Pharmacology - I

Unit - I

1. General Pharmacology:-

Introduction to Pharmacology:- Pharmacology is the science of drugs which deals with their Pharmacological action.

(Greek: Pharmacon - drug; logos - discourse in)

↓ i.e Pharmacodynamics and Pharmacokinetics.

Father of Pharmacology:- Oswald Schmiedeberg

Father of Indian Pharmacology:- Sh. Ram Nath Chopra.

Pharmacodynamics:- — what the drug does to the body. This includes physiological and biochemical effects of drugs and their mechanism of action at organ system levels.

Eg. Adrenaline → interaction with adrenoceptors → G-protein mediated stimulation of cell membrane bond adenylyl cyclase →

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→ increased intracellular cyclic AMP (Adenosine monophosphate)

Cardiac stimulation, hepatic glycogeno-lysis and hyperglycaemia.

Pharmacokinetics:- What the body does to the drug. This refers to movement of the drug in and alteration of the drug by the body; includes absorption, distribution, storage, biotransformation and excretion of the drug.

eg. Paracetamol is rapidally and almost completely absorbed orally attaining peak blood levels in 30-60 min.

Drug:- It is the single active chemical entity present in a medicine that is used for diagnosis, prevention, cure of disease.

Pharmacotherapeutics:- It is the application of pharmacological information together with knowledge of the disease for its prevention, mitigation or cure.

Clinical Pharmacology:- It is the scientific study of drugs in man. It includes pharmacodynamic and pharmacokinetic investigation in healthy

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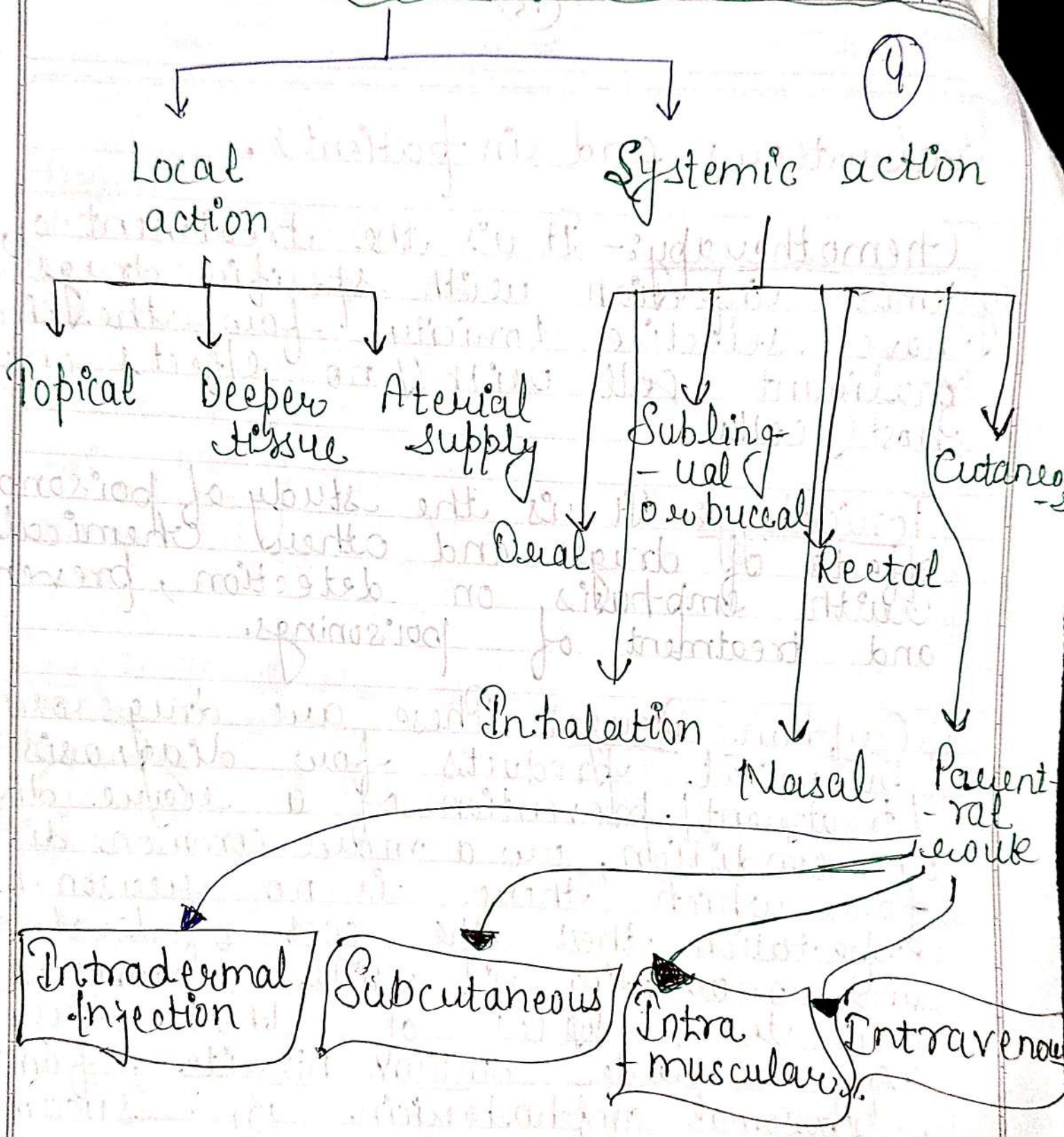
volunteers and in patients.

Chemotherapy:- It is the treatment of systemic infection with specific drugs that have selective toxicity for the infecting malignant cell with no effects on the host cells.

Toxicology:- It is the study of poisonous effects of drugs and other chemicals with emphasis on detection, prevention and treatment of poisonings.

Ouphan Drugs:- These are drugs or biological products for diagnosis / treatment / prevention of a rare disease or condition, or a more common disease for which there is no reasonable expectation that the cost of developing and marketing it will recovered from the sales of that drug. eg. includes sodium nitrite, famepizole, liposomal amphotericin B, succimer etc.

Routes Of Drug Administration.



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Most of drugs can be administered by a variety of routes.

Routes can be broadly divided into these two

(a) Local action
(b) Systemic action

(a) Local Routes:- These routes can only be used for localized lesions at accessible sites and for drugs whose systemic absorption from these sites is minimal or absent.
eg:- glyceryl trinitrate (GTN) applied on the skin as ointment or transdermal patch.

Mainly local routes are:

1. Topical:- This refers to external application of the drug to the surface for localised action. Drugs can be efficiently delivered to the localized lesions on skin, nasal mucosa, eyes, ear canal, in the form of lotion,

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ointment, cream, powder, paints, drops, spray and pessaries.

2. Deeper tissues:- Certain deep areas can be approached by using a syringe and needle, but the drug should be in such a form that systemic absorption is slow, eg. intra-articular injection, infiltration around a nerve or intrathecal injection (Lidocaine), retrobulbar injection

3. Arterial supply:- Close intra-arterial injection is used for contrast media in angiography; anticancer drugs can be infused in femoral or brachial artery to localise the effect for limb malignancies.

(b) Systemic routes The drug administered through systemic routes is intended to be absorbed into the blood stream and distributed all over, including the site of action, through circulation.

(i) Oral routes:- Oral ingestion is the oldest and commonest mode of drug administration. ~~It is~~

→ It is safe, more convenient, does not need assistance,

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the medicament need not be sterile and so is cheaper. eg. Tablets, capsules

ii) Sublingual (S.L) or buccal
The tablet or pellet containing the drug is placed under the tongue/or crushed in the mouth and spread over the buccal mucosa.
→ In sublingual (S.L) or buccal route only lipid soluble and non-irritating drugs can be be so administered.
→ Absorption is relatively rapid - action can be produced in minutes.
→ Drugs given sublingually are- GTN, buprenorphine, desmopressin, oxytocin.

3) Rectal:- Certain irritant and unpleasant drugs can be put into rectum as suppositories or retention enema for systemic effect.

→ This route can also be used when the patient is having recurrent vomiting or is unconscious.

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→ In this route, absorption are ir
irregular.

→ Drugs are given in rectally, Diazep
, indomethacin, paracetamol, and ergotamin

(iv) Cutaneous

→ Highly lipid soluble drugs can be appli
-ed over the skin show slow and
prolonged absorption.

→ The drug can be incorporated in an
ointment and applied over specified
area of skin.

→ Absorption of the drug can be enhanced
by rubbing the preparation, by using
an oily base.

(v) Inhalation:- Volatile liquids and gases
are given by inhalation for systemic
action, eg. general anaesthetics.

→ Absorption takes place from the vast surface
of alveoli.

→ In inhalation, the action is rapid

→ Irritant vapour (ether) cause inflam-
-mation of respiratory tract and
increase secretion.

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(vi) Nasal:- The mucous membrane of the nose can readily absorb many drugs; digestive juices and liver are bypassed.

→ Only certain drugs like GnRH agonists and desmopressin applied as a spray or nebulized solution have been used by this route.

→ This route is being tried for some other peptide drugs like insulin, as well as to bypass the blood-brain barrier.

(vii) Parenteral (Par- beyond, enteral - intestinal.

Parenteral refers to administration by injection which takes the drug directly into the tissue fluid or blood without having to cross the enteral mucosa.

→ In parenteral, the action of drug is faster/rapid.

→ Liver is bypassed.

Disadvantages of parental:-

→ The preparation has to be sterilized and is costlier.

→ The technique is painful - eg. insulin by diabetics, there are chances of local tissue injury.

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The important parenteral routes are

(a) Subcutaneous (S.C):- The drug is deposited in the loose subcutaneous tissue which is richly supplied by nerves (irritant drugs cannot be injected)

→ In subcutaneous the absorption of drug is slow than intramuscular.

→ This route should be avoided in shock patients who are aqueous suspensions can be injected for prolonged action.

Some special forms of this route are:

(a) Needle-jet:- In this method needle is not used; a high velocity jet of drug solution is projected from a microfine orifice using a gun like implement.

→ The solution passes through the superficial layers and gets deposited in the subcutaneous tissue.

→ Painless.

(b) Pellet implantation:- The drug in the form of a solid pellet is introduced with a cannula.

→ This provides sustained release of the drug. Few weeks and month eg. DOCA, testosterone.

b) Sialistic (non biodegradable) and biodegradable implants :-

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→ Crystalline drug is packed in tubes or capsules made of suitable materials and implanted under the skin.
→ The nonbiodegradable implant has to be removed later on but not the biodegradable one.
→ This has been tried for hormones and contraceptives (eg. NORPLANT).

ii) Intramuscular (i.m) :- The drug is injected in one of the large skeletal muscles — deltoid, triceps, gluteus maximus etc.
→ Muscle is less richly supplied with sensory nerves.
→ In I.m. the absorption of drug is faster.
→ less painfull.
→ eg. I.m. should be avoided in anticoagulant treated patients, because it can produce local haematoma.

iii) Intravenous (i.v) :- The drug is injected as a bolus means (lump) or infused slowly over hours in one of the superficial veins.

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eg. ⊛ (Sodium nitroprusside), titration. the dose with the response is possible.
→ This is the most risky route – vital organs heart, brain etc.

(iv) Intradermal injection:- The drug is injected into the skin raising a bleb (eg BCG vaccine, sensitivity testing) or scratching of the epidermis through a drop of the drug is done.

Combined effect of Drugs

When two or more drugs are given simultaneously, they may be either indifferent to each other or exhibit synergism or antagonism.

Synergism [Syn – together, ergon – work]

When the action of one drug is facilitated or increased by the other, they are said to be synergistic.

Synergism may be two types.

(a) Additive

(b) Supra-additive drug combinations

a) Additive

Effects of drugs A and B = effect of drug A + effect of drug B.

Additive drug Combinations	
Aspirin + Paracetamol	as analgesic / antipyretic
Nitrous oxide + halothane	as general anaesthetic
Amlodipine + atenolol	as antihypertensive

(b) Supra-additive drug combinations

effect of drug A+B > effect of drug A + effect of drug

Drug pairs	Basis of potentiation
Acetylcholine + Physostigmine	Inhibition of break down
Adrenaline + cocaine	Inhibition of neuronal uptake.
Tyramine + MAO inhibitors	Use releasable CA store.
Enalapril + hydrochlorothiazide	· Taking two contributory features.

Antagonism :- when one drug decreases the action of another, they are said to be antagonistic.

effect of drugs A+B < effect of drug A + effect of drug B

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(a) Physical antagonism:- Based on the phy property of the drugs, eg. charcoal adsorbs alkaloids and can prevent their absorption - used in alkaloid poisonings.

(b) Chemical antagonism:- The two drugs react chemically and form an inactive product eg.
$KMnO_4$ oxidizes alkaloids - used for gastric lavage in poisoning.

(c) Physiological / functional antagonism
The two drugs act on different receptors, but have opposite overt effects on the same physiological function.

eg. Histamine and adrenaline on bronchial muscles and BP

(d) Receptor antagonism:- One drug blocks the receptor action of the other. This is a very important mechanism of drug action.

→ Receptor antagonists are selective ie an anticholinergic will oppose contraction of intestinal smooth muscle induced by cholinergic agonist but not induced by histamine or 5HT

Receptor antagonism can be competitive or non-competitive.

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Competative antagonism:

→ Antagonist binds with the same receptor as the agonist.
→ Intensity of response depends on the concentration of both agonist and antagonist.
→ eg, Ach – Atropine

Non-competetitive

→ Binds to another site of receptor. Does not resemble
Maximal response depends only on the concentration of antagonist
eg. Diazepam – Bicuculline

Factors modifying Drug action

Factors modifying drug action:

(a) Quantitatively:- The plasma concentration and the action of the drug is increased or decreased.
(b) Qualitatively:- The type of response is altered, eg. drug allergy, idiosyncrasy.

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Various factor are discussed b

(1) Body size:- It influences the concentrat of the drug attained at the site of a In children, dose may be calculated o body weight Basis

Individual dose = BW (Kg) / 70 × average adult dose

(2) Age:- The dose of a drug for children is often calculated from the adult dose.

(Young's formula) Child dose = Age / Age + 12 × adult dose

(Dilling's formula) Child dose = Age / 20 × adult dose

(3) Sex:- Females have smaller body size and requires doses that are on the lower side of the range.

→ Maintenance treatment of heart failure with digoxin is reported to be associate with higher mortality among women than among men.

(4) Genetics:- The ~~drug~~ dose of drug to produce the same effect may vary by 4-6 fold among different

individuals.
→ All key determinants of drug response, viz. transporters, metabolizing enzymes ion channels, receptors with their couplers and effectors are controlled genetically.

Pharmacogenetics:- The study of genetic basis for variability in drug response is called Pharmacogenetics.

(5) **Route of administration:-** Route of administration governs the speed and intensity of drug response.
→ Parenteral administration is more rapid and more predictable drug action eg. A drug may have entirely different uses through different routes, eg. magnesium sulfate given orally cause purgation applied on sprained joints.
↓
use swelling, while intravenously
↓
It produces CNS depression and hypotension.

(6) **Environmental factors:-** eg. food interferes with absorption of ampicillin, but a fatty meal enhances absorption of griseofulvin and flumefenturine.

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7.) Psychological factors:- Efficacy of a drug can be affected by patient's beliefs, attitudes and expectations.
eg. a nervous and anxious patient requires more general anaesthetic.

Placebo:- This is an inert substance which is given in the guise of a medicine.
Placebos are used in two situations;
① As a control device in clinical trial of drug (dumy medication)
② To treat a patient who, in the opinion of the physician, does not require an active drug
* Placebo do induce physiological responses eg. they can release endorphins in brain causing analgesia.

8.) Other drugs:- Drugs can modify the response to each other by pharmacokinetic or pharmacodynamic interaction b/w them.

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

Liver disease:- Liver disease (especially cirrhosis) can influence drug disposition in several ways:

(a) Serum albumin is reduced - protein binding of acidic drugs (diclofenac, warfarin etc.) is reduced and more drug is present in the free form.

(b) Prodrugs needing hepatic metabolism for activation, eg., bacampicillin are less effective and should be avoided.

Other examples of modification of drug response by pathological states are:-

→ Antipyretics lower body temperature only when it is raised.

→ Atropine, furosemide can cause urinary retention in individuals.

2. Tolerance:- It refers to the requirement of higher dose of a drug to produce a given response. Tolerance is a widely occurring adaptive biological phenomenon.

Drug Tolerance

Natural

Species is inherently less sensitive to the drug eg. rabbits are tolerant to atropine

Acquired

This occurs by repeated use of a drug in an individual who was initially responsive. eg. Tolerance develops to the sedative action of phenobarbitone but not as much to its antiepileptic action.

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→ Tolerance occurs to analgesic and euphoric action of morphine, but not much to its constipating and miotic actions.

Cross tolerance:- It is the development of tolerance to pharmacologically related drugs, eg. alcoholics are relatively tolerant to barbiturates and general anaesthetics.

eg. Partial cross tolerance blw morphine and barbiturates but complete cross tolerance blw morphine and pethidine.

Mechanism of drug action:-

Pharmacodynamics is the study of drug effects. It starts with describing what the drug do, and goes on to explain how they do it.

Principle of drug action:-

Drugs donot impart new functions to any system, organ or cell; they only alter the pace of ongoing activity ~~However, this alone~~.

Basic types of drug action can be broadly classified as;

① Stimulation:- It refers to selective enhancement of the level of activity of specialized cells, eg, adrenaline stimulates heart, pilocarpine stimulates salivary glands.

Depression:- Selective diminution of activity specialized cells. eg. barbiturates depress CNS.

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② Irritation:- Nonselective, noxious effect and is particularly applied to less specialized cells. Strong irritation results in inflammation, ulceration, necrosis.

③ Replacement:- This refers to the use of natural metabolites, hormones or their cogeners in deficiency states, eg. levodopa in parkinsonism, iron in anaemia.

④ Cytotoxic action:- Selective ~~action~~ CA on invading parasites or cancer cells, eg. penicillin, chloroquine etc.

Mechanism of drug action:-

(1) Enzymes:- Enzymes is a biological catalyst, which is synthesised by living cells.

→ Enzymes are a very important ~~drugs~~ target of drug action. Drugs and either increase or decrease the rate of enzymatically mediated reactions.

→ Stimulation of an enzyme increases its affinity for the substrate so that rate constant (KM) of the reaction is lowered.

→ Apparent rise in enzyme activity can also occur by enzyme induction, i.e. synthesis of more enzyme. Induction is synthesis of more enzyme protein.

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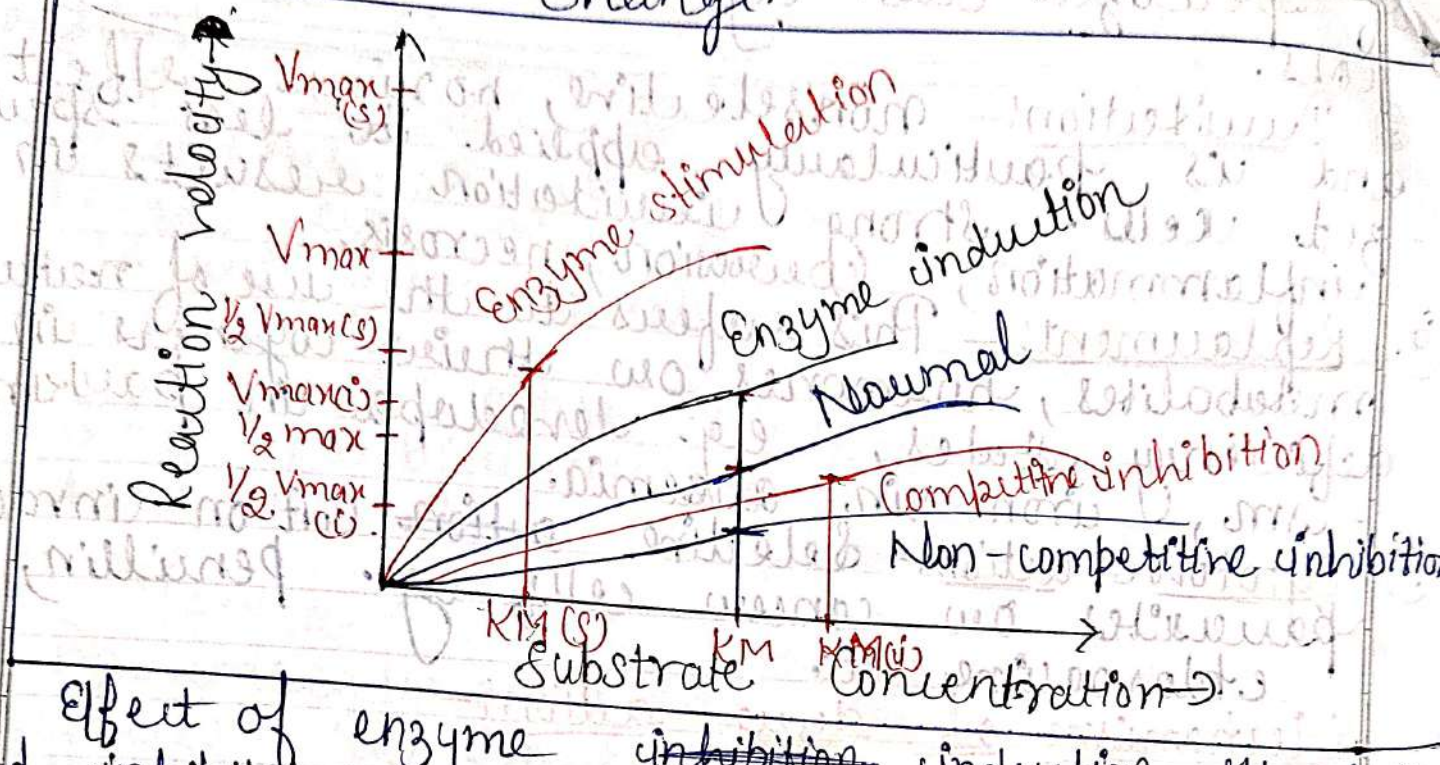
cannot be called stimulation because K_M does not change.



Effect of enzyme ~~inhibition~~ induction, stimulation and inhibition on kinetics of enzyme reaction.

Vmax — Maximum velocity of reaction.

Vmax (S) — of stimulated enzyme.

Vmax (i) — in presence of non-competative inhibitor, K_M — rate constant of the reaction, K_M (S) — stimulated enzyme, K_M (i) — in presence of competative inhibitor.

Enzyme Inhibition:— Some chemicals (heavy metal salts, strong acids and alkalies) denature proteins and inhibit all enzyme nonselectively. Such inhibition is either competitive or non-competitive.

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Competitive :- The drug being structurally similar competes with the normal substrate for the catalytic binding site of the enzyme so that the product is not formed.

A nonequilibrium type :- of enzyme inhibition can also occur with drugs which react with the same catalytic site of the enzyme but either form strong covalent bonds or have such high affinity for the enzyme that the normal substrate is not able to displace the inhibitors. eg:

Organophosphates react covalently with the esteratic site of the enzyme cholinesterase.

ii) Non-competitive :- The inhibitors reacts with an adjacent site and not with the catalytic site, but alters the enzyme in such a way that it loses its catalytic property, KM is not changed but Vmax is reduced.

Non-competitive inhibitors	Enzyme
Acetazolamine	- Carbonic anhydrase
Aspirin	- Cyclo-oxygenase
Omeprazole	- H^+, K^+ ATPase
Digoxin	- Na^+, K^+ ATPase

② Transporters:- Many drugs produce their effects by directly interacting with the solute carriers (SLC) class of transporter proteins to inhibit the ongoing physiological transport of the metabolite. Examples are:-

① Desipramine and cocaine block neuronal reuptake of noradrenaline by interacting with norepinephrine transporter

② Amphetamines selectively block dopamine reuptake in brain neurons by dopamine transporters (DAT)

③ Receptors:- It is defined as a macromolecular binding site located on the surface or inside the effector cell that serves to recognize the signal molecule and initiate the response to it, but itself has no other function.

Various terms are used in describing drug-receptor interactions:-

Agonist:- An agent which activates a receptor to produce an effect similar to that of the physiological signal molecule.

Inverse agonist:- An agent which activates a receptor to produce an effect in the opposite direction to that of the agonist.

Opoid analgesics and Antagonists

Algesia - (Pain) → unpleasent body sensation

A drug that reduces the pain by acting the CNS

* Excessive pain may lead to produce other effects - sinking sensation, sweating, nausea, palpitation, rise or fall in BP, tachyponea, type of sensation and urge to vomit.

Analgesics.

- unpleasent feeling
- heart is racing pounding, ~~thump~~ -ing a beat
- Breathing that is abnormally rapid and often shallo

Opium
Opiod narcotic morphine like analgesics

NSAIDs

* Opoid analgesics obtained faum opium

Opium :- A dark brown, resinous material obtained from poppy (papaver somniferum) Capsule.

(opium (two types of alkaloids))

(Phenanthrene derivative) | (Benzoisoquinoline derivative)

→ Morphine (10% in opium)
→ Codeine (0.5%)
→ Thebaine (0.2%), (Non-analgesic)

→ Papaverine (1%)
→ Noscapine (6%)
Non-analg

① Morphine :- Pain medication
↓
found naturally in a num
of plants and animals
including humans
↓
directly act to the CNS system to
use the feeling of pain.
↓
taken Both acute pain and
chronic pain

FDA approval - 1941

* Donot take the morphine if you have severe asthmatic breathing problems
* a blockage in your stomach or intestines
* Do not use morphine if you have used an MAO inhibitor in the past 14 days.

