy :

In this, combination of three regimes is advised.

1. INH + R + S or E, all drugs given daily for two months, followed by INH + R for seven months.
2. INH + R + S + Z daily for two months followed by :
   INH + R..... twice a week / daily OR
   INH + S + Z twice a week for 4 months.

(b) Two drugs therapy :

This includes daily supervised administration of INH + S + E or PAS/T for two months. Followed by daily self administration of INH + E or PAS + or T for 16 months in non-cavitary cases and 22 months in cavitary cases.

(c) Intermittent, supervised treatment :

Includes administration of

INH + S
OR INH + E twice a week for 18 months.

(d) Low cost regime :

This includes administration of

INH + R daily for two months followed by
INH + T for 8 months.

Signs of Improvement :

1. Clinical improvement is characterized by weight gain, relief from cough and fever.
2. Bacteriological improvement is characterized by negative sputum cultures within three months.
3. Radiological improvement is indicated by cavity closure or its disappearance.
4. By periodic determination of ESR – Erythrocyte Sedimentation Rate.

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B. C. G. VACCINE

Definition :

Bacille Calmette Guerin is a stain of bovin tubercle bacillus. It was developed by Calmette and Guerin.

Aim of Vaccination :

The main objective of vaccination is to increase the patient's resistance by producing an artificial primary tuberculous infection by an organism, which causes local lesions and swelling of lymph nodes.

Mode of Administration :

- It is usually given within first six months of life or immediately after birth.
- Tuberculin test is carried out before vaccination.
  In this test 0.0001 mg or 5 test units of Purified Protein Derivative – PPD – obtained from mycobacterium is injected intradermally on ventral surface of forearm.
- If the above test remains negative, it is repeated again after 6 weeks. If after six weeks also tuberculein test remains negative, then follows vaccination.
- 0.1 ml of the vaccine is injected intradermally in the deltoid region. This leads to formation of Papule, ulcer with 4 - 6 weeks.
- After vaccination tuberculein test becomes positive within a period of 6 - 12 weeks indicating development of immunity against tuberculosis.
- Glandular cold abscess is the most likely complication, but occurs rarely.

(a) Standard / Primary Anti-tuberculous Agents :

No.	Drug	Mechanism of action	Side effect	Trade name	Preperation/ dose
1.	Isoniazid	Inhibits phospholipid synthesis and damages the cell membrane of tubercle bacilli. It is bactericidal.	Nephrotoxicity, Hepatotoxicity, Convulsion	Nydrazid INH	Isoniazid tablet, I.P. 100 mg, Dose – 200 mg daily oral.
2.	Rifampicin	Acts by inhibiting bacterial DNA-Dependent – RNA-polymerase and thus interferes with RNA synthesis It is bactericidal.	Influenza, abdominal upset, Respiratory disturbances	Rifampin Rifaclin Rimactance	600 mg orally / day before meal, 10 mg/ kg in children.
3.	Ethambutol	Depresses RNA synthesis. It is bacteriostatic.	Ocular toxicity, with blurring of and loss of red-green perception	Myambutol	15 mg / kg / day.
4.	Streptomycin	It is bactericidal	Deafness	-	0.75 g / day
5.	Pyrazinamide	Bactericidal	-	-	-

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ANTIFUNGAL AGENTS

Definition :

Antifungal agents are drugs used to kill or inhibit the growth of common mycotic infestations local as well as systemic.

Fungal infection can be discussed in three groups :

- Dermatophytic
- Systemic
- Candidal

The dermatophytic infections involve the skin, hair, nails.

The systemic mycotic infections are a serious problem. They are chronic in nature and difficult to diagnose. Systemic infections are caused due to eryptococcosis, aspergellosis, blastomycosis etc. The candidal infections are caused in human by candida albicans. Candidiasis affects moist skin, mucous membrane, including gastrointestinal tract and may cause systemic disease.

Ideal Properties of Antifungal Agents :

3. It should be fungicidal.
4. It should be non-staining and non-irritating to the skin and free from sanitation reactions.
5. It should be able to penetrate into the hair, nails and layers of skin.
6. It should have some antibacterial activity.

Types of infection	Drugs	Antifungal	Side effect	Trade spectrum	Rate / dose
a) Dermatophytic infection	1. Griseofulvin	Effective against epidermophytori trichophyton.	Hepatotoxicity	Grisovin FP	500 mg orally after meals.
	2. Tolnaftate	Effective against epidermophyton, microsporum, trichophyton	Local irritation	Aftate	1% solution cream rubbed into lesion twice daily for 4 – 6 weeks.
	3. Haloprogin	Effective against epidermophytan, microsporum, trichophyton.	Local irritation	Halotex	1 % cream thrice daily.
	4. Clotrimazole	Skin and vaginal infection	Erythema, oedema	Mycelex	1% cream twice daily.

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b) Systemic fungal infection	1. Amphotericin B	Useful for systemic infection	Chills, fever, headache	Fungizone	Initial dose 0.25 mg/kg intravenous
	2. Flucytosin	For candida infection, torulopsis	Blood dyscrasis renal impairment	Ancobon	150-200mg/kg orally daily at 6 hour interval
c) Candidal infections	1. Candicidin	Fungistatic or fungicidal	Hypotension tachycardia	Candeptin	Tablet 3 mg manually inserted into vagina.
	2. Nystatin	Active against fungi	Nausea, diarrhoea	Mycostatin	Oral 500,000 unit t.i.d.
	3. Hamycin	Active against fungi and yeasts	Local irritation		In form of pessaries 100,000 units.

ANTIVIRAL AGENTS

Viruses :

Viruses are smallest biological structures. The complete viral particle is known as viron and consists of a protein and nucleic acid. The nucleic acid is either RNA or DNA.

Viruses show great variation in size and shape ranging from about 10 – 300 nm.

Some viruses are smaller than largest protein molecule and many are larger than the smallest bacteria.

Some viruses are spherical, some are ovoid, cubes or rod shaped.

Viruses are heat labile and sensitive to some agents that affect bacteria. They are highly resistant. They are readily destroyed at 60°C for 30 minutes.

Classification :

1. **Compounds interfering with the nucleic acid synthesis...**
   - Idoxuridine.
   - Adenine arabinoside.
   - Ribavirin.
   - Acyclover.
   - Trifluridine.
   - Azidothymidine.

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2. **Thiosemicarba zones...**
   - Methisazone.
3. **Natural substances...**
   - Interferon.
4. **Miscellaneous...**
   - Amantidine.
   - Antiviral antibiotics.
   - Gamma globulin.

Name	Uses
1. Idoxurindine	➢ Locally in herpetic ulceration of cornea. 0.1% eye drop.
2. Adenine arabinoside	➢ Used to treat herps simplex 3% ointment. ➢ To treat herps encephalitis in a dose 15 mg / kg body weight.
3. Acyclovir	➢ To treat corneal ulcer available as 250 mg powder for I.V. infusion.
4 Thiosemicarbazone	➢ Effective against vaccine and small pox viruses. ➢ 2 – 3 g daily individed doses.
5. Amantidine	➢ Suppress infection with influenza A virus, rubella virus dose – 100 mg once / twice daily for 10 – 30 days.
6. Gamma globulin	➢ In patients with hypogamma globulinemia. ➢ To treat infective hepatitis. ➢ In measles and rubella prophylaxis. ➢ Mumps and poliomylitis 0.025 to 0.05 gm / kg intramuscularly.

ANTI-LEPROTICS

Definition :

Leprosy is a chronic infectious disease caused by an acid fast bacillus, microbacterium lepre.

It is essentially a disease of peripheral nerves but also affects the skin, eyes, mucosa of upper respiratory tract, muscles, bones, testes.

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Types of Leprosy :

Clinically leprosy can be classified into four major groups :

1. Lepromatous leprosy.
2. Tuberculoid leprosy.
3. Indeterminate leprosy.
4. Dimorphic leprosy.

Symptoms :

1. Lepromatous Leprosy :

The typical lesion of lepromatous leprosy is a macule, hairless, hypopigmented, circular erythematous patch. Maculus are small and smooth, eye lashes fall off, nerves are affected later. It affects mainly face, nose, ears, eyes.

2. Tuberculoid Leprosy :

Initially nerves are affected. Tuberculoid lesion is large, flat, atrophic, hypopigmented skin area, with impairment of sensation.

Difficulties in the Treatment of Leprosy :

1. The bacillus multiply very slowly in the body and not in culture media. Hence leprosy vaccine is not available.
2. The mode of transmission of the disease is not well-defined.
3. Human leprosy cannot be easily transferable to animals, hence animal study for development of new drugs is not possible.

Classification of Anti-leprotics :

(a) Sulphones...
- Dapsone.

(b) Non-sulphones...

1. Antibiotics...
   - Rifampicin.
2. Phenazine...
   - Clofazimine
3. Thioureas...
   - Thiambutosin
4. Anti-inflammatory drugs...
   - Aspirin

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No.	Drug	Mechanism of action	Absorption fat excretion	Side effect	Trade name	Preparation dose
1.	Dapson	Antagonizes Para Amino Benzoic Acid (PABA), Acts as a bacteriostatic.	Slowly but completely absorbed from gastro-intestional tract. Distributed widely in liver, muscles, kidney, skin. Excreted in urine.	Gastro-intestinal upset, Renal failure, Drug fever.	DDS Novaphone Avlosulfon.	100 mg/day for five year or more.
2.	Clofazimine	Bacteriostatic	Well-absorbed orally excreted in urine.	Skin pigmentation. Nausea. Diarrhoea, Abdominal pain	Lamprene	100-300 mg orally.
3.	Rifampicin	Bactericidal	Completely absorbed from gut remains protein-bound excreted in bile and urine.	Haemolytic anaemia, Thrombocytopenia, Renal failure Hepatitis.	Refadin Tibirim Rimactane	600 mg oral once in a day.
4.	Streptomycin	Bacteriostatic effectively controls invasion of mucous membranes of upper respiratory tract.	Poor oral absorption excreted through urine.	Deafness	-	1 g / Intra muscular / day for one month.
5.	Thiambutasin	Bacteriostatic	Well-absorbed orally, excreted in urine.	Less toxic	-	500 mg orally alternate day.
6.	Aspirin	Anti-inflammatory controls lepra reaction	Irregular oral absorption.	Frank bleeding and ulcers.	Disprin	600-1200 mg four times daily.

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Chapter :14

PROTOZOAL INFECTIONS

ANTHELMINTICS

Introduction :

Helminthiasis is worm infestation. It is a common disease and is not restricted to tropical or subtropical areas, but also endemic in many regions because of poverty, illiteracy, lack of adequate sanitary facilities and pure water supply.

Types of Worms :

1. Nematodes : Round worms
2. Cestodes : Tape worm
3. Trematodes : Flukes

Symptoms :

Worm infestation is characterized by various gastro-intestinal symptoms with nutritional deficiencies, blood loss, urticaria, intestinal obstruction etc.

Diagnosis :

By examination of stools, urine, blood, sputum, tissues of host for worm investigation.

Anthelmintic Treatment :

Anthelmintics are pharmacological agents used to eradicate parasitic worms from the human body.

