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Pharmacology

→ Pharmacon + logy
(Greek) ↓ drug — ↓ To study

→ Scientific study of drug movement (ADME) & its effect on Human body

→ Disease
- dis ↓ alteration
- ease ↘ Normal physiology

⇓

(↑↓) 'altered physiology'

→ Medical science
↓
disease
- diagnosis
  - (↑↓ Physiology)
  - ↓
  - 'Pathology'
  - ↙ A&P ↓ B ↘ M
- Treatment
  - (↓↑ physiology)
  - ↓
  - drugs.
  - 'Pharmacology'
  - → Medicine
  - → Surgery.

Pharmacology
- Pharmacokinetics
  - drug ↓ movement
  - (study of drug movement)
- Pharmaco-dynamics
  - drug ↓ power
  - (study of drug power) → Effect

ADME
- → Absorption - (Blood)] आना
- → Distribution - (Tissue)] आना
- → Metabolism - (Chem. conversion)] जाना
- → Excretion. - (Removal)] जाना

Drug:— Chemical substance that is used for prevention, treatment, diagnosis & cure of disease in human being.

As per W.H.O. :— Chemical substance that is used to modify pathological state & change in physiology for the benefit of the recepient.

- **Pharmacotherepeutics :—** (Medicine) Use of drugs (PCM) according to their applications. → Fever

Chemical
- use + misuse → drug
- use → medicine

- **Chemotherapy:—** Treatment of systemic infection & neoplasm by the help of chemical agent.

- **Clinical Pharmacology :—** Study of kinetics & dynamics of a drug in a pt.

- **Toxicology :-** Study of toxic / poisonous effect of drug / chemical.

Chemical → Drug (Right amount)
Chemical → Toxic (wrong amnt.)

- **Pharmacy :-** It is art & science of compounding & dispensing of drugs.
  - It include collection, purification & synthesis of drugs.

Orphan drug :— Drugs that used in rare disease or used rarely.

e.g:- desferrioxamine in Wilson' disease.

Essential drug :— As per W.H.O. :— Drugs that satisfy priority, health care need of a population are called Essential drugs.

EDL :— Essential drugs list.
(Rajasthan).
↳ NLEM (India)
National list of Essential medicine.

Nomenclature of Drug :— IUPAC Name → Chemical Name
- difficult to remember
- Not popular

e.g:- Acetyl Salicylic acid © Railway SN 2014

→ Generic name
Genera (Basic structure) e.g:- Aspirin
- Salt Short name → Non-proprietary name
- Easy to remember
- Popular.

→ Proprietary name — Brand name e.g:- Ecospirin.
- Given by manufacturer.

Diclofenac → Diclofenac Sodium
↓ (salt of diclofenac drug)
Drug ↓
*Drug used in salt form → solubility ↑
→ stability ↑

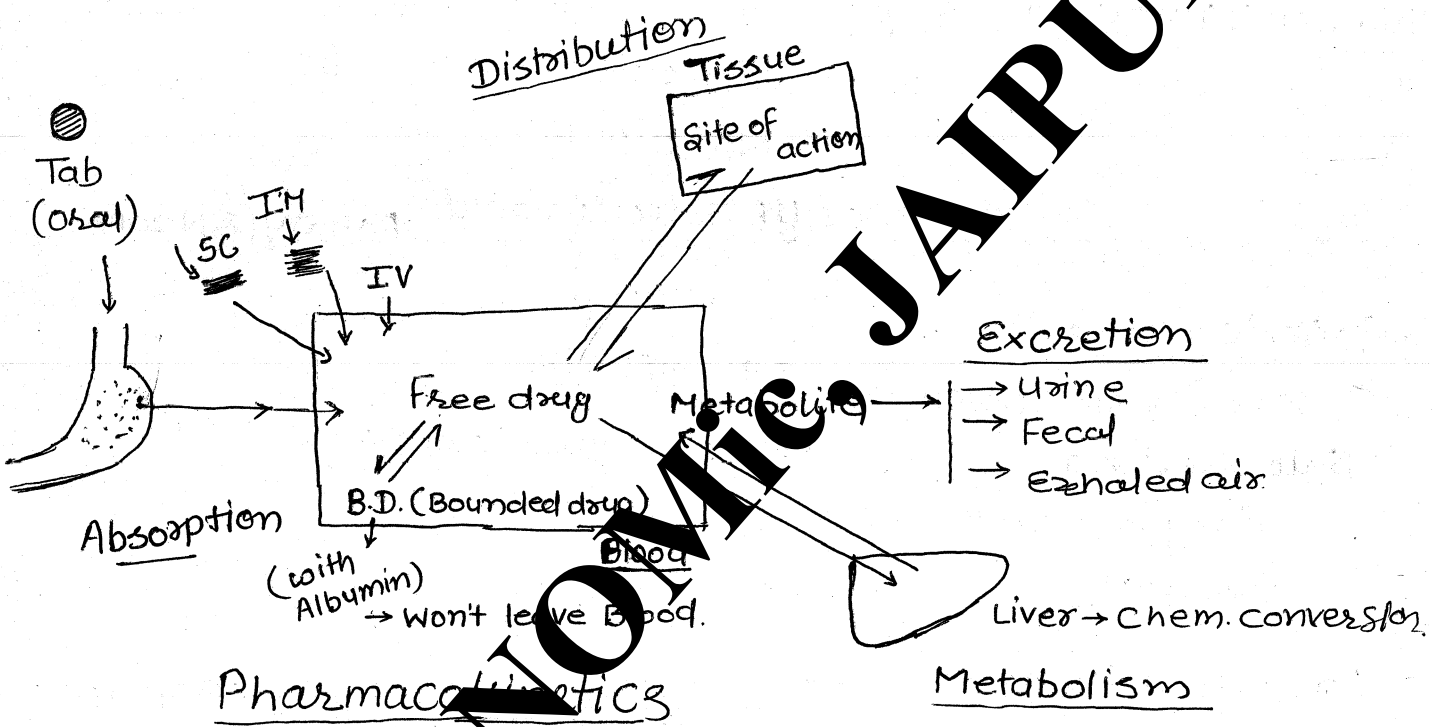
Pharmacokinetics → what the body does to the drug?

→ Study of drug movement in, through and out of the body.

→ It is quantitative study of A, D, M, E. [Drug movement]

→ All Pharmacokinetic processes [A, D, M, E] include movement of drugs across biological membrane.

** → Due to special structural design of biological membrane, it allows free passage to lipid-soluble drugs, while restrict water-soluble drugs (pass only via pores).



Absorption:- Movement of drug from site of admn. to systemic circulation.

S.O.A $\xrightarrow{\text{Drug}}$ S.C.

Factors :—

① **Aqueous Solubility** → For oral route.

→ Aspirin → Takes time to dissolve in water → absp. easily.

ⓑ Concentration :- Conc.↑ → absp.↑

ⓒ area of absorbing surface :-

Intestine → Large S.A → more absp.

Stomach → Less. Surf. area → less. absp.

ⓓ Vasculasity :-

- I.M → more vascular → Fast absp.
- Sub.cut. → less. vascular → Slow absp.

ⓔ Route :-

(i) ORAL :-

Most of the drugs.

↓

. weak organic acid / base

↓

Ionise ⇌ Unionise

(polar) GIT Epithelial (Non-polar)

↓ limit ↓

water sol. (Lipoidal nature) ↓

↓ lipid soluble

Not absorbed ↓

absorb.

(ii) SC / IM :- * Large pores in capillaries. (SC / IM) =

↓

Even ionise / polar / water soluble / large molecule

↓

absorb.