* Morphine interact with (u opoid receptors) → affinity high
* Morphine depress respiratory centre

~~Oral bio availability → 1/6th to 1/4th~~

Bioavailability — 80-100%.

Parenteral morphine — Tmax - 15 mintues
Oral " - " - 90 min.

volume of distribution — 5.3 1/kg.

Protein binding — 35%

Clearance — IV/Subcut - 1600 ml/min

Metabolism — 90% (liver by glucuronide conjugation)

Half life - 2-3 hours.

Toxicity · LD_{50} — 0.178 μg/ml in males and 0.198 μg/ml in females.

Food Interactions — Avoid alcohol

ADR of morphine :-

⇒ Sedation, mental clouding, lethargy

⇒ Idiosyncrasy and allergy

⇒ Apnoea of the newborn
↓ drug of choice -
Naloxone 10 μg/kg injected in the umbilical cord

Feeling of being very tired and have any energy.

⊗ * Specific antidote —
Naloxone 0.4 — 0.8 mg (~~I.M.~~) - i.v. repeated every 2-3 min

a medical condition in which somebody stop breathing for a short time while asleep

Interactions :-
Phenothiazines, tricyclic antidepressants, MAO inhibitors, amphetamines, neostigmine
Potentiate morphine

* Classification of opioids

Natural opium alkaloids	Semisynthetic opiates	Synthetic opoids.
⇒ Morphine	Diacetylmorphine (Heroin)	Pethidine (meperidine)
⇒ Codeine	Pholcodine	Fentanyl
	Ethylmorphine	methadone
		tramadol
		Dextropropoxy-phene

used in cancer pain

Codeine: It is methyl-morphine - occurs naturally in opium.
↓ less potent than morphine

*

* Originally approved in US in 1950

* used to treat pain, coughing, and diarrhea.

* used to treat mild to moderate degree pain.

* weak narcotic pain relieves and cough suppressant that is similar to morphine and hydro-codone

* Absorption – GIT
* Plasma concentration – 60 mintues
* Volume of distribution
3 L/kg – 6 L/kg.

* Protein binding – 7-25%
* Metabolism – 70 to 80%
(in liver by conjugation with glucu-nic acid
* Half life – approx. 3 hours.
* Clearance – 183 +/– 59 ml min-1

Side effects :-
=> Dizziness, nausea, vomiting, shortness of breath, sedation, allergic reaction, Rash, itching
Serious –
* Life-threatening respiratory depression
* Severe low blood pressure

Codeine – Tablets - 15, 30, 60 mg
sol → 15mg/5ml
Injection – 15-30 mg/ml.
Storage – 15°c to 30°c

MOA :- Codeine binds to receptors in the brain (μ opioid receptors).

Codeine — oral : parenteral ratio

[1:2]

Heroin :- (diacetylmorphine) 3 times more potent than morphine, more lipid soluble, cross Blood brain barriers. Banned in most countries except U.K.

Pethidine (Meperidine)

Pethidine was synthesized as an atropine substitute in 1939.

* their action with μ receptors, blocked by naloxone.

* IM injection, the onset of action is more rapid but duration is shorter (2-3 hours)

~~cough~~.

(oral : Parenteral)

Ratio — O:P — (1/3 to 1/4)

Plasma half life — 2-3 hours.

Side effects :- dry mouth, blurred vision, (tachycardia) → rapid heart beat (100 times per minute)

Overdose

tremors → unintentional and uncontrollable rhythmic movement of one part or the limbs of your body

delirium

mydriasis → dilation in pupil

hyperreflexia → overactive or overresponsive reflexes.

Serious disturbance in mental ability

Uses:- Pethidine is used in analgesia and in preanaesthetic medication but not for cough and diarrhoea

Dose:- 50–100 mg i.m. sc (may cause irritation, local fibrosis on repeated injection

Fentanyl:- A pethidine congener 80 to 100 times more potent than morphine, both in analgesia and respiratory depression

high lipid solubility → enters the brain → Produce peak analgesia in 5 min after iv injection

Duration of action — 30-40 min
elimination t1/2 is ~4 hours

* In injection form it is used in anaesthesia

* Transdermal fentanyl has become available for use in cancer

Methadone:- Synthetic opoid, analgesic, respiratory depressant, emetic, anti-tussive, constipation and biliary actions similar to morphine.

Ration :- Oral : Parenteral (1:2)

(4-6 hours i.m. injection)

Plasma protein binding - 90%

Metabolism - liver

Opoid receptors :-

μ receptor :- μ receptor is characterized by its high affinity for morphine, It is a major receptor mediating actions and its congeners.

* Endomorphins 1 and 2
↓
found in mammalian brain.

β-funaltrexamine — μ antagonist

K receptor:- This receptor is defined by its high affinity for Ketocyclazocine and dynorphin A.

Nor binaltorphimine → antagonist of K

Two types of K

K1 K3

δ receptor:- High affinity.
↓ Present in dorsal horn of spinal cord

Naltrindole → δ antagonist

* Opoid antagonists (~~analgesics~~)

① Agonist - antagonists (K analgesics)

→ Nalorphine
→ Pentazocine
→ Butorphanol

(2) Partial / weak μ agonist + κ antagonist → Buprenorphine

(3) Pure antagonists
Naloxone, Naltrexone, Nalmefene

(1) Nalorphine — N-allyl-normorphine
↓
first opioid antagonist introduced in 1951
⇒ not used clinically because of dysphoric and psychotomimetic effect
↓
a drug with psychotomimetic actions mimics the symptoms of psychosis, including delusions.
↓
State of feeling uneasy / unhappy / unwell.

⇒ used as antidote to reverse opioid overdose

(2) Pentazocine :- First agonist or antagonist to be used as an analgesic.
⇒ weak μ antagonistic and more κ agonistic actions.

* Pentazocine is effective orally.
* Oral : Parenteral ratio 1:3
* Plasma half life ($t_{1/2}$) - 3-4 hours.
* Duration of action of a single dose - 4-6 hours.

* Pentazocine is indicated for post-operative and moderately severe pain in burns, trauma, fracture, cancer

* Pure Opoid antagonists.

① Naloxone :- N- allylnor- oxymorphone and a competitive antagonist

* Blocks μ receptors at much lower doses
* Injected (i.v.) ⇒ (0.4 - 0.8 mg)
* Naloxone also blocks the action of endogeneous opioid peptides.
⇒ It blocks placebo, acupuncture, stress introduced analgesia
* Naloxone can't take orally because of high first pass metabolism.

Name —> Aman Thakur

t½ iv — 2-3 min.
Plasma t½ — 1 hour
Newborns — 3 hours

ADR effects — Rise in BP and pulmonary edema.

Uses:- Naloxone is the drug of choice for morphine poisoning (0.4 - 0.8 mg i.v. every 2 min. maximum 10mg)
=> used for treat overdose with other opioids and agonist - antagonist

* Endogenous opioid peptides.

In the mid 1970's, a no. of peptides having morphine - like actions were isolated from mammalian brain, pituitary, spinal cord and git.

⇓

Peptides are active in very small amounts, their actions are blocked by naloxone, and they with high affinity to opioid receptors.

① Endorphins :- β- endorphin (β-End) having 31 amino acids.

② Enkephalins

③ Dynorphins.

Antiseptics, Disinfectants and ectoparasiticides

Antiseptics and disinfectants

(which inhibits or kills microbes)

* Antiseptics are those agents which is used for skin, mouth

* Disinfectant are those agents which is used for instruments, privies, water supply.

Mechanism of action

(a) Oxidation of bacterial protoplasm

(b) Denaturation of bacterial proteins including enzymes.

(c) Detergent like action increasing permeability of bacterial membrane

Classification

1.) Phenol derivatives Phenol, cresol Chloroxylenol, Hexachlorophene

2.) Oxidizing agents Potassium permanganate Hydrogen peroxide, Benzoyl peroxide.

3.) Halogens :- Iodine, Iodophores, Chlorine Chlorophores.

4.) Biguanide :- Chlorhexidine

5.) Quaternary ammonium (cationic): Cetrimide, Benzalkonium chloride

6.) Soaps : soaps of sodium and potassium

7.) Alcohols :- Ethanol, Isopropanol

8.) Aldehydes :- Formaldehyde, Glutaral -yde

9.) Acids :- Boric acid, acetic acid (Bacteriostatic action) used in burn dress

10) Metallic salts :- Silver nitrate, silver sulfadiazine, mild

11) Dyes :- Gentian violet, acriflavin, Pro -vin

12) Furan derivatives :- Nitrofurazone

1) Phenol :- used to disinfect urine, faeces, pus, sputum
accumulates at the site of infe
a thick yellowish liquid that may form in a part of your body that has been hurt

2) Cresol :- used as disinfection for utensils, excreta and for washing hands.

3) Chloroxylenol (PCMX) : Para- chloro- me -xylenol - used for skin infection and cleaning surgical instrument

:⇒ commercially used as a dettol, household disinfectants and wound cleaners.

:⇒ 2.4% lubricating obstetric cream for vaginal examination, use on forceps.

:⇒ Potassium permanganate :-

* Condy's lotion is used for gargling, douching, irrigating cavities, urethra and wounds.
* used to disinfect water and for stomach wash in alkaloidal poisoning
* not good for surgical instruments.

⇒ Cetrimide :- used as 1-3% solution, it has good cleansing action, efficient removing dirt, grease, tar and coagulated blood from road side accident wounds.
⇒ used for surgical instruments utensils, baths etc.

⇒ Silver compounds :-
(1) $AgNO_3$ → used for hypertrophied tonsillitis and aphthous ulcer
A small, shallow sore inside the mouth or at the base of the gums.

=> used for ophthalmia neonatorum (Conjunctivitis of the newborn)

* It is an eye infection that occurs within the first 30 days of life.
* Infected with a STD.

Silver Sulfadiazine :- used for burns

Zinc Salts :- ~~highly used~~ They are astringent and mild antiseptics.

Zinc sulfate :- used for eye wash and in ear drops.

Calamine or zinc oxide :- mild antiseptic used as dermal protectives and adsorbents.

Crentian violet (crystal violet) :-

used on furunculosis, bedsores, chronic ulcers, infected eczema, thrush, Vincent's angina, ringworm etc.

progressive infection with ulceration, swelling of dead tissue from the mouth

painful

a painful pus-filled bump under the skin caused by infected inflamed hair foll

Acriflavine and proflavine (dyes) → used as disinfectant bacteriostatic against many gram positive bacteria.

Nitrofurazone:- used as a topical antibiotic ointment. effective against gram-positive bacteria, gram-negative bacteria; and can be used in the treatment of trypanosomiasis.

{ Sleeping sickness, is a vector-borne parasitic disease. }

* Nitrofurantoin and furazolidone are other furan derivatives used for urinary and intestinal infections respectively.

Ectoparasiticides:- These are drugs used to kill parasites that live on body surface.

Scabies:- Scabies is a skin infestation caused by a mite known as the sarcoptes scabiei.

Pediculosis :- Is an infestation of the hairy parts of the body or clothing with the eggs, larvae or adults of lice.

⇒ Insect feed on human blood which can result in severe itching

Drugs used are :-

① Permethrin → used to treat scabies and lice.
② Lindane (BHC) → used for agricultural insecticide and S. and L.
③ Benzyl benzoate → insect repellent. S and L
④ Crotamiton → both scabicidal and antipruritic → used as a lotion based medicine
⑤ Sulfur → treat scabies in newborns, infants and pregnant women.
⑥ Dicophane (DDT)
⑦ Ivermectin.

↓
used for many types of parasitic infestations.

↓
head lice, scabies, lymphatic filariasis, river blindness

⇒ Taken in mouth or applied to the skin.

Vitamins

* Vitamins are substance that your body needs to grow and develop normally.
* Vitamins as drugs is primarily in the prevention and treatment of deficiency diseases.

Vitamins

- Fat-soluble
  - A, D, E, K
  - These are stored in the body for prolonged periods and are liable to cause cumulative toxicity after regular ingestion of large amounts.
- Water soluble
  - B Complex, C
  - These are meagerly stored: excess is excreted with little chance of toxicity.

Fat soluble vitamin:-

Vitamin A:-
- Vit A_1 → Retinol
- Vit A_2 → Dehydroretinol

① Vit A_1 is an unsaturated alcohol containing an 'ionone' ring. Marine fish (Cod, shark, halibut) liver are such sources.

* Appreciable amounts are present in egg yolk, milk and butter.

② Vit A_2 :- It is present in fresh water fishes. Carotenoids are pigments found in green plants (carrot, spinach (leafy veg)), β carotene is the most important carotenoid.

1 ug of retinol = 3.3 IU of vit. A activity

(β carotene - Provitamin)

* Vitamin A stored in liver

- Vit A deficiency mainly in infants and children.

Functions of Vitamin

⇒ Vitamin A helps form and maintain healthy teeth, skeletal and soft tissue, mucus membrane, and skin.

⇒ It is also known as retinol because it produces the pigments in the retina of the eye.

⇒ Vit A promotes good eyesight, especially in low light.

⇒ Necessary for the maintenance of normal epithelium.

⇒ Necessary for reproduction. ⇒ Good for spermatogenesis and fetal development.

⇒ act as a anti-oxidant.

⇒ β caretene prevents heart attack.

⇒ Bone growth.

Deficiency symptoms :-

* Xerosis (dryness) of eye, Bitot spot, softening of cornea, night blindness.

* Dry and rough skin
papules
↓
tend
on th

(Hyperkeratinization)

↓

(disorder of the cells lining the inside of a hair follicle)

→ corneal opacities → eye problems can lead to scarr
or clouding of the
cornea.

⇒ unhealthy gastrointestinal mucosa
, diarrhoea.

⇒ ~~Sterilization~~ sterility due to faulty spermatogenesis, abortions, foetal malformations.

⇒ Growth retardation.

Therapeutic uses:-

Vitamin E (α-Tocopherol)

Functions ⇒ antioxidant, protecting unsaturated lipids in cell membrane

Deficiency :- RBC breakage, nerve damage, degenerative changes in spinal cords, haemolytic anemia.

Side effects :- impaired wound healing, abdominal cramps, loose motions and lethargy ⇒ feeling of being tired and not having any energy

Toxicity :- Interferes with blood-clotting drugs.

Food sources :- Vegetable, nut oils, seeds and nuts, wheat germ and whole grains.

Water soluble vitamins :-

Vitamin B :- Vitamin B_1 (Thiamine) (antiurine)
↓
contain pyrimidine and thiazol ring

Presence → rice polishing, pulses, nuts, green vegetables (yeast), egg and meat

* Pyrithiamine and oxythiamine are synthetic thiamine antagonists
* Tea (also contains a thiamine antagonist)

Deficiency symptoms:-

(Dry beri-beri) (Wet beriberi)

↓ ↓

neurological symtoms. — Polyneuritis with numbness, tingling muscular weakness

Cardiovascular System disease mainly affected — palpitation, Breathlessness, high output cardiac failure and ECG changes

Major functions :- Energy metabolism

* Vitamin B_2 (Riboflavin) - yellowish colour

Sources:- milk, egg, liver, green leafy vegetables, grains.

Major functions:- Energy metabolism

Deficiency:- Inflammation of the mouth, skin, vascularization of cornea.

* Vit B_3 (Niacin) { Nicotinic acid / Nicotinamide

Provitamin - Tryptophan

Sources — liver, fish, meat, cereal husk, nuts and pulses.

⇒ Energy metabolism.

Deficiency:- Pellagra.

Toxicity Niacin flush, liver damage, impaired glucose tolerance.

* Vitamin B_5 (Pantothenic acid)

Functions — Protein, fat and carbohydrate metabolism

D.C — Extremely rare

Toxicity - Mild intestinal distress.
Sources - ~~fo~~ avocadoes, broccoli, meats.

(Vit B6) — Pyridoxine, pyridoxal (pyridoxamine)

↓↓ functions
Protein and fat metabolism.

Deficiency.
Toxicity :- scaly dermatitis, anemia, convulsions.

Toxicity :- Nerve degeneration.

Source — Protein-rich foods
↓
liver, meat, egg, soybean vegetables and whole grain

Vitamin B7 (Biotin)

↓↓ function.
Protein, fat and carbohydrate metabolism, beneficial to hair, skin and nails.

Deficiency symptoms - alopecia, anorexia, muscular pain

Source:- Egg yolk, liver, peanuts, also produced by gut-bacteria

* (Vit B9) — folate, folic acid, folain

functions = Helps make DNA for new cells, activates B12

* Sources:- Egg yolk, liver, bean fortified grain products vegetables, legumes.

Toxicity - masks a B12 deficiency

Deficiency :- Anaemia, birth defects

* (Vit B12) — (Cobalamin)

↓ functions (cynocobalamin), (Methylcobalamin)

Helps make DNA for new cells, activates folate, protects nerve cells.

Deficiency:- Anemia, irreversible nerve damage and paralysis.

Sources:- Meat, fish, poultry, eggs, milk products.

Vitamin C (ascorbic acid)

↓ functions.

antioxidant, collagen synthesis, immune function.

Deficiency — Scurvy

Toxicity — Diarrhoea

Sources - fruits and vegetables (Citrus)

Fat soluble :-

* Vitamin D :- (Calciferol, CD_2)
(Cholecalciferol, CD_3)
(Calcitriol)

↓ functions

(Bone growth and maintenance, absorption of calcium)

Deficiency effects :- Rickets, Osteomalacia

Toxicity — Calcium imbalance

Sources :- Sunlight, fortified milk, fatty fish, eggs, liver

Vitamin K (Phylloquinone (1)
Phytonadione (K_1)
Mena-quinone (K_2)
Menadione (K_3)
Acetomenaphthone

↓ functions
Blood clotting
, bone health.

Deficiency symptoms :- Hemorrhage

Sources :- Dark leafy greens, cabbage family, liver

* NSAIDS

↳ NSAIDs are members of a drug class that reduce pain, ↓ses fever, prevents blood clots, ..

Classification of NSAIDS

(A) Non - selective COX inhibitors (traditi-onal NSAIDS)

1.) Salicylates :- Asprin

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

3) Fenamate :- Mephenamic acid

4) Enolic acid derivatives :- Piroxi
Tenoxicam.

5) Acetic acid derivatives: Ketorolac
Indometacin, Nabumetone

6) Pyrazolone derivatives :- Phenylbut
Oxyphenbutazone

B) Preferential COX-2 inhibitors

⇒ Nimesulide
⇒ Diclofenac
⇒ Aceclofenac
⇒ Meloxicam
⇒ Etodolac

C) Selective COX-2 inhibitors
Celecoxib, Etoricoxib, Parecoxib

D) Analgesic- antipyretics and
poore anti-inflammatory action

E) Paraaminophenol derivatives
⇒ Paracetamol (acetaminophen)

Salicylates

Aspirin:- also called acetylsalicylic acid, is a medication used to reduce pain fever, or inflammation.

Aspirin is used to treat include. Kawa disease, pericarditis, and rheumatic fever. Aspirin given shortly after a heart attack lowers the risk of death.

Plasma $t_{1/2}$ = 15-20 min

Route of administration by mouth, rec

Bioavailability — 80-100%
Protein binding — 80-90%
Metabolism — liver, gut wall

Elimination half-life - dose dependent

~~Excree~~
Excretion :- urine (80-100%)
sweat, saliva

crosses the BBB

Vasodilation → relaxation of smooth mu

Vasoconstriction — narrowing of blood vessels

Aspirin :- Pharmacological actions

① Weak analgesic, anti-inflammatory action (3-6g/day or 100 mg/kg/day).

② ·↑se in utilization of glucose. → ↓ Blood Sugar

③ Aspirin has no direct effect on heart or blood vessels in therapeutic dose

⇒ Large dose → ↑se cardiac output
↓
cause vasodilation

⇒ Toxic dose depends vasomotor centre
↓
BP may be fall

④ Aspirin irritate git. mucosa
↓
cause epigastric distress, nause and vomiting.

* Adverse effects of NSAIDs

⇒ ·gastric mucosal damage and peptic ulceration.

⇒ Hypersensitivity and idiosyncrasy

⇒ acute salicylate poisoning

Uses :- as analgesic

→ headache (mild migraine)
→ myalgia ⇒ muscle pain - mild to
→ joint pain
→ toothache
→ Neuralgias → pain that travels along the length of a nerve.

aspirin
⇒ as antipyretic ⇒ effective in feves

⇒ acute rheumatic fever :-

aspirin is first therapy. ~~in all cases~~

⇒ Rheumatoid arthritis :-

Aspirin - 3-5g/day

⇒ relief of pain, swelling and morning stiffness

⇒ Osteoarthritis

but paracetamol is the first choice analgesic.

⇒ Post my cardial infarction and post-stroke patients

6.) Propionic acid derivatives

Ibuprofen was the first member of this class to be introduced in 1969

ADR:- headache, dizziness, blurring of vision, tinnitus and depression.

→ cannot prescribed to pregnant women and should be avoided in peptic ulcer patient.

* Plasma proteins (90-99%)

Uses:- used as simple analgesic and antipyretic, widely used in rheumatoid arthritis, osteoarthritis

*Naproxen:- Strongest antiinflammatory activity ~~its strongest~~ and it is particularly potent in inhibiting leucocyte migration

also recommended for rehemutoid arthritis and ankylosing spondylitis (mostly affecting the spine and large joints)

→ regular use supress platelet function

Keloron Ketoprofen:— - inhibit LOx
same as Ibuprofen

Mephenamic acid:— inhibits synthesis of PGs. (Prostaglandin)

ADR:- Diarrhoea, skin rashes, dizziness, Haemolytic anaemia.

Pharmacokinetics:— Oral absorption — slow
Plasma $t_{1/2}$ ⇒ 2-4 hours.

Uses:- used as an analgesic in muscle, joint and soft tissue pain.
quite effective in dysmenorrhoea.

Keborolac:- arylacetic acid NSAID
has potent analgesic
↓
rapidly absorbed ← by oral and im admin
Plasma $t_{1/2}$ is 5-7 hours — ration

ADR:— Nausea, abdominal pain, dyspepsia, loose stools, headache, dizz
pruritus → uncomfortable, irritating sensation in the
↓ upper part of the body
indigestion (upper abdominal discomfort)

used in postoperative, dental and acute muculoskeletal pain. (oral, iv, im) ⇒ used in renal colic

renal colic
↓
{ intense pain caused by kidney dysfunction }

Diclofenac sodium

⇒ inhibits PG synthesis
⇒ well absorbed orally
Plasma protein — 99%
Plasma t1/2 — 2 hours
ADR:- mild epigastric pain, nausea, headache, dizziness, rashes.

Paracetamol

↓
active metabolite of phenacetin
1950
Given orally, Plasma t1/2 = 2-3 hours
- Oral dose - 3-5 hours.

Paracetamol Poisoning ⇒ acetylcysteine (NAC, Parvolex)
I.V injection, activated charcoal

Uses:-

Paracetamol is most commonly used over the counter drug, analgesic for headache, mild migraine, dysmenorrhea (↓ cramps and pelvic pain with menstruation, causes due to heavy flow, clots and endometriosis)

⇒ first choice analgesic for osteoarthritis, one of the best drugs to be used as antipyretic especially in children (no risk of Reye's syndrome)

Reye's syndrome

Encephalopathy + liver damage (Brain dysfunction)

used in pregnant women for breastfeeding

Topical NSAIDs:-

Diclofenac – Volini gel, 1% gel, Naproxen, Ketoprofen, Nimesulide, Piroxicam

* Antirheumatoid drugs

↓

those drugs which supress the rheumatoid process and retard disease progression

Rheumatoid authritis :- autoimmune disease in which there is joint inflammation, synovial proliferation and destruction of articular cartilage.

Classification :-

1.) Disease modifying antirheumatic drugs

(A) Nonbiological drugs

1.) Immunosuppressants :- Methotrexate Azathioprine, Cyclosporine.

2) Sulfasalazine

3) Chloroquine or Hydroxychloroquinine

4) leflunomide

B) Biological agent :-

1. TNF-α inhibitors :- Etanercept, Inf-mab, Adalimumab

2) IL-1 antagonist :- Anakinra

11) Adjuvant drugs

* Corticosteroids — Prednisolone and others.

* Methotrexate are contraindicated in pregnancy, breast-feeding, liver disease, leucopenia, peptic ulcer.

Drugs used in Gout (Normal plasma urate 2-6 mg/dl)

↓

metabolic disorder

↓

Characterized by hyperuricaemia

↓

When blood levels are high, it precipitates and deposits in joints, kidney

Drugs used in gout are:-

* For acute gout

NSAIDS, Colchicine, Corticosteroids

* For chronic hyperuricaemia

(a) Uricosurics — Probenecid, sulfinpyrazone

(b) Synthesis inhibitors:- Allopurinol, Febuxostat

Acute Gout:

↓

Severe inflammation in small joint due to precipitation of joint space. ↓ Joints becomes used. ↓ Painful :- require

① NSAIDS :-
naproxen, ibuprofen, etoricoxib.

② Colchicine :-
used in a gout, one of the oldest drug neither analgesic nor anti-inflammatory but specifically actions, gout inflammation.