- Wormicidal – These anthelmintics when administered, kill the parastic worm.
- Wormifugal – These anthelmintics when administered paralyse the parasitic worm.

Types of infestation	Drug	Pharmacological action	Trade name	Route dose
A. Nematodes (Round worm)	Pyrantel pamoate	Leads to spastic paralysis of worms.	Combantrin	200 mg tab orally. 250 mg / 5 ml suspension

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	Piperazine	Causes flaccid paralysis of the muscles of worms.		Tablet 300 mg
	Tetramisole	Cause spastic paralysis of the worms	Decaris Levamisole	2.5 mg / kg oral
	Mebendazole	Blocks uptake of exogenous glucose by parasite.	Mebex	100 mg twice a day for 3 days
	Thabendazole	Interferes with metabolic pathway in worms.	Mintezol	25 mg / kg after evening meal for 3 days orally.
B. Cestode infection (Tape worms)	Niclosamide	Vermicidal	Niclosan	Two tablets (1g) in the morning on empty stomach, to be chewed and not to be swallowed
	Paromomycin	Vermicidal		1 gm every 4 hours for four doses orally.
	Chloroquin	Vermicidal		0.6-0.8 gms (3 – 4 tablets) repeated after 6 weeks.
	Dichlorophen	Vermicidal		75 mg/kg : adults 2.4 g :children
C. Trematodes infection (Flukes)	Praziquantal	Vermicidal	Biltricide	40 mg/kg orally
	Oxaminiquin	Vermicidal	Vansil	15 mg/kg orally
	Niridazole	Vermicidal	Ambilhar	25 mg/kg/day orally

ANTI-MALARIALS

Malaria

Cause :

It is caused by parasitic pratozoa of the genus plasmodium, which includes four major types :

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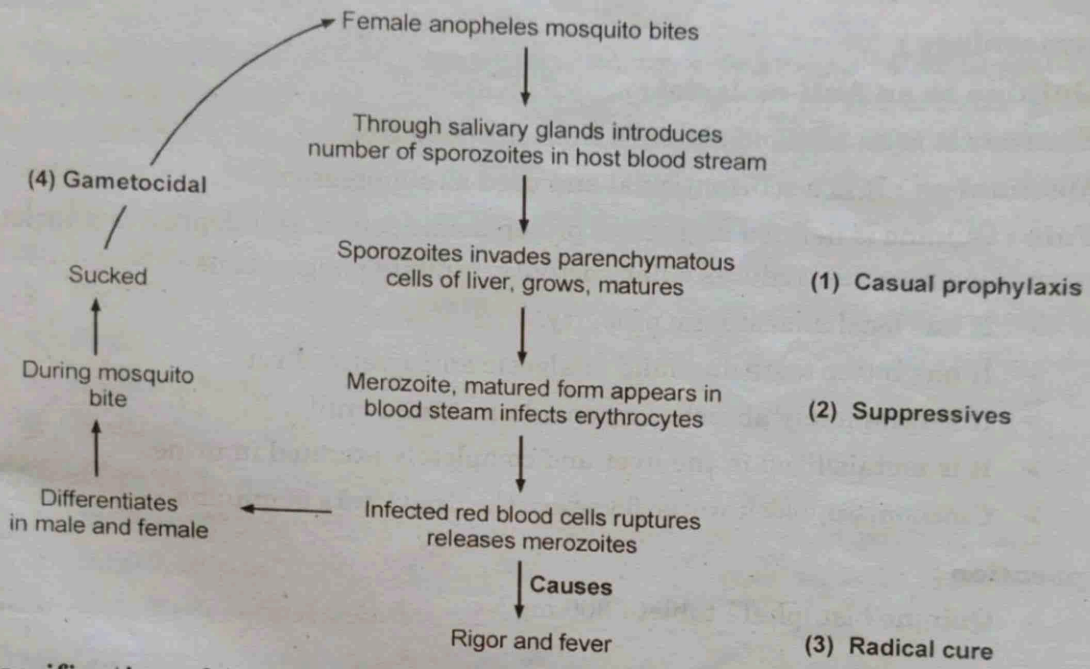
Plasmodium vivax	-	Benign tertiary
Plasmodium falciparum	-	Malignant tertiary
Plasmodium ovale	-	Last 48 hours
Plasmodium malariae	-	Quatan

Life Cycle :



Classification of Anti-malarial Drugs :

1. *Casual prophylactics :*

   Prevent maturation of sporozoites or destroy sporozoites within infected hepatic cells.

   - Primaquin
   - Pyrimethamine
   - Proguanil

2. *Suppressive :*

   Prevents erythrocytic schizogony and prevents rupture of infected erythrocytes.

   - Quinine
   - Mepacrine
   - Proguanil
   - Pyremethamine

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3. *Radical cure :*

   Eradicates erythrocytes and erythrocytic schizogony

   - Primaquin

4. *Gametocidals :*

   - Primaquin

Pharmacology :

Quinine as an Anti-malarial :

Source : It is an alkaloid obtained from cinchona tree.

Mechanism : It is a schizonticidal and used as suppressive.

Fate : Quinine is defined as general protoplasmic poison as it depresses a variety of enzymatic processes, reduces ciliary activity, inhibits phagocytosis.

- It has local anaesthetic property.
- It has bitter taste and mild analgesic antipyretic effect.
- It is completely absorbed when administered orally.
- It is metabolized in the liver and completely excreted in urine.
- Cinchonism, block water fever are the drawbacks of quinine.

Preparation :

- Quinine bisulphate tablet : 300 mg

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Chapter...15

CHEMOTHERAPY OF CANCER

CANCER

"Cancer" is defined as "life threatening" disease and a major killer in mankind. Cancer is a disease of cells characterized by the loss of normal cellular growth, maturation and multiplication, which disturbs the homeostasis. The main features of cancer are :

1. Excessive cell growth (usually in the form of tumour).
2. Invasiveness.
3. Undifferentiated cells or tissues.
4. Ability to metastasize.
5. A type of hereditary disorder.
6. A shift of cellular metabolism.

Difficulties in Treatment of Cancer :

1. Anticancer drugs are not specific and have a lower than margin of safety.
2. Inspite of satisfactory treatment, possibility of recurrence always remains.
3. Neoplastic cells can develop resistance to drugs.

Classification of Anticancer Drugs (Antineoplastic) :

[A] *Alkylating agents :*

- Nitrogen mustards
- Mechlorethamine
- Cyclophosphamide
- Melphalan
- Uracil mustard
- Busulfan

[B] *Antimetabolites :*

- Methotrexate
- 6 – mercaptopurine
- Fluorouracil

[C] *Radio-active isotopes :*

- Radio iodine
- Radio gold

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[D] *Antibiotics :*

- Actinomycin – D
- Mitomycin – C
- Rubidomycin

[E] *Miscellaneous :*

- Vinca alkaloids – vinblastin, vincristine

[F] *Hormones :*

- Androgens
- Estrogens
- Progestins
- Corticosteroids

Mechanism of Action, Site of Action of Anticancer Drugs :

1. The antimetabolite type of anticancer drugs, act by affecting either enzymes or substrates, which affects DNA synthesis or function.
2. The alkylating type of drugs affects substrates, usually the DNA macromolecule.
3. The vinca alkaloids bind to microtubular proteins necessary for cell division and dissolve this protein, causing death of cell during mitosis.

Adverse Effects of Cancer Chemotherapy :

1. In initial phase – Nausea, vomiting.
2. After 10 – 14 days of therapy – bone marrow depression.
3. Gastro-intestinal toxicity includes, bleeding ulceratin, diarrhoea etc.
4. Neurotoxicity.
5. Hepatotoxicity.
6. Teratogenecity and infertility.
7. Immunosuppression.

Groups	Drug	Trade	Therapeutic use	Preparation dose
A. Alkylating agents	Nitrogen mustard	Mustin	Lung cancer Breast cancer	200-600 mcg/kg I/V in single dose.

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	Cyclophospha -mide	Cytoxan	Acute lymptocytic leukemia, wilm's tumour, ovarian cancer, multiple myeloma.	30 – 40 mg / kg I/V every three week.
	Chlorambucil	Leukeran	Chronic lymphocytic leukemia, multiple myeloma.	10 – 30 mg/ day orally.
	Melphalan	Alkeran	Multiple myeloma, breast and ovarian cancer.	10 to 30 mg / day orally.
	Busulphan	Myleran	Chronic granulocytic leukemia.	4 – 8 mg / day orally.
B. Anti-metabolites	Methotrexate	Amethopterin	Acute lymphoblastic leukemia, chorio carcinoma, breast, testis, lung cancer.	2.5 – 5.0 mg / kg per day orally or intra-muscularly
	Fluorouracil	5-Fluorour-acil (– 5 FU)	Carcinoma of the colon, rectum, breast, stomach, pancreas.	12 mg /kg day orally.
	6 – mercapto-purine	Purinethol 6 MP	Acute lymphocytic leukemia chronic granulocytic leukemia.	2.5 mg / kg/ day orally.
C. Natural products	Vinca alkaloids			
	Vincristine	Oncovin-VCR	Acute lymphoblastic leukemia lymphosarcoma.	2 mg / m^2 I/V.
	Vinblastin	Velban-VLB	Hodgkins disease chorio carcinoma, breast, testicular carcinoma.	0.1 mg / kg I/V.

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D. Hormones	Adrenocorti-costeroid			
	Prednisone		Acute and chronic lymphocytic leukemia.	10-100 mg orally.
	Androgen Testosterone propionate		Breast carcinoma	100 mg IM orally.
	Diethylstilbo-estrol		Prostate carcinoma breast carcinoma	15 mg orally.
E. Radio-active	Sodium phosphate solution p^{32}	Phosphotope	Polycythemia vera chronic lymphocytic granulocytic leukemia.	6 millicuries orally.
	Sodium iodide solution I^{131} (iodotope)	Iodotope	Thyroid carcinoma hyperthyroidism	4 –10 millicuries orally.
	Radio-gold solution Au198	Aureotope	Malignant pleural effusions.	85 – 100 millicuries I/Peritonially.

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Chapter...16

ANTISEPTICS AND DISINFECTANTS

ANTISEPTICS AND DISINFECTANTS

Introduction :

Antiseptics and disinfectants are collectively used as anti-infective agents. These are useful in decreasing the bacterial flora when applied directly to the skin, infected wounds, instruments or excreta. Most of these drugs are highly toxic if used for systemic purpose because of their lower margin of safety (Low therapeutic index). Hence, these agents are preferred for local use in clinical practice for :

- Sterilization of skin.
- Sterilization of surgical instruments prior to surgical process (operation).
- Disinfection of wound and ulcer.
- Infections of skin, hair.
- Disinfection of rooms.

These agents are also added to toothpastes, soaps, aftershave lotions, etc.

Definitions :

1. Antiseptics : These are pharmacological agents that are applied directly to living tissues so as to kill bacteria or inhibit their growth. These agents are mainly bacteriostatic in action.

2. Disinfectants : These are pharmacological agents which are applied to inanimate objects like surgical dressings, instruments, bed pans, rooms, wards, lavatories etc., to destroy microorganisms and prevent infection. These agents are mainly bactericidal in action.