(iii) Topical :- (Body surface)

Skin. mucous memb

Eye, Nose, Ear (Body cavities)

Local Effect

* Highly Lipid Soluble

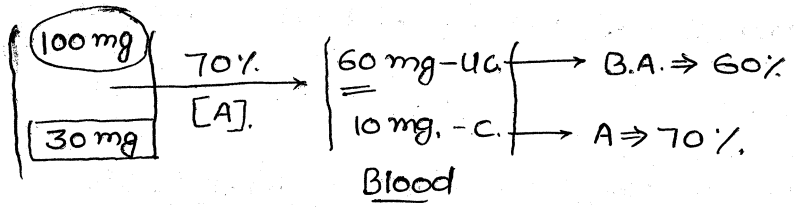
↓

absp. via skin / MM

↓

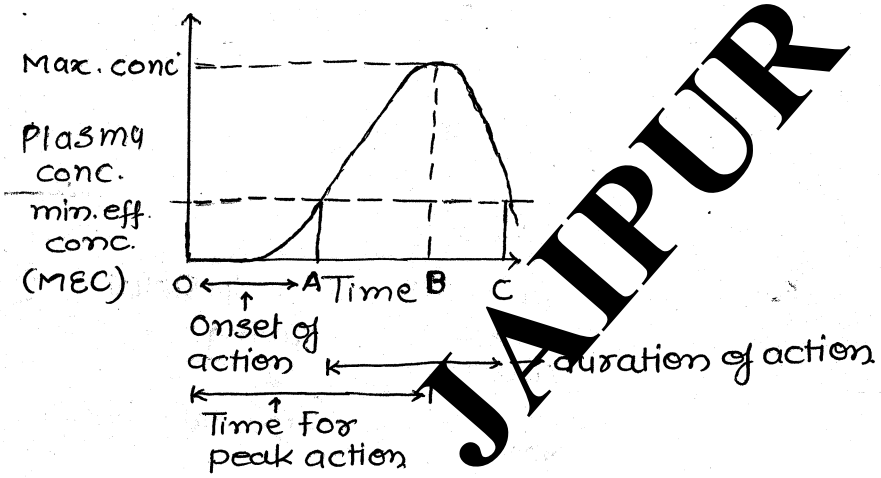
Systemic effect

* **Bioavailability** :- Fraction of administered dose that reaches in systemic circulation in unchanged form. → useful.



→ Availability of drug in system at a time.

→ It denote by plasma conc.- time curve



Bioavailability governs :- Rate, onset

① Route :- absp. → IV > IM > SC > Oral.

② Dose :- conc. > MEC → action.
↓ min effective conc.

③ Onset

④ Duration

⑤ Peak action

⑥ Frequency → drug in blood.
⇓ (action)
Frequency.

Distribution :- Movement of drug from blood to tissue.

Blood $\xrightarrow{[D]}$ Tissue

Factors :-

① Lipid / Water Solubility :-

② Ionisation :-

③ Plasma protein binding (PPB) :-

◉ Barriers :-

⑨ Placental barrier :- Passage across placenta.

Placenta :- Lipoidal memb.

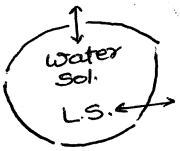
→ Lipid solubles easily cross it. while it restricts water soluble.

** Placenta incomplete barrier →*

→ If water soluble +nt in High conc. for long time then they also cross placenta.

E.g:- Vita B_9 (Folic acid) – daily given → cross placenta

⑥ Blood-brain barrier :- penetration into brain & C.S.F.



Normal capillaries.

Blood Brain barrier (Tight vascular junction)

*BBB :- only lipid sol. cross it.

Plasma Protein Binding :- Binding of drug with Plasma protein Generally with Albumin.

→ Bound drug (BD) :- Fraction of drug that bound with Plasma prot.

→ Unbound drug / Free drug :- Drug that don't bound with P.P. (Fraction)

→ Bound drug is pharmacokinetically & dynamically inert. (not available for dist., meta, excr & even for action)
until not get unbound (Free drug).

→ Bound get unbound to maintain Free drug concentration. in equilibrium,

When Free drug conc. ↓se due to elimination [M+E].

- So Plasma prot. binding generally act as temporary storage of drug, that makes drug a long-acting.*

Drug displacement :— When two drug bind to same plasma prot on same site, in this situation First drug displaced by second drug.

↓

First drug Free drug conc. ↑se.

↓

Toxicity of First (displaced) drug

Eg:- Phenytoin displace Warfarine → [illegible]

↳ 2nd

Tissue Storage → accumulation of drug in body tissue that is based on affinity.

Drug	Tissue
→ Tetracycline	Bone & Teeth.
→ Chloroquine	Retina & Liver
→ Iodine	Thyroid Gland

* → It will lead to destruction of same organ. (Toxicity)

Drug Metabolism (Biotransformation):-

Chemical conversion of drug inside body to convert Lipid Soluble (unionised / Non-polar) to water soluble (ionise/ Polar) for excretion.

Lipid Soluble (unionised / Non-polar) → reabsp → excn (by crossing memb. easily)

water soluble (ionise/ Polar) → no reabsp → excn

* Water soluble / ionise/ Polar do not need metabolism.

Biotransformation:- Chem. conversion of drug inside body. (Liver, Kidney, Gnt., Lungs, Plasma)

Addition (Anabolism) / Breakdown (Catabolism) → **Drug Metabolism**

(Liver, Kidney, Gnt., Lungs, Plasma) = Enzymes

Enzymes → Non-microsomal → Mitochondria, Cytoplasm

Enzymes → Microsomal → Smooth Endo. reticulum

Plasma → (only non-microsomal)

Chem. Rxns.

- Phase-I (Non-Synthetic)
- Phase-II (Synthetic) → new products formed

① **Inactivation:-** ** Most of the drugs inactive after metabolism.

Drug (Active) → Metabolite (Inactive)

② **Active to Active:-**

Drug (Active) → Metabolite (Active)

depression → Imipramine (A) → Desipramine (A)

→ This makes drug Long-acting.

③ **Activation:-** Inactive → Active

Drug (Inactive) → Metabolite (active)

e.g:- Levodopa → Dopamine

→ Drugs that are inactive, active after metabolism are called 'Prodrug'. e.g:- Levodopa.

* Both microsomal & Non-microsomal enzymes are deficit in newborn. upto the age of Few months.
  ↳ Baby can't process. drugs c̄ Heavy metabolism.

* Microsomal enzymes inducible by drugs [Rifampacin, phenobarbiton], smoking & barbaque Food. ⟶ ↑se Metabolism.

* Rifampacin ↑se OCP Metabolism → Failure of OCP. (↓se duration of action).
  Meta. ↑
  24 hr → 16 hr.

* Phenobarbiton ↑se bilirubin conjugation. → ↓se unconjugated billirubin.
  ↳ removable Form.
  (℞ of Neonatal Jaundice)
  ↑se Glucoronide
  removes billirubin.