Rheumatoid arthritis :-
Rapid absorption — orally
Metabolism — liver
Excreted — Bile

(there is no effect on blood uric acid levels.)

uric acid inhibit the production

uric acid crystals in the swollen, and external immediate. treatment strong NSAIDs eg. Indomethacin.

alkaloid form colchicum isolated in 1820

anti-inflammatory suppress

Toxicity:-

Nausea, vomiting, watery or bloody diarrhoea and abdominal cramps.

* accumulation of drug in intestine and inhibition of mitosis.

kidney damage, CNS depression due to muscular [illegible]

Overdoses:-

Intestinal bleeding, death due to respiratory failure.

paralysis and

Uses:-

It is used for acute gout. It is used only when due to high toxicity NSAIDs are ineffective. Intraarticular injection [illegible]

37 Corticosteroids:-

given for acute gout. Highly effective and produce nearly as rapid a response as colchicine.

Chronic Gout:- repeated episodes of pain and inflammation. more than one joint may be affected.

Probenecid:- highly lipid soluble organic acid derivative in 1951 to inhibit tubular secretion of penicillin

* Interactions :-

* Probenecid inhibits the urinary excretion of cephalosporins, sulfonamides In addition of penicillin

* It inhibits biliary excretion of rifampicin.

* Pyrazinamide and ethambutol interfere with uricosuric action of probenecid.

* Probenecid inhibits tubular secretion of nitrofurantoin.

* salicylates blocks uricosuric action of probenecid.

ADR :- Dispepsia, common side effect rashes and hypersensitivity phenomena are rare.

2. Sulfinpyrazone :- It is a pyrazolone derivative.

⇓

It inhibits tubular reabsorption of uric acid.

↓

It inhibits platelet aggregation.

Allopurinol :-

↓

used to decrease high blood uric acid levels.

↓

used to prevent gout, prevent specific type of kidney stones. and it can be taken by mouth or injected into vein.

(Enzyme responsible → Xanthine oxidase for uric acid)

Short acting $t_{1/2}$ - 2 hours.

* Competitive inhibitor of xanthine oxidase, but its major metabolite alloxanthine.

* 80% orally administration

Interactions :- Allopurinol inhibits the degradation of 6-mercapopurine and azathioprine.

* Probenecid given with allopurinol has complex interaction, while probenecid shortens $t_{1/2}$ of alloxanthine, allopurinol prolongs $t_{1/2}$ of probenoid

* Allopurinol has been reported incidence of skin rashes. when ampicillin is given to patients on allopurinol.

* Allopurinol can potentiate (increase the power, effect) azathioprine and theophylline by inhibiting their metabolism.

ADR:- Common - Gastric irritation (headache, nausea and dizziness

rare
Stevens-Johnson syndrome:- a rare, serious disorders of the skin and mucus membranes.

* Contraindicated in pregnancy and lactation.

* If patient suffering from kidney or liver disease. then allupurinol cannot given.

Uses:- Allopurinol is the first line drug therapy for chronic gout.

=> It can be used both over production and under excretors of uric acid.

Kala-azar: Allopurinol inhibits Leishmania by altering its purine metabolism.

Black fever

Febuxostat: - non-purine xanthine oxidase inhibitors, low the blood uric acid level, orally absorbed, highly plasma protein bound.

Plasma $t_{1/2}$ = ~ 6 hours

ADR:- liver damage

Side effects:- Diarrhoea, nausea and headache.

Contraindication:- It is contraindicated in patients being treated with azathioprin or mercaptopurine.

↓

immunosuppressive medication.

Histamine

(tissue amine)

almost present in animal tissues and plants

nitrogenous

It is an organic compound involved in local immune responses

regulating physiological function in the gut and acting as a neuro-transmitter for the brain, spinal cord, and uterus.

mostly present within storage granules of mast cells.

also present in blood, most body secretions, venoms and pathological fluids.

Play an important role in gastric acid secretion

maximally it present in lungs skin and GIT

Synthesis:- Storage and destruction

Histamine is β imidazolyethylamine.

* Synthesized locally from the amino acid histidine ↓

and degraded rapidally by oxidation and methylation.

* Increase in intracellular cAMP ↓ inhibit

histamine release

↓

can't take orally because liver degrades all histamine

Histamine receptors:-

* H_1 receptors:- ↑ Ca^{2+}

→ Smooth muscle contraction
→ Increased capillary permeability
→ Vasodilation
→ Sensory nerve endings pain and itching

H_2 receptors:- Adenylyl cyclase activation ⟵ cAMP↑

→ ↑gastric acid secretion ⟵ Phosphorylation of specific proteins.
→ Bloods vessels - dilation
→ ↑se capillary permeability

H_3 ~~ant~~ receptors:- (a) Restricting Ca^{2+} influx
(b) K^+ channel activation (c) cAMP↓

↓

→ ↓ histamine release
→ secretion
→ vasodilation.

Uses:- not used therapeutically but in the past it has been used to test acid secreting capacity of stomach, bronchial hyperreactivity in asthmatics, and flow cytometry of pheochromocytoma, but these pharmacological tests are rarely.

Side effects:- Dry mouth, Dizziness, nausea and vomiting, Blurred vision, Confusion

agonist of histamine

H_1 → 2-methylhistamine
H_2 → 4-methylhistamine
dimaprit
impromidine

H_3 — (R) α-methylhistamine
Imetit

Anti-histamine

↓

a drug that reduces or eliminates the effects mediated by chemical histamine.

Classification:-

1.) Highly sedative

→ Diphenhydramine (Benadryl)
→ Dimenhydrinate
→ Promethazine
→ Hydroxyzine

2.) Moderately sedative

Pheniramine
Cyproheptadine
Meclozine

→ cinnarizine

3.) Mild sedative

→ Chlorpheniramine
→ Dexchlorpheniramine
→ Triprolidine
→ Clemastine

4.) Second generation antihistamine

Fexofenadine, Loratadine, cetirizine Levocetirizine, Mizolastine, Rupata -dine, ebastine.

~~Dihydr~~ ~~D~~ diphenhydramine

* used to treat allergies.
→ used for insomnia, common cold remove in parkinsonism * orally
→ IV
→ SC are applied to the skin

Promethazine — first generation used to treat allergies, trouble sleeping, and nausea

Chlorpheniramine — used to treat runny nose, sneezing, itching and watery eyes caused by allergies or flu

* Fexofenadine — active metabolite of terfenadine

→ cannot cross BBB
→ does not produce sedation
$t_{1/2}$ — 11–16 hours
duration — 24 hours
of action.

* Cetirizine → active metabolite of hydroxyzine.

→ Levocetirizine — used for the treatment of allergic rhinitis and long term hives of unclear cause less sedating. taken by mouth. side effects ↓ sleepiness, dry mouth cough, vomiting.

used in scabies because itching will decrease during scabies

5 - Hydroxytryptamine

(antagonist and drug therapy of migraine)

monoamine neurotransmitter

5-HT - (Serotonin) → Chemical that has a variety of functions in the human body.

⇓

called as happy chemical, because it contributes to wellbeing and happiness.

⇓

mainly found in the brain, bowels, and blood platelets.

* 90% of body's content of 5-HT is localized in the intestines, also found in (wasp) and scorpion sting, and widly distributed in (invertebrates) and plants (banana, (pear), pineapple, tomato, stinging, cowhage.)

$C_{10}H_{12}N_2O$

(animals without a backbone or bone skeleton.)

Synthesis, storage and destruction

* 5-HT is β-aminoethyl-5-hydroxy-indole.
* Synthesized from the amino acid tryptophan and degraded primarily by MAO and small extent by aldehydrogenase.
* Stored within storage vesicles.
* VMAT-2 is inhibited by reserpine
  ↓
  which cause depletion of As
  as well as 5-HT
  ↓
  (Catecholamine)
* Secreted from the enterochromaffin cells.

Serotonin receptors:-

1) $5HT_1$ → Use cellular levels of cAMP.
   ⇒ Inhibitory

2) $5\text{-}HT_2$ → Use cellular levels of IP3 and DAG.

Excitatory

5-HT3 — Ligand-gated Na^+ and K^+ cation channel.

Mechanism — depolarizing plasma membrane

Excitatory

5-HT4 — ↑se cellular levels of cAMP

Excitatory.

5-HT5 — ↓sing cellular levels of cAMP → Inhibitory

5-HT6 — ↑sing cellular levels of cAMP. → Excitatory.

5-HT7 — ↑sing cellular levels of cAMP. Excitatory.

~~5HT3 — agonist :-~~

5HT3 — antagonist

↳ Cyproheptadine — (Periactin), is a first generation antihistamine, antiserotonergic, and local anesthetic properties.
used to relieves allergy symptoms ; watery eyes, runny nose, itching.

Side effects :- drowsiness, dry mouth, ataxia (Impaired balance (cannot due to damage to brain, nerves or muscles)

② Clozapine :- (Clozaril) an atypical antipsychotic medication. used for schizophrenia.

Side effects :- hypotension, fever, tachycardia, constipation weight gain, nausea

③ Ondasetron :- (Zofran) — is a medication. used to prevent nausea and vomiting caused by cancer chemotherapy, radiation therapy, or surgery.

Ergot alkaloids :- Ergot is fungus Claviceps purpurea

Ergotamine :- ergopeptine and part of the ergot family of alkaloids ; it is structurally and biochemically closely related to ergoline.

Drug therapy of migraine

Migraine :- Migraine is a mysterious disorder characterized by pulsating headache, restricted to one side, which comes in attacks lasting 4-28 hours and is often associated with nausea, vomiting, sensitivity to sound and light, flashes of light

Two types

- Migraine with aura
- Migraine without aura

Stages

- Prodrome → Duration 15 to 20 min
- Aura → 15-30 hours
- Head-ache → 4-72 hours
- Post-drome → 2 days

① Mild :- Simple analgesics / NSAIDs
↓
Paracetamol (325-1g)
aspirin — (300-600mg)
NSAIDs - Ibuprofen (400-600mg)
, naproxen, diclofenac (50mg
Antiemetics :- metoclopramide (10
oral / im)
domperidone (10 - 20mg)

② Moderate migraine :-

→ NSAIDs
→ ergot preparation or sumatriptan

③ Severe migraine :-
Ergot alkaloid, sumatriptan.

① Ergotamine → most effective ergot alkaloid for migraine.
* Oral route, 1 mg is given at half hours intervals.

② Selective · 5-HT1b/1d agonists.
Sumatriptan
Rabid oral absorption but 84% presystemic elimination

Bioavailability · Pg 154.

⇒ 25-100 mg

⇒ Intranasal spray 5-20mg

ADR:- fatigue, muscle weakness. sedation, vomiting, nausea

② Eletriptan ③ zolmitriptan
④ Naratriptan ⑤ frovatriptan
⑥ Rizatriptan

Newer triptan:- (Lasimiditan)
↓
selectively binds to the 5-HT$_{1F}$ receptor subtype.

Prophylaxis of migraine:-

① Antihypertensive drugs
(a) Beta blockers — Propranolol, nadolol, atenolol, metoprolol
(b) Ca^{2+} channel blockers — Flunarizine
(c) Clonidine
(d) Candesaktan

② Anticonvulsants:- Topiramate, valproate, gabapentin, zonisamide.

③ Antidepressants— amitriptyline, nortriptyline, venlafaxine.

Autocoids

autocoids are ↓biological factors which act like local hormone

Classification:-

① Amine derived:- Histamine, Serotonin
↓
Tryptophan

② Peptide derived:- Angiotension, Bradykinin

③ Lipid derivative:-
→ Prostaglandins, Leukotrienes, Interleu-kins, Platelet ~~activit~~ activating factor etc.

* Respiratory system drugs

* Drugs for cough and asthma

Cough :- protective reflux

↓

expulsion of respiratory secretions of foreign particles from airs passage

Demulcents and expectorants (mucokinetics)

↓ ↓

Sooth the throat and reduce afferent impulses

↓

neural impulse which travel from sensory organ and to the CNS.

a medicine which promotes the secretion of sputum by the airs passages, used to treat coughs.

↓

and also lubrica-ting the irritated respiratory tract.

① Pharyngeal demulcents :- Lozenges, cough drops, linctuses containing syrup, glycerine, liquorice.

2) Expectorants

(a) Bronchial secretion enhancers:-

→ Sodium or Potassium citrate.
→ Potassium Iodide
→ Guaifenesin,
→ Balsm of Tolu
→ Vasaka
→ Ammonium chloride

(b) Mucolytics:- Bromohexine, ambroxol, acetylcysteine, Carbocisteine.

Bromohexine:- A derivative of the alkaloid vasicine obtained from Adhatoda vasica (Vasaka), is a potent mucolytic and mucokinetic, induce bronchial secretion.

Side-effects:- rhinorrhoea and lacrimation, nausea, gastric irritation, hypersensitivity.

rhinorrhoea → it is a condition where the nasal cavity is filled with a significant amount of mucus fluid

Ambroxol :- metabolite of bromohexine having similar mucolytic action

Carbocisteine :- It liquifies viscid sputum
↓
contraindicated in peptic ulcer patients.

Side-effects :- gastric discomfort and rashes.

Anti-tussives :- a drug that suppresses coughing possibly by reducing the activity of the cough center in the brain.

⇓

used only for dry nonproductive cough

⇓

also called cough centre suppressants

Classifications

- Opoids
  - → Codeine
  - → Ethylmorphine
  - → Pholcodine
- Antihistamine
  - → Chlorpheniramine
  - Diphenhydramine
  - Promethazine
- Non opoids.
  - → Noscapine
  - → Dextromethorphan
  - → Clophedianol
- Peripherally acting
  - → Prenoxdiazine

1) Codeine :- centrally acting narcotic opioids a prodrug that is bioactivated by CYP2D6 into morphina in the liver

cough suppression — shows

* antitussive action is blocked by (naloxone).
* Side-effects :- Overdose related to respiratory depression and drowsiness
* Contraindicated in asthma patients

2) Ethylmorphine :- used for cough suppression.

3) Noscapine :- opium alkaloid of the benzoisoquinolone series

↓

depress cough, useful in spasmodic cough.

Side-effect :- Nausea, vomitting, Headache

* It release histamine and produce bronchoconstruction. in asthmatics.

4) Dextromethorphan :- Synthetic N-methyl (D- aspartate) receptor antagonist

* d- ... has antitussive action while l- isomer is analgesic.
* donnot depress mucociliary function

Side Effects:- drowsiness, nausea, drowsiness, high dose - hallucinations and ataxia.

Antihistamines:- relief in cough due to their sedative and anticholinergic actions. Have no expectorant property, they may reduce secretions by anticholinergic action.
Chlorpheniramine, Diphenhydramine, Promethazine.

Asthma:- It is a common chronic inflammatory disease of the airways characterized by variable and recurring symptoms, reversible airflow obstruction and bronchospasm.

Antiasthmatics:- used to treat asthma patients:-

Classifications:-

1) Broch

* Classification of antiasthmatics

1.) Bronchodilators

3- Sympathomimetics
- Salbutamol
- Terbutaline
- Salmeterol
- Ephedrine
- Formoterol

Anticholinergics
- Ipratropium bromide
- Tiotropium bromide

Methylxanthines
- Theophylline
- Aminophylline
- Hydroxyethyltheophylline
- Doxophylline

2.) Leukotriene antagonists
- Montelukast
- Zafirlukast

3.) Mast cell stabilizers
- Sodium cromoglycate
- Ketotifen

4.) Corticosteroids

(a) Systemic :- Hydrocortisone, Prednisolone

(b) Inhalational :- Beclomethasone dipropionate, Budesonide, Fluticasone propionate, Flunisolide

v) Anti-IgE antibody
(Omalizumab)

Bronchiodilators Action:

β-agonists

Stimulates β2-adrenergic receptors of bronchi

Anticholinergic drugs

reduce tonus of vagus

Smooth muscle relaxation

Inhibit Phosphodiesterase

Methylxanthines

* β-agonist are used for the treatment of asthma acute.

4. (Salbutamol) → Highly selective β-agonist with less cardiac side effects.

* Inhaled salbutamol produce bronchodilation within 5-min and the action lasts for 2-4 hours.
* used for acute asthmatic attack

Side-effect:- Palpitation, nervousness, throat irritation, and ankle edema.

Metabolism:- metabolism in gut, oral bioavailability is 50%.
→ Duration of action:- 4-6 hours.

→ ~~Terbutaline~~:-

Bambuterol:- Bicarbamate ester of prodrug of terbutaline
⇒ slowly hydrolysed in plasma and lung by pseudocholinesterase to release the active drug over 24 hours.
⇒ used in chronic bronchial asthma

Hypokalaemia :- low level of K+ in blood stream.

* Salmeterol :- First long acting selective β2 agonists with slow onset of action
* used for nocturnal asthma

Methylxanthines :- Theophylline and its derivative are most commonly used for COPD and asthma.

Theophylline :- Orally absorbed.
Plasma protein - 50%
Metabolism - liver
t 1/2 in adults - 7-12 hours.

ADR :- Headache, nervousness and nausea.
Rapid I.V injection causes precordial pain.

uses :- COPD and Apnoea in premature infant

* Theophylline decreases the effect of - phenytoin, lithium.

* Theophylline enhances the effect of - furosemide, sympathomimetics, digitalis, oral anticoagulants, lithium.

Anticholinergic:-

a) Ipratropium bromide is a short acting inhaled anticholinergic bronchodilator
duration — 4-6 hours

(b) Tiotropium bromide:- long acting (24 hours)

Leuckotriene antagonists:-

↓

inflammatory molecule, one of the several substance which are released by mast cells during asthma attack

↓

responsible for bronchoconstriction

block

Leukatriene are derived from arachidonic acid, the precursor of prostaglandins.

Montelukast- and Zafirlukast-

* Both have similar actions and clinical utility.

* competively antagonize cysLT1 receptor mediated bronchio-construction, airway mucus secretion, increased vascular permeability.

$t_{1/2}$ — 3-6 hours ↑ 8-12 hours

* Montelukast and zafirlukast are indicated for prophylactic therapy of mild to moderate asthma, as alternatives to inhaled glucocorti-coids
* Side-effects:- headache and rashes.

Mast cell stabilizers:-

(1) Sodium cromoglycate (cromolyn sodium)
synthetic chromone derivative
inhibits degranulation of mast cells
orally — cannot taken.
It can be administered as an aerosol through metered dose inhaler.
uses: Bronchial asthma, allergic rhinitis & allergic conjunctivitis

(2) Ketotifen:- anti-histaminic (H_1) with some cromoglycate like action;

↓ enhance the β adrenergic stimulated muscle response
these are not bronchodilators
↓
but will reduce bronchial hyperactivity

Hydrocortisone :- used for asthma and COPD

50mg i.v — 4 times a day for two days followed by low dose oral prednisone. Is as effective in resolving acute severe asthma as 200 - 500 mg of hydrocortisone.

Beclomethasone dipropionate :-
↓
* intranasal spray → effective in perennial rhinitis.

Budesonide :- nonhalogenated glucocorticoid with high topical inhalation administration

Side-effects :- nasal irritation, sneezing, itching of throat

Fluticasone propionate :- inhaled gluco-corticoid - high potency.

Inhalational dose — 100-250 µg BP (max 1000 µg/day.)

Flunisolide :- Topical steroid is available for prophylaxis and treatment of seasonal and perennial rhinitis

Anti-IgE antibody :-

* Omalizumab :- humanized monoclonal antibodies against IgE.

S.C — administered

* Choice of treatment :-

① mild - episodic asthma :- β-agonist ↓ less than once daily

② Seasonal asthma :- Regulers chromo-glycate / low dose inhaler steroid (200-400 micro mg/day)

③ Mild chronic asthma with occasional exacebration :- Symptoms once daily ⇒ inhaled steroid + chromoglycate

④ Moderate asthma → ~~500~~ - occurs daily. ↑ dose of inhaled steroid + β2 agonist (long-acting.

5) Severe asthma: Continous symptoms
Regular high dose of Inhaled steroid (2000 mg/day + long acting β_2 agonist twice daily

Hormones and related drugs.

Substance of intense biological activity that is produced by specific cells in the body.

Body functions	Major regular hormone
availability of fuel	Insulin, glucagon, Growth hormone
Metabolic rate	Tri iodo thyronine, thyroxine
Somatic growth	Growth hormone, insulin - like growth factors
Sex and reproduction	Gonadotropins, androgens, estrogens, Progestins
5.) Circulating volume	Aldosterone, antidiuretic hormone

6) Adaptation to stress — Gluco-corticoid adrenaline

7) Calcium balance — Parathormone ? calcitonin, Vit D.

Endocrine glands

1) Pituitary (Pineal gland — smallest endocrine gland in the human body)

(a) Anterior — Growth hormone, Prolac-tion, adrenocorticotropic hormone Thyroid stimulating hormone (TSH, Thyrotropin) Gonadotropins - FSH and Leutenizing hormone.

(b) Posterior:- Oxytocin, Anti diuretic hormone (ADH, vasopressin)

2) Thyroid (largest endocrine gland) - Thyroxine (T_4), Triiodothyronine (T_3), Calcitonin.

3) Parathyroid Parathormone. (PTH)

4) Pancreas — (Islet of Langerhans) Insulin, glucagon.

5) Adrenals:-

(a) Cortex glucocorticoids (Hydrocortisone) mineralocorticoids (Aldosterone) Sex steroids (dehydroepiandro-sterone)

(b) Medulla:- Adrenaline, Noradrenali-ne.

6.) Gonads :- Androgens (testosterone)
Estrogens (estradiol)
Progestins (Progesterone)

(Placenta also secretes many hormones)

Chorionic gonadotropin, estrogens. Placental (lactogen, Prolactin, Progesterone, chorionic thyrotropin.

largest gland :- liver
Smallest " :- Pineal gland.
largest internal organ :- liver 3.5 pounds (1.6 kg)
largest external " = skin
smallest internal organ — Pineal
longest bone — femur
largest artery - aorta
largest vein - inferior vena cava

Anterior pituitary hormones

↓

master glands.

↓

Secretion is controlled by hypothalamus

(GH) :- Somatotrophin :- 191 amino acid single chain, M.W - 22000

⇒ Promote growth of bones, brain and eye.

⇒ Promote retention of nitrogen, calcium, promote utilization of fat and spares carbohydrates.

GH Inhibitors :- Somatostatin (i.v)

, octreotide (i.v).

lanreotide - long-acting analogue of somatostatin. (i.m)

Prolaction :- (luteotropic, luteotropin)

↓

199 amino acid, MW - 23000

↓

Secretion of milk from

- lactation • Prolactin surge during labor

- essential for initiation of lactation.

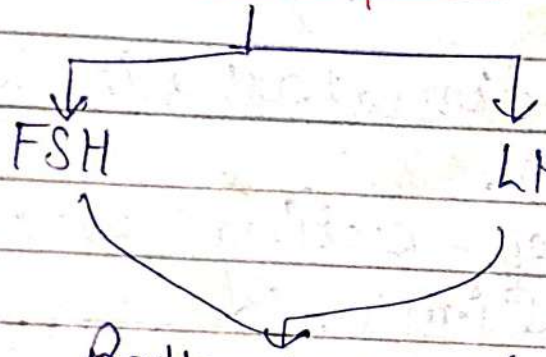
- Immune function • Stimulates

lymphocyte development
- Reproduction — Essential for rodents

* Prolactin
↓
Secretion is regulated by hypothalamus, i.e. dopamine
↓
produced by the hypothalamus.

* Prolactin Inhibitor
⇒ Bromocriptine, cabergoline
↓
new D2 agonist

Gonadotropins (Gns)



Both are glycoproteins containing 23–28% sugar and consist of two polypeptide chain

α- chain (92 AA) common LH, FSH
β- chain (111 AA), LH (121 AA)

⇒ FSH and LH act in concert to promote gametogenesis and secretion of gonadal hormones.

(Gonadotrophin inhibitors)

⇒ Nafarelin, Goserelin, Leuprolide, triptorelin.

Thyroid stimulating Hormone (TSH, Thyrotropin)

↓

210 amino acid, two chain glycoproteins (22% sugar), MW 30000

Functions:- TSH stimulates thyroid to synthesize and secrete thyroxine (T_4) and triiodothyronine (T_3). Its action are:-

⇒ Induces hyperplasia and hypertrophy of thyroid follicles and the blood supply to the gland.

↓

- Enlargement of an organ or tissue by an increase in the reproduction rate of its cells

↓

Use and growth of muscle cells.

(Adrenocorticotropic Hormone)

↓

39 amino acid single chain peptide.

MW – 4500

∴ Secreted by pituitary gland

↓

Stimulating the adrenal cortex

⇒ Regulate levels of the steroid

⇒ Regulate the activity of the cortex of the adrenal gland.

Uses :- ACTH is used primarily for the diagnosis of disorders of pituitary adrenal axis.

Thyroid hormones and thyroid inhibitors.