Ideal Properties of an Antiseptic and Disinfectant :

- They should have a wide antimicrobial spectrum.
- They should be lethal to the bacteria (more parasitotropic) should not produce any adverse effect on host cell (less organotropic).
- The agents should have quick onset of action, high penetrating property and more chemical stability.
- Their potency should not be affected by presence of pus, tissue fluid, blood and pH of tissues.

Mechanism of Action :

The various mechanisms by which the antiseptics and disinfectants act are as follows :

1. by coagulation of bacterial proteins.

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2. by altering properties of bacterial cell wall.
3. by binding to – SH – sulfhydryl group essential for enzyme action.
4. by competition with essential substrates for the important enzymes in the bacterial cell.

Classification :

[A] Physical Agents :

- Heat
- Ultraviolet light

[B] Chemical Agents :

1. Acids :

- Boric acid
- Benzoic acid
- Mandelic acid
- Salicylic acid

2. Oxidizing Agents :

- Potassium permangnate
- Hydrogen peroxide
- Sodium perborate

3. Phenolic Compounds :

- Phenol
- Cresol
- Resorcinol
- Thymol

4. Surfactants :

- Soap
- Cetrimide

5. Alcohol :

- Ethyl alcohol
- Isopropyl alcohol

6. Halogens :

- Iodine
- Iodophores
- Chlorine

7. Aldehyde :

- Formaldehyde

8. Antiseptic dye :

- Crystal violet
- Brilliant green

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9. **Heavy metal :**
   - Mercuric chloride
   - Silver nitrate
10. **Antibiotic :**
   - Bacitracin
   - Neomycin
   - Polymyxin – B
11. **Miscellaneous :**
   - Nitrofurazone

Commonly used Local Anti-infective Agents :

1. HEAT

It is the most important sterilizing agent. Heat may be applied either in the form of moist heat or dry heat.

Pasteurization, boiling in water, steam are several ways by which moist heat can be applied.

The various materials that can be sterilized by moist heat are, dressing packs, surgical instruments, laboratory equipments, culture media and pharmaceutical products.

Dry heat can be used in several ways like flaming, incineration, hot air etc. Glass syringes, instruments, laboratory glassware, materials used in pathology labs. can be sterilized by dry heat method.

The method of disinfection by using ultraviolet rays is highly costly.

2. ACIDS

[a] Boric acid :

Pharmacology : It is a weak bacteriostatic agent.

Uses :
- Antiseptic eye ointment.
- Eye lotion.
- Eardrops.
- Throat pain.

Preparation dose : 1 to 5%.

[b] Benzoic acid :

Pharmacology : It is a bacteriostatic.

Uses :
- As a preservative in foods and drinks.
- Antifungal in the treatment of ringworm infection of skin.

Preparation Dose : 0.1% to 3%.

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[c] Salicylic acid :

Pharmacology : It has weak bacteriostatic, antifungal action.

Uses :

- As keratolytic.
- For the removal of corns or warts.

Preparation Dose : 1 – 5 % as ointment.

3. OXIDIZING AGENTS

[a] Potassium permangnate :

Uses :

- As a disinfectant and deodorant.
- To disinfect ponds and wells.
- To disinfect bed pans and septic discharges.
- 1:100, 1:500 solutions of 1:4000 to 1:1000 are used as gargle or mouth wash in stomatitis.
- Dilute solutions are used as bladder or urethral wash.
- For gastric lavage in case of poisoning.

[b] Hydrogen peroxide :

Uses :

- For cleaning wounds.
- As a mouthwash and deodorant in aphthous stomatitis, tonsilitis, diphtheria.
- In dental practice as cleanser and helps to remove stains from teeth.

4. PHENOLIC COMPOUNDS

[a] Phenol :

Uses :

- As a local antiseptic.
- As disinfectant against gram-positive, gram-negative bacteria.
- Effective against fungus, viruses.

[b] Dettol : (Chloroxylenol)

Uses :

- As germicide.
- For cleansing wounds.
- 5% solution with 70% alcohol is used for disinfection of surgical instruments.

[c] Cresol :

Use :

- As a commercial disinfectant and a preservative in medicinal preparations.

[d] Resorcinol :

Use :

- As an antiseptic ointment.

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[e] Hexiresorcinol :

Uses :

- As an anthelmintic.
- In throat lozenges.

5. SURFACTANTS

[a] Soaps :

Use :

- Weak germicidal.

[b] Cationic surfactant :

like benzalkonium chloride, benzethonium chloride

Uses :

- As a rinse for diapers and for bed linen.
- Underclothes of patients suffering from urinary incontinence to prevent dermatitis.

[c] Cetrimide :

Uses :

- For disinfection and cleansing of wounds.
- Pre-operative preparation of skin.
- Sterilization of surgical instruments.

6. ALCOHOLS

[a] Ethyl alcohol :

Uses :

- For cleansing the skin prior to parenteral injection.
- As a local antiseptic to prevent bed sores.
- May be injected near the nerve to produce conduction block for temporary relief of pain.

[b] Isopropyl alcohol :

Uses :

- As a germicidal.
- As skin disinfectant
- In sterilization of syringes and needles.

7. HALOGENS

[a] Iodine :

Use :

- As antiseptic.

[b] Chlorine :

Uses :

- As germicidal.
- Effective against gram-positive and gram-negative bacteria.

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[c] Chlorinated lime :

Uses :

- As a disinfectant.
- As a deodorant.

8. ALDEHYDES

[a] Formaldehyde :

Uses :

- Effective germicide.
- For disinfection of surgical instruments and excreta.

9. DYES

[a] Acraflavin hydrochloride :

Use :

- Used in the treatment of wounds, burns and other infections of skin and mucous membranes.

[b] Gentian violet :

Uses :

- For disinfection of skin.
- To treat infectious eczema.

[c] Brilliant green :

Use :

- In the treatment of burns.

10. HEAVY METALS

[a] Thimerosal :

Uses :

- In sterilization of skin, mucous membranes.

[b] Silver nitrate :

Use :

- For gonococcal ophthalmia in neonates.

[c] Zinc oxide :

Uses :

- As astringent.
- As antiseptic.
- To treat eczema.

11. ANTIBIOTICS

[a] Dicophane (DDT) :

Use :

- As insecticide.

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Chapter...17
MISCELLANEOUS

PHARMACOLOGICAL TERMS

Achyliagastria	Absence of gastric juice.
Achlorhydria	Absence of free hydrochloric acid in gastric juice.
Acidemia	Abnormal acidity of the blood, having increased hydrogen ions and a low pH.
Acne	Inflammatory pilo-sebaceous disease characterized by pus filled cysts in the skin.
Actinomycosis	Fungal disease caused by actinomycetes.
Addison's disease	Disease of deficient secretion from adrenal cortex.
Adenoma	A non-malignant tumour of glandular tissue.
Aldolescence	Age between puberty and full maturity (youth).
Aerosol	Atomized particles suspended in gaseous form inhalation.
Agranulocytosis	Marked reduction of granulocytes in WBC.
Albuminuria	Presence of albumin in urine.
Alopecia	Baldness or falling off of hair from scalp.
Amenorrhoea	Absence of menses during adult life in women.
Amnesia	Partial or complete loss of memory.
Anaphylaxis	Immediate and acute type of severe allergy often associated with hypotension and shock.
Anaemia	Symptom complex characterized by loss of appetite, restlessness, breathlessness and loss of weight and is due to decreased oxygen carrying capacity of blood, due to decreased haemoglobin or RBC count.
Angina pectoris	Constricting type of chest pain, often radiating to left arm due to diseased cardiac condition : cardiac ischemia.
Angioneurotic oedema	Severe form of allergy, involving face, hands, genitals or throat with sever oedema.
Anorexia	Loss of appetite.
Antisera	Supernatant fluid containing anti-bodies.

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Anuria	Absence of secretion of urine by the kidneys.
Anxiety	Feeling of apprehension, worry, uneasiness and mental tension.
Appendicitis	Inflammation of vermiform appendix.
Aplastic anaemia	Anaemia with less number of RBC, as well as less WBC and TC due to bone marrow depression.
Apnoea	Transitory ceasation of breathing.
Arrhythmia	Any deviation from the normal rhythm of heart beat.
Arthralgia	Pain in joints specially of non-inflammatory type.
Arthritis	Inflammation of joints.
Asthma	Spasmodic chronic disease characterized by breathlessness, cause by narrowing of the bronchial passages (spasm of bronchioles) especially during exhalation.
Astringent	As agent which contracts organic tissue, thus lessening the secretion and hardening of the surface.
Ataxia	Defective muscular control, resulting in irregular and jerky movement.
Atherosclerosis	Hardening and narrowing of arteries.
Auricular fibrillation	Irregular and rapid atrial contractions of the heart.
Auricular flutter	Rapid and regular atrial rhythmic contractions of the heart.
Azoospermia	Absence of spermatozoa in semen.
Bactericidal	Agent that kills bacteria and microbes (bacteria).
Bacteriostatic	Agent that prevents the multiplication of microbes (bacteria).
Beriberi	Disease of Vitamin B_1 deficiency.
Blood dyscrasias	A diseased state of blood.
Bradycardia	Slow rate of contraction of heart.
Breathlessness	Excessive conscious breathing.
Bronchitis	Inflammation of bronchi.
Carcinoma or cancer	A malignant tumour – dangerous, virulent spreading growth, developing metastasis, resulting from chronic irritation.
Cataract	Development of opacity in lens of the eye.

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Chemoreceptor trigger zone	Area located in the fourth ventricle (area postrema) of medulla oblongata responsible for initiating vomiting.
Chey-stoke's breathing	Intermittent stopping of breathing.
Choriocarcinoma	Malignant tumour arising from chorion cells of the embryo.
Cirrhosis	Hardening of the organ, e.g. cirrhosis of liver.
Colic	Abnormal contraction of a hollow viscera, e.g. abdominal colic.
Colitis	Inflammation of colon.
Coma	A state of profound unconsciousness.
Conception	The act of becoming pregnant.
Congestive cardiac failure	Inadequate output of blood from one or both ventricles of the heart, resulting in a failure of congestive type (CCF).
Congenital	Hereditary, existing from birth.
Conjunctivitis	Inflammation of conjunctiva.
Constipation	Formation of hard stools and/or delayed normal defecation.
Convulsions	Violent, spasmic and paroxysmal, contractions of voluntary muscles.
Cretinism	Thyroid deficiency disease present from the birth and characterized by retarded physical and metal growth of children.
Cryptorchism	A developmental defect in man whereby the testes do not descend into the scrotum.
Crystalurea	Appearance of crystals in urine.
Cushing's syndrome	A disorder due to excessive adrenal cortical hormone.
Cyanosis	Bluish tinge due to lack of oxygen in the blood.
Cycloplegia	Loss of accommodation of eye due to paralysis of cilliary muscles of eye.
Dandruff	Infective inflammatory scaling disease of scalp, face and sometimes other areas of body.
Delirium	Abnormal mental condition characterized by confusion, hallucinations and restlessness.
Dermatitis	Inflammation of the skin.