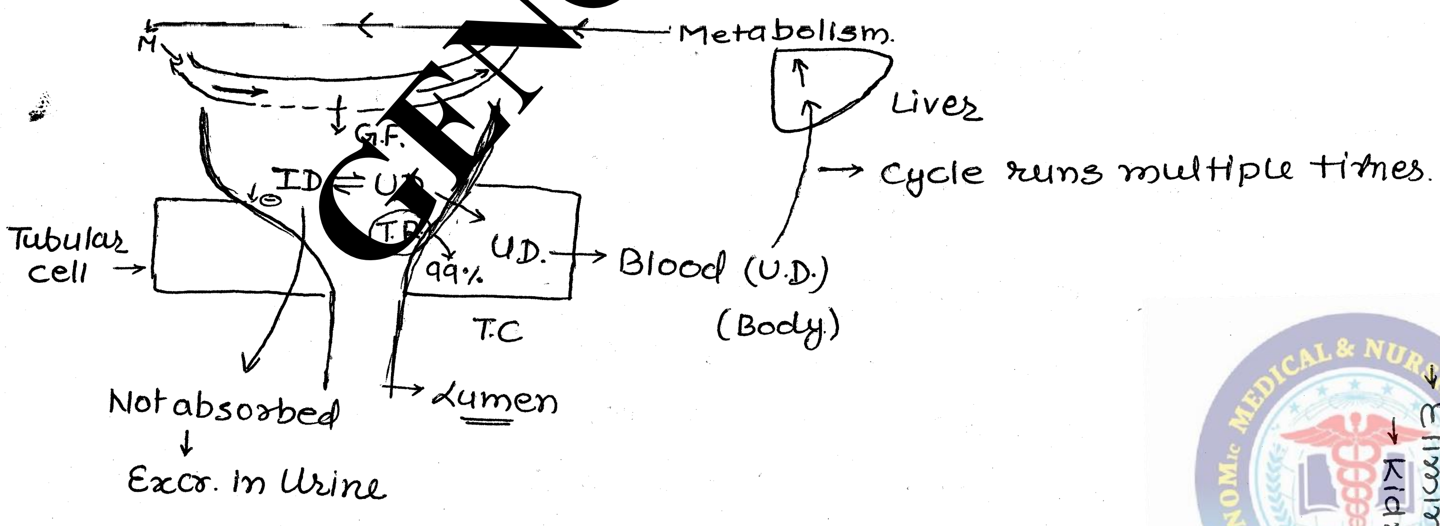
* Drugs are enzyme inhibitors also. e.g:- Omeprazole, Fluconazole.
  ↓
  ↓se metabolism.
  ↓
  ↑se duration

* Excretion:- Passage out of systemically absorbed drug from body.

- Drugs & their metabolites. excrete via various channels. like, urine, feces, Exhaled air, ~~Fat~~, saliva, milk & tear. sweat

(a) Urine :- (Through Kidney) → 'Renal Excretion'

RE = GF + T.S − T. Reabsp.



Elimination:- Kidney, Liver, Lungs

* Major Channel of Excretion → Most of the drugs excr. by urine.

(b) Feces :- (through liver) → Billary Excretion.

→ Bulky drugs eliminate by liver in Feces.

e.g:- Amphicillin.

Blood → Liver → Bile → Intestine → Stool

→ Glucoronide conjugation → make drugs more bulkier.

(c) Exhaled Air :- Volatile & liquids & gases eliminate by lungs. ↳ M+Excr.*

e.g:- Nitrous Oxide. (Gen anes)

→ Sweat, Saliva, Tear, Milk are minor channel of excretion

- Sweat, Tear → Rifampacine.*
  ↳ (Orange-Red colour)#

- Saliva → Lithium.
  ↳ (bitter taste in mouth)

- Milk → Basic drug. → Ca cause prob. in baby.

→ Elimination (Metabolism) + (Excretion)

Liver, Lung, Kidney

↓ Major Metabolism.

↳ Major organ for Excretion.

• First Pass Metabolism :- When drug taken through Oral Route,

↓

during its absp.

↓

before entering in Systemic Circ.

↓

Drug get metabolised in intestinal wall & Liver during its I st pass From there

→ Hydrocortisone & Lignocaine not use orally due to High First Pass metabolism.

→ Plasma Half Life :- ($t_{1/2}$) It is time taken by a drug to remain in half amnt of its original value in plasma.

* → In 4 to 5 $t_{1/2}$, drug almost eliminate from body.

↓ $t_{1/2}$ → Fast Elimination

→ Study of drug effect sequence.
(What the drug does to the Body?)

Drug
↓
Chemical
↓
Physiological Changes
(Pharmacological effect)
↙ ↘
Wanted (Therapeutic) | Unwanted (Adverse)

→ How the Drug act on Human Body?
↙ ↘
① Principle of drug action. | ② Mechanism of Drug action.

→ Principle of Drug action :—

ⓐ Stimulation :- Enhancement of specialised cell/organ activity.
e.g:- Adrenaline stimulate Heart.

ⓑ Depression :- Diminution of specialised cell/organ activity.
e.g:- Diazepam depress CNS.

ⓒ Irritation :- Mild irritation may start associated function.
e.g:- Bitters ↑se Gastric acid secretion.
↙ ↘
↑ Secr. | ↑ motility

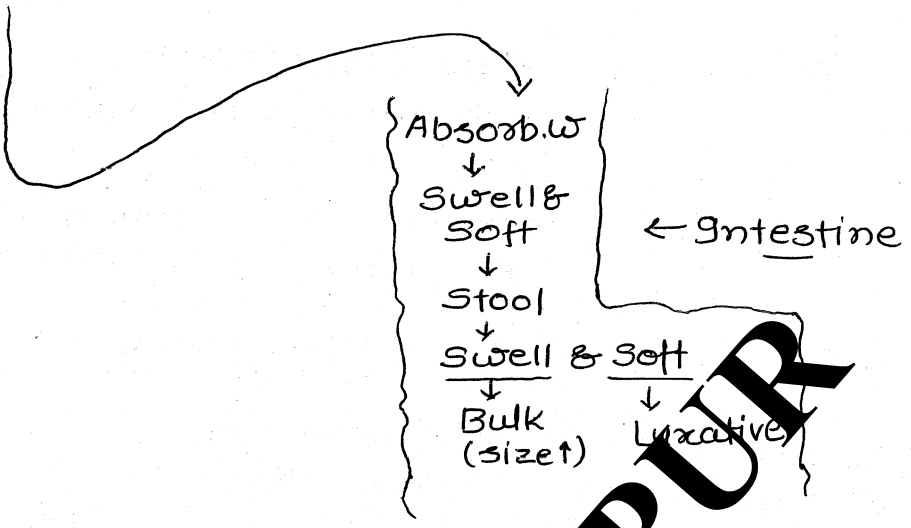
ⓓ Replacement :- Endogenous deficiency of hormone, mineral, vitamins can be replaced from outside.
e.g:- Iron in I.D.A. (Iron def. anemia)

ⓔ Cytotoxic (killing of cell) :—
↙ ↘
Pathogen (Guest cell) | Cancer cell (Host cell)
↓ ↓
In case of Infection. | In case of Cancer.

→ Mechanism of Drug action:—

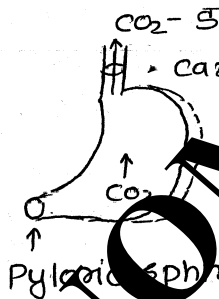
1. Physical action :- Action due to physical property.
eg. (mass., Radiation)

- Isapghulla as bulk laxative
↓
with lukewarm water or milk.



2. Chemical action :— action due to chemical property (Acid, base)

$$\underset{\text{Acid}}{HCl} + \underset{\text{Base}}{NaHCO_3} \longrightarrow H_2O + NaCl + \underset{\text{डकार}}{CO_2\uparrow}$$



↓ HCl → ↑ PH → Alkalosis

↑ HCl → ↓ PH → Acidosis.

3. Through Enzyme :— Imp. target for drug action.

Drug
↓
Enzyme ↕
↓
Chem. Rxn
↓
↕ Physiology.