↓ secretes

↓ ↓ ↓

Thyroxine (T4) | Triiodothyronine (T3) | Calcitonin

Calcitonin produced by interfollicular 'C' cells. It is chemically

* Plasma t 1/2 → T4, (6-7 days) Plasma t 1/2 → T3 (1-2 days)

* Regulation:- controlled by anterior pituitary

used:- Thyroid inhibitors

these drugs lower the functional capacity of the hyperactive thyroid gland

Classification:- (Anti-thyroid)

1.) Inhibit hormone synthesis
* Propylthiouracil, Methimazole, Carbimazole

2.) Ionic inhibitors (inhibit iodide trapping)
Thiocyanates; Perchlorates (ClO_4), Nitrates (NO_3)

3.) Inhibit hormone release.
Iodine, Iodides of Na and K, Organic iodide

4) Destroy thyroid tissue
Radioactive Iodine. (^{131}I, ^{125}I, ^{123}I) (hyperthy-roidism)

Propylureacil used to treat hyperthy-roidism. Hyperthyroidism due to grave's disease and toxic multinod-lar goiter.

Vmp
radioiodine → used as first-line therapy for hyperthyroidism
Propylthiouracil → 2nd line

First line for Hypothyroidism
↓
Synthetic thyroid hormone
levothyroxine

* Toxic inhibitors:- are toxic and not clinically used
Thiocyanates — cause liver & kidney, bone marrow and brain toxicity.

Pericarditis — Produce rashes fever, aplastic anaemia.

* uses of Iodine and iodides

- Thyroid storm :- life-threatening health condition, during T.S. an individual heart rate, blood pressure, and body temperature can soar to dangerously high levels. (rise)

- Prophylaxis of endemic goitre
- Antiseptic — tincture iodine, povidone, iodine etc.

Radioisotope iodine :- stable isotope of iodine — ^{127}I.

^{131}I — physical half-life 8 days

uses :- Hyperthyroidism due to graves disease or toxic nodular goit

* β adrenergic blockers :- Propano have emerged as an important form of therapy to rapidly alleviate manifestations of thyr -otoxicosis, that are due to sympathetic overactivity.

Cyrare disease

↓

Basedow's disease.

↓

an immune system disorder of the butterfly shaped gland in the throat.

↓

mainly affect the thyroid gland

↓

radioactive iodine treatments and anthyroid drugs.

↓

But in some cases surgery is the best approach

Insulin :-

Hypoglycemia :- can also be caused by a problem with the pituitary or adrenal glands, the pancreas, the kidneys, or the liver.
↓
Because pituitary gland control the body's production of some of the hormones.

DM :- It is metabolic disorder characterized by hyperglycaemia, glycosuria, hyperlipidemia, -ve Ketonaemia, nitrogen balance
↓ excretion of glucose into the urine

↓
Presence of an abnormally high conc^n. of ketone bodies in the blood.

Type-I diabetes :- Juvenile disease
↓
a chronic condition in which the pancreas produce little or no insulin.
⇒ appear in adolescence.

→ destructions of β cell in pancreas
- HC islets.

1. Type :- NIDDM :- no loss or moderate reduction of β cell
↓ caused by
Both genetic and environmental factor

Insulin :- discovered by 1921
→ It obtained in pure crystalline form in 1926 and the chemically structure was fully worked out in 1956 by Sanger.

* Pancreas → Produces → digestive enzyme
↓
also produces insulin, ← also located in abdomen behind the stomach
↓
a hormone that helps regulate blood sugar levels.
↓
the cell that produce insulin are called β-cells.

of Langerhans.

Insulin C. two polypeptide chain

(Chain A 21) (Chain B 30 amino acid.) 51 amino acid

*A and B chain are held together by two disulfide bonds.

Preproinsulin — 110 AA from which 24 AAs. — are first removed to produce Proinsulin.

store in granules with C Peptide - 35 AA

assay :- Bioassayed by measuring blood sugar depression in rabbits

~~C + U reduces Blood glucose of the~~

Regulation :- secretion of insulin from β-cells is regulated by chemical, hormonal and neural mechanism.

hormonal → eg. GH, corticosteroids

Somatostatin → inhibits release of insulin as well as GH and glucagon.

GH inhibitors

action of Insulin:

↓ direct and indirect

on cells.

stimulates the uptake of glucose

↓

insulin decreases blood glucose concentration by inducing intake of glucose by the cells. Also insulin activates the enzymes.

↓

Phosphofructokinase and glycogen synthase. which are responsible for glycogen synthesis.

mechanism of action of insulin

Binding of insulin on α subunit

↓

Phosphorylation of β - subunit

↓

Phosphorylation of (IRs)

Insulin receptor substrate proteins

↓

Changes in

gene expression ← → Metabolism

↓

Growth

Fate of insulin: It is distributed only extracellularly. It is a peptide; gets degraded in the g.i.t if given orally.

Insulin is injected by

↓

Portal vein of from pancreas

(upper arms, abdomen, thighs lower back)

* Types of insulin preparations and insulin analogues:-

① Rapid acting:- (quickly act)

	Onset	Peak (hr)
Insulin lispro	0.2–03	1–1.5
Insulin aspart	0.2–0.3	1–1.5
Insulin glulisine	0.2–0.4	1–2

Duration (hr) 3-5

Can be mixed Regular, NPH

↓

isophane insulin

↓

3-5

↓

Regular NPH

↓

3-5

↓

Regular NPH

Short acting

→ Regular insulin — 0.5-1 — 2-3 — 6-8 — It Rep

→ Intermediate acting

Insulin zinc suspension 1-2 8-10 20-24 Re
of lente

~~In~~ NPH 1-2 8-10 20-24 Regu

Long acting

Insulin glargine 2-4 8-10 - 24 - Non
Insulin detemir 1-4 ~~8-10 24~~ 20-24 - N

Human Insulin

In the 1980, the human insuli
were produced by rDNA techn
-logy in E. coli

NPH (Isophane)

Insulin analogues:-

Insulin lispro Insulin glargine

Insulin aspart

⇒ used
, Hyperosmolar coma.

Newer Insulin delivery devices:-

⇒ Insulin syringes, Pen devices
, Inhaled insulin, insulin pumps
, Implantable pumps.

Oral Hypoglycaemic drugs

↓

lower the blood sugar level and are effective orally

Classification:-

A) Enhance Insulin secretion

1.) Sulfonylureas (KATP channel blocker)

↓ ↓

First generation | 2nd gen^n

Tolbutamide | Glibenclamide (Glyburide), Glipizide, Gliclazide, Glimepiride

↓

Type 2 diabetes

2.

2.) Meglitinide / phenylalanine analog
Repaglinide, Nateglinide

3.) Glucagon - like peptide - 1 (GLP-1) receptor agonists (injectable drug)
Exenatide, Liraglutide

4.) Dipeptidyl peptidase - 4 (DPP-4) inhibitors
Sitagliptin
Vildagliptin
Linagliptin.
Saxagliptin
Alogliptin

5.) Overcome Insulin resistance

Biguanide
(AMPK activator)
⇒ Metformin

Thiazolidine dione
(PPAR activator)
⇒ Pioglitazone

C. Miscellaneous antidiabetic drugs

1.) α-glucosidase inhibitors
Acarbose, Miglitol, Voglibose

2. Amylin analogue
Pramlintide

3. Dopamine D2 receptor agonist
Bromocriptine

4) Sodium-glucose cotransport-2 (SGLT-2) inhibitors
Dapagliflozine

Sulfonyl urea:- Basically used in type 2 diabetes; first generation tolbutamide is frequently used.

Mechanism of action:-
SUR1 receptors on pancreatic β cell membrane
Binding to receptors
⇓
Reduced conductance of ATP sensitive K+ channels
↳ Depolarization of membrane
⇓
Enhance Ca2+ influx
⇓
Degranulation of insulin vesicles.

* Tolbutamide :- 1st generation
K+ channel blockers.
⇓
used in type -2 diabetes.

* Stimulate the secretion of insulin
the pancreas.

Meglitinide / D- phenylalanine analogue
(KATP channel blockers
⇓
these are KATP channel blocke
⇓
quick short lasting insulin
-mic action.

Repaglinide :- invented in 1983.
⇓
oral medication used in addition
to diet and exercise for blood
sugar control in type 2 diabe
mellitus.
⇓
quickly absorbed

side effects :- mild headache
(dyspepsia, arthralgia
and weight gain.

→ type-2 DM, not used for disease patient.

Nateglinide:- D-phenylalanine derivative

↓

Stimulates the 1st phase insulin secretion by closing β cell K ATP channel

↓

result in fast onset and shorter lasting hypoglycaemia than repaglinide.

↓

Side-effect - dizziness and nausea

symptoms - joint pain

↓

used as type 2 DM → to control post prandial rise in blood glucose.

* **Glucagon-like peptide-1 (GLP-1) receptor agonists**

GLP-1 is an important incretin released from the gut in response to ingested glucose.

↓

Use insulin release from pancreatic β cells.

inhibit glucagon release from
K cells, slow gastric emptying
and supresses. appetite by
activating specific GLP-1 receptor

* They are not clinically used because
of rapid degradation by the enzyme
dipeptidase-4 (DPP-4)

Exenatide :- Synthetic DPP-4 resistant
analogue.
Plasma t1/2 is ~3 hours

Side effect :- nausea and vomiting

Uses :- lowering of postprandial
as well as fasting blood glucose

Liraglutide :- recently developed
GLP-1 agonist.

(DPP-4) Dipeptidyl peptidase-4
inhibitors.

⇓

oral diabetic drugs

⇓

also called
gliptins

they are usually prescribed
for people with type 2 diabetes
⇓
of metformin and sulphonylureas
cannot respond.
(Januvia)

Sitagliptin :- First DPP-4 inhibitors introduced in USA in 2006.
⇓
used to treat type-2- diabetes mellitus.
⇓
metabolised in liver
side effect :- upset stomach, stomach pain, URI
⇓
Prevent Kidney damage, blindness, nerve problems, loss of limbs.

Vildagliptin :- 2nd DPP-4 inhibitors longer duration of action - (12-24

Biguanide :- (AMPK activator)
Phenformin and metformin
↓
Introduced in 1950 s.

Phenformin is banned in India since 2003, because of higher risk of lactic acidosis.

Metformin:- Glucophage

first-line medication for the treatment of type 2 diabetes

also used in the treatment of polycystic ovary syndrome.

Side effects:- Nausea, vomiting, stomach, metallic taste in mouth.

MOA:- It uses hepatic glucose production

use intestinal absorption of glucose, and improve insulin sensitivity by increasing peripheral glucose uptake and utilization.

Pioglitazone (Actos)

Currently available.

Rosiglitazone was banned in India since 2010 due to ↑ycardial infarction, ↑CHF, stroke and death.

PPAR-γ → Peroxisome proliferator-activated receptor-γ → expressed in fat cells

↓

used to treat type-2 diabetes.

↓

used with combination of metformin, SU and insulin.

MOA :- Also stimulates the nuclear receptors PPAR-δ and PPAR-α

↓

modulates the transcription of the genes involved in the control of glucose and lipid metabolism in the muscle, adipose tissue, and the liver.

Banned June 2013 due to lack of evidence used

(Glucagon)

Peptide hormone ⇒ produced by α-c of the pane of the pancreas

nd its ⇓ works to raise th
main catabolic concentration of glu
hormone of the and fatty acids in th
body. blood stream

⇓

Single chain polypeptide containing 29 amino acids, MW – 3500

MOA:- Glucagon through its own receptor and coupling G Protein activates adenylyl cyclase

⇓

↑se cAMP in liver, fat ce heart

inactive orally ⊗, t½ – 3-6 min.

Uses:- Hypoglycaemia

Dose – 0.5–1.0 mg iv, or im.

→ Cardiogenic shock

Corticosteroids

adrenal cortex secretes steroidal hormones which have glucocorticoid, mineralocorticoid and weakly androgenic activity

↓↓

lowers inflammation in the body

↓↓

~~allow~~ also used to treat disease like: asthma, ~~a~~rthritis

Glucocorticoid:- ~~used at~~ It is composed from its role in regulation of glucose metabolism.

↓↓

Synthesis in adrenal cortex

use:- adrenal insufficiency, allergic, autoimmune disorders (- asthma, organ transplant

gluco-corticoid actions:-

- carbohydrate and protein metabolism
- Fat metabolism, calcium metabolism

Relative activity of systemic corticosteroids

Glucocorticoids :- ① Cortisol (hydrocortisone)

act rapidly

But short duration of action

used Replacement therapy - 20mg morning + 10mg afternoon orally.

shock, acute adrenal insufficiency - 100 mg i.v bolus.

② Prednisolone :- 4 times more potent than hydrocortisone.

used allergic, inflammatory, autimmune disease

orally, i.m., intraarticular, also topically.

③ Methylprednisolone :- Slightly more potent & more selective than Prednisolone ; 4 - 32 mg/day oral.

Methylprednisolone acetate has been used as a retention enema in ulcerative colitis.

Triamcinolone 1-32 mg/day oral, 5-40 mg im. & intra articular

Dexamethasone:- used for inflammatory and allergic condition orally 0.5-5 mg/day oral. for shock, cerebral edema 4-20 mg/day used as typically

Betamethasone:- Similar to dexamethasone 0.5-5 mg/day oral.

2) Deflazacort (Newer steroid)

Fludrocortisone, Desoxycorticosterone (DOCA) Aldosterone.

↓

(Mineralocorticoids)

Uses:- Replacement therapy

↓ acute adrenal insufficiency

↓ addison disease

↓ adrenal glands donot produce enough hormones.

↓ Adrenogenital

adrenogenital syndrome

↓

a group of genetic condition limiting [illegible] produce [illegible] glands

Androgens and drugs for erectile dysfunction

male sex hormone.

are substances which cause development of secondary sex characters.

Natural androgens:- Testosterone

- 95 part of which is converted in extra-glandular tissue to more active dihydro-testosterone.

5-12 mg daily

Androsterone - metabolite of testosterone; 1/10 of the activity of testosterone.

Synthetic androgens:-

Methyltestosterone and fluoxymesterone are 17-alkyl substituted derivatives of testosterone which are orally active

Regulation:- Testosterone is secreted by the interstitial (Leydig) cells of the testes under the influence of pulsatile secretion of LH from pituitary.

Testosterone is inactive orally.

↓

i.m. injection.

Plasma $t_{1/2}$ - 10-20 min.

Transdermal androgen:- Recent delivery of androgen across skin.

* Fix combinations of testosterone with yohimbine, strychine and vitamins are banned in India.

Side-effects:- Virilization, acne, salt retention and edema, Hepatic carcinoma.

Uses:- Testicular failure, AIDS related muscle wasting, aging

Anabolic steroids:- synthetic androgens, higher anabolic and lower androgenic activity

Drugs :- Nandrolone, Oxymetholone, stanozolol and methandienone.

Side effects :- jaundice and worsen lipid profile.

Uses :- catabolic states, Osteoporosis, to enhance physical ability in athletes.

Anti- androgens

Danazol, Cyproterone acetate, Flutamide, Bicalutamide.

5-α reductase inhibitors :-

Finasteride, Dutasteride.

Drugs for erectile dysfunction

↓

inability of men to attain and maintain an erect penis with sufficient rigidity to allow sexual intercourse.

Sildenafil :-

marked in USA in 1998 and 2 years later in India for treatment of erectile dysfunction.

Orally active,

oral bioavailability — ~40%

t1/2 in men — < 65 yr - 4 hairs.

ADR :- vasodilation — headache, nasal congestion, dizziness, facial flushing

Use in BP, loose motions.

Tadalafil :- more potent and cogener of Sildenafil t1/2 18 hours. duration 24-36 hours.

side effects :- ~~vasod~~ same as sildenafil

- Vardenafil
- PDE1

Estrogens, Progestins and contraceptives

(female sex hormones)

development and regulation of the female reproductive system.

Natural estrogens :- estradiol is the major estrogen secreted by ovary, estrone, estriol.

Synthetic estrogens :-

Steroidal	Non-steroidal
⇒ ethinylestradiol	⇒ Diethylstilbestrol
⇒ Mestranol	⇒ Hexestrol
⇒ Tibolone	⇒ Dienestrol

Regulation of secretion

Synthesis and secretion of estrogens is stimulated by follicle-stimulating hormone.

↓

controlled by the hypothalamic gondatropin releasing hormone.

Uses :- used as contraceptive and hormone replacement therapy in postmenopausal women

used for Hormone Replacement therapy, used for treatment of postmenopausal osteoporosis and endometriosis.

(Antiestrogens and (selective estrogen receptor modulators)

Clomiphene citrate
Tamoxifen citrate

Binds to both estrogen receptors α and ERβ

and act as a pure estrogen antagonist

used in: In vitro fertilization

also used in men (oligozoospermia)

chemically related to clomiphene

used for treatment of albright syndrome

used to prevent breast cancer in women

⇒ Tamoxifen citrate
⇒ Raloxifene

2nd drugline therapy for treatment of osteoporosis in postmenopausal women.

he use in men

* Aromatase

⇓ They are used in the treat of breast cancer.

x Letrozole :- orally active nonsteroi Compound that reversibly inh aromatization.

⇓

100% oral bioavailability

$t_{1/2}$ = ~40 hours.

⇒ Letrozole is a fine line drug f adjuvant therapy after mastecto in ER+ive postmenopausal wome ADR:- Hot flushes, nausea, diar , dyspepsia and thinning of hai

Anastrozole :- more potent tha letrozole and suitable for s daily dosing, used as breast ca palliation of advanced cases i postmenopausal women.

Side effects :- Hot flashes, hea , trouble, sleeping, dizzines , stomach upset, constipa , less of appetite.

first line therapy for breast cancer in postmenopausal women.
dose: 1mg OD (tablet).

Exemestane:- Sold under the brand name aromasin. Is a medication used to treat breast cancer.
side effect - Vaginal bleeding, fatigue, nausea, Hot flashes, insomnia.

Progestins:- A synthetic form of progesterone that is similar to the hormone produced naturally by the body.

Natural Progestins:- Progesterone, a 21C-steroid, is the natural progestins and it is derived from cholesterol.
not orally, i.m. inj.

↓

Secreted by corpus luteum in the later half of menstrual cycle

Synthetic progestins:- Synthetic progestins with high oral activity.

1) Progesterone derivatives:-
- Medroxyprogesterone acetate.
- Megesterol acetate, Dydrogesterone
- Hydroxyprogesterone caproate
- Nomegestrol acetate

2.) Norethisterone derivatives

Oldest

⇒ Norethindrone
⇒ Lynestrenol
⇒ Ally lestrenol
⇒ Levonorgestrel (Gonanes)

⇓

Weak estrogenic, androgenic, anabolic and potent antiovulatory action.

Newest (Estranes)

⇒ Desogestrel
⇒ Norgestimate
⇒ Gestodene

⇓

very potent progestins, antiovulatory action, little estrogenic, androgenic properties.

⇒ Preferable in women with hyperandrogenemia

3.) Norprogesterone derivative

⇒ Nomegestrol

⇓

weak antiandrogenic property, less antiovulatory, strong antiestrogenic effect on endometrium.

A:- Desogestrel and Norgestimate are progestins.

* $t_{1/2}$ — 5-7 min, degradation occurs in the liver

ADR:- Breast engorgement, headache, rise in the body temperature, oedema, irregular bleeding.

uses:- Dysfunctional uterine bleeding, as contraceptive, endometriosis, Hormone replacement therapy, premenstrual syndrome/tension, endometrial carcinoma.

Antiprogestin:-

Mifepristone:- 19-norsteroid with potent antiprogestational and significant anti-glucocorticoid, antiandrogenic activity.

⇓

also called as RU-486.

⇓

typically used in combination with misoprostol to bring about an abortion during pregnancy.

⇓

also effective in the 2nd trimester of pregnancy.

* Interaction with CYP3A4 inhibitors (erythromycin, Ketoconazole) and inducers (rifampin, anticonvulsants) has been reported.

Uses:- Termination of pregnancy, cervial ripening, Postcoital contra-ceptive, Cushing syndrome

↓

condition that occurs from exposure to high cortisol levels for a long time.

↓

mostly use of steroid drug

Mifepristal:- It is a selective progesterone receptor modulator used for the purposes of emergency contraception and the treatment of uterine fibroids

absorption = 60-90 minutes.

Side effects:- Headache, nausea, vomiting, abdominal pain and menstruation delay.

Hormonal contraceptives:-

Birth control methods that act on the endocrine system.

Female contraception:-

⇓

With these drugs ~~[illegible]~~, fertility can be suppressed.

Types of methods:

① Combined pill:-
Contains an estrogen and a progestin in fixed dose.

① Norgestrel (0.3mg) + Ethinyl estradiol (30ug) + ~~[illegible]~~
② Norgestrel (0.5mg) + Ethinyl estradiol (50ug)
③ Levonorgestrel (0.25mg) + ethinyl " (30ug)
④ " (0.15mg) + (30ug)
⑤ " (0.1mg) + " 20ug
⑥ Desogestrel (0.15mg + " (30ug)
⑦ " (0.15mg) + " 20ug)
⑧ third generation pills containing newer progestins like desogestrel 1990s.

② Phased pills:-
Triphasic regimens have been introduced to permit reduction in total steroid dose.

Levonorgestrel 50-75-120ug. Ethinylestradiol 30-40-30ug

⑨ Now ethindrone
0.5 – 0.75
– 1.0 mg

Ethinylestra...
35
– 35 µg

③ Postcoital Pills:-

① Levonorgestrel + Ethinylestradiol (0.25 mg)

④ Mini Pills:-

① Nor ethindrone
② Norgestrel
— efficacy is ↓.

* Injectable:- highly effective, over 50 million women have used.

(a) Depot medroxyprogesterone acetate (DMPA) 150 mg at 3 month intervals. i.m. injection peak blood levels are reached in 3 weeks and decline with a t½ of ~ 50 days.

(b) Nor ethindrone enanthate mg at 2 – month intervals.

1 ml vial
↓
i.m inj^n

* Not suitable for adolescent girls and lactating mothers.

Implants:- drug delivery systems implanted under the skin.

Norplant / → 6 capsules each containing 36mg levonorgestrel. for S.C. implantation is available.

Progestasert 52mg of levonorgestrel

ADR:- Nausea, vomiting, weight gain, acne, chloasma.

Serious → leg vein thrombosis and pulmonary embolism, rise in BP, genital carcinoma, Gallstones.

Contraindicated:- Cerebrovascular disease; moderate to severe hypertension; hyperlipidaemia.

Ormeloxifene:- (Centchroma)
↓ Brand name - Sahe
selective estrogen receptor modulators (SERM)
↓
act on the estrogen receptor
↓
Best known as a nonsteroidal oral contraceptive.
↓
Potent anti-cancer activities in breast, head and neck

*Antara (fenofibrate) → used to high cholesterol and high triglyceride levels.

Male contraceptive:-

These are the drugs which supress - spermatogenesis.

⇒ antiandrogens, estrogens and progestins, androgens, cytotoxic drugs

↓

cadmium, nitrofurazone

Oxytocin

Secreted by the posterior lobe of the pituitary gland.

↓

Pea-sized structure at base of the brain

Uterine stimulants (uterotonics)

are medications given to cause a women's uterus to contract

↓

or to increase the frequency and intensity of the contractions

Classifications of Uterine stimulants (Oxytocics, Abortifacients)

1. Posterior pituitary hormone
   Oxytocin, Desamino Oxytocin
2. Ergot alkaloids :- Ergometrine, methylergometrine.
3. Prostaglandins :- PGE_2, $PGF_{2\alpha}$, 15-methyl $PGF_{2\alpha}$, Misoprostol.
4. Miscellaneous :- Ethacridine, Quinine.

(Oxytocin :-) → nonpeptide.

↓

Secreted by the posterior pituitary (ADH → vasopressin)

→ Pituitary along ~~with vasopressin~~ extract was first used in labour in 1909.

→ contraction of the womb (uterus) during childbirth and lactation.

→ Oxytocin stimulate the uterine muscle to contract and also increase production of prostaglandins, which increase the contraction further

Physiological role :-

① Labour - ② Milk ejection reflex
③ Neurotransmission.

* inactive orally, by im or iv. route
Plasma $t_{1/2}$ — 6-12 min.

Use: Induction of labour
① Uterine inertia
② Breast engorgement
-ADR: rupture of uterus

* Ergometrine, methylergometrine

⇒ increase force, frequency and duration of uterine contractions.
⇒ E, M weaker than constrictors
⇒ In GIT, High dose can use peristalsis.

Plasm $t_{1/2}$ — 1-2 h

ADR :- Nausea, vomiting and rise in BP

Uses :-
control post partum haemorrhage. 0.2-0.3 mg i.m.

Prognosis for variant angina.

Prostaglandins:

PGE2, PGF2α and 15-methyl PGF2α are potent especially for the later part of pregnancy (and cause softening of cervix.

Ethacridine:

Which injection is given for labour pain
⇒ epidural (lower back) and a plastic tube is placed through which drug are released which hormone makes you go into labour
⇒ Oxytocin

What are the 3 hormones that bring on labour
⇒ Oxytocin, β-endorphins, epinephrine and norepinepherne (the hormone excitement), Prolactin

How much pain can a person take
45 Del Cunits — normal human
57 Del (units) — at a child birth
unit of pain — dolaceimeter

(Uterine relaxants)

(Tocolytics)

⇓

drugs which use

⇓

used to delay or postpo labour.

* Drug relaxes the uterus — Terbuta

⇒ arrest abortion.

⇒ Dysmenorrhoea.

Premature labour is done only if cervical dilation is <4cm.

Classification

1) Adrenergic agonist:-

⇒ Ritodrine

⇒ β2 selective agonist

⇒ Supress premature labour and delay delivery.