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Diabetic coma	Coma pertaining to diabetic condition of profound unconsciousness.
Diabetes insipidus	Deficiency of vasopressin in posterior pituitary hormone (anti-diuretic hormone component) leading to excessive urine production.
Diabetes mellitus	Insulin deficiency disease characterized by excess of sugar in blood and urine.
Diarrhoea	Inflammation, swell or stretch out from within resulting in liquid stools.
Diplopia	Double vision.
Dizziness	Giddiness.
Drug fever	Hypersensitive state leading to increase in body temperature due to administration of a drug.
Dwarfism	Decreased linear growth of the body due to growth hormone deficiency.
Dysmenorrhoea	Painful menstruation in women.
Dysphoria	Exaggerated feeling of depression and unrest.
Dyspepsia	Indigestion in stomach.
Dyspnoea	Difficulty in breathing.
Dystrophy	Defective nutrition (muscular dystrophy – genetically determined, primary degenerative nyopathy).
Edema	Abnormal infiltration of tissue with fluid.
Embolism	Obstruction of blood vessel by thrombi, air or any other material, away from the site of origin.
Emesis	An act of vomiting.
Endocarditis	Inflammation of the inner lining (endocardium) of heart.
Endometritis	Increased eosinophil count in the WBC of blood.
Epilepsy	Organic brain disorder, associated with attacks of convulsion and unconsciousness.
Epistaxis	Bleeding from the nose.
Erythema	Redness of the skin (an allergic reaction).
Euphoria	An exaggerated feeling of well being, ecstasy.
Exopthalmos	Abnormal protrusion of eye balls.
Extrapyramidal	Akinesia, tremor and rigidity caused by deficiency or dopamine in extrapyramidal tracts of the brain.

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Extrasystole	Premature extra-beat of the heart.
Fibrillations	Repeated asynchronous contractions.
Gastric lavage	Washing out of the stomach through a rubber tube by siphon action.
Gastritis	Inflammation of gastric mucosa in stomach
Gastroenteritis	Inflammation of the mucus membrane of the stomach and intestine.
Gestation	Pregnancy
Gigantism	Increased linear growth of the body due to excessive growth hormone.
Glaucoma	Eye condition where the intraocular pressure is raised.
Glomerulonephritis	Inflammation of the glomeruli of the kidney.
Glossitis	Inflammation of tongue.
Giutre	Enlargement of thyroid gland.
Gout	A form of metabolic disorder in which sodium biurate is deposited in the cartilages of joins and ear.
Granulocytopenia	Abnormal reduction in number of granulocytes of WBC in the blood.
Grave's disease	Thyrotoxicosis, i.e. excessive formation of thyroid hormone.
Gynaecomastia	Enlargement of male mammary gland.
Haematemesis	Vomiting of blood.
Haematuria	Presence of blood in urine.
Hemoglobinaemia	Decrease of haemoglobin in the blood plasma.
Haemoptysis	Coughing of blood.
Haemorrhage	Bleeding.
Heart block	Inhibition of speed of conduction of the impulse from auricle to ventricle of the heart. It may be partial or complete.
Heart-burn	Hyperacidity state with gastric contents coming into the mouth and causing burning sensation in the chest.
Haemorrhoids	Swelling containing varicose (dilated) veins in the mucous membrane of anus (piles)
Hepatitis	Inflammation of liver.

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Hepatoxicity	Harmful effects in liver.
Hirsutism	Excessive growth of hair on the body.
Hodgkin's disease	Progressive disease of RES showing enlargement of lymphatic glands.
Hyperglycemia	Increase in blood sugar level.
Hyperkalaemia	Increase in potassium content above normal, in the blood.
Hyperplasia	Excessive formation of cells or over growth in gingival region.
Hypertension	High blood-pressure.
Hypersensitivity	Abnormal sensitivity to a stimulus of any kind.
Hyperthyroidism	Condition caused by excessive secretion of thyroid hormone from thyroid glands.
Hyperuricemia	Abnormal amount of uric acid in blood.
Hypoglycemia	Decrease of blood sugar level.
Hypokalaemia	Decrease in potassium content below normal level in blood.
Hypotension	Low blood-pressure.
Hypothermia	Fall in the body temperature.
Hypoxia	Diminished amount of oxygen in the tissues.
Impotence	Inability of the male to attain or sustain erection satisfactorily for normal coitus.
Infection	Disease transmissible from one person to another.
Inflammation	Tissue reaction to injury, infection or irritation characterized by heat, redness, pain and swelling.
Insomnia	Chronic inability to sleep.
Iritis	Inflammation of iris.
Ischemia	Reduced blood supply.
Jaundice	A condition characterized by raised bilirubin level in the blood, leading to yellowish skin and conjunctiva.
Kala-azar	An infectious disease resulting in leishmaniasis.
Labour	Physiological process by which the foetus is expelled from the uterus at term.
Lacrimation	Outflow of tear.
Lactation	Breast feeding.

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Laryngospasm	Spasm of laryngeal muscles.
Leucocytosis	Increase in total WBC count about 11,000/cmm.
Leucopenia	Decrease in total WBC count below 4,000/cmm.
Leukaemia	Increase in leucocyte (total WBC) count above 50,000/cmm, with immature cells from bone marrow.
Malignant growth	Rapidly growing, worsening with metastasis, cancer, sarcoma.
Mania	A type of mental disease characterized by undue elation of mood and psychomotor excitation, alternating with depression of mood.
Meningitis	Inflammation of the meninges of brain.
Menopause	Permanent stoppage of menses, heralding old age in women.
Myalgia	Muscle pain.
Myasthenia gravis	An autoimmune disease characterized by marked weakness of the voluntary muscles.
Mydriasis	Dilation of the pupil of the eye.
Myeloma	Multiple tumours in bones and their marrow.
Myositis	Inflammatory and degenerative changes in muscles.
Myotonia	Difficulty in relaxing the muscles after they have been contracted.
Myxoedema	Clinical condition of hypothyroidism in adults with a decrease in BMR.
Narcolepsy	Tendency to fall asleep.
Narcosis	Unconsciousness produced by the drug.
Nausea	Vomiting sensation without, or prior to, vomiting.
Necrosis	Localized death of tissue.
Nephritis	Inflammation of the kidney.
Neurogenic	Originating in nerve cells.
Nystagmus	Involuntary and jerky movement of eye balls.
Obesity	Abnormal increase of fat in the body.
Oliguria	Decrease in production of urine.
Orthostatic	Caused by upright position (e.g. Orthostatic hypotension).

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Osteoarthritis	Degenerative condition of large joint causing stiffness.
Osteoma	Tumour of bony tissue.
Osteomalacia	Adult rickets (Disease of Vitamin – D deficiency)
Osteomyelitis	Inflammation of bone marrow or bone.
Osteoporosis	Loss of bone density due to excessive absorption of calcium and phosphorous from the bone.
Palpitation	Rapid heart beat.
Paralysis	Complete or incomplete loss of nervous function of a part of the body.
Parkinsonism	Condition of Parkinson's and similar nervous diseases; blank face and tremors, movement of thumb, muscular rigidity, etc.
Paroxysmal tachycardia	Marked increase in frequency of heart beat of temporary but sudden origin.
Peptic ulcer	Circumscribed ulceration of gastric mucosa.
Pericarditis	Inflammation of the covering membrane of the heart.
Peripheral neuritis	Inflammation of peripheral nerves.
Peritonitis	Inflammation of the peritoneum of the abdomen.
Petit mal	Clouding of consciousness with no convulsions, type of epilepsy.
Pheochromocytoma	Tumor of adrenal medulla.
Photophobia	Abnormal sensitiveness of eyes to light.
Pleurisy	Inflammation of pleura.
Pneumonia	Acute infection and/or inflammation of the alveolar spaces of lungs.
Poliomyelitis	Destruction of upper motor neurons causing flaccid paralysis and wasting of muscles.
Polyuria	Excretion of excessive amount of urine.
Pericardial	Pertaining to the area of chest immediately over the heart.
Prophylactic	Preventive.
Puberty	The age at which reproductive organs become functionally active (pre-youth state)
Raynaud's syndrome	Spasm of the digital arteries, producing pallor or cyanosis of fingers or toes.

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Refractory period	Resistant period during a cardiac beat.
Rheumatism	The term referring to disease characterized by affection of the smaller peripheral joints, accompanied by joint deformities and muscle wasting.
Rickets	Disease of Vitamin D deficiency in children.
Scabies	Infectious parasitic disease in children.
Scabies	Infectious parasitic disease of skin characterized by itching and minute superficial burrows in the skin.
Scurvy	Disease of Vitamin C deficiency.
Schizophrenia	A group of mental illness characterized by disorganization of the patient's personality.
Tachycardia	Excessive rapid rate of heartbeat.
Tachyphlaxis	Quickly developing tolerance, with decreasing drug effect.
Tetany	Condition of hyper-excitability in which, mild stimuli produce cramps and spasms.
Thrombocytopenia	A reduction in the number of platelets (TC) in the blood.
Thrombosis	Intravascular formation of blood clot.
Thyrotoxicosis	Condition due to excessive production of thyroid hormone.
Tonsillitis	Inflammation of the tonsils in the throat by infection.
Trachoma	Contagious inflammation affecting conjunctiva, cornea and eyelids.
Trauma	A wound or injury especially produced by external force.
Tremor	Involuntary trembling of skeletal muscles.
Tumour	An abnormal mass of tissue, the growth of which is extreme and uncoordinated and persists even after cessation of the stimulus which evoked this change.
Ulcer	Local defect or an open sore, with pus, on or in the body.
Vaginitis	Inflammation of the vagina.
Vasoconstriction	Narrowing of the lumen of blood vessels.
Vasodilatation	Widening of the lumen of blood vessels.

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Vertigo	Giddiness.
Virilism	Appearance of secondary male characteristics in the female.
Xeropthalmia	Vitamin A deficiency disease of the eyes.