Drug

- Enzyme Stimulation
  - e.g:- Adrenaline
  - ↓
  - ↑se Adrenal Cyclase
  - ↓
  - ↑se Cyclic-AMP
  - ↓
  - ↑se Cardiac Activity
  - ↓
  - ↑se Force & rate
- Enzyme Inhibition
  - Specific
    - Competitive
      - e.g:- Sulfonamide competitively inhibit Folate Synthase enzyme.
    - Non Competitive
      - e.g:- Aspirin inhibit Cox Non-comparitively
  - Non-Specific

→ Non Specific :- Acid alkali, phenol and heavy metal inhibit enzymes non-specifically by alter in pH or structure.

(iv) ~~GMP~~.

4. Gon Channel :- Fastest Mechanism*

gon channel keep opening closing :-

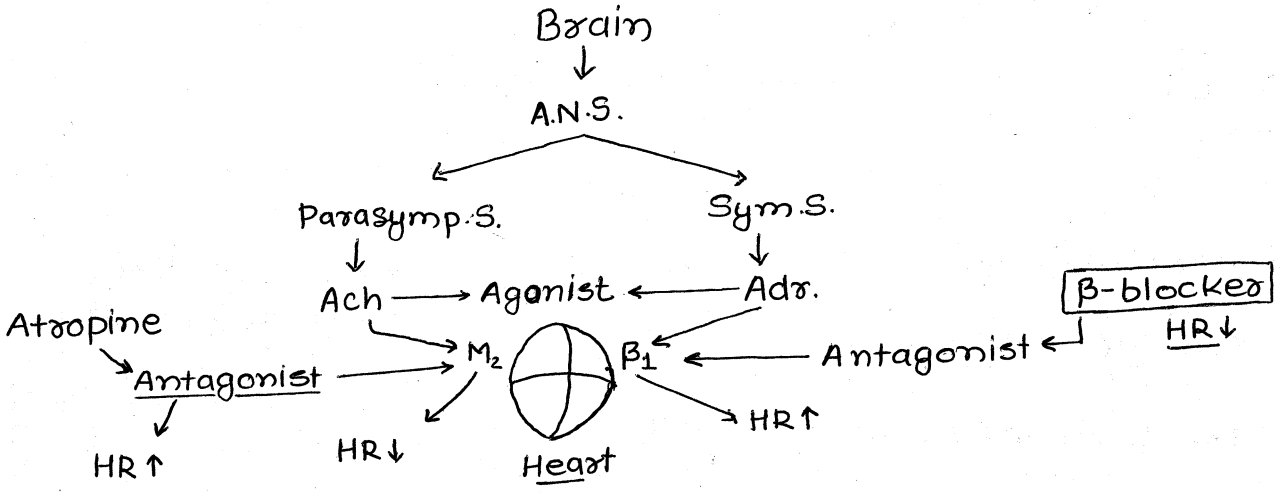
Drug

- ↑ Opening Time (open For more time)
  - ↓
  - • Gon channel opener.
  - E.g:- Nicorandil ~ (K^+ Channel opener)
- ↑se Closing time (Close for more time)
  - ↓
  - • Gon channel blocker
  - e.g:- Amlodipine ~ (Ca^{+2} channel blocker)

5. Receptor :- Maximum drug act through this.

↳ Macromolecule, protein in nature, ⊕nt on cell surface & inside cell (cytoplasm, nucleus).

↳ Act as a site of action for various hormones, N.T. & drugs for action.



Agonist :— attach and activate receptor.
↓ Affinity ↓ intrinsic activity.

Antagonist :- attach & occupy receptor.
↓ only affinity but no intrinsic activity
↳ prevent action of agonist. ↳ shows effect only in the presence of agonist.

Drug action :- Drug act on receptor. (→ attach)

Drug effect :- Physiological changes.

Drug dose :- Appropriate amount of drug that is needed to produce certain response in a patient.

@ According to effect (use) :-
(i) Prophylactic dose :- For Health benefits.
(ii) Therapeutic dose :- For Treatment.
(iii) Toxic dose :- Toxic effect.

ⓑ According to need :-
(i) Standard dose :- Same For all.
e.g:- O.C.P.
(ii) Regulated dose :- dose adjusted according to physiological need.
e.g:- Anti-hypertensive drugs.

(iii) Target-level dose :- Dose adjusted according to target therepeutic concentration.

e.g:- Anti-depressant

(iv) Titrated dose :- Dose adjust a/c. to acceptable adverse effect.

e.g:- Anti-cancer drug.

Factors affecting Effect of Drugs :-

1. Body weight / Body Size :-

B.W. / B.S. / Dose

Higher the Body wt. → Higher the body size → Higher dose

→ Children & a Elder require lesser dose as compared to Adults due to their lesser body size.

Clark's Formula →

(Individual dose)

$$I.D. = \frac{\text{Body wt.}}{70} \times \text{Adult dose}$$

↳ (If wt is in kg).

→ India
↳ M.K.S.

Q. Body wt. = 7 kg. Adult dose → Ceftriaxone → 1000mg.

$$ID = \frac{7}{70} \times 1000mg = 100\ mg$$

Q. Body wt = 21 kg. Ofloxacin A.D = 200mg

$$ID = \frac{21}{70} \times 200 = 60mg$$

$$ID = \frac{B.W.}{150} \times A.D.$$

If wt is in pound. → Britain
↳ F.P.S.

B.H.U. 2018

* Body wt. / Body size :- Best method (accurate) for child dose calculation.

② Age :- Child dose calculate according to age in routine.

Young Formula

$$\frac{\text{Age}}{\text{Age}+12} \times \text{A.D.}$$

Diling Formula

$$\frac{\text{Age}}{20} \times \text{A.D.}$$

E.g. PCM = 500 mg A.D.

→ if age = 8. ⇒ $\frac{8}{8+12} \times 500 = 200\,mg$

⇒ $\frac{8}{20} \times 500 = 200\,mg.$

→ if age = 12 ⇒ $\frac{12}{12+12} \times 500 = 250\,mg$

⇒ $\frac{12}{20} \times 500 = 300\,mg$

→ if age = 16 ⇒ $\frac{16}{16+12} \times 500 \Rightarrow \frac{16^{4}}{28_{7}} \times 500$

$= \frac{2000}{7} \simeq 285.7\,mg$

⇒ $\frac{16}{20} \times 500 = 400\,mg.$

→ Young Formula applied below 12 yr. age

Q. A.D. = Cefotaxime - 1000 mg.
Calculate dose for 14 kg child.

Sol. ⇒ $ID = \frac{14^{2}}{\cancel{10}} \times 1000 = 200\,mg.$ ✓

→ If age in months :- Fried formula :-

$$ID = \frac{\text{Age (months)}}{150} \times \text{AD.}$$

③. Body Surface area :-

$$I.D = \frac{B.S.A\ (m^2)}{1.7} \times A.D.$$

③ Sex :- Female require lesser dose as compared to male specially drugs acting on C.N.S., due to their lesser body size and mental makeup.

E.g:- Sleeping pills

→ Succinate Choline Muscle relaxant

4. Psychological Factors :- Pt. attitude & belief may affect the effect of drug.

E.g:- Anxious Pt. require more dose of G.A.

5. Disease condition :- Kidney and Liver disease affects elimination of drugs. → Drug remain in body → Toxicity.

e.g:- Streptomycin nephron toxicity ↑se in Renal failure

6. Tolerance :- Effect ↓se on prolonged use, to maintain effect ↑se dose req...

e.g:- Sleeping pills

7. Tachyphylaxis :- when indirectly acting drug administer in quick succession repeatatively, Loss of effect due to unavailability of mediator.

of drug ... for sometime and on again use effects become usual due to unavailability of mediator.

Eg:- Epinadrine
↓
↑ Nor-Adr. → mediator.
↓
Effect.

⑧ Idiosyncrasy :- It is genetically determined abnormal reactivity, towards a chemical.

e.g:- Aspirin induce Asthma.