⇒ use 50 µg/min i.v infusion

Side effects:-

- Cardiovascular
- metabolic
- complication.
- anxiety

Calcium channel blockers:- Reduce the tone of myometrium and oppose contraction.

Having smooth muscle relaxant action.

Postponed labour. Dose — 10mg oral every 2 to 30 min.

Magnesium sulfate:

Control convulsions and reduce BP in toxaemia of pregnancy.

5% IV infused

first line drug for prevention and treatment of seizures in pre-eclampsia and eclampsia.

Oxytocin antagonist:- → Peptide analogue of oxytocin act as antagonist at receptor.

Atosiban → not approved in India and USA.

↓

supress premature uterine contraction and postpone preterm delivery

Miscellaneous drugs:- Ethyl alcohol, nitrates, progesterone, PGI's synthesis.

→ Halothane is an efficacious ~~uterine~~ relaxant that have been used as the anaesthetic ~~when external use~~

Drug affecting Calcium Balance

Calcium:- Total body Ca^+ = 1 - 1.5 kg

99% in bones and teeth, 1% in body fluids and tissue.

Sources:- Milk and ~~dairy~~ dairy products Egg yolk, fish, G.L.V., beans.

Cow milk 100 mg/100ml
Human " - 30 mg/100 ml

Daily allowance:-

Adults - 500 mg/day
Children - 1200 mg/day
Pregnancy and Lactation - 1500 mg/day

Absorption:- First part and 2nd part of duodenum.

Plasma calcium level:-

Regulated by 3 hormones.
① Parathormone. ② Calcitonin and calcitriol.

Normal plasma calcium ⇒ 9-11 mg/dl

function:-
① Mineralization of Bones (mineralized connective tissue) and teeth
② Coagulation of Blood
③ Activation of enzymes.
④ Secretion of hormones.
⇒ Calcium mediates secretion of Insulin, Parathyroid hormone, calcitonin, vasopressin.
⇒ Heart functioning, GIT

Side eff ⇒

uses:- Tetany (involuntary contraction of muscles.), as dietary supplement, osteoporosis — (bone become weak and brittle.)

① (Parathyroid Hormone) Parathormone
↓
84 amino acid Polypeptide

Secretion of PTH is regulated by plasm Ca++ concentration through CaSR.
Plasma t1/2 = 2-5min.

⇒ Action :- ↑se reabsorption of Ca and Bone.
⇒ Kidney :- ↑se. Ca+ reabsorption in the distal tabule
⇒ Hypoparathyroidism :- low plasma Ca+ level
* Hyperparathyroidism :- due to parathy - roid. tumor
Bone Symptoms
. Bone pain, muscle weekness, long bone fractures, Kidney stone.
Treatment :- Cinacalcet (Sensipar)
↓
Block the level of PTH

* In hypoparathyroidism ~~consist~~ the vit D and calcium is to be given.

uses:- not used in hypoparathyroidism because plasma calcium can be elevated.

Teriparatide :- form of parathyroid hormone. → Consisting of 1st 34 amino acid
↓
which is the bioactive portion of the hormone.
↓
effective anabolic agent used in the treatment of some form of osteoporosis.
↓
used speed fracture healing.
(forsteo, terisone, forteo)
⇒ Subcutaneous — once daily.
~~600 mcg / 2.4 ml~~
⇒ It is secreted by the PTH.
⇒ (PTH 1-34) → recombinant Technology
⇒ only agents which stimulates bone formation
S.C. ⇒ inject Plasma t 1/2 = 1 hr
contraindicated in Hypercalcaemia :-
↓
Too much Ca2+ in the blood
Pagets disease.
↓
disrupts the replacement of old bone with new bone

Calcitonin → Hypocalcaemic hormone

discovered by Copp in 1962.

32 amino acid single chain Polypeptide (MW 3600)

Produced by parafollicular 'C' cells of thyroid gland.

mainly in Humans, animals

reduce blood calcium, opposing the effects of PTH

mainly found in fish, reptiles, birds and mamals.

Calcitonin ↑ → sign of thyroid cancer

Normal calcitonin level — 10pg/ml. (men having higher.)

⇒ inhibit bone resorption. by direct action of osteoclasts.

Prep^n and unitage :- Salmon Calcitonin more potent and longer acting

1 IU = 4 µg

* Calsynar, Zy.calcit : Synthetic salmon calt 100 IU/ml amp for i.m or S.C. inj

Uses :- Hypercalcaemic states

* For emergency treatment of Hypercalcaemia 5-10 IU/kg may be diluted in 500ml saline and infused i.v over 6 hours.

(cephallic vein is basically used)

IV infusion :- used for fluid volume replacement, to correct electrolyte imbalances, to deliver medications, and for blood transfusion

IV catheter may feel painful.

② Postmenopausal osteoporosis — i.m, s.c calcitonin, Nasal spray formulation 200 IU per actuation.

⇒ Mia Calcin Nasal SPRAY

⇒ Osto spray 2200 IU MDI. (metered dose inhaler)

⇒ Calcinase 200 IU / actuation

3.) Paget's disease - 100 IU i.m./s.c.
4.) Diagnosis of medullary carcinoma of thyroid.

Vitamin D

⇓

Synthesized in Human body and found in foods activated by UV radiation.

D_3 :- Cholecalciferol :- Synthesized in the skin under the influence of UV rays.

D_2 :- Calciferol :- ~~synthesized~~ present in irradiated food - yeasts, fungi, bread, milk.

Deficiency of vit D = Rickets

~~Activation of vit D :-~~

Vit D is ~~consdi~~ considered a hormone because it synthesize in body (skin).

Actions :- ↑se absorption of Ca^{2+} and phosphate from intestine.

osteoporosis, rickets, ↓ Deficiency

↓ bone becomes weak and brittle.

↓ disorders caused by a lack of vit D, Ca^{2+} and Phosphate.

↓↓

leading to softening and weakening of bones.

Hypervitaminosis D

↓↓

you take much vit D.

⇒ High level of Ca^{+} in the blood.

Vit D absorbed from the intestines in the presence of bile salts.

$t'_{1/2}$ = 1-1'8 days

Fanconi syndrome.

↓↓

disorders of kidney tubule function

↓↓

that results in excess amounts of glucose, bicarbonate, uric acid, K^{+} and Amino acid

Fanconi anemia:- mainly affect bone marrow

Interactions:- Cholestyramine and chronic uses of liquid paraffine can reduce vit D absorption.

⇒ Phenytoin and phenobarbitone reduce the calcitriol.

Bisphosphonates:- analogues of pyrophosphate. ⇓ inhibit bone reabsorption and have recently attracted considerable attention

Classification:-

⇒ Ist generation BPNs
- ⇒ Etidronate
- ⇒ Tiludronate

⇒ II gen^{n} BPNs
- Pamidronate
- Alendronate
- Ibandronate

⇒ III generation BPNs
- Risedronate
- zoledronate.

Uses:- Osteoporosis ⇒ 2nd and third gen^{n} BPN (eg. alendronate, risedronate)

② Paget's disease:- II and III gen^{n}

③ Hypercalcaemia of malignancy
Pamidronate (60-90 mg i.v. over 2-4 hours) zoledronate (4mg i.v over 15 min).

other drugs for osteoporosis

=> Strontium ranelate. 75mg. patients

=> Denosumab - monoclonal antibody

Drug acting on peripheral somatic nervous system.

Skeletal muscle relaxants.

are these drugs that act peripherally at neuromuscular junction

to reduce a muscle tone.

=> give with anaesthetic

to provide muscle relaxation during surgery.

=> Centrally acting muscle relaxants are used mainly for painful muscle spasm and spastic neurological conditions.

* Peripherally acting muscle relaxants

(I) Neuromuscular blocking agents

A) Nondepolarizing (Competitive) blockers

1) Long-acting
   - ⇒ d-Tubocurarine
   - ⇒ Doxacurium
   - ⇒ Pancuronium
   - ⇒ Pipecuronium.

2) Intermediate acting :- Vecuronium, atracurium, Cisatracurium, Rocuronium, rapacuronium

3) Short-acting :- Mivacurium.

B) Depolarizing blockers :-

- ⇒ Succinylcholine (Suxamethonium)
- ⇒ Decamethonium (C-10).
  + not used clinically.

(II) Directly acting agents

Dantrolene sodium
Quinine

Curare :- Plant extracts used by south America tribals as arrow poison. Natural sources of curare, are strychnos toxifera. Italy 1930s

1) d- Tubocurarine:-

histamine releasing, ganglion blocking and CVS actions.

⇓

d-TC can't used

⇒ use of neuromuscular blockers as adjuvants to general anesthesia

⇒ N.M.B.A are not given orally, i.v, i.m, admin is available.

⇒ Muscle weakness is the side effect ⇒ depends upon dose limiting.

* Centrally acting muscle relaxants:-

⇓

which reduce skeletal muscle tone by a selective action of Central spinal axis.

Classification:-

(i) Mephenesin congeners

Mephenesin
Carisoprodol
Chlorzoxazone
Chlormezanone

(i) Methocarbamol
(ii) Benzodiazepines Diazepam and others
(iii) GABA mimetic Baclofen, Thiocolchi-cosides
(iv) Central α agonist Tizanidine

Carisoprodol :- sedative activity ratio and weak analgesic, antipyretic and anticholinergic.
↓
used in musculoskeletal disorders.

Methocarbamol :- less sedative and used for orthopedic procedures and tetanus.
limitation.
Gastric ~~acid~~ and sedation are most important side effects

Baclofen :- analogue of inhibitory transmitter GABA.
orally

Thiocolchicosides :- related to the colchicine

NSAIDS + T ⇒ used for painful muscle spasms such as torticollis sprains.

uses:- acute muscle spasm, Torticollis, lumbago, backache, neuralgia, anxiety and tension, spastic neurological diseases, tetanus, electroconvulsive therapy, orthopedic manipulations.

Local anaesthetics

These are those drugs which upon topical application or local injection.

Classification:-

a) Injectable anaesthetic

⇒ Low potency, short duration
Procaine
Chloroprocaine

⇒ Intermediate potency and duration
Lidocaine (Lignocaine)
Prilocaine

⇒ High potency, long duration
Amethocaine (Tetracaine)
Bupivacaine
Ropivacaine
Dibucaine (Cinchocaine)

b) Surface anaesthetic

Soluble
Cocaine
Lidocaine

Insoluble
Benzocaine
Orethazaine

(I. drugs)

(Bedamben)
(I. drugs)

* Mepivacaine, Etidocaine, Prilocaine, Dyclonine, Propanocaine are other local anaesthetics, used in some countries

* Some other drugs Propanolol, chlorpromazine, H_1-antihistamines, quinidine

↓↓

Significant activity, but are not used for pain this purpose because of local irritancy

* LA's weak bases with amphiphilic property

ester linked LAs - Cocaine, procaine, chloroprocaine, tetracaine, benzocaine

Amide-linked LAs:- Lidocaine, bupivacaine, dibucaine, prilocaine, ropivacaine

ADR:- Systemic toxicity due to rapid i.v. injection, CNS effects are - dizziness - CVS toxicity

* Often methylparaben added as preservative in certain LA solutions is responsible for the allergic action.

Precautions and Interactions:-

* Before injecting the LA, aspirate lightly to avoid intravascular injection.

* Propranolol may reduce metabolism of lidocaine and other amide LA, by reducing hepatic blood flow.

* Vasoconstrictor (adrenaline) containing LA should be avoided for patients with ischaemic heart disease, cardiac arrhythmia.

Cocaine:- Natural alkaloid from the leaves of erthroxylon coca.

↓

rapidally absorbed from buccal mucous membrane. (1884)

↓

Trade names - Neurocaine

↓

administered by mouth, insufflated Nasal spray.

⇒ used.
⇒ Donot given by injection.

Lidocaine (Lignocaine):- (Xylocaine.)

Introduced in 1948, mostly used in LA.

Injected around a nerve it blocks conduction within 3 min.

used as nerve block, epidural, spinal and i.v regional block

⇒ used to treat ventricular tachycardia and to perform nerve blocks.

Duration of action : 10 min to 20min (IV.)

Transdermal patch of lidocaine

⇓

fore skin to relief burning pain

⇓

due to postherpetic neuralgia

Prilocaine:- It is similar to lidocaine but does not cause vasodilation. ⇒ one of its metabolites cause ⇒ methaemoglobinaemia. used as infiltration, nerve block and i.v regional anaesthesia

Eutectic lidocaine / prilocaine

two sodi solid are mixed

↓↓

25°c → resulting oil is emulsified into water

↓

to form a cream.

Lemlox 5% cream

Amethocaine :- Highly lipid soluble PABA ester, more potent and more toxic; donot used in eye, nose, throat, used as a ointment and powder free soln

useful in vaginal delivery.

Bupivacaine :- A potent and long acting amide linked LA; used for infiltration, nerve block, epidural and spinal anaesthesia injected epidurally.

Epidural anaesthesia with 0.75% bupivacaine during labour.

Ropivacaine :- Bupivacaine congener

Cinchocaine / Dibucaine :- most potent long acting LA.

low the eye, has little anaesthetic
Produces corneal anaesthesia. potency.

Benzocaine and butylaminobenzoate
↓
Produce long acting anaesthesia
↓
they are used as lozenges for
stomatitis, sore throat, etc as a
ointment on wounds, used as piles.

Uses and techniques of local anaes-
-thesia:- ① surface anaesthesia
Produced by topical application of a
surface anaesthetic to mucous
membranes and abraded skin.
Lidocaine: (10%) sprayed in the throa-
-t acts in 2-5 min and produces
anaesthesia for 30-45 min.

Infiltration anaesthesia:- Diluted
soln of LA is infiltered under
the skin in the area of opera-
-tion → block nerve endings.
Lidocaine = 30-60 min. & bupivacaine
-90-180 min. Infiltration is used
for minor operations eg.
incisions, excisions, herniorrhaphy

3.) Conduction block:
LA is injected around nerve trunks
↓
area to be anaesthesised and paralysed.

Lidocaine (1-2%) - short duration
Bupivacaine — long acting

4.) Spinal anaesthesia: the LA is injected in the subarachnoid space btw (L2-3) or (L3-4.) vie below the lower end of spinal cord.

⇒ used for operations on the lower limbs, pelvis, lower abdomen. eg. fracture setting.

Complication of spinal anaesthia: —
* Respiratory paralysis, Hypotension
, Headache, Cauda equina syndrome
, septic meningitis, nausea and vomiting.

5.) Epidural anaesthesia: The spinal dural space is filled with semiliquid fat through which nerve roots.

(ii) the midthoracic region.
(iii) Lumbar :- epidural space.

(iv) Caudal :- Injection is given in the sacral canal through the sacral hiatus. - procedures anaesthesia of pelvic and perineal region. most used in vaginal delivery, anorectal Lidocaine (1-2 %) and bupivacaine (0.25 - 0.5 %)

If we add adrenaline prolong the action.

6) Intravenous regional anaesthesia (Intravascular infiltration anaesthesia) ⇒ injection of LA in a vein of a tourniquet occluded limb. Lidocaine i.v. under pressure.

General anaesthetics

are drugs which produce reversible loss of all sensation and consciousness.

Cardinal features of general anaesthesia :-

- Loss of all sensation
- Sleep and amnesia
- Immobility and musele relaxation
- Abolition of somatic and autonomic reflexes.

Mechanism of general anaesthesia

a wide variety of chemical agents produce general anaesthesia.

GA action had been related to some common physicochemical property of drugs.

Minimal alveolar concentration (MAC)

is the lowest concentration of the anaesthetic in pulmonary alveoli needed to produce immobility in response to a painful stimulus.

in 50% of cases. The MAC of a number of GAs shows excellent correlation with their oil/gas partition coefficient

Stages of analgesia - (1) 2

- Starts from beginning of anaesthetic inhalation and lasts up to loss of consciousness.
- Pain is progressively abolished.
- Patient remains conscious, can hear and see, and feels a dream like state.
- Reflexes and respiration normal.
- Some minor operation carried out, limited to short procedures.

(1) (2) Stage of excitement

(3) Surgical anaesthesia
extends from onset of regular respiration to cessation of spontaneous breathing

(4) Stage of medullary paralysis.
cessation of breathing leading to failure of circulation and death

Techniques of inhalation of anaesthe-tics:-

- Open drop method
- through anaesthetic machines.

Classification:-

1) Inhalational
   - Gas
     - Nitrous oxide
   - Volatile liquids
     - Ether, Halothane, Isoflurane, desflurane, sevoflurane

2) Intravenous
   - Fast acting drugs
     - Thiopentone sodium
     - Methohexitone sod.
     - Propofol
     - Etomidate.
   - Slower acting drugs
     - ① Benzodiazepines
       - ⇒ Diazepam
       - ⇒ Lorazepam
       - ⇒ Midazolam
     - ② Dissociative anaesthesia.
       - Ketamine
     - ③ Opioid analgesia
       - ⇒ Fentanyl

① Nitrous oxide weak general anesthetic and not generally used. 70% N_2O conc^n + 30% oxygen ; more potent general ; analo anesthetic agents

→ as a sole agent, N_2O (50%) has been used with O_2 for dental and obstetric analgesia, nontoxic to liver, kidney and brain..

⇒ It can be quickly removed from the body by lungs.

② Halothane :- (fluothane) ⇒ ~~It is~~ potent anaesthetic.

For induction = 2-4%

maintenance = 0.5-1% is delivered by the use of a special vaporizer.

* supression of cough :- dilate the bronchi. ⇒ they preferred for asthmatics.

* During labour can prolong delivery and the postpartal blood loss.

* Halothane is popular anaesthetic
→ Cheap and nonirritant, noninflammable, pleasant, rapid action
→ toxicity is less.

Intravenous anaesthetics:-

Fast acting drugs

Produce loss of consciousness in one arm — brain circulation time. (~ 11 sec.)

Sedative- Hypnotics

Sedative:- slow the brain activity

also called tranquilizers are depressants, sedatives have a calming effect and ~~can also~~ without inducing sleep

Hypnotics:- commonly known as sleeping pills, to induce sleep and to be used in the treatment of insomnia, are surgical anaesthesia

Classification

Barbiturates :-

Long acting
⇒ Phenobarbitone

Short acting.
⇒ Butobarbitone
⇒ Pentobarbitone

Ultra short acting
⇒ Thiopentone
⇒ Methohexitone

Benzodiazepines :-

Hypnotic	Antianxiety
⇒ Diazepam	"
⇒ Flurazepam	Chlordiazepoxide
⇒ Nitrazepam	Oxazepam
⇒ Alprazolam	Lorazepam
⇒ Temazepam	Alprazolam
⇒ Triazolam.	

Anticonvulsant :- Diazepam, Lorazepam
Clonazepam, Clobazam.

3.) Newer nonbenzodiazepine hypnotics.

Zopiclone Zolpidem Zaleplon

(Paraldehyde, & chloral hydrate)

Benzodiazepine antagonist

(Flumazenil) :- BZD analogue which has little intrinsic activity.

⇒ given to the patient with i.e.v. injection.

⇒ used as reverse BZD anaesthesia.

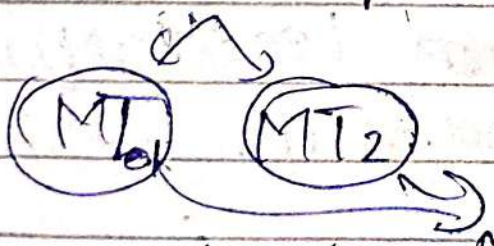
⇒ BZD overdose

⇒

Melatonin :- principle hormone of the pineal gland which is secreted at night ↓

important role in entraining the sleep - wakefulness cycle with the circadian rhythm.

Two receptors



found in brain.

⇒ used to induce sleep (take orally)

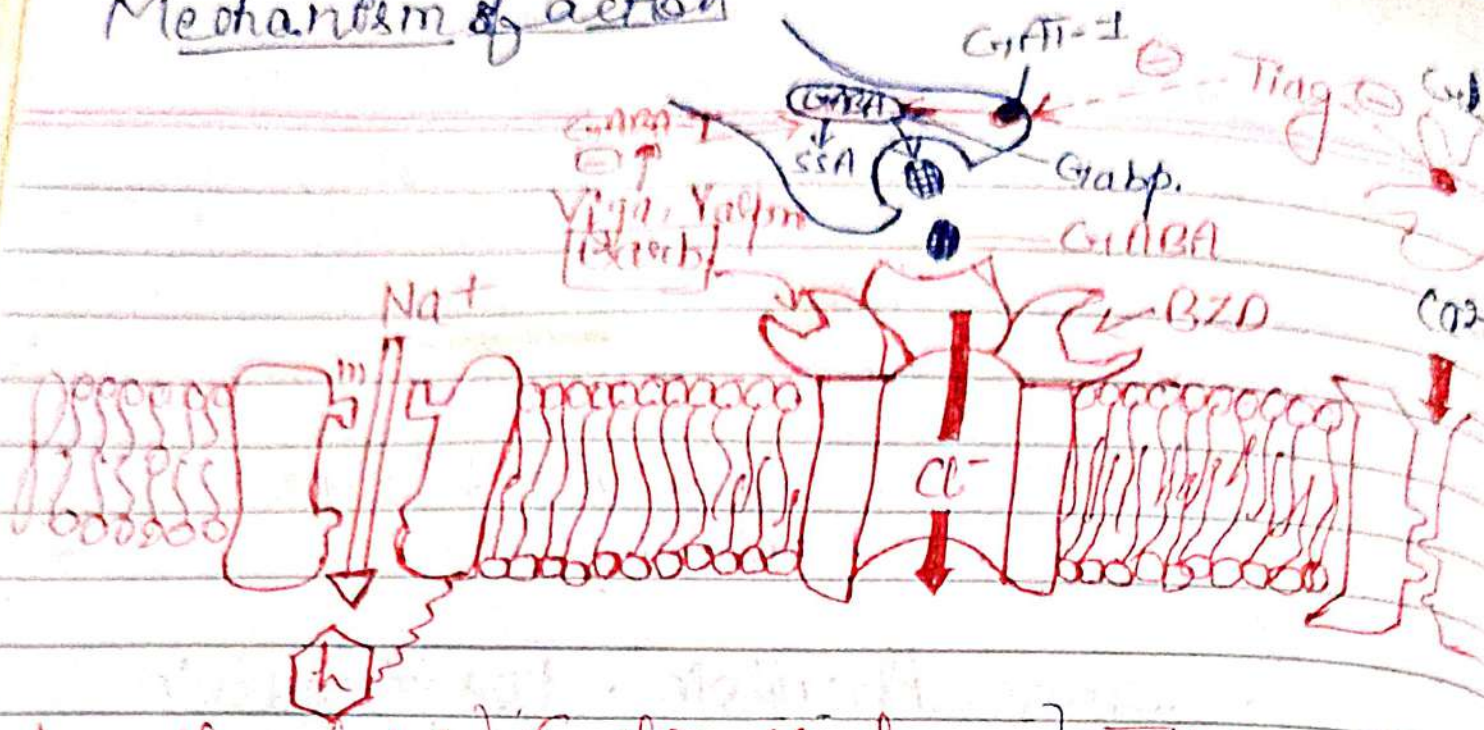
Antiepileptic drugs :-

These are the drugs which are used to treatment of epilepsy. (disorders of CNS)

Classification :-

1) Barbiturate :- Phenobarbitone
2) Deoxy-barbiturate :- Primidone
3) Hydantoin :- Phenytoin, Fosphenytoin
4) Imino-stilbene :- Carbamazepine
   Oxcarbazepine
5) Succinimide :- Ethosuximide
6) Aliphatic carboxylic acid :- Valproic acid
   (Sodium valproate)
   , Divalproex
7) Benzodiazepines :- Clonazepam, diazepam, Lorazepam, clobazepam
8) Phenyltriazine :- Lamotrigine, ~~gaba~~
9) cyclic GABA :- ~~gaba~~pentin, Pregabalin
   analogues
10) Newer drugs :- Topiramate
    zonisamide, levetiracetam
    Tigabine, Vigabatrin, Tiagabetrin
    Lacosamide

Mechanism of action



Prolongation of Na^+ channel inactivation.	Facilitation of Gaba. mediated Cl^- channel opening	Inhibition of T type Ca^{2+} current
⇒ Phenytoin	Barbiturate	Ethosuximide
Carbamazepine	BZD	Valproate
Valproate	Vigabatrin	Zonisamide
Lamotrigine	Valproate	
Topiramate	Gabapentin	
Zonisamide	Tiagabine	
Lacosamide		

Phenobarbitone:-

⇒ 1. First efficacious drug introduced in 1912.

2. Cheap and less toxic antiepileptic

It has broad spectrum efficacy in generalized tonic-clonic, simple partial and complex partial seizures

⇒ Phenobarbitone sodium may be injected (i.m. or i.v.)

(not effective in absence seizures)

* Phenytoin (Diphenylhydantoin)

Synthesized in 1908 as a barbiturate analogue.

Action:- action is given by blocking the axonal Na channel that gives membrane stabilizing action.

ADR:- Gum hypertrophy, hirsutism (acne in girls), megaloblastic anaemia; osteomalacia

* Tetrogenic effect as hydantoin syndrome, synaptic cleft, hare lip.