DRUGS – TRADE NAMES

Drugs	Trade name
Acetazolamide	Diamox
Allopurinol	Ciploric
Aluminium hydroxide gel	Divol
Ampicillin	Roscilline
Analgin	Novalgin
Bleomycin	Bleocin
Butobarbitone	Soneryl
Carbamazepine	Mazeptol
Carbenicillin sodium	Carbelin
Chlorambucil	Leukeran
Chloramphenicol	Chloromycetin
Chlordiazepoxide	Librium
Chloroquin	Nivoquin
Chlorphenaramine maleate	Piritone
Chlorpromazine	Largactil
Chlorpropamide	Diabenese
Chlortetracyclin	Auromycin
Clofazimine	Lamprene
Clofibrate	Lipomid
Clonidine	Catapres
Dapson	Novophone
Dexomehason	Decadron
Diazepam	Calmpose, Valium
Digoxin	Lanoxin
Erythromycin	Althrocin
Ethambutol	Mayambutol

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Ehtosyximide	Zarintin
Frusemid	Lassix
Glyceryltrinirite	Angised
Griseofulvin	Grisovin
Guanehedine	Ismelin
Haloperidol	Halidol
Hydralazine	Nepresol
Hydrochlorothiazide	Esidrex
Ibuprofen	Brufen
Imipramine	Dapsonil
Isoprenaline	Isoprin
Isosorbide dinirate	Isordil
Kanamycin	Kanacin
Leptazole	Cardiozole
Levamisole	Vermisol
Levodopa	Levopa
Lignocaine	Xylocaine
Lorazepam	Larpose
Mebendazole	Mebex, Wormin
Macamylamine	Merasin
Mefanamic acid	Meftal
Meprobamate	Euqanil
Metformin	Glyciphase
Mehotrexate	Equanil
Niostigmine	Prostigmine
Nystatin	Mycostatin
Orciprenalline	Alupent
Orphenadrine	Disipal
Oxazepam	Serepax
Oxymetazoline	Nasivion
Oxyphenbutazone	Suganril

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Oxytetracyclin	Terramycin
Oxytocin	Pitocin
5-flurouracil	Fluracil
Para amino benzoic acid	Paraminol
Paracetamol	Crocin, Calpol
Pentobarbitone sodium	Nembutal
Pthalylsulfa thiazole	Thalazole
Pheniramine maleate	Avil
Phenobarbitone	Gardinal
Pheynylbutazone	Zolandin
Phenytoin	Dialantin
Pilocarpine	Pilocar
Piperazine	Antepar
Prednisolon	Hostacortin
Primidone	Mysolin
Probenecid	Benemid
Procaine	Navocaine
Promethazine	Avomine
Propranolol	Inderal
Reserpine	Serpasil
Rifampicin	Tibamycin
Salbutamol	Asthalin
Secobarbitone	Shortal
Spironlactone	Aldactone
Sulfa cetamide	Albucid
Sulfa methizole	Urolucosil
Thiopentone sodium	Petothal sodium
Tubocaranine chloride	Tubarin
Vexpamil	Isoptin
Warfarin	Uniwarfin
Xylometazoline	Otrivin

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CONDITIONS – DRUG CONTRAINDICATED

Condition	Drug should not be used (Contraindicated)
Glaucoma	Atropine
Prostate enlargement	Propranolol
Intestinal obstruction	Atropine, Morphine
Cirrhosis of liver	Phenobarbitone sodium
Head injury	Morphine
Insomnia	Analeptics
Pheochromocytoma	Adrenaline
Peptic ulcer	Salicylates
Impairment of renal function	Sulfa drugs
Hypertension	Adrenaline
Congestive cardiac failure	Quinidine
Myasthenia gravis	Streptomycin and Kanamycin
Therapy with MAO inhibitor	Cheese, butter, milk

CONDITIONS – DRUGS OF CHOICE

No.	Conditions	Drugs of choice
1.	Alcoholism	Disulfiram
2.	Insomnia	Phenobarbitone Diazepam
3.	Anxiety	Diazepam
4.	Grand mal epilepsy	Phenytoin
5.	Petit mal epilepsy	Trimethadione. Ethosuximide
6.	Status epilepsy	Diazepam, phenobarbitone
7.	Diarrhoea	Tincture opium and Tincture belladonna
8.	Pyrexia	Salicylates, Paracetamol
9.	Rheumatoid arthritis	Ibuprofen, indomethacin, paracetamol
10.	Gout	Colchicin, Probenecid, Allopurinol.
11.	Schizophrenia	Chlorpromazine
12.	Mania	Imipramine, Desipramine

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13.	Narcolapsy	Amphetamine, Caffeine
14.	Parkinsonism	Levodopa, Amantidine
15.	Myasthenia Gravis	Neostigmine, Prednisone, Ephedrine
16.	Glaucoma	Physostigmine, Carbachol, Pilocarpine
17.	Anaphylactic shock	Adrenaline, Diphenhydramine
18.	Bronchial asthama	Adrenaline, salbutamol, Orciprenaline
19.	Obesity	Amphetamine
20.	Pheochromo cytoma	Propranolol, Phentolomine
21.	C.C.F.	Digoxin, Digitoxin
22.	Angina pectoris	Glyceryl trinitrate, Amylnitrite
23.	Atheriosclerosis	Clofibrate, Probucol
24.	Cardiac arrhythmia	Quinidine, Procainamide, Propranolol
25.	Megaloblastic anaemia	Folic acid
26.	Pernicious anaemia	Cynocobalamine (vit – B_{12})
27.	Thrombosis	Heparin, Coumarine, Vitamin K
28.	Myocardial infarction	Coumarine, Vitamin K
29.	Oedema	Chlorothiazide, Furosemide
30.	Graves Disease OR Hyperthyroidism	Propyl thio uracil
31.	Diabetes mellitus	Chlorpropamide, Insulin
32	U.T.I infections	Cotrimaxol, Ciprofloxacin
33.	Bacillary dysentery	Ampicillin, Co-trimoxazole
34.	Sexually transmitted diseases – syphilis and gonorrhoea	Penicillin – G
35.	Typhoid	Chloramphenicol
36.	Tuberculosis	Streptomycin, Isonicotinic hydrozide
37.	Leprosy	Diphenyl-di-amino sulphone
38.	Malaria	Chloroquin, Primaquin
39.	Worm infestation	Mebendazole, Pyrantel pamoate
40.	Breast cancer	Mustine, Methotrexate, Vinblastin
41.	Duodenal ulcer	Alluminium hydroxide, Calcium carbonate
42.	Constipation	Liquid paraffin

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43.	Hypertension	Hydralazine hydrochloride + Propranolol + Furosemide
44.	Morphine poisoning	Naloxon, Nalorphine
45.	Paroxysmal atrial tachycardia	Methacoline
46.	Multiple myeloma	Cyclophosphamide
47.	Diabetes insipidus	Benzathioazides
48.	Hepatic cirrhosis	Spirolactone
49.	Atony and bladder	Carbachol, Methacholine
50	Motion sickness	Pheniromine maleate

DRUGS – SIDE EFFECTS

No.	Drugs	Side effects
1.	Atropine	Dryness of mouth, intense thirst, blurring of vision, constipation.
2.	Adrenaline	Palpitation, hypertensive crisis, glucose tolerance.
3.	Propranolol	Postural hypotension
4.	Morphine	Pin point miosis, respiratory depression, cynosis.
5.	Salicylates	Nausea, vomiting, epigastric distress, frank bleeding and ulcer.
6.	Phenobarbitone sodium	Chyne strokes breathing, nystagmus hangover, amnesia obstructive jaundice.
7.	Diphenyl hydantoin	Hyperplasia, hypertrophy of gums.
8.	Chlorpromazine	Pseudopregnancy, gynaecomastia, weight gain.
9.	Penicillin	Anaphylactic shock.
10.	Tetracyclins	Bone and teeth deformity, osteomalacia, jarish herxmier reaction, benign intracranial, hypertension.
11.	Chloramphenicol	Grey baby syndrome, bone marrow depression.
12.	Streptomycin	Deafness.
13.	Quine	Cinchonism, embolism, black water fever.
14.	Digitalis	Constipation.

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DRUG – ROUTE OF ADMINISTRATION – COMMON USE – DOSE

Sr. No.	Name of the Drug	Route of Administration	Common use	Dose
1.	Thiopentone sodium	Parenteral – Intravenous	General Anaesthetic	2.5% solution Initial dose : 100 to 150 mg repeated if necessary
2.	Piperazine citrate	Oral	Anthalmintic – In the treatment of Ascaris infections	3.5 gms once daily for two consecutive days.
3.	Dapsone	Oral	Anti-leprotic	100 mg/day for five years or more
4.	Streptomycin	Parenteral – Intramuscular	Antitubercular Antileprotic	1 gm / day for one month.
5.	Insulin	Parenteral – Subcutaneous	Anti-diabetic	40/80/100/500 units/ml as per requirements of patients.
6.	Trinitroglyceri ne	Oral – Sublingual	For the relief of acute angina – pectoris	0.4 to 0.6 mg
7.	Hamycin	Oral, Topical – vaginal	Anti-fungal	
8.	Digoxin	Oral, parenteral – Intravenous	In the treatment of congestive cardiac failure	First 24 hours : Oral – 0.75 to 1.5 mg I/V – 0.5 to 1.0 mg Maintenance dose : Oral – 0.125 to 0.5 mg I/V – 0.05 to 0.2 mg
9.	Chlorpromazine	Oral, parenteral – Intramuscular	Antipsychotic in Schizophrenia	Oral dose : 100 to 1000 mg/day
10.	Imipramine	Oral	Antidepressant and mood elevator	75 to 300 mg / day
11.	Atropine sulphate	Oral, parenteral – Subcutaneous, Intramuscular, Instillation into eyes	Antispasmodic – Intestine, Urinary and biliary colics, mydriatic, Pre-anaesthetic	Oral – 0.25 to 2 mg Parenteral – 0.5 to 1 mg Ophthalmic – 1 to 2 %

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12.	Pethidine	Oral, parenteral – Subcutaneous I/m	Analgesic for moderate and severe pains	25 to 100 mg
13.	Meprobamate	Oral	Anti-anxiety drug used to relieve tension, fear etc.	200 to 400 mg t.i.d.
14.	Adrenalin tartrate	Parenteral – Subcutaneous Intramuscular Intra-cardiac	Bronchodilator in Asthma Anti-allergic In heart block and cardiac arrest	0.2 to 0.5 ml (1 in 1000 solution) 0.5 to 1.0 ml (1 in 1000 solution) 0.3 to 0.6 ml (1 in 1000 solution)
15.	Levadopa	Oral	In the treatment of Parkinsonism	Initial dose : 125 mg b.i.d.
16.	Quinidine sulphate	Oral Parenteral – Intramuscular	In the treatment of cardiac arrythmias	Oral – 0.2 to 0.3 gm t.i.d Parenteral – 0.2 to 0.4 gm
17.	Chloramphenicol	Oral Intravenous (Parenteral)	In the treatment of typhoid and meningitis	1.5 to 3 gm/day in 3 to 4 divided doses
18.	Naloxone	Intravenous or Intramuscular	Narcotic antagonist	0.4 mg (1 ml) repeated after every 5 –10 minutes.
19.	Phenobarbitone	Oral	Anti-epileptic	60 – 80 mg divided doses or a single dose at night.
20.	Epinephrine (Adrenalin)	Subcutaneous or intramuscular	• In allergic emergency • To control bleeding • To treat heart block and cardiac arrest	1 : 1000 aqueous solution 0.1 to 0.5 ml subcutaneous
21.	Warfarin sodium	Oral	To treat... • Venous Thromboembo-lism • Arterial thrombosis • Acute myocardial infarction	30 – 50 mg / day

contd...