- diff in gene proto among individu

Adverse Effects:—

Unwanted, undesirable, unintended effect of drug that can be trivial, serious, or even fatal.

- Adverse effect
  - Predictable — Type-A
    - → Side effect
    - → Toxic effect
    - ↳ Reduction of dose require
  - unpredictable — Type-B
    - → Idiosyncrasy
    - → Drug allergy.
    - ↳ stop the drug & not use again.*

Side Effect:- effect other than targeted side.

Teratogenecity:— Abnormal effect of drug on Fetus when drug taken by preg^n woman

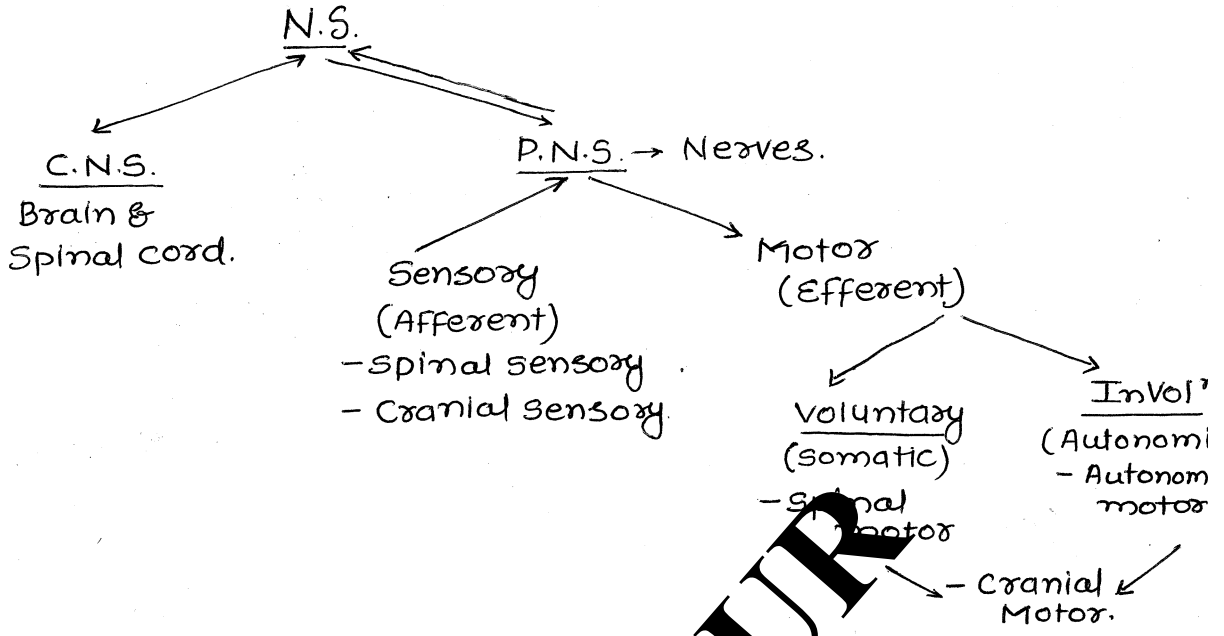
Teretogen	Teretogenic effect
• Thalidomide (For morning sickness)	Phocomelia ↳ Seal like limbs.
• Phenytoin	Cleft Palate
• Alcohol.	T.O.G.R.

Combined Effect of Drug :—

- Synergism (↑se effect)
  - Addition → Effect equal to total
  - Superaddition (Potentition) → Effect greater than total.
- Antagonism (↓se effect)

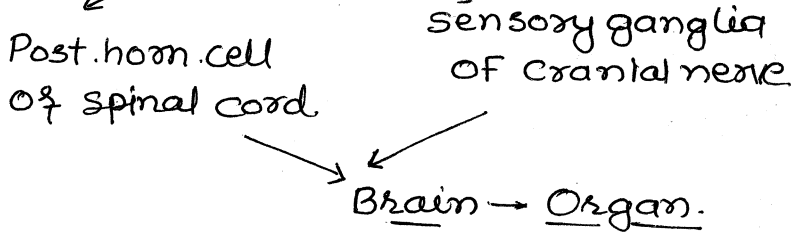
Drugs acting on A.N.S.

General consideration:—

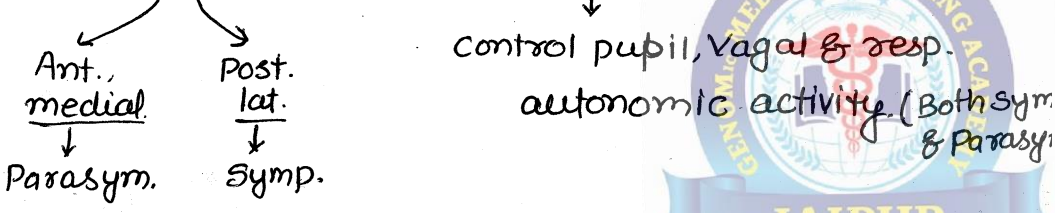


A.N.S. → Involuntary Motor (efferent) of the body
- control visceral organ function and largely function below the level of consciousness.
- Autonomus working :-

Autonomic Afferent :— Most of the visceral nerves
↓
Mixed nerve
↓
Carry non-mylinated sensory (afferent) Fibre.



Autonomic Centre :— Higher Centre of Brain.
(Hypothalamus, mid-brain & Medulla).