Fall in BP and arrhythmia in only IV

Interactions

* Phenobarbitone competitively inhibits phenytoin metabolism.
* Carbamazepine and phenytoin induce each other's metabolism.
* Valproate displaces protein bound phenytoin and ↓s its metabolism
* Chloramphenicol, isoniazid, cimetidine and warfarin inhibit phenytoin metabolism - can ppte its toxicity
* Phenytoin competitively inhibits warfarin metabolism.
* Sucralfate binds phenytoin in g.i.tract and ↓s its absorption.

Uses:- Phenytoin is a first line antiepileptic drug, overdose cause to produce neurotoxicity.

Fosphenytoin:- Prodrug of phenytoin

Phenytoin cannot be injected in a drip of glucose or

Because it get applied.) fosphenytoin can be injected with both saline and glucose.

Carbamazepine:- Chemically related to imipramine, it was introduced in the 1960-s for trigeminal neuralgia. first line antiepilepic neuralgia drug.

Carbamazepine exerts a lithium like therapeutic effects in mania and bipolar mood disorder used as antidiuretic action.

ARRs:- Sedation, dizziness, vertigo ataxia.

Interactions:- As an enzyme inducer; can reduce efficacy of haloperidol, oral contraceptives, lamotrigine, valproate and topiramate.

∴ Metabolism of carbamazepine is induced by phenobarbitone, phenytoin.

Carbamazepine is not useful in diabetic, traumatic and other form of neuropathic pain.

Valproic acid (sodium valproate)

It is a branched chain aliphatic carboxylic acid with a broad spectrum anticonvulsant action.

side effects of valproate: used during pregnancy, it has produced spina bifida and other neural tube defects

used:- drug of choice for absence seizures.

Interactions:-

- Valproate increases plasma level of phenobarbitone and lamotrigine by inhibiting their metabolism
- It displaces phenytoin from protein binding site and decreases its metabolism → Phenytoin toxicity
- Valproate inhibits hydrolysis of active epoxide metabolite of carbamazepine

Lorazepam:- 0.1mg/kg injected iv.

Gabapentin — lipophilic GABA derivative crosses to the brain
first line drug therapy

Choice of antiseizures drugs

Type of seizure	Ist choice drugs	Second line drug	Add on drug
Generalised tonic-clonic simple partial with or without generalization	Carbamazepine, Phenytoin	Valproate, Phenobarbitone	Lamotrigine, Gabapentin, topiramate, primidone, Levetiracetam.
② Complex partial with or without generalization.	Carbamazepine, Valproate, Phenytoin.	Gabapentin, Lamotrigine, Levetiracetam	Clobazam, Clonazepam
③ Absence	Valproate.	Ethosuximide, Lamotrigine	Clobazam, clonazepam
④ Myoclonic	Valproate	Clonazepam, Lamotrigine	Levetiracetam, Lamotrigine
⑤ Atonic	Valproate	Clobazam, Topiramate	Clonazepam
⑥ Febrile convulsion	Diazepam (rectal)	Clonazepam, clobazam	Lamotrigine
⑦ Status epilepticus	Lorazepam (i.v.), Diazepam (i.v.)	Fosphenytoin, Phenobarbitone	Gen. anaesthetics

Phenobarbitone - 80-120
Phenytoin - 12-36
Carbamazepine - 10-40
Ethosuximide - 30-50
Valproate - 10-15
Clonazepam - 20-40

(Antiparkinsonian Drugs)

Parkinsonism :- It is an extrapyramidal motor disorder characterized by rigidity, tremors and hypokinesia.

(PD) Parkinson's disease is a progressive degenerative disorder, mostly affecting older people, first discovered by James Parkinson in 1817.

The most consistent lesion in PD is degeneration of neurones in the substantia nigra pars compacta (SN-PC) and nigrostriatal tract results in deficiency of dopamine in the striatum which controls muscle tone and movements.

Belladonna alkaloids had been especially used in PD.

Classification :-

i) Drugs affecting brain dopaminergic system

(a) Dopamine precursor : Levodopa (L-dopa)

(b) Peripheral decarboxylase inhibitors - Carbidopa, Benserazide

(c) Dopaminergic agonist :- Bromocriptine, Ropinirole, Pramipexole.

(d) MAO-B inhibitor: Selegiline, Rasagiline

(e) COMT - inhibitors - Entacapone, Tolcapone

(f) glutamate (NMDA receptor) antagonist (Dopamine facilitatory): Amantadine

ii) Drugs affecting brain cholinergic system

(a) Central anticholinergic : Trihexyphenidyl (Benzhexol), Procyclidine, Biperiden.

(b) Antihistaminics :- Orphenadrine, Promethazine.

Levodopa :- class of medications called CNS agents. It works by being converted to dopamine in the brain.

=> Levodopa + Carbidopa are used to treatment of parkinson's disease.

side effect :- Dizziness, lightheadedness, nausea, vomiting, Loss of appetite, trouble sleeping.

* First line drug therapy for parkinsons is Levodopa

* absorb in small intestines

* (After prolonged therapy)

1) abnormal movements, (face, tongue thrusting)
2) Behavioural effects
3) fluctuation in motor performance

Peripheral decarboxylase inhibitor

carbidopa and benserazide

Lodosyn is a drug given to people with parkinson's disease in order to inhibit peripheral metabolism of levodopa.

Carbidopa inhibits aromatic-L-amino-acid-decarboxylase, an enzyme important in the biosynthesis of L-tryptophan to serotonin and in the biosynthesis of L-DOPA to dopamine.

side-effects:- uncontrolled muscle movements in face., worsening of tremors, severe nausea, vomiting, depression, suicidal thoughts.

[levodopa + carbidopa] => Co-careldopa

Dopaminergic agonists:-

(act with striatal DA receptors.)

Bromocriptine:- ergot derivative which acts as potent agonist on D2,
oral dose ÷ Bromocriptine
side effects:- vomiting, hallucinations, hypotension.
largely replaced by the newer DA agonists ropinirole and pramipexole.

Ropinirole and pramipexole:- nonergoline selective D2/D3 receptor agonists,
* side-effects similar to bromocriptine
* now frequently used as monotherapy in early PD.

absorbed orally, 40% plasma protein bound, $t_{1/2} = 6$ hours, longer du..., fewer hallucina... than Levodopa.

side effects — nausea, dizziness.

[Ropinirole is FDA approved for use in restless leg syndrome.]

Pramipexole:- Twice as potent as ropinirole and comparable in efficacy and tolera-bility.

Restless legs syndrome:- Peculiar sensory motor disorder affecting the legs during periods of relaxation, especially sle...

MAO-B inhibitors:-

Selegiline (Deprenyl)

It is selective and irreversible MAO-B inhibitor.

The isoenzyme forms of MAO,

↓ MAO-B → Selegiline
↓ MAO-A

→ Both are adrenergic structures and intestinal mucosa.

Higher doses can produce hypertensive interactions with levodopa

Metabolism ⇒ intestines and liver

Half life ⇒ 1.2 - 2 hours

It were used in tremor (↓ involuntary movement of muscle), muscle stiffness & difficulty to movements

used with combination of (levodopa and carbidopa)

Rasagiline:- irreversible inhibitor of monoamine oxidase-B used as a monotherapy to treat symptoms of PD

metabolism = liver

Azilect (rasagiline) — increasing the levels of certain chemicals in the brain. sometimes the used with other medicine (levodopa)

COMT inhibitors

are a class of me
-cations. that doctor
used in combination with
levodopa, to treat the motor
symptoms of parkinson's disease.
(catechol - O - methyl transferase) (COMT
that break down levodopa, to extend the
time of levodopa activity.

COMT inhibitors:- blocking the action of
(Tolcapone and entacapone)

Glutamate (NMDA receptors) antagonist

Amantadine:- Brand name- Gocovri.
medication used to treat dyskinesia
associated with parkinsonism and influenza
caused by type A influenza viruses.
* acts rapidly but less efficacy than
levodopa; subdues motor fluctuations and
abnormal movements.

100 mg - BD in day.

side effects - wakefulness, confu
, night mares anti'ohelines

Central neurologics

Trihexyphenidyl:- It is most commonly used drug. It is an antiparkinsonian agent of the antimuscarinic class, used as medical for decades. Trihexyphenidyl alters unusual nerve impulses and relaxes stiff muscles.

Side effect - dry mouth, blurred vision, dizziness, nausea.

* Drugs used in mental illness

Antipsychotic and antimanic drugs that controlling

Antimanic drug - any drug stabilizes mood by the symptoms of abnormal psychological state of excitement.

Antipsychotic sedative also known as neuroleptics, are a class of medication primarily used to manage psychoses (including delusions, hallucinations, paranoia or disordered thought).

* Lithium used for excitement and mania

Tranquilizers
a drug which reduces mental tension and produces calmness without inducing sleep or depressing mental faculties.

Antipsychotic drugs (Neuroleptics)

Classification:-

1) Phenothiazines
Aliphatic side chain:- Chlorpromazine, Triflupromazine
Piperidine side chain:- Thioridazine
Piperazine side chain:- Trifluoperazine, Fluphenazine

2) Butyrophenones:-
Trifluoperazine, Haloperidol
Penfluridol
Fluspenthixol
Pimozide
Lorapine

3) Thioxanthenes:-

Other heterocyclics:-

4)

High potency piperazine side chain phenothiazines.
↓
decanoate given as a depot i.m injection.

* II generation antipsychotics
Clozapine :- first atypical antipsychotic
metabolized by CYP1A2, CYP2C19
* High dose can induce seizures even in nonepileptics.
- Clozapine is used as a reserve drug in refractory schizophrenia.

Risperidone :- Brand name Risperdal. used to treat schizophrenia, bipolar disorder.

Schizophrenia :- a disorder that affects a person's ability to think, feel and behave clearly
* serious mental disorder in which people interpret reality abnormally.

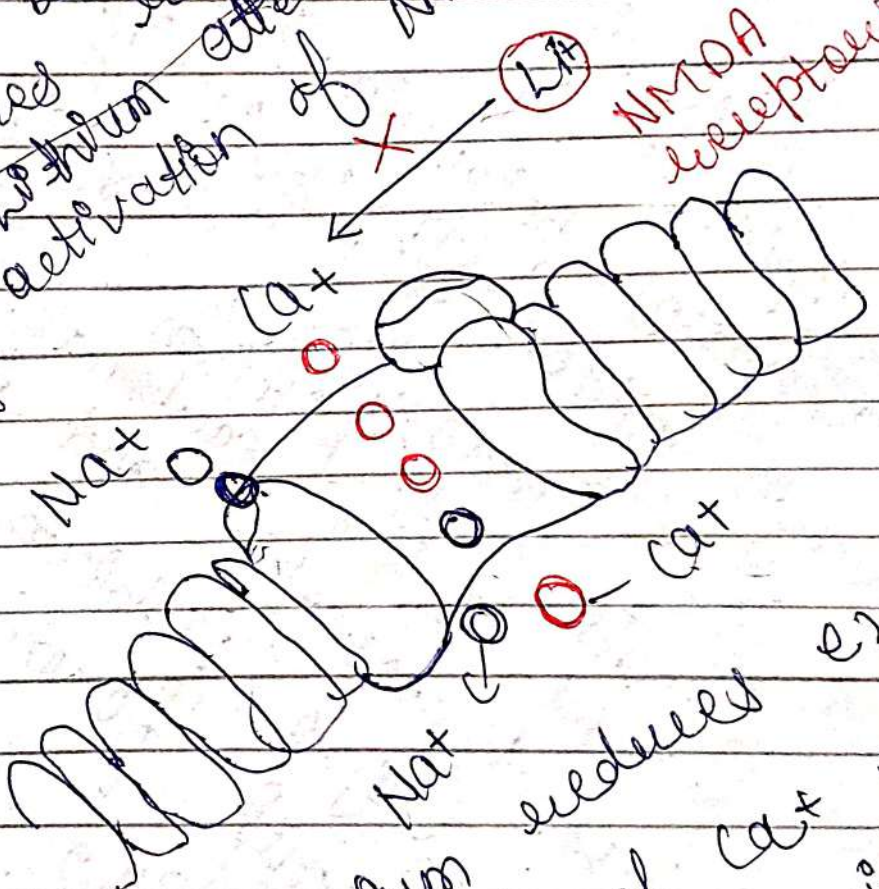
Anti-manic and stabilizing drugs (Drugs for bipolar disorders).

Drugs used for bipolar disorders.

Lithium carbonate:

It is an anti-manic agent used to treat manic depressive disorders, used to treat manic episodes, cluster headache. It smoothes out the depression. In bipolar disorder, patients by lessening the balance of neurotransmitters sometimes referred to as mood, it stabilizes the brain chemicals. Lithium alternates calcium influx after activation of NMDA receptor

MOA:-



Lithium reduces excitatory modulation of Ca^+ entry and via inhibition of calpain pathway which is a protease that play a role in apoptosis.

* MF:- Li_2CO_3
* Element of the alkali metal group
* Extended release tablet contains 300mg of Li_2CO_3
* For acute mania:- 1800mg/day
Morning 3 tablets - Night time 3 tabs (300mg)
* Long-term control:- 1200mg/day

Indications:- Lithium carbonate extended-release tablets USP is indicated in the treatment of manic episodes of Bipolar disorder.

ADR:- Tremors, polyuria → excessive passage of urine.

No specific antidote for poisoning

Interactions:- Tetracyclines, NSAIDs and ACE inhibitors can also cause lithium retention.

Uses:- It is used as its carbonate salt because this is less hygroscopic and less gastric irritant than lithium citrate i.e. Li_2CO_3.

Lithium formulations used as syrup.

→ acute mania, prophylaxis in bipolar disorder.

Alternative to lithium:-

① Sodium valproate which is used in Ist treatment of acute mania in faster. High dose valproate acts and lithium. Then lithium. Combination of Naval prak

② Carbamazepine :- ③ Lamotrigine. ④ Atypical antipsychotics. ⇒ Olanzapine, risperidone, aripiprazole, quetiapine, with or without BZD.

→ It are used first line for acute mania.

(Hallucinogens.) to control the drugs which these are thought and perception alter mood, behaviour, to in manner similar to the psychosis.

1) Indole amines:- 1) Lysergic acid diethylamide (LSD) 2) Psilocybin 3) Harmine (4) Bufotenin

2) Phenylalkyl amides Mescaline

3) Arylcyclohexyl amines:- Phencyclidine

(4) Cannabinoids:- Tetrahydrocannabinol
Bhang, Ganja, Charas

LSD :- one of the most potent mood-changing

* chemicals. acid, which found lysergic, ergot and other

that grows on rye

grains.

* Antidepressant and antianxiety drugs

Antidepressant are medications used to treat major depressive disorders, some anxiety disorders and help to manage some addictions.

Classifications :-

i) reversible inhibitors of MAO-A (RIMA)

1) Moclobemide, Clorgyline

ii) Tricyclic antidepressants (TCAs)

(A) NA + 5-HT reuptake inhibitors

Imipramine, Amitriptyline, Doxepin, Dothiepin

Trimipramine, Clomipramine

(B) Predominantly NA reuptake inhibitors

Desipramine, Nortriptyline, Amoxapine, Reboxetine

(III) Selective serotonin reuptake inhibitors (SSRIs)
Desipramine, Nortriptyline, Amoxapine, Rebadetine
Fluoxetine, Fluvoxamine, Paroxetine
Sertraline, Citalopram, Escitalopram
Paroxetine.

(IV) Serotonin and noradrenaline reuptake inhibitors (SNRIs)
Venlafaxine, Duloxetine

(V) Atypical antidepressants
Trazodone, Mianserin, Mirtazapine, Bupropion
Tianeptine, Amineptine, Atomoxetine

Moclobemide:- It is a reversible inhibitor of monoamine oxidase A drug used to treat depression and social anxiety disorder

Mechanism of action:- MAO-A This reversible inhibition leads the destruction of monoamines and neurotransmitters. in the metabolism of monoamines in the brain.

t-½ hours - Half life

ADR:- nausea, dizziness, headache, insomnia, liver damage.

First line agents for initial treatment bupropion, fluoxetine, paroxetine, duloxetine.

Pruritus ← drugs used to relieve itching in atopic dermatitis.

↓
Itching

Anti-anxiety drugs

↓
Emotional state, discomfort
To reduce CNS depressants

Antianxiety:-

Classification:-

1) Benzodiazepines:- Diazepam, Chlordiazepoxide, Oxazepam, Alprazolam, Lorazepam

2) Azapirones:- Buspirone (Gepirone, Tspapirone)

Sedative antihistamine. Hydroxyzine

Blocker- Propranolol

β

CNS Stimulants and Cognition Enhancers.

Those drugs whose primary action is to stimulate the CNS globally

Classification:- (1) Convulsants (Pic rotoxin, Strychnine, Bicuculline, Pentylenetetrazol (PTZ), Picrotoxin)

2) Analeptics:- Psychostimulants:- Doxapram, Amphetamines, methylphenidate, Atomoxetine, Modafinil, Armodafinil, caffeine.

4) date) Pemoline (Cocaine, Respiratory stimulants)

* Cognition enhancers:- these are developed for cerebral heterogenous disorders. group of drugs use in dementia and other

(a) Cholinergic activators:- Tacrine, Rivastigmine, Donepezil, Galantamine

(b) glutamate (NMDA) antagonist M.emantine

(c) Miscellaneous (cerebroactive drugs) Piracetam, Pyritinol, Nicergoline, Citicoline, Ginkgo biloba, Pirfenidone

Drugs affecting renin angiotensin and plasma kinins System

Renin - It is an octapeptide angiotension - It is an octapeptide generated in plasma from a precursor plasma α2 globulin.

ACE inhibitors and ARB's - Drugs

ACE inhibitors :- captopril, Enalapril, Lisinopril, Perindopril, fosinopril, Ramipril and Imidapril, Benazepril etc.

ARB :- Losartan, candesartan, valsartan and telmisartan.

Angiotension receptor blockers (ARB)

Two types inhibitors -

Direct renin inhibitors - (Aliskiren) → used to treat cardiovascular and renal disease

* half life = 24 hours.

* Contraindicated in pregnancy.

AT1

AT2

Plasma Kinins

(Bradykinin and K-allidin)

Plasma kinins are polypeptides split off from a plasma glob kininogen by the action of specific enzymes (kallikreins).

Two Kinins → Kallidin (decapeptide)
→ Bradykinin (nonapeptide)

Bradykinin → slow response
→ to slow
→ to move

Kininogens → LMW (low molecular weight form)
→ HMW (High molecular wt. form)

Kallikreins :- Kallikreins are glycoprotein enzymes produced in the liver as prekallikreins and present in plasma and in several tissue, including the kidneys, pancreas, intestine etc

* Cardiac glycosides and drugs for heart failure

cardiac glycosides are a class of organic compounds that increase the output force of the heart and increase its rate of contractions by acting on the cell sodium - potassium ATPase pump.

Therapies used in heart failure

* Chronic systolic heart failure
  - Diuretics, aldosterone receptor antagonists, ACE inhibitors, angiotensin receptor blockers, beta-blockers.
* Acute Heart failures
  - Diuretics, vasodilators, beta-agonist, Bipyridine, Natriuretic peptide, Left ventricular assist device

Drugs used in heart failure

* Digitalis drugs used in heart failure
  - shows positive inotropic effect in heart
* Bipyridines :- Milrinone
* Beta adrenoreceptor agonist :- dobutamine

* Drugs without positive inotropic effects used in heart failure

⇒ Diuretics, ACE inhibitors, Angiotension receptor blockers, vasodilators, β - adrenoreceptor blockers

Digitoxin

⇒ Absorbed orally. Absorption varies from zero to nearly 100%

⇒ Toxicity of digitalis is high, margin of safety is low.
Therapeutic index = 1·5-3

Higher cardiac mortality has been reported among patients with steady - state plasma digoxin levels > 1·1 ng/ml.

Antidote for overdose of digoxin:-

Digoxin Immune fab or Digoxin - specific antibody.

⇒ used in the treatment of congestive heart failure and cardiac arrhythmias.

* ~~Before the~~

Antiarrhythmic drugs

↓

drugs used to prevent or treat irregularities of cardiac rhythem.

Classification of antiarrhythmics

* Class I :- sodium channel blockers, or membrane stabilizing Depress Phase 0
* Class IA :- Quinidine, Novocainamide, disopyramide
* Moderate Depression of Phase 0 depolarization
* Prolong the AP duration, have slow Kinetics.
* Class IB :- Lidocaine, Mexiletine (phenytoin (Difenin))

Depress Phase 0 slightly
shorten the AP duration, have fast kinetics.

Class IC :- Flecainide
ethmozin (Moracizin)

Marked depression of Phase 0 depolarization.

* Profound slowing conduction, rare very slow kinetics.

Class II (β- blockers)
non- selective : propranolol
selective :- metoprolol

Class III (K+ channel blockers)
amidarone, sotalol, dofetilide, azimilide

Class IV (Ca2+ channel blockers)
verapamil, diltiazem

Others- adenosine, digoxin, mag- sulfate, atropine
- neostigmine

Drugs for PSVT

Drugs for A-V Block

Choice and use of antiarrhythmic drugs.

* Supraventricular arrhythmias only
⇒ adenosine, verapamil, diltiazem, Dronedarone, Digoxin.

* Supraventricular and ventricular arrhythmias.
Amiodarone, β- blockers, propranolol, sotalol, Esmolol

Lidocaine, Mexiletine

* Atrial fibrillation:- iv amiodarone, sotalol, oral verapamil, diltiazem

* Atrial flutter:- verapamil, propranolol, Amiodarone

* Wolf-parkinson-white syndrome
Tachycardia ⇒ propafenone, procainamide, verapamil, propranolol, amiodarone

* Ventricular fibrillation:- amiodarone (iv), propanolol

* Antianginal and other anti-ischaemic drugs

Angina pectoris:- pain syndrome due to induction of an adverse O_2 supply/demand situation in a portion of the myocardium.

- Classical angina (Stable angina): By exercise, emotion, eating & cold and subside during sleep
- Variant angina: rest angina, rest or sleep

Classifications:-

1) Nitrates:-

(a) Short acting: Glyceryl trinitrate (GTN, nitroglycerine)

(b) Long acting:- Isosorbide dinitrate (Short acting by sub-lingual route) Isosorbide mononitrate, erythrityl tetranitrate.

2) β-blockers:- Propranolol, Metoprolol, atenolol, and others.

3) Ca+ channel blockers:-

(a) Phenyl alkylamine - Verapamil.

(b) Benzothiazepine :- Diltiazem

(c) Dihydropyridines :- Nifedipine, Felodipine, amlodipine, Nitrendipine, Nimodipine, Lacidipine, Benidipine

4) Potassium channel openers:- Nicorandil.

5) Others:- Dipyridamole, Trimetazidine, Ranolazine, Trabradine, Ephedrine

Clinical classification:-

(A) used to abort and terminate the attack - GTN, Isosorbide dinitrate

(B) used for chronic prophylaxis - All other drugs

Nitrates:- Prodrug that are sources of nitric oxide (NO)

Nitroglycerin:- First synthesized in 1846 by Sobrero.

also known as glyceryl trinitrate (GTN), is a medication used for heart failure, high BP, anal fissures, painful periods and to treat and prevent chest pain from not enough blood flow to the heart or due to cocaine.

* taken by mouth, under the tongue applied to skin or by inj in vein

* Side effects — headache, low blood pressure
* can't give to other medications
* Sildenafil (PDE5) inhibitors due to risk of ↓BP:

* used for the treatment of angina, acute myocardial infarction, severe hypertension and acute coronary artery spasms.

ADR:- Flushing of the face, tachycardia, blurred vision, syncope, cyanosis

oral bioavailability — 60-85%.
volume of distribution = 6-8 l/kg
t1/2 — 36-40 hours.

β- Blockers

β-Blockers are prophylaxis used in the angina by exceptional. reducing the myocardial demand below the oxygen. that would provoke an angina attack.

Propranolol:- sold under the brand name Inderal, is a medication of the β-blocker class, used to treat high blood pressure, a no. of type of irregular heart rate, thyrotoxicosis, anxiety, tremors, cardioselective and

Calcium channel blockers:- more rate, (verapamil, diltiazem) use heart rate contractility, which leads to a reduction in myocardial oxygen demands.

Ethanol is involved in the inhibition of L-type calcium channels.

Natural calcium channel blockers
↓
Magnesium

Verapamil:- used for the treatment of ↑BP ~~pre~~, angina, and supraventricular tachycardia. also be used for the prevention of migraines and cluster headaches. It is given by mouth or by inj into vein.

Side effects: slow heartbeat, constipation, headache, dizziness, nausea, trouble breathing

Overdose: It increases plasma digoxin level by decreasing its excretion

Interaction: It should not used along with other cardiac depressants like quinidine and disopyramide. less potent

Diltiazem:- vasodilators than nifedipine and verapamil, BP, angina and medication used to treat high * certain heart arrhythmias. * used in hyperthyroidism if β- blockers cannot be used. * taken by mouth or injection into a vein.

Side-effects:- dizziness, tired feeling, weakness, flushing

* To prevent chest pain, relaxing the blood vessels in the body. Blood can flow more easily and your heart less hard to pump blood. Diltiazem works dilates coronaries.