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22.	Chlorpropamide	Oral	Anti-diabetic drug	100 – 250 mg tablet 0.1 – 0.5 g single dose.
23.	Cimetidine	Oral	As an ulcer healing agent	200 mg three times per day for 4 weeks.
24.	Griseofulvin	Oral	Antifungal agent	Microcrystalline form 500 mg in single or divided doses after meals.
25.	Thiopentone sodium	Intravenous	For induction of anesthesia • Anaesthetic for minor operation	2.5% solution initially 100 – 150 mg over 10 – 15 sec. Repeated if necessary
26.	Morphine	Intramuscular or sub-cutaneous injection	• As narcotic analgesic for pre-anaesthetic medication. • For acute left ventricular failure.	10 mg / 70 kg body weight.
27.	Paracetamol	Oral	Mild analgesic, Antipyretic	0.5 – 1 gm (1 – 2 tablets) after every 4 to 6 hours.
28.	Ephedrine hydrochloride	Nasal drops, Sprays, Oral Subcutaneous	To treat mild or moderate cases of Bronchial Asthma	15 mg – 50 mg
29.	Benzyl penicillin	Oral Intramuscular Intravenous	To treat... • Pneumococcal infection • Staphylococcal infection • Streptococcal infection	400,000 units orally / intramuscularly 10 million units daily intravenously
30.	Chloroquin	Oral Intramuscular	Acute malarial attack suppression of malaria, Hepatic amoebiasis	100 mg after meal.
31.	Mebendazole	Oral	Anthelmintic	100 mg chewable tablet twice a day for three days.
32.	Lbuprofen	Oral	Non-steroidal analgesic anti-Rheumatic	200 mg, 300 mg, 400 mg tablet dose 400 mg t.i.d. or 300 mg g.i.d.

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33.	Aspirin	Oral	Analgesic, antipyretic, anti-Rheumatic	300 – 650 mg
34.	Nifedepine	Oral – Sublingual	Use in Angina pectoris and cardiac arrythmias	10 mg t.i.d.
35.	Diazepam	Oral Parenteral – I/V	Sedative and hypnotic Anxiolytic Pre-anaesthetic medication	Oral dose – 2 to 5 mg I/V dose – 200 to 500 mcg/kg
36.	Choral hydrate	Oral	Sedative and hypnotic	1 gm
37.	Nalorphine	Parenteral – Intravenous	Narcotic antagonist in opiate poisoning	I/v dose 5 to 10 mg
38.	Promethazine	Oral	Anti-allergic in motion sickness	25 to 50 mg
39.	Propoxyphene	Oral	Antitussive	50 to 100 mg for every four hours.
40.	Aminophylline	Parenteral – Intravenous	Bronchodilator in conditions like bronchial asthma and pulmonary oedema	250 to 500 mg by slow I/v infusion.
41.	Frusemide	Oral Parenteral – Intravenous	Diuretic to treat various conditions of oedema	20 to 80 mg
42.	Heparin	Parenteral – Intravenous	Anticoagulant	10,000 to 12,500 I.U.
43.	Tolbutamide	Oral	Antidiabetic in the treatment of diabetic ulcers.	0.5 to 3.0 gm/day in divided doses.
44.	Ranitidine	Oral	In the treatment of gastric and peptic ulcers	150 mg b.i.d.
45.	Gallamine	Parenteral – Intravenous	• Muscle relaxant used alongwith general anaesthetic • To reduce muscle spasm in tetanus	Dose – 80 mg I/v

contd...

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46.	Gentamycin	Parenteral – Intramuscular topical	Antibiotic for gm – ve infections used for septicaemia, meningitis, U.T.I. and topical skin infections	80 mg I/m 8 hourly
47.	Sodium cromoglycate	Inhalation	Antiasthmatic – Useful in prevention and control of bronchial asthma	20 mg every 4 to 6 hours by inhalation route
48.	Castor oil	Oral	Purgative	15 to 60 ml
49.	Diclofenac	Oral	Analgesic, Antipyretic, Anti-inflammatory	

JUSTIFY BY GIVING REASONS

[Means you have to write whether given sentence is correct. If so why and if it is not how ?]

1. Acetyl choline is never used in therapeutics.

Ans. Acetyl choline is never used in therapeutics. Yes ... it is true, because...

(a) Being a quaternary ammonium compound it is not effective orally.

(b) When administered parenterally it is destroyed in the plasma by the enzyme psuedo choline esterase and at the site of action by the specific enzyme true choline esterase.

(c) Thus it has extremely transient (short duration) type of action.

Hence it cannot be used for any therapeutic purpose.

2. Atropine produces photophobia.

Ans. Yes... it is true, because...

(a) When atropine is instilled in the eye, it causes paralysis of cilliary smooth muscle and tightening of suspensory ligament.

(b) This result in flattening of lens, causing increase in size of pupil.

(c) The increase in size of pupil is defined as mydriasis. Because of mydriasis, individual is able to see the objects which are far away but fails to observe the objects which are near.

(d) This paralysis of accommodatin is termed as 'cycloplegia'. Because of cycloplegia, individual fails to constrict the pupils in response to bright light. This is termed as 'photophobia'.

Hence it is true that atropine produces photophobia.

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3. Edrophonium is used in the diagnosis of myasthenia gravis. OR Edrophonium is preferred over to neostigmine in the diagnosis of myasthenia gravis.

Ans. Edrophonium is used in the diagnosis of myasthenia gravis. Yes... it is true, because...

(a) When neostigmine is administered in a single intramuscular injection 1 to 1.5 mg in the diagnosis of myasthenia gravis, it produces marked improvement in muscle power, which remains for 3 to 4 hrs, while edrophonium 10 mg when administered intravenously, effect remains only for 10 minutes.

(b) The muscarinic side effects are negligible and can easily be countered by atropine.

Hence edrophonium is preferred in diagnosis of myasthenia gravis.

4. Adrenaline is added to injections of local anaesthetics.

Ans. Yes... it is true, because...

Local anaesthetics are employed to elicit local effects at desired site without affecting the degree of consciousness.

Adrenaline is the sympathomimetic amine and is known to constrict peripheral blood vessels owing to its 'α' (alpha) receptor action.

Thus when adrenaline is added to local anaesthetics.

(a) adrenaline limits absorption of local anaesthetic from site of infiltration.

(b) Adrenaline prevents systemic toxicity.

(c) As adrenaline limits local anaesthetic at the site of infiltration and prevents its systemic circulation, it prolongs duration of action of local anaesthetic.

5. Neostigmine is the drug of choice in myasthenia gravis.

Ans. Yes... it is true, because

(a) Neostigmine being the parasympathomimetic cholinergic agent it acts on nicotinic receptor of skeletal muscle and improves muscle power in myasthenic patient.

(b) Neostigmine being choline esterase inhibitor blocks pseudo and true choline esterase and sets free acetyl choline which in turn acts on nicotinic receptor of skeletal muscle and improves muscle power.

(c) Thus, in a single therapeutic dose, neostigmine produces marked striking improvement in muscle power in myasthenic individuals.

6. In the treatment of myasthenia gravis, along with neostigmine, atropine is administered.

Ans. Yes... it is true, because...

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Myasthenia gravis is the disease characterized by skeletal muscle weakness. Skeletal muscles belongs to nicotinic group of reactor.

Neostigmine being a parasympathomimetic, acts on both muscarinic as well as nicotinic receptor.

When neostigmine is employed in the treatment of myasthenia, it is expected that it should produce only nicotinic action on skeletal muscle, without acting on muscarinic receptors of heart, eyeball, blood vessels etc.

To mask this unwanted muscarinic actions of neostigmine, an anti-cholinergic, anti-muscarinic atropine is administered with neostigmine.

7. Tincture belladonna (atropine) is used in diarrhoea.

Ans. Yes... it is true, because...

Atropine is the parasympatholytic, anti-cholinergic drug. When administered, it acts on muscarinic receptors of smooth muscles of intestine and causes decrease in tone, motility and peristalsis and produces constipation.

Diarrhoea is the clinical condition in which tone, motility and peristalsis of smooth muscles of intestine is markedly increased, leading to increase in frequency to pass stools.

Hence to reduce tone, motility and peristalsis an anti-spasmodic atropine is used.

8. Atropine is used in peptic ulcer.

Ans. Yes... it is true, because...

(a) Hyper secretion of hydrochloric acid is one of the causes of peptic ulcer. Hydrochloric acid is secreted by oxyntic cells of stomach (gastric glands).

(b) Atropine is the anti-cholinergic, anti-muscarinic agent which acts on exocrine gland and blocks all exocrine secretion.

(c) Atropine as an anti-secretary agent when used in peptic ulcer blocks hydrochloric acid secretion and assist ulcer healing process.

9. Atropine is used with ether when ether is used as general anaesthetic.

Ans. Yes... it is true, because...

(a) Ether vapours are too irritant, when used as volatile inhalatory anasthetic agent. It irritates respiratory, lacrimal, nasopharngeal passage and stimulates their secretions.

(b) These secretions interfere with normal respiration, as well as with anaesthetic process.

Hence atropine as an anti-secretary agent, is advised to be taken in combination with ether, which when administered, blocks all secretions and assists the anaesthetic process.

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10. Atropine substitutes are preferred over atropine in fundoscopic examination of eye.

Ans. Yes... it is true, because...

Atropine when used for fundoscopic examination of eye.

(a) It produces mydriasis within 30 minutes but recovery occurs within 10 days.

(b) It is not specific mydriatic, but when instilled in eye, produces pharmacological actions on other organs of the body.

(c) As it is 'natural' in origin, may be allergic to individual.

To avoid these, atropine substitutes are used.

(a) For their shorter duration of action (mydriatic effect remains only for 1 – 3 days).

(b) For selective mydriatic action.

(c) In case of atropine intolerance.

11. Adrenaline is not given orally.

Ans. Yes... it is true, because...

Adrenaline, on oral administration, is rapidly inactivated (destroyed) in the gut and liver.

12. Adrenaline is used in asthma.

Ans. Yes... it is true, because...

(a) It induces prompt bronchodilation.

(b) It leads to shrinkage of mucosa.

(c) It inhibits mucoid secretion.

13. Adrenaline is found in the emergency kit of physician.

Ans. Yes... it is true, because...

Adrenaline is the life saving drug in various clinical conditions.

(a) It is drug of choice in anaphylactic shock.

(b) It is drug of choice in cardiac shock.

(c) It is drug of choice in asthma.

(d) It is used as haemostatic to stop nasal and dental bleeding.

(e) Adrenaline is frequently added to local anaesthetic injection.

Hence it is always found in emergency kit of physician.

14. Adrenaline is never administered intravenously.

Ans. Yes... it is true, because...

Adrenaline is the sympathomimetic, catecholamine. It acts on peripheral, skeletal muscle blood vessel and on the heart directly and is a known cardiac stimulant.

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If adrenaline is administered intravenously, sudden high blood levels may prove to be harmful and hence not advised.

15. Adrenaline is used in the treatment of epistaxis (nose bleeding). OR Packs soaked in adrenaline are preferred in dental practice after tooth extraction.

Ans. Yes... it is true, because...

Adrenaline is peripheral vasoconstrictor. When used as topical haemostatic agent, it produces vasocostriction which stops bleeding.

16. Ephedrine is used as mydriatic in elderly people.

Ans. Yes... it is true, because...

(a) Ephedrine is non-catecholamine, combines 'α' (alpha) receptors of eye.

(b) Ephedrine produces mydriasis without cycloplegia and photophobia.

Whereas, if some other agents, like atropine or homatropine are used, these agents also produce mydriasis, but with cycloplegia and photophobia, which lasts for 1 to 10 days.