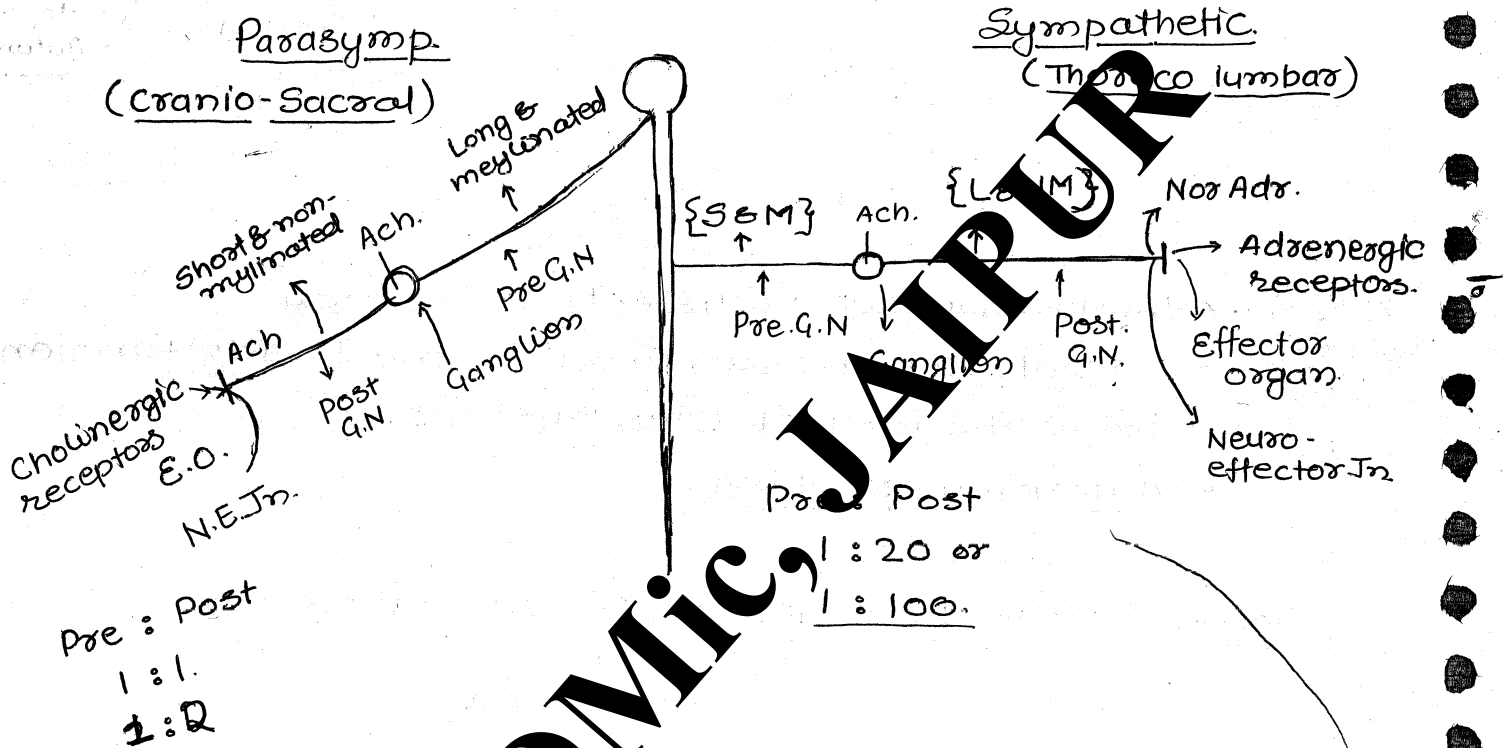


Autonomic Efferent:- Anatomically divided into two:-

Parasympathetic | Sympathetic

- Most of the organs recieves both and both functions antagonistic in nature. So autonomic activity at a time depends on sum total of Parasym. & Symp. tone.
  ↳ according to situation, and need, one of them goes dom^{n}.

* Cilliary, gastric and pancreas recieves only parasym.
* While in most of the Blood vessels, sweat gland, hair follicle & Spleen recieves only Sympathetic.



① Origin :- Cranio-Sacral
III, VII, IX, X & S_2-S_4.

② Pre-Gang nerve :- L & M

③ Post Gang nerve :- S./abst & NM.

④ Ganglion :- Near & on organ.

⑤ N.T. :- Ach.

⑥ Pre-Post ratio :- 1:1 / 1:2.

⑦ Distribution :- Limited to Head, neck & Trunk.

⑧ Major fn :- Assimilation of Food & conservation of Energy.

① Origin :- Thoraco-lumbar
(T_1-L_2 or L_3)

② S. & M.

③ Long & NM

④ Away from organ.

⑤ Nor. Adr. & Adr.

⑥ 1:20. / 1:100

⑦ Wide

⑧ Tackling stress & Emergency.

Parasympathetic Nervous System → 24 hours working

- But dominant at Night time. (resting)

- Cranio-Sacral (spinal nerve)
- III, VII, IX, X, S_2-S_4.
  - III → Meiosis
  - VII, IX → ↑se Secretion
  - X → 75% of Parasym. activity.
  - S_2-S_4 → Bladder, Bowels & Genital → Penile erection

P.S.A. → Involn activity.

→ Parasym. Activity is because of Ach that is released by post Gang. P.S. Nerve at NEJn. Activity is via Cholinergic (Muscarinic) receptor on Effector Organ.

Ach
↓
Cholinergic receptor

- Nicotinic (no significant role in PSA)
  - NN → on (Autonomic Ganglia) → Nerve-Nerve
  - NM → somatic Nervous System → Neuro-Muscular Jn.
- Muscarinic (Effector Organ) — P.S.A. ⇑
  - M_1 → Gastric → ↑se HCl
    - CNS → Learning & Memory
  - M_2 → Heart → ↓ HR
  - M_3
  - M_4 → CNS → Unknown.
  - M_5

M_3.
→ Smooth Muscle → Contraction
→ Gland → ↑se secretion
→ Eye → Miosis.

Parasym. Drugs

- Parasympathomimetic (↑ PSA)
- Parasympatholytic (↓ PSA)

* Parasympathomimetic / Cholinomimetic / Cholinergic recep agonist / Muscarinic recep. agonist / Vagomimetic / cholinergic :-

→ Drugs used to ↑se P.S.A.

→ Drugs that have action similar to Ach either by acting as Cholinergic recep. agonist (Act like Ach.) and by acting as Anticholinesterase (↑se Ach level.)

Drugs :-

1. Cholinergic Receptor Agonist :-

e.g:- Acetylcholine
Carbachol
Methacholine
BETHANACHOL
} - Cholinester.

PILOCARPINE :- alkaloid

2. Anticholinesterase :- ↑ Ach level.

(a) Reversible Anticholinesterase :

e.g:- Physostigmine
Neostigmine
Edrophonium
Pyridostigmine
Galantamine
Rivastigmine
Donepezil.

(b) Irreversible Anticholinesterase :-
(Organophosphate / insecticide)

e.g:- Malathion
Parathion
} known for poisoning
→ not prefer clinically.

Pharmacological Action of Ach. (P.S.A.):-

1. **Heart :-** ↓HR.

Vagus → Ach → M_2 (SA Node) → depress. SA Node → HR ↓

P.S.A / Vagal action on Heart → ↓ HR
(stimulation)

2. **Smooth Muscles :-** Contract

Ach → M_3 (SM) → contract.

- → Bronchospasm,
- → Bladder spasm
- → Abdomen spasm
- – Involn micturation & Defecation.

→ used in post-op Pt., (absence of signal for mict & defec.) - eff. of anesthesi

3. **Gland (M_3) :-** ↑se Secretions

→ ↑se Saliva, Sweat, Tear, Gastric and Resp. secretions.

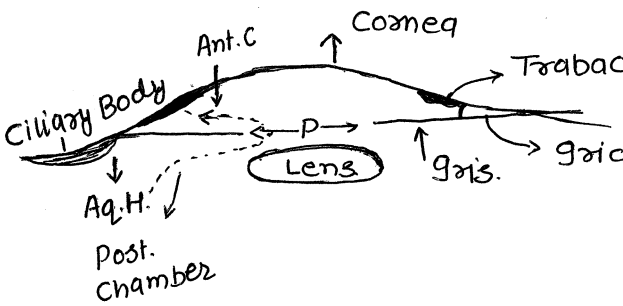
4. **Blood Vessels :-** Vasodilation

– only in Few blood vessels. (Bcz most of the BV only have symp.)

– No Clinical Importance.

Ach
↓
M_3 (Endothelial cells) ← B.V.
↓
Nitric oxide → Relax → Vasodilation
(Smooth muscles of vessels)

5. **Eye :-** Meiosis and ↓I.O.P.

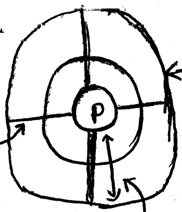


Eye

(III CN) OM

Ach → Circular m. (Iris) (M_3)
↓
Contract
↓
Miosis.
↓
- Iris thin and stretch.
↓
Remove pupilary block. ⟶ ↑se Aqueous Humor OutFlow/drainage

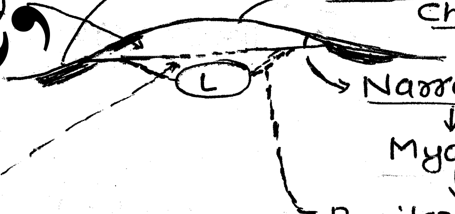
Ach → Ciliary muscles (M_3) (attached c̄ ciliary body)
↓
Contract
↓
Improve Trabeculae allignment
↓
↑se Aqueous Humor OutFlow/drainage
↓
↓se I.O.P.



Sympath. → Adr → Radial muscles (α) → Contr. → Mydriesis (dilation of pupil)

Parasym. (Ach) → Circular muscle (M_3) → Contract → Miosis (Constriction of Pupil).