* Diltiazem should not given to patients with breastfeeding

ADR:-

Nifedi...
sold under the bra...
brand name. ...
It is a medication ... high ... It is one
manage angina, Raynaud's ... choice for
pressure, premature labor. ... may be used to
and the treatments of ... blood pressure in pregnancy.
of total angina. It ... high ... flushing, weakness,
treat severe ... Dizziness, headache

Side effects:- swelling ankles/feet, Trouble breathing.

Overdose:- Dihydropyridine (DHP)

Amlodipine
sold under the brand name Norvasc among
used to treat high blood pressure and coronary
artery disease, not recommended in heart
failure - cannot be used in other medi-
cations.

Calcium channel blockers

Mechanism of action
inhibits the transmembrane
influx of calcium ions
into vascular smooth muscle
and cardiac muscle.

Side effects:- slow the movement of
Ca+ into the cells of
the heart and blood
vessel walls.

Natural vasodilator:

Leafy greens, - spinach and collard greens are high in nitrates, which your body converts into nitric oxide, a potent vasodilator.

Amlodipine:-

Dose 5-10 mg OD.

S(-) Amlodipine - The single enantiomer preparation is effective at half the dose and is claimed to cause less ankle edema. Dose 2.5-5 mg OD

Nicorandil, Pinacidil and cromakalim

↓ Potassium channel openers used to prevent or reduce painful signs

common side effects:- Headache ADR - nausea, vomiting dizziness and flushing

↓ vasodilator drug.

↓ used to treat angina.

other antianginal drugs

1) Dipyridamole — coronary dilator
1) Trimetazidine
2) Ranolazine — Novel drug
3) Ivabradine → alternative to β-blockers
4) Oxyphedrine → sustain Hypoxia.

Drugs for peripheral vascular diseases

a circulatory condition in which narrowed blood vessels reduce blood flow to the limbs.

① Cyclandelate → It is a papaverine like general smooth muscle relaxant which increases cutaneous, skeletal muscle and cranial blood flow
Dose - 200 - 400 mg TDS.
cyclospasmol, cyclogyn 200 400mg T/C.

② Xanthinol nicotinate (Nicotinyl xanthinate)

vasodilator, ↑se blood flow in many vascular beds

300-600mg TDS oral; 300mg by I.M. I.V.

Pentoxiphylline (oxpentifylline)
a weak phosphodiesterase inhibitor - selectively PDE-3 inhibitor.
Cilostazol
Drugs therapy in myocardial infarction.

① Pain, anxiety and apprehension - 3 dosed of CDTN (an opoid analgesic (morphine / Pethidine) or diazepam is administered parenterally

② Oxygenation:- By O_2 inhalation and assisted respiration.

③ Maintenance of blood volume, tissue perfusion and microcirculation.
slow i.v. infusion of saline / low molecular wt. dextran.

④ Correction of acidosis:- acidosis occurs due to lactic acid production can be corrected by i.v. sodium bicarbonate infusion.

5. Prevention and treatment of arrhythmias :- Prophylactic i.v. infusion of a β - blocker ~~Lidocai~~

* Tachyarrhythmias may be treated with i.v. lidocaine, procainamide or amiodarone.

6. Pump failure :- Furosemide, vasodilator (or) ; Inotropic agents - dopamine or dobutamine i.v. infusion.

GTN (i.v) or nitroprusside.

First line drug therapy for Cardiac (sudden) attack :- Nitroglycerin.

~~2nd drug :-~~

First - line therapy for cardiac arrest :- Vasopressin

Antihypertensive drugs

Normal range of BP :- 120/80 mm Hg

Systolic B.P →

Good pulse rate :- 60 - 100 beat/min

	Elevated	High.
Systolic	120/139	140 or above
Diastolic	80/89	90 or above

Drugs used for Systolic blood pressure

⇒ Diuretics (water pills) to help your kidneys flush water and sodium from your body.

⇒ β- blockers. (— to slow the heart rate

⇒ ACE inhibitors, angiotensin II receptor blockers, Calcium channel blockers to relax your blood vessels.

angiotensin :- It is a chemical in your body that narrows your blood vessels.

AT_1 subtype of angiotensin II receptors.
location Heart, blood vessels, kidney, adrenal cortex, lung and circumventricular organ of brain, basal ganglia, brainstem.

Diastolic B.P drugs:- Enalapril, Lisinopril, ARB blockers.

1) Which of the following is renin inhibitor?
⇒ Remikiren.

2) Altered taste sensation, it's caused by Captopril (502).

3) Which of the following anti-hypertensives was once used as antipsychotic
⇒ Reserpine (but withdrawal of suicide initiated)

4) The most significant ADR of ACE inhibition.
⇒ Hypotension.

5) Which of the following is a K^+ channel opener
(Minoxidil)

6) Drug of choice of [illegible] in Pregnancy is :-

Methyldopa :-

* Hydralagine is used in (HTN) emergency in pregnancy
* Nifidipine is a 2nd line drug

7) Which of the following drug uses plasma renin activity
=> Clonidine

*enalaperil, Nifidipine, Hydralagine

↑se Plasma renin activity.

* ~~diuretics~~ Methyldopa, β - Sympato - lytics,

↓se renin secretion

8) Which of the following is not a frontline antihypertensives.

Atenolol :-

9) Antihypertensive which can be used in gout, with diabetes mellitus is

→ Enalapril.

10) Which of the following does not cause bradycardia:-

Hydralazine → reflex tachycardia cause.

Sympatholytics (Propanolol, clonidine Respin Reserpine)

↓
bradycardia

11) Which of the following antihypertensive in vesicular uptake of NA.

Reserpine :- inhibit vesicular uptake of NA, 5HT and dopamine.

↓

effect MOA enzyme deplete into NA.

12) Trimetazine is used for

↓

⇒ angina inhibit fatty acid oxidation.

↓

drugs are the partial inhibitors. fatty acid oxidation and inhibit lipid peroxidation and by reducing the free radicals

↓ ↓

⇐ reduce the generation

these can be used in chronic angina pectoris.

13) Drug not used in prinzmetal angina. i's.

* Propanolol.

β- blockers are contraindicated

⇓

because they cause constriction of coronary artery due to vasoconstriction.

⇓

they donot give into the prinzmetal angina

14) Sublingual nitroglycerin for treatment of acute chest pain can cause:-

Headache

cause vasodilation.

↓ causes.

⇒ Palpitation,

⇒ Headaches, Tachy

⇒ Cardia, Brady Cardial.

15) Nitroglycerin causes all except:-

Hypotension and bradycardia

16) Class I antiarrhythmic drugs are Na^+ channel blockers.

(2) β-blockers (3) K^+ channel blockers
(4) Ca^+ channel blockers.

17) Best used in digoxin induced arrhythmia.

Lignocaine ⇒ ~~first~~ drug of choice.

Phenytoin :- alternative drug for digitalis induced arrhythmia.

18) Drug of choice of paroxysmal supraventricular tachycardias.

Adenosine - first choice.

2nd choice - (2) Verapamil or diltiazem. (Ca+ channel blockers)

19) Which of the following drugs can cause torsades de pointes.

Quinidine ⇒

20) The following drug is contraindicated in Pregnancy :-

⇒ ACE inhibitors.

Safe ⇒ Hydralazine, methyldopa, labeta
- lol, cardioselective β- blockers
, prazosin and clonidine.

Unsafe :- Diuretics, ACE inhibitors, Non-selective β- blockers, α+β Blockers, sodium nitroprusside, reserpine.

(21) Nitroglycerine is effective as sublingual medication because:-

(a) Non ionic, Highly lipid soluble

Depends on → absorption :- ✓ sublingual route

drug is non ionic

then they are Highly lipid soluble.

(22) Why adenosine has a short half life.

- uptake in RBC and endothelial cells.

short half life. — 10sec Half life.

(23) Dofetilide is which class of antiarrhythmic drugs.

Class III

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CHEMOTHERAPUTICS AGENT

Chemotherapy ⇒ Chemo + Therapy

↓ ↓

Chemical Treatments

↳ of Infectious disease

↓

caused by micro-organism

eg:- Virus, fungus, Bateria etc

"The use of drug (chemical) substance derived from micro organism with selective toxicity against infection of viruses, bacteria, protozoa, fungi & helminthes is called Chemotherapy"

OR

It is a type of treatment which are used in the treatment of cancer & infectious disease

Antimicrobial drugs:- These are those drug which kill or inhibit growth of micro-organism.

* **Antibiotics**:- are substance produced by micro-organism, which selectively supress the growth of or kill other micro organism

Chemotherapeutic agent :- those agent which destroy or inhibit the growth of micro-organism without damaging host tissue, known as chemotherpeutic agent.

Classification of Anti-microbial agent or chemotherapeutic agent.

A) Chemical structure
B) Mechanism of Action
C) Types of Organism
D) spectrum of Activity
E) Types of Action
F) Source of Antibiotics

⇒ Antimicrobial chemotherapeutic agent can be classified as

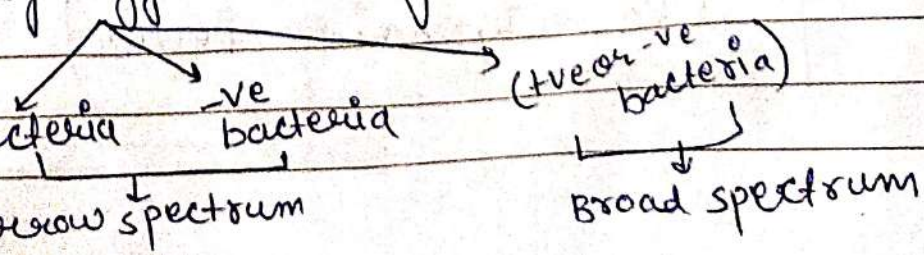
Bactericidal Agents	Bacteriostatic Agents
⇒ These agent kill bacteria.	- These agents prevent the growth the bacteria
Eg:- penicillin, Cephalosporin, Aminoglycaside, Fluoroquinolones	Eg:- Tetracycline, Chloram-phenical, Sulphonamide

⇒ Antimicrobial agent :-
Fungi ⇒ penicillin, Griseofulvin, Cephalosporin
Bacteria ⇒ Polymyxin B, Tyrothricin, Bacitracin
Actinomycetes ⇒ Aminoglycoside, Macrolides, Tetracline

Mechanism of Action of Antimicrobial drugs

Antibiotic mainly effective against

⇒



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✗ Basic principles of chemotherapy of Infections & Infestations

Infections: Cause small micro-organism

Infestations: Cause parasites or large M.O

(1) Diagnosis

→ site of infection
→ Responsible organism (which organism respo
→ sensitivity of drug

(2) select the drug.

→ Antimicrobial activity of drug.
→ Pharmacokinetic factor.
→ (physiochemical properties of drug)
→ patient related factor. Previous
eg Allergy, renal disease, Medication history.

(3) frequency & Duration of drug Administration. (OD, BD, TD)

→ low dose, can develop resistance, imidiate dose may not cure infection.
→ So, optimise dose, should be used for therapy.

(4) Continue therapy -

→ Acute infection treated for 5-10 days.
→ But some of bacterial infection takes a long time like - Typhoid, fever, Tuberculosis

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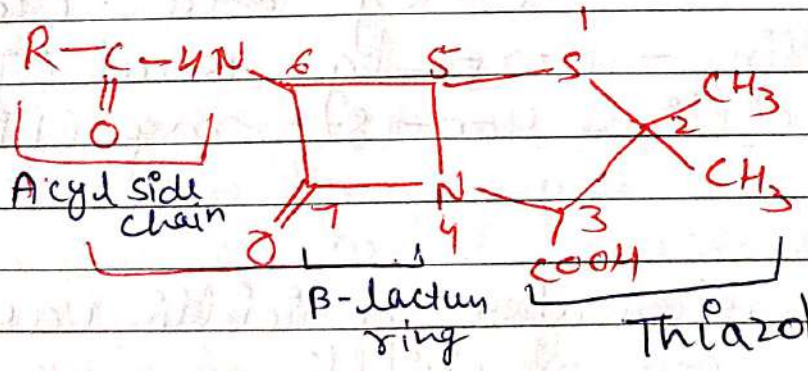
(5) Test for cure (After medication)
→ After therapy symptom & sign may disappear before pathogen eradicated
↳ Not completely died
↳ To check

(6) Prophylactic Chemotherapy:-
→ To avoid, surgical site infection etc.

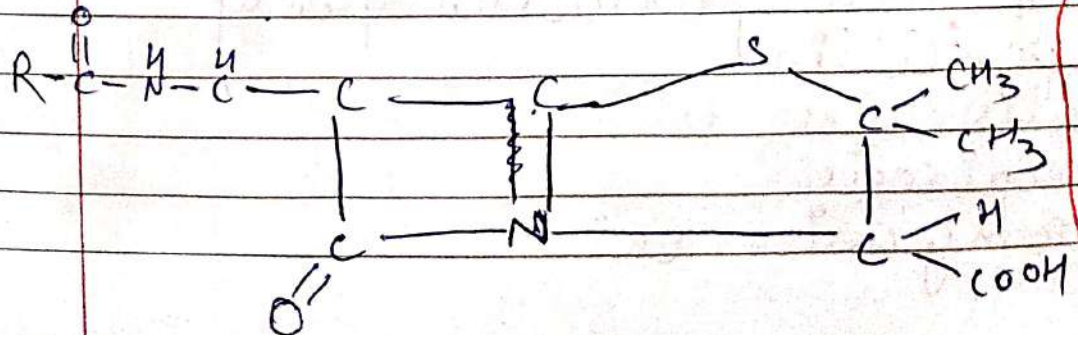
✱ Penicillin Drug

→ penicillin is the first Antibiotic
→ It was obtained from fungus (penicillium notatum) in 1928 or 1929. by Alexander fleming.
→ first antibiotic clinically used in 1941
→ Penicillin is a group of antibiotic which include - Penicillin-G, PenicillinV etc.

Chemically structure of Penicillin



β-lactum
↓ bind
peptidoglycan layer of bacterial cell
(Protein layer) (PG)
↓ cause
binding prevent cross-linking (PG)
↓
Lack of cross linkage
Result in lack of cell wall formation in bacteria
↓
Without cell, bacteria undergo lysis
↓
Ultimately, result in bacterial (death)
Bactericidal effect.



Classification

① Natural penicillin
- penicillin G
- (procain, Benzyl Penicillin) etc.

② Pebicillinase Resistance Penicillins
- Methicillin
- Oxacillin
- Cloxacillin.

③ Amino penicillins.
- Ampicillin
- Amoxicillin
- Bacampicillin

④ Carboxy penicillin
- Carbicillin
- Ticanicillin.

Dose :-
- penicilline G - 0.5 - 5 MU im/i.v
- Ampilicine - 0.5 - 2 g oral. (Tab)
- Amoxicillin - 0.25 - 1g oral (TDS)
- Bacampicillin - 400 - 800 mg (BD)

Indication
- The indication for penicillin vary depending upon pbenicillin group.

Natural penicillin
→ Syphillis.
→ Leptospirosis
→ Actinomycosis etc.

(2) penicillinase Resistant Penicillins
→ Syphilis
→ Pneumonia
→ tetanus
→ Diptheria ... etc

(3) Amino penicillins
→ pneumonia.
→ urinary tract infection.
→ skin infection.
→ fever.

* Contraindication
→ In lactation
→ previous history Allergy rxn,
→ In stevens Johnson syndrom
→ Drug pregnance
→ patient with renal disorder.

Cephalosporin

"C" ← obtained from the fungus cephalosporium

Defination :- These are second major group of β-lactum Antibiotic. derived from
→ these are the group of semi-synthetic antibiatics
→ It is a broad spectrum antibiotic
→ used to treat gram (+ve) & gram (-ve) bacterial infection.

Classification :- first generation to 5th gruop

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1st generation (Phaolfa)
→ Cefazolin) Parenteral
→ cephalexin) Oral
→ Cefadroxil)

2nd generation
– Cefaclor) O
– ~~Cefuroxime~~ (Cefoxitin) P
– ~~Cefazolin~~ (Cefprozil) O

→ 3rd generation
→ Cefixime) O
→ Cefotaxime) P
→ Cefpodoxime proxetil) O
→ Cefdinir) O

Fourth generation
P – Cefepime
– Cefpirome

5th generation.
→ Cefazolin fosamil
→ Ceftobiprole medocaril

MOA
Chephalosporin
↓
Bind to PBP (cell binding protein) (penicillin Binding protein-I) or PBP-1 / or PBP-3
↓
Inhibit the synthesis of peptidoglycan layer
↓
Inhibit cell wall synthesis

Dose :-
Cefixime – 400mg / od. (per day)
Cefazolin – 0.5g 8 hourly (mild case) (im / iv)
Cefadroxil → 0.5 – 1g (BD)

Uses
→ To treat skin infection
→ To treat fever / Typhoid
→ Gonorrhoea – gynecological infection
→ To " UTI
→ Osteomyelitis.
→ gonorrhoea.

Contraindication :-
→ Renal failure → Nep
→ Hepatic impairment
→ Hypersensitivity
→ pregnancy --- etc.

Aminoglycoside (AGs)

→ Aminoglycosides are called bactericidal antibiotics because they kill bacteria directly.

→ Aminoglycoside are normally used to treat serious infections

Classification of Aminoglycoside drug.

→ **Systemic aminoglycoside :-**

→ Streptomycin, Amikacin, Gentamicin, Sisomicin, Kanamycin, Tobramycin.

Topical aminoglycoside :-

→ Neomycin, Framycetin.

Dose :-

① Streptomycin - 1-2 g/d. (IM)
② Gentamycin - 3-5 mg/kg/day in 3 divided dose (im/iv)
③ Tobramycin - 3-5 mg/kg/day in 3 divided dose (im/iv)
④ Amikacin - 15 mg/kg/day in 2-3 divided doses (im/iv)
⑤ Netilmicin - 4-6 mg/kg/day in 2-3 divided dose (im/iv)

Indication (uses)

→ To treat skin injection
→ To treat lung "
→ To treat UTI "
→ To treat respiratory "
→ To treat tuberculosis.
→ Tuberculosis, soft tissue, ear, eye etc.

Contraindication

→ Renal disease
→ pregnacy
→ Hypersensitivity

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MOA (Aminoglycoside)

↓

Bind with 30s ribosomal unit

↓

Inhibit the initiation of Protein synthesis

↓

Cause misreading genetic code on recognition region of ribosome

↓

Insertion of wrong amino a

↓

Destruction of cell membrane.

* Fluoroquinolones

→ Fluroquinolones are bactericidal antibiotics,

→ They are commonly used to treat respiratory & urinary track Injection.

→ They are active against gram (+ve) & gram (-ve) bacteria. (Broad spectrum Antibiotics)

→ Many advantageous pharmacokinetic properties including high oral bioavailability, large volume of distribution & broad spectrum antimicrobial activity

Classification

① First generation :- Nalidixic acid, Cinoxacin

② 2nd generation :- Norfloxacin, ofloxacin, ciprofloxacin.

③ 3rd generation :- Levofloxacin, sparfloxacin.

④ 4th generation :- Tovafloxacin.

Indication :-

→ Urinary Tract infection. (UTI)
→ Throat infection.
→ Ear infection, Dental infection
→ Pneumonia.
→ sinus infection.... etc.
→

Contraindication :-

→ lactation.
→ Hypersensitivity.
→ Pregnancy.... etc.

Dose :-

→ levofloxacin - 250-500 mg/day
→ ofloxacin - 250 (BD)
→ ciprofloxacin - 250 mg TDS.

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Macrolides

→ They are broad spectrum antibiotics

→ They are bacteriostatic in nature.

→ They are mainly active against gram (+ve) and gram -ve bacteria

→ These are antibiotic having a macro-cyclic lactone ring & attach sugars.

→ Erythromycin was 1st member discovered in 1950s.
Roxithromycin, calrithromycin & azithromycin later added.

MOA :- Macrolides

↓

Bind to 50s ribosomal unit

↓

Inhibit polypeptide chain elongation & protein synthesis inhibition

↓

Result in inhibitions of growth & multiplication

Classification

① Macrolides :- Erythromycin, Clarithromycin Azithromycin, Roxithromycin Spiramycin.

Ketolides :- Teli-thromycin.

Indication:- ① Pneumania
② Inflamation nasal cavity.
③ Peertussis (Respiratory Tract infection)
④ Diptheria.
⑤ Covid-19.
⑥ Tetnus
⑦ Syphillis
⑧ Skin Infection ointment.

⇒ Contraindication.
→ Hypersentivity.
→ Liver or kidney disease
→ Myasthenia gravis
→ Pregnancy & breatfeeding.

Dose :-
Erythromycin :- 250mg/d
Azithromycin :- 500 - 1500mg/d.

Tetracyclines

→ Tetracyclines are a class of antibiotics,
→ which are chemical substances produce by a micro-organism that are able to kill other micro-organism.
→ It will not work you cold, flu or other viral infec
→ It is also used along with other medication to treat acne.

Classification :-
① Short acting (6 hours half life)
Chlortetracycline, Oxytetracyclin.

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② Intermediate Acting (16 hours half life)
→ Demeclocycline.

③ long acting (18-24 hours)
Doxycycline, minocycline.

Indications

→ Acne
→ Chlamydia.
→ Trachoma
→ Respiratory Tract Infection.
→ UTI, genital or Intestinal.
→ Eye.

contra indication

→ Pregnancy & lactation.
→ Hypersensitivity
→ Renal & hepatic failure.

Dose

Chlortetracyclin - 250 mg/6h.
Doxycycline - 100-200 mg/d.

MoA

Tetracycline

↓

Bind to A (aminoacyl t-RNA) site of 30s ribosomal submit.

↓

Prevent binding of t-RNA to A site

↓

Chain fail to grow

↓

Prevent protein synthesis.

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Sulphonamides :- They are also known as sulpha drugs.

→ They are bacteriostatic in nature

→ Sulphonamide were the first antimicrobial agent.

→ They are a group of man-made (synthetic) medicines that contains the sulfonamide chemical group

→ Many people use of the terms sulfonamide only for antibiotic However, there are several non-antibiotic sulfonamides that have been developed by observations.

→ These are used for a range of condition such as diabetes and pain relief.

Classification :-

(1) Short acting (4-8 hrs) :- Sulfadiazine.
(2) Intermediate acting :- sulfamethoxazole, sulfamoxole.
(3) Long acting (7 day) → sulfadoxine, sulfamethopyrazine.

Indications :-

(1) Bacterial Infection :- sulfamethoxazole,
(2) Crohn's disease :- sulfasalazine.
(3) Ulcerative colitis :- sulfasalazine.

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Contraindication

→ Hypersensitivity
→ pregnancy & lactation

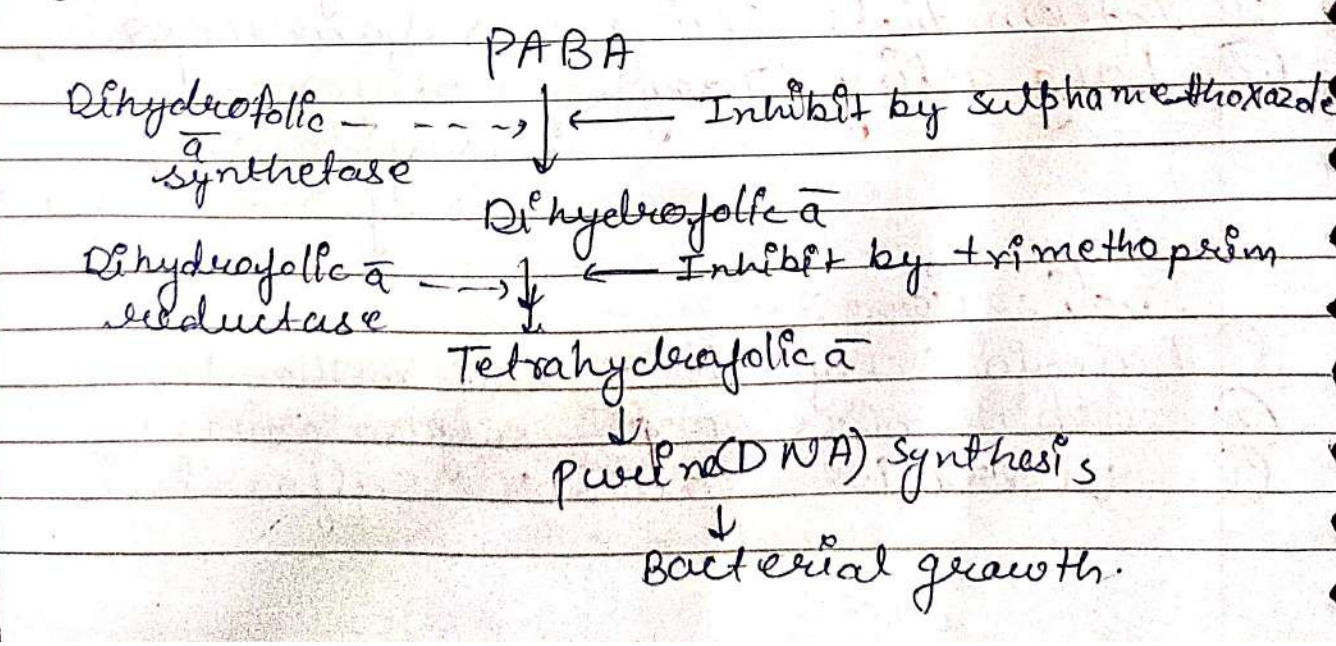
Dose

→ Sulfones (Dapsone) - 50-100mg/d
→ sulfomethazole - 800 mg/d
→ sulfadiazine - 0.5-1g ... etc.