To avoid such visual activity in old people, ephedrine is preferred.

17. Ether is stored in amber coloured bottles.

Ans. Yes... it is true, because

(a) Ether is a colourless volatile liquid, with pungent odour. It has a boiling point of 35° C.

(b) Ether vapours are irritating.

(c) Ether when exposed to air or moisture or light, may form ether peroxide or acetic aldehyde, which are irritants.

(d) To avoid this conversion, ether is marketed in sealed containers or amber coloured bottles covered with black paper.

18. Chloroform is a good anaesthetic.

Ans. No... it is not true, because...

(a) Chloroform is liquid anaesthetic used previously.

(b) It is not used now because of its toxic effects on liver, kidney and heart.

(c) As it produces hepato, nephro, cardiac toxicity and because of its lesser margin of safety, it is not a good anaesthetic.

19. Halothane and cyclopropane are costly anaesthetic.

Ans. Yes... it is true, because...

(a) Halothane and cyclopropane are poor analgesics and poor muscle relaxants. Hence require pre-anaesthetic medication, which adds to the cost of therapy.

(b) Halothane and cyclopropane need special apparatus.

Hence they are expensive.

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20. Tincture opium is used in diarrhoea.

Ans. Yes... it is true, because tincture opium contains morphine, which in therapeutic dose, reduces tone, motility and peristalsis and produces constipation.

Hence used in diarrhoea.

21. Morphine is strictly contraindicated in cases of brain injury.

Ans. Yes... it is true, because...

(a) Morphine if administered in case of head / brain injury, it increases cerebrospinal fluid pressure (C.S.F.).and worsens the bleeding.

(b) It depresses respiration.

(c) It causes pin point miosis.

(d) It causes mental clouding.

As it worsens the existing condition, it is strictly contraindicated in head / brain injury cases.

22. Morphine should not be given for abdominal pain before diagnosis is made.

Ans. Yes... it is true, because...

(a) Morphine is a potent narcotic analgesic, when administered for abdominal pain, it relieves the pain temporarily.

(b) This false relief masks the signs of diagnosis and interferes with the judgement.

(c) As morphine relieves pain temporarily, without diagnosing the cause of abdominal pain, it should not be given before diagnosis.

23. In the treatment of billiary colic (spasm with pain) morphine is always used with atropine.

Ans. Yes... It is true, because...

(a) Billiary colic means pain due to billiary tract spasm (vigorous contractions).

(b) To abolish spasm, anti-spasmodic atropine is used.

(c) To block pain due to spasm, analgesic morphine is used.

As Morphine and atropine acts synergistically, morphine is combined with atropine in the treatment of billiary colic.

24. Morphine is strictly contraindicated in children, old people and carrying women.

Ans. Yes... it is true, because...

(a) Morphine, if administered in children, may decrease the rate and depth of respiration, as the various systems in children, are not yet properly developed to detoxify the drug.

(b) In old people administration of morphine develops bronchospasm and symptoms like asthma.

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(c) In carrying women, if morphine is administered, it may cross placental barrier and may depress the foetal respiration.

Hence not advised.

OR

25. Morphine causes addiction.

Morphine is the worst drug, though it is a good analgesic.

Ans. Yes... it is true, because...

(a) Morphine relieves severe types of pains associated with burns, parturation, fractures, palpitation, tumors, malignancy (cancer) etc. As it gives quick relief from severe pains, it is a good analgesic.

(b) Morphine, when consumed in the absence of pain / disease, produces a pseudo sensation of well being and of security, called euphoria.

(c) Thus to enjoy this euphoria, in the absence of pain / disease an individual is compelled to continue the drug, and soon develops a habit and becomes dependent on, and tolerant and addicted to it.

26. Aspirin is not used in patients with peptic ulcer. OR

Aspirin is strictly contra indicated in patients with ulcer.

Ans. Yes ... it is true, because ...

(a) Aspirin, when administered, precipitates the protective glycoprotein component of gastric mucus and allows free H^+ ions to attack the mucosa. These free H^+ ions causes gastric erosion, gastritis.

(b) It is known to decrease prostaglandin levels which allows ulceration.

(c) As aspirin administration itself causes gastric erosion, gastritis, gastric ulcer it is avoided in patients with history or suffering with ulcer, it's administration may worsen the existing condition.

27. Salicylates are always advised on full stomach or with milk. OR

Aspirin is generally taken after meal or in association with $NaHCO_3$ (sodium-bicarbonate).

Ans. Yes ... it is true, because ...

Salicylates if administered on empty stomach, it causes gastric irritation, gastrittis, nausea, vomiting, ulcers.

To avoid these gastric complications, aspirin like salicylates are advised on full stomach.

28. Reserpine is never prescribed for immediate quietening of maniac patient.

Ans. Yes ... it is true, because...

(a) Reserpine depletes catecholamines on large scale and affects vital site like myocardium.

(b) Reserpine stimulates central nervous system excessively. This leads to firing of all central neurons synchronously developing epilepsy.

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(c) Reserpine initially stimulates central nervous system followed by profound depression under the influence of which individual may commit suicide.

To avoid all the above complications, reserpine is never advised in immediate quietening of maniac patient.

29. Eating of cheese is forbidden while on MAO inhibitor therapy.

Ans. Yes... it is true, because...

(a) Food products like milk, butter, cheese, soyabeans and chocolates contains tyramine, which inturn is converted into adrenaline.

(b) Mono-amino-oxidase inhibitors (MAO inhibitor) blocks 'mono-amino-oxidase' enzyme and prevents destruction of adrenaline and may increase plasma-adrenaline level which may prove to be risky and may create some or other cardiac complexity. Hence it is avoided.

30. Salicylate therapy is always supported with vitamin K.

Ans. Yes... it is true, because...

(a) Salicylates on administration, causes frank bleeding and ulcers.

(b) Vitamin K favours coagulation, i.e. clotting by increasing prothrombin level.

Hence vitamin K is combined with salicylate.

31. During the treatment of epilepsy drugs should be discontinued/ withdrawn gradually. **OR**

Anti-epileptics should not be withdrawn abruptly.

Ans. Yes... it is true, because...

If anti-epileptic drugs are discontinued abruptly, individual may suffer from rebound epileptic attack, which may be severe than the previous one.

Hence, to avoid this, epilepsy drugs are withdrawn gradually.

32. Dilantin sodium is always combined with barbiturates in the treatment of grand mal attack.

Ans. Yes... it is true, because...

(a) Dialantin is combined with barbiturates to achieve additive effect.

(b) The two drugs in combination overcomes each other's side effects.

(c) The combination reduces cost of therapy.

(d) Low doses are effective. Hence used in combination.

33. Chorpromazine is called largactil.

Ans. Yes... it is true, because...

(a) Chlorpromazine when administered in schizophrenic patients, it reduces aggressiveness by inducing tranquillizing effect.

(b) Person on chlorpromazine therapy develops interest in the surroundings.

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(c) Schizophrenic under the influence of chlorpromazine develops interest in food.

(d) Chlorpromazine reduces emotional out brusts and causes psychomotor slowing.

(e) It possess atropine like activity.

(f) It has anti-hystaminic property.

(g) It causes weight gain.

(h) In schizophrenic female it develops pseudopregnancy and in schizophrenic male it produces gynacomastia.

(i) It is anit-emetic.

As chlorpromazine posses large number of pharmacological actions, it is called 'largactil'.

34. High fluid intake is advised with sulfa drug. OR
Large quantities of fluids are advised with sulfa drug. OR
Alkalinisation of urine is advised during sulfa therapy.

Ans. Yes... it is true, because...

(a) Sulfonamides in therapeutic dose cause renal damage, crystal urea, haematuria.

(b) To avoid renal complications and to favour excretion of sulfa, large amounts of fluid intake and alkalization of urine is advised.

35. Sulfa methoxazole is combined with trimethoprim.

Ans. Yes... it is true, because...

(a) Sulfonamides inhibit conversion of para-amino-benzoic-acid (PABA) to folic acid while trimethoprim inhibits conversion of folic acid to folinic acid.

Thus they are synergistic to each other.

(b) In combination, these agents overcomes each other's side effects.

(c) In low doses they are effective.

(d) Their half-lives are approximately the same, hence clearance occurs at a same time.

half life of sulfamethoxazole ..... 10 hrs.
half life of trimethoprim ..... 16 hrs.

As they are synergistic to each other, sulfamethoxazole is combined with trimethoprim.

36. Sulfa is not effective in pus.

Ans. Yes... it is true, because...

(a) Pus contains large amount of para-amino-benzoic acid (PABA), with which sulfa cannot compete and is hence ineffective.

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(b) This is so because, if doses of sulfa are increased above the therapeutic limit, to compete with pus, then these high doses of sulfa may produce renal damage, crystal urea, haematuria and other renal complications.

(c) To avoid the above, sulfa is not used in pus.

37. Penicillin is life saving as well as life threatening drug.

Ans. Yes... it is true, because...

(a) Penicillin is used in different types of life threatening diseases like...
(i) Syphillis and gonorrhoea, (ii) dipheria, (iii) gangrene, (iv) tetanus and (v) meningitis.

(b) Penicillin in therapeutic dose, if randomly administered without checking for an allergic reaction in individuals, it produces anaphylactic shock.

Hence it is life saving as well as life threatening.

38. Tetracycline is not effective orally.

Ans. Yes... it is true, because...

Tetracycline forms insoluble complexes on chelation with Ca^{++} and Al^{+++} and hence if administered orally, its absorption is variable, poor and inadequate.

39. Tetracycline is contraindicated with milk.

Ans. Yes... it is true, because...

(a) Milk contains Ca^{++}, Mg^{++}, Al^{+++} ions.

(b) Tetracycline if administered with milk, forms insoluble complexes by chelating with these ions.

(c) This makes it absorption variable, poor and inadequate and reduces it's efficacy.

Hence, to avoid its chelating and thus efficiency, tetracycline is not given with milk.

40. Tetracycline is contraindicated in carrying women.

Ans. Yes... it is true, because...

(a) Tetracycline forms insoluble complexes by chelation with Ca^{++}, Mg^{++}, Al^{+++} ions.

(b) These ions are essential for development of bone and teeth as well as proper linear growth of body.

(c) If tetracycline is administered in carrying women, or in small children, because if its chelating property, it may produce deficiency of these ions, i.e. Ca^{++}, Mg^{++}, Al^{+++}, required for bone and teeth formation.

(d) Such children may suffer from bone and teeth deformity. Hence it is contraindicated.

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41. Frequent blood cell counting / tapping is essential during prolonged administration of chloramphenicol.

Ans. Yes... it is true, because...

(a) Chloramphenicol, when employed in treatment of typhoid fever, even in therapeutic doses, it causes bone marrow depression, disturbs erythropoeisis and leads to aplastic anaemia and in children, gray baby syndrome.

(b) So, to keep a constant check on the count of red blood cells, to know whether they are affected by chloramphenicol or not, and if at all they are affected, then to take immediate precautions to avoid aplastic anaemia, frequent blood cell count is taken during prolonged therapy with chloramphenicol.