Ciliary mus. → contract → Improve trabacular allign. → Trabacular → A.C → ↑se A.H. drainage → ↓se IOP



Circular (Iris)
↓
Contract
↓
Miosis.
↓
Iris thin & Stretch
↓
Remove pupilary block
↓
P.C $\xrightarrow{A.H.}$ A.C ✓

Shallow Ant Chamber
↓
Narrow (ICA)
↓
Mydriasis
↓
Pupilary Block
PC $\xrightarrow{(X)\ Aq.H}$ Ant. C.
↓
↓ Aq. H outflow/drainage
↓
↑ I.O.P.
(Acute congestive Glucoma) / (Angle closure Glucoma)

When circular is relaxed, it rests on Lens ⇒ Pupilary block ⇒ Aq.H. ⇒ remain in Post. chamber

Drugs:-

I. Cholinergic Receptor Agonist :-

- Acetylcholine

  Ach ⇒ Natural, neurotransmitter but not preferred clinically
  → destroy in second (Blood)

- Carbachol :- Not use in current.

- Methacholine :- was. Occasionaly used in P.S.V.T. (In history).
  - not prefer in current.
  - Nurse :- used to notice breathing sound during methacholine therapy.

  ↓
  M_2 agonist
  ↓
  ↓se HR
  ↓
  Use :- in P.S.V.T. (Paroxymal Supra Ventricular Tachycardia)

  Bronchospasm.

  {In current → Adenosine. (D.O.C in P.S.V.T.).}

- Bithanachol (Urotonin) (25 mg T...)

  ↓
  M_3 (detrusser bladder)
  ↓
  contract detusser
  ↓
  Micturation

  use :- post operative non obstructive urinary retention.

- Pilocarpine (0.5-4% Eye drop)

  (a) as miotic

  (i) Glucoma (↓IOP)

  # • (Angle closure glucoma)
  (Remove → Pappilary block)
  contract → Circular mus.
  PC → AC

  * open angle glucoma :
  ↓se trabacular paten...
  ∈ the age
  ↑se IOP

  • Open Angle Glucoma
  (contract → Cilliary mus.)
  A.C. —A.H.→ Trabacul.
  (Trabacular allignment)

  • Aphakic Glucoma (⊖Lens)

  (ii) To counter Mydriesis

  (iii) To break adhesion b/w iris & lens or iris & cornea.

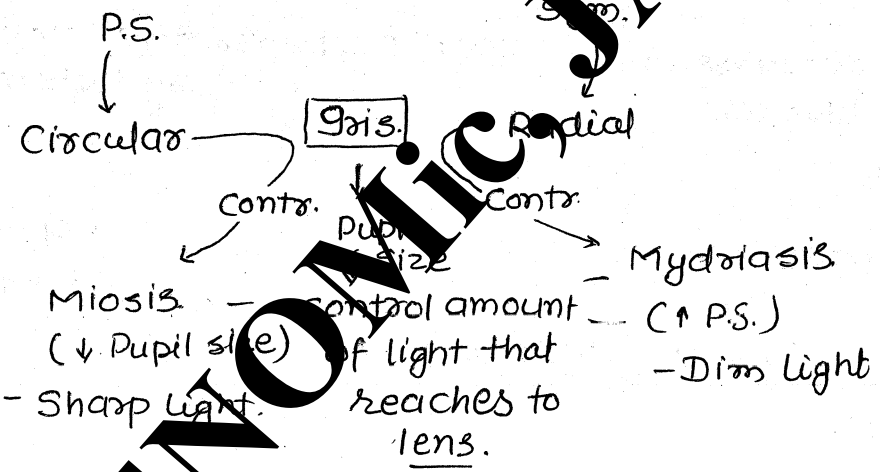
(b) diagnosis of Cystic Fibrosis:- (sweat test)*

Pilocarpine → locally ē cotton → sweat
↓
Take as sample
↓
Check Cl^-
↓
If excess.
↓
C.F.

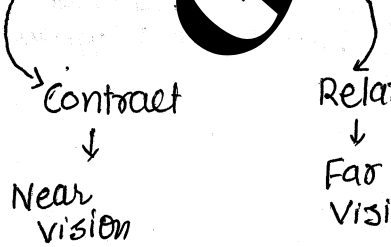
Adverse Effects :-

→ Miosis (Circ. muscles)
↓
(i) ↓se vision in dim light.

→ Cilliary - contraction
↓
(ii) - spasm of accomodation
(iii) - Brow pain
(iv) Stinging sensation in Eye.



Cilliary (adjust Focal length)



II. Anticholinesterase :- ↑se Ach level.

Ach (choline ester)
⊖ → | cholinesterase
Hydrolysis

(a) Reversible Anticholinesterase :-

• Physostigmine :- 0.5 mg/ml. inj. S.C. / IM / I.V.
'Eserine' - 0.25% Eyedrops

- Natural
↓
Lipid Soluble
↓
Cross. B.B.Br.
↓
'Central Effect'

- Penetrate Cornea. → Opthalmic use.

* Usage :- 1. Central use :- Atropine / Belladonna Poisoning.

physostigmine (cross BBBr) → ↑se C.A. in Brain also.

Atropine → cross BBBr. → Anticholinergic → ↓se cholinergic activity in Brain also

2. Opthalmic use :- Glaucoma (↓se I.O.P.) {Eyedrop}

• Neostigmine :- 0.5 mg/ml. inj. S.C. / I.M / I.V.
↓
Synthetic
↓
Water soluble.
↓
Only peripheral use.

Usage :- 1. Mysthania Gravis :- To ↑se muscle strength
↓
Auto-immune disease
↓
affects N-M Jn.
↓
Muscle weakness.

* Mysthania Gravis :- 1 in 10,000 incidence

↓ A.I.D.

developement of Ab.

↓

At N-M Receptor

↓

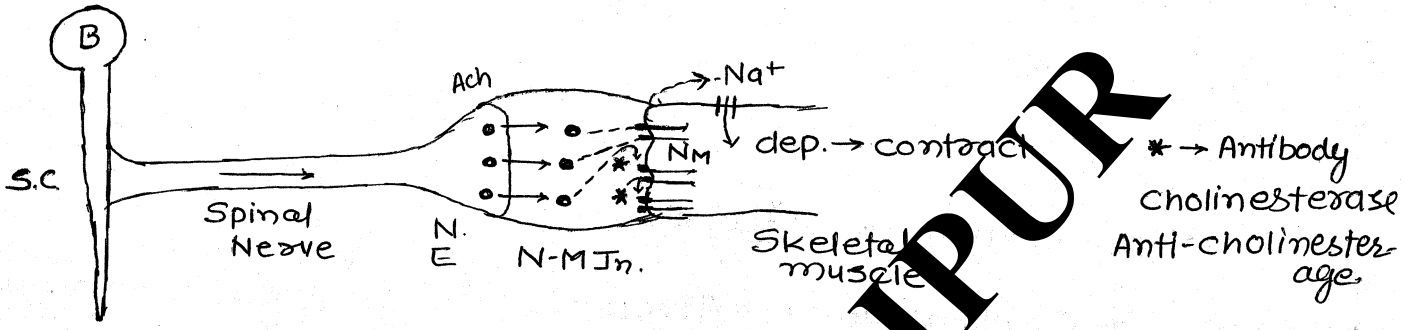
↓ Free N-M receptors. (upto 1/3 or less)

↓

↓ se Ach action on skeletal muscles.

↓

muscle weakness



Neostigmine

↓ (by inhibition of Cholinesterase)

↑se availability of Ach at N-M Jn.

(sustain availability)

↓

↑se Ach attachment c̄ large area of remaining receptors (Free Nm recep.)