Sulphonamides

⇒ Why sulphamethoxazole is combined with trimethoprim?

- sulphamethoxazole is combined with trimethoprim in 5:1 ratio.
- These two agents acts synergistically by blocking the formation of folic acid & its utilisation.
  The combination is called cotrimoxazole.



ANTI-TUBERCULAR AGENTS

Tuberculosis is a disease caused by an organism Mycobacterium tuberculosis.

Antitubercular Agents :-

The drug which are used in the treatment of tuberculosis are called Antitubercular drugs.

Classification of Antitubercular Agents

1. Standard drug / Primary drug / first line drug

Eg:→ Isoniazid (INH)
→ Rifampicin (R)
→ Ethambutol (E)
→ Streptomycin (S)
→ pyrazinamide (Z)
→ p-aminosalicylic acid (PAS)

2. Reverse drugs / secondary drug / second line drug

Eg:- → kanamycin (K)
→ capreomycin (Cm)
→ cycloserine (C)
→ Amikacin
} P

→ ofloxacin
→ Levofloxacin
} O

Isoniazid (Isotonic Acid Hydrazide) (INH)

It is most effective & cheapest antitubercular agent.

Isoniazid (INH) - Antitubercular agent
↓
INH inhibit mycolic acid synthesis
↓

Mycalic acid is essential component of the tuberculosis bacteria's cell wall

↓

disruption of cell wall formation weakens the bacteria

↓

This disruption ultimately leads to the death of tuberculosis bacteria.

Adverse effect :-

→ peripheral neuritis
→ Hepatotoxicity
→ anemia
→ convulsion, loss of memory
→ loss of self-control

Dose

① Isoniazid tab IP : 200-300mg/d in single dose

② Rifampicin tab IP :- 10mg/kg

② Rifampicin :- is semi-synthetic derivate of rifamycin, an antibiotic.

MoA

Rifampicin
↓
Bind with β subunit of DNA dependent
↓
RNA polymerase Inhibition of mRNA synthesis
↓
Tuberculocidal effect.

Dose :- 10 - 20mg/kg of body weight

Adverse effect :-
→ Hepatotoxicity
→ flu-like synthentic.
→ staining of secreation

Uses
① Tuberculosis & atypical mycobacterial Infection.
② Leprosy & prophylaxis
③ Resistant staphylococcal infection.

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ANTI-FUNGAL INFECTION

Fungal infection

→ Any disease caused by fungus is known as fungal infection.

→ A fungal is heterotropic micro-organism.

→ A fungal infection is also called mycosis, a skin disease caused by a fungus.

→ Mycotic infection of human are

① Dermatophytosis is a contagious superficial skin infection.

② These disease produced ringworm of foot. ringworm of skin, hair, nails.

③ Candidiasis can affect the skin & mucus membrane.

④ saprophyte invade skin & penetrate deep causing lymphatic pulmonary & systemic mycoses.

Fungal infection are

① Candidias :- caused by yeast-candida

② Blastomycosis :- Caused by the fungus Blastomyces.

③ Ringworm: A common fungal infection

④ Vaginal candidias

⑤ Mucormycosis :- Caused by Mucormycetes

Anti-fungal agent:-
The drugs which are used in the treatment of fungal infection are called anti-fungal agent.

Classification

Anti-fungal antibiotics:-

→ (a) polyene macrolides:- e.g amphotericin, nystatin
Antibiotics

(b) Non-polyene :- griseofulvin

(2) Synthetic:-

(a) Imidazole derivatives:- e.g ketoconazole, } Para
miconazole, }
clotrimazole. } Topic
Azoles

(b) Triazole derivatives:- ~~Undecylenic acid~~.
fluconazole, itraconazole.

Allylamine :- Terbinafine.

Topical Agents:- Tolnaftate, Butenafine, Benzoic acid.

Mon polyenes griseofluvin

→ Broad spectrum antifungal antibiotics are amphoteric in nature.

→ Obtained from ~~streptomyces nodosus~~ Penicillium griseofulvum.

selectively effective in dermatophyte infection of the skin, nails & hair.

MOA:- It inhibits fungal mitosis by interfering c microtubule function.

Therapeutic Uses:-
- As an antifungal agent.
- To treat fungal infection of skin, scalp, hair & nails.
- Used to treat ringworm infection.
- Effective in aspergillus & Candida infection.

Adverse effects
- Nausea, Vomiting
- flushing
- peripheral neuritis
- Mental confusion

Contraindication
- severe liver disease
- porphyria.

Brand Names: ① Gri-flavin ② Grisovin-FP

Doses:- ① Griseofulvin tablet 500mg daily single or divided dose orally.

② fluconazole — 150-400mg (OD)
③ Itraconazole - 200-400mg (OD)
④ Amphotericin B via I.V route & dose can range from 0.3-1.5 mg/kg/day.

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ANTI-VIRAL DRUGS

→ The drugs are used to treat viral infections are called antiviral drugs.
Virus are tiny (smaller than bacteria) contain genetic material.

→ They cause common infectious disease like comm cold, flu, and warts; while they malso can severe illnesses such as HIV/AIDS, small po and haemorrhagic.

→ Virus invade (enter, attack & take control of) the living, normal cells of an individual and use them to multiply.

→ This ultimately kills the cells & the individ becomes sick

→ Since the viruses live inside the body's cell treatment of viral disease is hard.

→ Antibiotic cannot cure viral disease, & a few antiviral drugs are avilable.

→ However, vaccine can prevent the occur of Many viral disease.

* Maximum antiviral drug traget the viral DNA & RNA.

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⇒ Classification of Non-retroviral drugs

Class		Drugs.
① Anti-Herpes Virus Drugs		① - Idoxuridin, Trifluridine, Acyclovir, Valacyclovir, Famciclovir, Ganciclovir.
② Anti-Influenza Virus Drug		① - Amantadine, Rimantadine Zanamivir, Peramivir, Oseltamivir
③ Anti-Hepatitis Virus Drugs	for hepatitis B	Lamivudine, Adefovir, Tenofovir ② ④ Dipivoxil
	for hepatitis C	Ribavirin, Interferon α, sofosbuvir, Ledipasvir, simeprevir.

Indication:- Used to treatment of Influenza A virus, Herpes virus

- Cytomegalovirus (CMV) infection.
- Hepatitis B & C virus, some virus cause warts & eye infection

Contraindication:-

- previous history of allergy to the drug, Renal Impairment.
- pregnancy & lactation.
- Severe CNS Disorder
- Hepatic dysfunction, Bone marrow suppress

Dose: ① Acyclovir – Adult is 200mg five time daily or 400mg 3 time day for (5–10 days)

② Oseltamivir – Adult ~~& Pedo~~ weighing 40 mg or more 75 mg (BD) for (5 days)

③ Ribavirin :- Oral dose for adult is 600mg (BD) for (3–7 days)

Acyclovir

→ It is the fastest acting drug.

→ It is a synthentic, purine nucleoside analogue that has anti-herpes activi

* It is more effect HSV-I & HSV-II than varicella zoster virus infection.

→ Available for oral, topical & IV administrat

MOA

Acyclovir —(Thymidine kinase; Virus kinase)→ Acyclovir monophosphate —(Cellular kinase; Host kinase)→ Acyclovir triphosphat

↓

Inhibit Viral DNA synthesis & viral replication

Acyclovir is taken up by virus infected cell. Convert ed to Acyclovir triphosphate (by viral thymidine kinase).
This inhibit viral DNA synthesis by viral DNA polymerases. Causing DNA chain termination.

Pcokinetic
→ Only about 20% of an oral dose of Acyclovir has been absorbed.

-Dose: Adult dose 200mg (5-time)] - 5 to
400mg (3-time)] - days.

Use:- Genital Herpes, Herpetic encephalitis, Herpes zoster, chickenpox.

Anti-Amoebic Agent. (Amoebiasis)

→ Amoebiasis is an infection of intestine or liver caused by Protozoa Entamoeba histolytica.

→ It infective stage is called Trophozoite. Occasionally, trphozoite pass into the blood stream, reach in the liver via portal vein & cause amoebic liver abscesses. Other organ like lung, spleen, kidney & Brain & rarely involved in extra intestinal amoebiasis.

→ It causes infection when ingesting contaminated water with infected feces.

Classification of Antiamoebic drugs

① Tissue amoebicides

ⓐ For Intestinal + Extraintestinal amoebiasis

→ Nitroimidazole :- Metronidazole, Tinidazole, Ornidazole.

→ Alkaloids :- Emetine or Dehydroemetine.

ⓑ for extraintestinal amoebiasis only

→ Chloroquine.

② Luminal Amoebicides

ⓐ → Amides :- Diloxanide furoate, Nitazoxanide.

ⓑ → Antibiotic :- Tetracyclin; Paramomycin.

Metronidazole → explain.

④ Indication :-

It is used to treatment of

→ Amoebiasis.
→ Giardiasis.
→ Trichomoniasis.
→ Anaerobic bacterial infection.
→ H. Pylori infection.

⑤ Contraindication :- Individual who have encountered certain ① blood disorders, ② pregnent women & ③ Alcoholics are advise against consuming Antiamoebic

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(8)

Dose :- (1) Metronidazole · Adult :- 500 or 750 (mg) milligram
3 time (TD) for 5-10 days

IV :- 15 mg/kg
Capsule :- 375 mg.

(1) **Metronidazole**

→ Broad-spectrum bactericidal activity against anaerobic protozoa.

→ Effect against E. histolytica, Giardia lamblia & Trichomonas vaginalis.

→ Metronidazole & diloxanide drug are useful in the treatment of both intestinal + extraintestinal symptoms of amoebiasis in orally.

→ It has a plasma $t_{\frac{1}{2}}$ of 8 hours.

(2) **MOA** :- Metronidazole diffuses into the organism, inhibit protein synthesis by interacting with DNA & cause a loss of helical DNA structure & strand breakage.

Dose · Adult **Adverse effect**
Headache, stomatitis, glossitis, furry tounge.

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Anthelmintics

also known as nematocides, Endectocide.

→ Anthelmintic are a type of medicine that kills helminths. Helminths are worm like parasites such as flukes, round worms & tapeworms.

→ It is important that anthelmintics are selectively toxic to the parasite and not the host

→ some work by inhibiting metabolic process that are vital to the parasite but absent or not vital in the host.

Classification

→ Classes	Drugs
① For Roundworm, Hookworm, Pinworm	① Mebendazole, ② Albendazole, ③ Pyrantel pamoate, ④ Piperazi ⑤ Levamisole
② For Threadworm	① Ivermectin ② Albendazole
③ For whipworm, Trichinella spiralis	① Albendazole ② Mebendazole
④ For filariasis	① Diethylcarbamazine (DEC) ② Ivermectin ③ Albendazole
⑤ For ~~filariasis~~ Tapeworm	praziquantel, Niclosamide, Albendazole

For Hydatid Disease	Albendazole, Mebendazole.

⇒ **Mebendazole** :- It is a broad spectrum anthelmintic (worm. roundworm, hookworm & pinworm & strong gyloides infestation.

MOA :-

Benzimidazole
↓ Bind
β-tublin of parasite
& high affinity
↓ Inhibit
synthesis of micro tubules

→ These microtubules are essential for several metabolic processes in the parasite

→ Benzimidazole also inhibit glucose uptake in the parasite.

pharmaco-kinetics

→ Mebenadazole is poorly absorbed (10%) from the gut & also undergoes 1st pass metabolism.

→ Fatty food enhances absorption.

Dose:- Mebendazole is 100mg (BD) for 3 day for most type of infection

Uses :- Used to treatment of Roundwo Hookworm, Pinworm, Tapeworm, Trichuriasis & Hydatid disea

Contraindication

→ pregnancy
→ Breastfeeding
→ Severe diarrhea.
→ Malnourishment
→ Hepatic or renal disease.

Dose :- ① Albendazole (400mg) OD 1-3 da for most type of Infe

② Mebendazole is 100mg taken (BD) fo 3 days (most type of infection like ~~tapeworm~~, whipworm infection)

③ pyrantel ~~in~~ 11mg/kg

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Anti-Malarial Agent

→ The drugs are used to treat malaria are called Anti-Malarial Agent.

Malaria :-

→ It is caused by parasitic protozoa of the genus Plasmodium which includes four types:-

① Plasmodium vivax ② Plasmodium Ovale
③ " falciparum ④ " malariae.

Life cycle of Malarial parasite in Human

① Mosquito Bite (Injection stage)

Anopheles mosquito inject Sporozoites

↓

Enter bloodstream

↓

② Liver stage (pre-erythrocytic cycle)

sporozoites → Liver cell → develop into Schizonts

Release Merozoites ← Schizont Rupture

↓

③ Blood stage (Erythrocytic Cycle)

Merozoites Inject RBCs → convert into → Trophozoites → Develop into schizonts ← RBC rupture

↓

More merozoites release

↓

④ Symptoms Appear (Cyclic, fever, Anemia)

↓

Due to RBC rupture & toxin release

↓

⑤ Gametocyte formation (sexual stage in human)

↓

some parasite become Gametocytes (male & female) → Taken up by mosquito.

↓

⑥ Mosquito stage (Sporogonic Cycle)

Gametocyte develop in mosquito

↓

From Sporozoites → Migrate to mosquito salivary gland

↓

(7) Transmission to Human (Cycle Repeats)

Mosquito bites another person

↓

Injects sporozoites

↓

Injection start again

Objective & use of antimalarial agents

→ The aim of using drug in relation to malarial infection are

→ To prevent clinical attack of malaria (prophylactic)

→ To treat a clinical attack of malaria (Clinical curative)

→ To cut down on human - to mosquito

Classification

Classes	Drug
(1) 4-Aminoquinolines	chloroquine, Amodiaquine, peperaquine
(2) Quinoline-Methanol	Mefloquine
(3) chinchona Alkaloid	Quinine, Quinidine.
(4) Biguanide	Proguanil (Chlorguanide)

(5)	Diaminopyrimidine	pyrimethamine
(6)	8-Aminoquinolines	Primaquine, Tafenoquine
(7)	Sulfonamide/Sulfone	sulfadoxine, sulfamethopyrazine, Dapsone
(8)	Antibiotics	Doxycycline, Clindamycin.
(9)	Sesquiterpenes-Lactonis	Artesunate, Artemether
(10)	Amino-alcohol	Halofantrine & Lumefantrine

Indication :- Used in the treatment of
→ Malaria
→ Chloroquine is used ~~+~~ metronidazole in amoebiasis
→ ~~It is~~ Chloroquine is used in Arrhythmia.
→ In Rheumatoid arthritis.

Chloroquine

→ This drug is a 4-amino quinoline derivatives.
→ Used in the treatment of malaria & amoebiasis.
→ It cause fewer toxic effects & is used in the suppressive treatment of malaria.

MOA

Chloroquine —enter→ RBC —enter→ Acidic food vacuole of the parasite

Inhibit heme polymerase → Accumulation of toxic heme → parasite membrane lysis → Death of the parasite

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Pharmacokinetic

→ It is absorbed rapidly & almost completely from the gut; peak serum conc. are obtained within 1 or 2 hours.

→ The half-life is 3 to 5 days.

→ It is excreated in the urine breast milk & faeces.

→ It crosses the placenta.

Dose :- Adult 500mg (OD) for 1 week for malaria.

Contraindication

→ nausea, vomiting
→ Headache
→ Dizziness
→ Muscular pain
→ Diarrhea, cough, fever & chills

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Anti-Neoplastic Agents / Anticancer Agent.

→ Cancer:- Cancer is a disease of cell characterised by the loss of normal cellular growth, maturation & multiplic which distrub the homeostasis.

1) Neoplasia:- It is new, uncontrolled growth of cell that is not under physiologic control. A "tumor" or "mass lession" is simply a "a growth" or "enlargement" which may not be neoplastic.
They are called as anticancer drug or also known as cytotoxic agents.

→ These are the agent used in the treatment of cancer.

→ The ultimate cause of cancer is not known, but it involves disorder in normal mechanism of cell developme and integration

Anti-neoplastic agent are used for the treatment of cancer.

→ Neoplasm (In Greek 'neo' mean 'new' & 'plasm' means formation). So, it refers to a group of disease caused by several agent - namely chemical or radiant energy.

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→ Cancer is characterized by abnormal & uncontrolled division of cell, which produce tumors & invade adjacent normal tissue.

→ Often, cancer cells separate themselves from the primary tumours and carried by lymphatic system, reach distant site of organ where they are divide & form secondary tumours.

→ Cancer is classified a/c to the tissue & type of cell in which new growth occur.

(1) Carcinoma:- Malignant tumours derived from epithelial cells.

(2) Sarcoma:- Malignant tumour derived from connective tissue.

(3) Lymphoma & leukemia :- Malignancy derived from hematopoietic (blood-forming) cell.

(4) Germ cell tumor:- tumors (usually) derived from totipotent cell.

⇒ Blastic tumour:- resembles an immature or embryonic tissue. Many of these tumours are common in children.

Treatment of cancer :-

→ Treatment of cancer includes surgical invention, radiation, immuno-therapy chemotherapy using neoplastic Agent.

→ some type of tumours are currently treated first with chemotherapeutic agent

→ Cancer chemotherapy is generally non-specific means drugs kill not only cancerous cell but also normal cells.

→ special strategies developed to increase the potential of destroying cancerous cell and lessing toxic effect on normal tissue.

Classification :-

Class	sub-class	Drugs
① Alkylating Agent	① Nitrogen Mustard	1-chlorambucil 2- Cyclophospha-mide 3- Ifosphamide 4- Uracil mustard 5- Mechlorethia-mine.

	(ii) Nitroso-urea	1- Carmustine, 2- Lomustine 3- Semustine 4- Cholorzotocin
	(iii) Azilidine	1- Thiotepa, 2- Benzotepa, Altretamine.
	(iv) Alkyl sulfonates	1- Busulfan
	(v) Methyl hydrazine	1- Procarbazine.
	(vi) Miscellaneous	1- Dacarbazine, 2- Streptozocin
(2) Anti-metabolites	(1) Folic a antagonist or analogue	1- Methotrexate 2- Trimetrexate 3- Azathioprine.
	(3) Pyrimidine analogue	5-Fluorouracil & Cytarabine Floxuridine & Capecitabine.
	(2) Purine antagonist or analogue	(1) 6-mercapto purine (2) 6-Thioguanine, (3) Fludarabine.
(3) Antibiotic	(1) Anthracyclins	(1) Daunorubicine, (2) Doxorubicine (3) Carminomycin (4) Idarubicine.
	(2) Miscellanous	(1) Actinomycine D, Mithra-mycine, Bleomycin, Mitomycin C.

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	Drugs.
(4) Plant Alkaloids	(1) Vinca alkaloids :- Vincristine, Vinblastine,
	(2) Epipodophyllotoxins - ① Etoposide. Teniposide
	(3) Taxol — paclitaxel, — Docetaxel
(5) Enzyme	① L- Asparaginase ② pegaspargase.
(6) Hormones	Mitotane, Tamoxifen
(7) Camptothecin Analogue/ Topoisomerase-I Inhibitor	Topotecan, Irinotecan
(8) Epipodophylotoxin	Etoposide.

① Cyclophaphamide, ② Chbrambucil ③ Cisplatin
④ Methotrexate. ⑤ Fluorouracil (5-FU)

→ Alkylating Agent

Alkylating agents are the compounds that work by adding an alkyl group (a type of chemical group) to the DNA of cancer cells.

This addition prevents the DNA from correctly pairing up preventing the cancer cell from replicating & dividing. This can lead to the death of cancer cell.

MOA

DNA Double Helix

Alkylating Agent
↓ Alkylates Guanine Base
Alkylated DNA
↓ Forms
Cross-linking
↓ Leads to
prevent DNA unwinding
↓ Result in
Inhibit DNA Replication

Cyclophosphamide :-

⇒ It is an alkylating agent used as anti-cancer agent.

→ It is less toxic to platelets & has immunosuppressant properties.

MOA → Cyclophosphamide alkylates DNA & RNA, inhibit enzyme that do synthesis of amino a in proteins The drug also help cross link DNA strand.

→ Its activity in the cell cycle phase is not clear. It acts as an antineoplastic agent.

Therapeutic uses :-

drug are used to treat the

1. Breast cancer
2. Lung cancer
3. Cancer of ovary
4. Hodgkin's disease, Ewing's sarcoma
5. Neuroblastoma.
6. Malignant lymphoma
7. Cancer of ovary
8. Chronic leukaemia.
9. It is used as an immunosuppressive agent.

Dosage :- Dose - 40-50 mg/kg divided dose by I.V.

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Brand Name:- Cycloxan, Cytoxan, Endoxan.

Contraindication:- pregnancy, lactation, Radiation Therapy.

Drug Interactions:- ↑se toxicity ℄ aminoglycosides; ℄ Thiazide ↑se bone marrow depression.

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Biologicals

Definition:- Medical products

→ Derived from human Blood, living organism (Animal & Plant, Bacterial) or its products like protein. (use biotech.)

Used in the prevention, diagnosis or the treatment of cancer & other disease.

Examples:- → Vaccine, Antibodies
→ Blood hormones
→ Interleukins...

Definition:- Biological are the medicine which are derived by using large scale cell culture of bacterias, yeast plants or animal.

→ Biological are also known as biological therapeutics or biologics or biopharmaceuticals

→ Biological are used for prevention or treatment of diseases.

→ Biologicals may be produce through biotechnology in living system.

Types:-

→ Immunotherapy :- Cytokines, cancer treatment vaccine, antibody.

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2. Targeted therapies:
   (1) Biological response modifier therapy (BRM therapy)
   (2) Biotherapy.
3. Blood components, blood derivatives, Whole blood.
4. Protein, xenotransplantation product.
5. Cellular and gene therapies.
6. Allergenic extract.

Sources:-

1. Mammalian cell culture
2. Insect cell culture
3. Plant cell culture
4. Avian cell culture (growing of cell from birds in lab setting)
5. Bacteria
6. Yeast
7. Transgenics
8. Humans.

Vaccines:-

→ Vaccine are prepⁿ of antigenic materials that are administered with the objective of including in recipient specific & active immunity against infectious micro-organism or toxin produce by them.

→ Immunization is the process whereby a person is made immune or resistant to an infectious disease, typically by the administration of a vaccine.

→ They contain living or killed micro-organism bacterial toxoids or antigenic material from the particular parts of bacterium rickettsia, or virus.

Classification of Vaccine

Class	Sub-class	Drugs
① Killed (inactivated) vaccines	Bacterial	Typhoid-parathyroid, cholera, wooking cough, Haemophilus Influenza type B., plague.
	Viral	Poliomyelitis inactivated Rabbies, Influenza, Hepatitis A, Hepatitis B
② Live attenuated vaccine	Bacterial	BCG, Typhoid Ty21a
	Viral	poliomyelitis oral vaccine (sabin), Mumps, Measles, Rubella, Varicella
③ Toxoids		Tetanus, Diptheria.

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Gene therapy

→ Gene therapy is a technique that involves the replacement of defective gene ε healthy ones in order to treat genetic disorder.

→ It is an artificial method that introduce DNA into the cell of the human body.

→ The first gene therapy was successfully accomplished in the year 1989.

Application of gene therapy:-

→ It is used in the replacement of gene that cause medical illness-health

→ The method generally destroey problem causing gene.

→ This method employ to treat disease such as cancer, ADA deficiency, cystic fibrosis etc.

Recombinant therapeutic

→ Are bio-engineered proteins that can be used to prevent or treat a disease

→ These ~~disease~~ proteins can replace protein that is abnormal or deficient in particular disease

→ These are produced by Recombinat DNA technology.

Indications :- some indications for biological agent along with examples

(1) Infectious disease :- (i) Vaccine such as HPV vaccine & Influenza vaccine are used to prevent the spread of the respective disease.

(ii) Monoclonal antibodies such as infliximab (Remicade) are used to treat viral infection such as hepatitis B and C.

(2) Hormonal deficiencies :-
→ Recombinant DNA products such as Human Growth hormone (HGH) are used to treat growth hormone deficiency.
→ Insulin is used to treat diabetes.

(3) Genetic disorder :-
Gene therapies such as lentiviral vector gene therapy are used to treat severe combined immunodeficiency.

(4) Neurological disorder
→ Monoclonal antibodies such as Ocrelizumab (Ocrevus) are used to treat multiple sclerosis.

(5) Cancer :- (i). Monoclonal antibodies such as Trastuzumab (Herceptin) are used to treat breast cancer.

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Side effects of biologicals

→ Most biologicals produce allergic hypersensitivity reactions.
→ Most biologics are given by
↓
→ IV site reaction (cause)
→ IV infusion rxn

→ Other side effect
① Chills
② weakness
③ diarrhoea
④ Nausea
⑤ fever
⑥ Shortness of breath
⑦ rash
⑧ Insomnia ---etc.

The serious side effect include:-
→ Anaphylaxis, serious infection,
→ CHF (congestive heart failure)
→ bleeding
→ cancer
→ thyroiditis
→ Hepatitis ....etc.