42. Chloramphenicol therapy is supplemented with haematinic or iron preparations.

Ans. Yes... it is true, because...

(a) Chloramphenicol, in therapeutic doses, also causes bone marrow depression, hampers erythropoeisis and leads to aplastic anaemia.

(b) To prevent these side effects, which cause aplastic anaemia, and to favour erhthripoeisis (synthesis of red blood cells.) haematinics are advised.

43. In the treatment of tuberculosis, drugs are always given in combinations.

Ans. Yes... it is true, because...

(a) This avoids drug resistance.

(b) Avoids viability and multiplication of bacilli during treatment.

(c) Achieves synergistic effect.

(d) Avoids caseation, which tends to block the blood vessels supplying to necrotic area and making penetration by anti-tubercular drug difficult.

44. Use of purgative is essential with piperazine. **OR**

Anthelmintics are administered with purgative.

Ans. Yes... it is true, because...

Piperazine is anthelminc.

(a) Anthelminic are either wormicidal (kills worm) or wormifungal (paralyse worm).

(b) To expel worms from the body through faecal matter, supportive agents like purgatives are advised.

(c) This combination acts synergistically to each other.

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45. Toxicity of digitalis is increased by chlorothiazide.

Ans. Yes... it is true, because...

(a) Loss of potassium enhances digitalis toxicity.

(b) In congestive cardiac failure, because of increased sodium retention and disturbed aldosterone mechanism, body already suffers from potassium deficiency.

(c) In addition, if an individual suffering from congestive cardiac failure is kept on prolonged diuretic therapy may further increase potassium loss. Hence if chlorothiazide like diuretics are administered with digitalis, it naturally increases the toxicity.

46. Digitalis controls ventricular rate in atrial fibrillation.

Ans. Yes... it is true, because...

(a) Digitalis protect the ventricles from the too rapid atrial impulses by depressing conduction across the A – V bundle and A – V node.

(b) Digitalis thus when administered in atrial fibrillation, reduces ventricular rate and improves circulation.

47. Digitalis is referred to as 'Cardio-tonic'.

Ans. Yes... it is true, because...

(a) Digitalis directly acts on myocardium, increases rapidity and force of systolic contraction of heart muscle.

(b) More forceful contractions result in more complete ventricular emptying with rise in stroke output.

(c) At the same time duration of systole is reduced, allowing greater time for ventricular filling as well as heart rest.

(d) It also reduces diastolic size of heart and there by oxygen expenditure.

(e) Thus digitalized heart can do same work with less energy or more work with same energy expenditure.

Hence digitalis is called the 'cardio-tonic'.

48. Procainamide is preferred over procain in the management of cardiac arrythmia.

Ans. Yes... it is true, because...

(a) On the one side...

- Procain is not effective orally.
- If administered directly in blood stream, it stimulates central nervous system, producing convulsions.
- It produces short duration of action as destroyed by esterase in plasma.

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(b) On the other side...

- Procainamide is effective orally.
- It does not stimulate central nervous system if administered directly in the blood steam.
- It has sufficient duration of action.

Hence procainamide is preferred over procaine.

49. Antihypertensives are used along with diuretics.

Ans. Yes... it is true, because...

(a) Excess plasma–Na^+ levels, excess plasma–Ca^{++} levels and excess plasma in circulation is thought to be one of the causes of hypertension.

(b) To eliminate excess Ca^{++}, excess Na^+ in the form of their salts and to excrete excess circulating plasma, diuretics are used.

50. Aluminium hydroxide is combined with magnesium oxide.

Ans. Yes... it is true, because...

(a) Aluminium hydroxide is nonsystemic antacid.

(b) Constipation is the only major adverse effect.

(c) To overcome this side effect, aluminium hydroxide is combined with magnesium oxide, as the later overcomes constipation.

DEFINE THE FOLLOWING TERMS WITH EXAMPLES

1. Analeptics :

These drugs when administered overcome narcolepsy by stimulating central nervous system.

e.g. Caffeine, Nikethamide, Strychnine.

2. Anticoagulants :

Anticoagulants are the pharmacological agents which when administered, inhibit the blood clotting process.

e.g. Heparin, warfarin.

3. Antacids :

These are the pharmacological agents which when administered neutralize gastric acid by raising the gastric pH above 4 to 4.5.

e.g. Sodium bicarbonate, Aluminium hydroxide gel.

4. Antipyretics :

These are the pharmacological agents which reduce the elevated body temperature (Pyrexia) by reducing prostaglandin levels and thereby resetting the body thermostat to normal.

e.g. Aspirin, Paracetamol, Ibuprofen.

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5. Antitussives :

These are the pharmacological agents used for symptomatic relief of cough.

e.g. Ammonium chloride, codeine, Bromhexine.

6. Anorexiants :

These are the pharmacological agents which promote weight loss by suppressing appetite.

e.g. Amphetamine, methamphetamine, phenylpropanol amine.

7. Anthalmintics :

These are the pharmacological agents used to eradicate worm infestation.

e.g. Piperazine, mebendazole.

8. Antiemetics :

These are the pharmacological agents used specifically to prevent or relieve nausea and vomiting.

9. Antiseptics :

These are the pharmacological agents that are applied directly to living tissues to inhibit the growth of bacteria (bacteriostatic).

e.g. Boric acid, Iodine, Povidon iodine, Neomycin, Hydrogen peroxide.

10. Anticonvulsants :

These are the pharmacological agents used to treat epileptic seizures.

e.g. Phenobarbitone, Phenytoin, sodium valproate.

11. Autocoids :

These anti-histaminics which when administered antagonizes effects of histamine on H_1 and H_2 receptors.

e.g. Diphenhydramine, chlorpheniramine.

12. Antineoplastic agents :

These are the pharmacological agents used in treatment of neoplastic diseases. (various types of cancers).

e.g. Methotrexate, vincristine, vinblastin.

13. Anti-anginal drugs :

These pharmacological agents when administered either prevent anginal attack or relieve the symptoms.

e.g. Nitroglycerine, Propranalol, Nifedepine.

14. Anti-arrythmic drugs

These are the pharmacological agents employed to correct various types of cardiac arrythmias.

e.g. Quinidine, Nifedepine, Verapamil

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15. Anti-hypertensive agents :

These are the pharmacological agents when administered reduce the blood pressure.

e.g. α-methy-dopa, Guanethidine, Reserpine.

16. Biotransformation :

Biotransformation of drug is its conversion into inactive metabolite suitable for excretion.

e.g. Diazepam – Deamination

Sulfonamides – Acetylation.

17. Chemotherapy :

Chemotherapy is defined as use of chemical compounds in the treatment of infectious diseases, so as to destroy offending organism without damaging the host tissue.

e.g. Sulphonamides, Antibiotics.

18. Cycloplegic drugs :

These are the drugs which cause increase in the focal length of lens and fixes the sight for far or longer vision due to which person can see the objects which are far away but fails to see the objects which are too near.

e.g. Atropin, Homatropin, Scoplamine.

19. Cardiotonics :

These are the pharmacological agents which when administered increases conductivity, automaticity, rhythmicity of heart and cardiac output so are employed in the treatment of congestive cardiac failure (C.C.F.)

e.g. Digitoxin, Digoxin, Oabain.

20. Drug Abuse :

Use of drugs for other than therapeutic purposes, mainly for addiction and dependence (both physical psychological) is termed as drug abuse.

Drug which are abused mainly are

e.g. Nicotine, opium alkaloids, cocaine, phencyclidine, diazepam.

21. Drug dependence :

It is a state of setting new equilibrium in the body due to repeated use of drug which may lead to increased dose requirement and chances of addiction.

e.g. Benzodiazepins in insomnia.

22. Disinfectant :

These are the pharmacological agents having bactericidal properties and can be directly applied to inanimate objects like surgical instruments, O.T. area, wards etc., for making them free from microorganisms.

e.g. Phenols, Formaldehyde

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23. Diuretics :

These are the pharmacological agents which when administered increase rate of formation of urine as well as excretion of urine.

e.g. Acetazolamide, Frusemide, Spironolactone.

24. Drug interactions :

It is defined as alteration in the duration or magnitude of pharmacological effect of one drug by concurrent administration of another drug.

e.g. 1) Antacid (Aluminium hydroxide gel) with Antibiotic (Tetracyclin)
Interaction : Chelate formation affecting absorption.

2) AO inhibitor antipsychotics like imipramine with cheese / butter containing tyramine.
Interaction : Hypertensive crisis.

25. Emetics :

These are the pharmacological agents which are used for induction of vomiting.

e.g. Apomorphine, mustard, Ipecacunha, sodium chloride.

26. Haematinics :

Haematinics are the pharmacological agents which when administered promotes erythropoeis, i.e. promote synthesis of erythrocytes.

e.g. Ferrous sulphate, Ferrous gluconate,
Ferrous fumerate, Ferric hydroxide.

27. Local Anaesthetics :

Local anaesthetics are the pharmacological agents which when applied or injected, block conduction as well as generation of impulses in localized area and bring loss of sensation without affecting degree of consciousness.

e.g. Procaine, Lignocaine, Benzocaine.

28. Miotics :

These are parasympathomimetics which when instilled topically in the eye, cause constriction of pupil and cause fall in the intraoccular pressure.

e.g. Pilocarpine, Carbachol, Physostigmine.

29. Mydriatics :

These are the pharmacological agents which when instilled into eye dilates the pupil.

e.g. Atropin, Homatropin, Scopolamine.

30. Nasal decongestants :

These are the pharmacological agents which when administered externally relieve nasal congestion.

e.g. Xylometazoline – HCl
Cyclopentamine – HCl

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31. Sedatives :

These are the pharmacological agents which when administered relieve anxiety, stress, by inducing drowsiness.

e.g. Barbiturates, Benzodiazepins.

32. Synergism :

When two or more drugs administered together, act on different receptors but produce same physiological action which is greater than the sum of their individual actions, the phenomenon is called as synergism.

e.g. Antihypertensive combination
Vasodilator – Hydralazine hydrochloride
+ β - Blocker – Propranolol
+ Diuretic – Frusemide

33. Tranquilisers :

These are anti-psychotics which when administered calm individuals without inducing sedation and hypnosis.

e.g. Chlorpromazine, Imipramine.

34. Tachyphylaxis :

When same pharmacological agent is administered in a same dose repeatedely without a time interval, then it fails to produce same pharmacological response. This reduction in pharmacological response is referred as "Tachyphylaxis".

e.g. Ephedrine (Bronchodilator)

ANTIDOTES FOR POISONING

1. Morphine poisoning
   a) Pure antagonist : Naloxan
   b) Partial antagonist : Nalorphine
2. Organophosphorous compound poisoning
   a) Atropine sulphate
   b) Enzyme reactivators : Obidoxime
      Pralidoxime
3. Mercury poisoning
   a) Symptomatic patients : Chelation therapy with dimercaprol
   b) Asymptomatic patients : Penicillamine
4. Atropine poisoning :
   Physostigmine 1 to 4 mg by slow I/V route
5. Arsenic poisoning :
   a) Dimercaprol
   b) Penicillamine
   c) Succimer

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