↓

↑se Ach action

↓

↑se Muscle strength

2. Post operative :- Recovery of anaesthesia.

• Curare + muscle relax.

↙ urinary retention | ↓ Paralytic ilius | ↘ decurarization. {* BHU2019} (To reverse musle relaxation)

3. Cobra bite → Neostigmine + Atropine (Muscarinic recep. blocker)

↓ Venom

↓ Curare like

↓ Resp. paralysis.

↓

↑se Ach

↓ Nicotinic (NM) → prevent resp. paralysis.

↓ Muscarinic → Bronchospasm

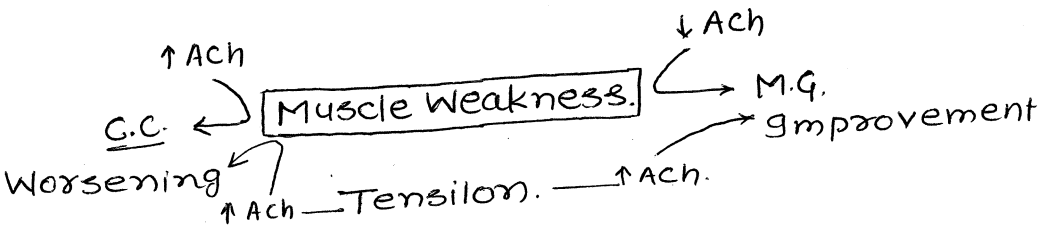
↓

prevent bronchospasm.

• Ult. Rx :- Antivenom.

• Edrophonium :— Short acting
(Tensilon) – Amelioration test. / Tensilon test.

2-10mg I/V → ⇓
- → Improvement → M.Gravis
- → Worsening → Cholinergic crisis.



• Pyridostigmine → 60 mg.
→ similar to Neostigmine
→ Long acting → better. *

Use :- → Mysthania Gravis [D.O.C.] *

- Rivastigmine
- Galantamine
- Donepezil.

→ Cross. B.B.Br. → Brain.
↓
agonist
↓
Improve learning & memory in Alzheimer's disease.

* Adverse Effects of Parasympathomimetic
→ Bronchospasm
→ Abdomenspasm
→ Bladderspasm
→ Involn micturation & defecation
→ ↑se secretions
→ ↓ se vision in dim light
→ Spasm of accomodation
→ Bradycardia.

* Contra-indications
→ Asthma, COPD.
→ Peptic Ulcer
→ Sick-sinus.
→ conduction defect
→ Obstructive bladder & colon.
→ Pregnancy.

Uses of Parasympathomimetic :-

1. Miotic :- Pilocarpine, Physostigmine
   - ↳ Glucoma :- ↓ IOP
   - ↳ To counter mydriesis
   - ↳ To break adhesion b/w Iris & lens / Iris & Cornea.

* Atropine use in Cholinergic Crisis to ↓se muscarinic effect.

2. Mysthania gravis
   - diagnosis → Edrophonium (Tensilon test)
   - Treat. → Neostigmine, Pyridostigmine [D.O.C.]

* Atropine used along ⊂ Neostigmine & Pyridostigmine in Rx of M.G. to counter (↓) muscarinic effect.

* currently :- Muscle biopsy (N-R Ab).

other used drugs :-
→ Prednisolone. (steroid)
Immunosuppresant.

3. Post Operative :- Recovery of Anesthesia. → [Neostigmine]- For all (Urin. Retention, Paralytic Ileus, decurarization)
   - {Bithanacol}
   - {Edrophonium}

4. Cobra bite :- Neost. + Atropine → To prevent Resp. paralysis.

5. Atropine / Belladona poisoning :- Physostigmine.

6. Alzehimer's disease :- Rivastigmine, galanta, donepezil.

* Organo Phosphate Poisoning / Insecticide / Irreversible anti-Cholinesterase :-

↑↑ Ach level

- Nicotinic
  - ↓
  - - Resp. paralysis.
    - ↓
    - death
  - - Muscle Fasiculation (twitching)

- Muscarinic → C.V.S. → Bradycardia, Vasodilation]- Hypotension
  - ↓
  - compensatory
  - ↓
  - Tachycardia
- → Resp. → Bronchospasm, ↑ Resp. secretions]- Dyspnoea
  - - Wheezing sound
  - - Froth.
- → Micturation, Defecation
- → Miosis → Pin point Pupil.
- → ↑se secretions. (saliva, sweat,

Classical Features:- Hypotension, miosis, ↑se secretions, dyspnoe

Treatment :- ① Termination of further exposure to poison.
→ Gastric lavage (If oral intake)
→ Wash the skin and mucus memb. C soap & water and take Pt. in Fresh air.

② Keep airway patent :- If ~~pres°~~ Pressure ↓se (saturation), use +ve pressure Respiration (ventilator).

③ Maintain B.P. and Hydration.

④ Control of Convulsions → Midazolam / Diazapam.

⑤ Antidote :- To ↓ cholinergic activity.

ⓐ By ↓se Ach action on musc. receptor. (Anticholinergic)
→ Muscarinic receptor blocker/antagonist
I priority - (Atropine) ↓ M.Eff.
{2 mg I/V} - repeated in every 10 min. till dryness of mouth upto 200 mg in 24 hrs

ⓑ ↓se Ach level. (Cholinesterase reactivator)
↓
By activa... cholinesterase.
↑Ach Hydrolysis → ↓se Ach.
e.g. - Pralidoxime (PAM)
II priority {1-2 gm IV infusion}
{20-40 mg/kg IV → child}

Parasympatholytic / ...cholinergic / Muscarinic {Vagolytic} Recep. Antagonist.
- Drugs that antagonise Muscarinic recep. effect of Ach. (↓ P.S.A.)

Drugs → Natural → Atropine
→ Hyoscine

→ Semi-Synthetic → Homatropine
- Ipratropium Bromide

→ Synthetic → ⓐ mydriatic → Tropicamide
- Cyclopentolate

ⓑ Anti-secretory
Anti-Spasmodic
- Pirenzepine
- Propanthaline
- Dicyclomine
- Glycopyrolate
- Valethamate Bromide.

© Vasicoselective (bladderselective):-

- Flavoxate
- Tolterodine
- Oxybutanin.

ⓓ Anti-Parkinson :- Benzhexol.

Pharmacological Action of Atropine :—

1. Heart :- Tachycardia.

Vagus → Ach →✗→ M_2 (S.A.Node) → ↑se H.R.
(Atropine)

2. Smooth muscles → Relax

- Relieve Broncheospasm
  Abdomenspasm
  Bladderspasm
- Cervix dilation.

3. Gland :- ↓se secretion (Saliva, Sweat, tear, gastric, resp) secretions.

4. Eye :- Relax circular (iris) & ciliary
   - circular → Relax → Mydriasis (Photophobia)
   - ciliary → Relax → Cycloplegia (paralysis) → {Blurring of Near vision}

5. CNS :- Stimulant effect.

→ Stimulate Medullary centre. → Overall effect HR ↑
   - V → Vasomotor
   - V → Vagal
   - R → Resp.

→ depress Vestibular excitation → Anti motion sickness effect.

↓ Vestibule → basal ganglia → cerebellum → Vomiting centre ↓

→ Supress. cholinergic activity in Basal Ganglia.
↓
Supress tremor & rigidity R/T Parkinsons.

→ On High dose (Toxicity) → Cortical excitation.
↳ Excitement, restlessness, delirium disorientation & Hallucination.

6. B.P. :- Low dose :- May ↑se B.P. (due to Vasomotor stimulation & H.R.↑)

**High dose (Toxicity) → ↓se BP (Hypotension)
- due to Histamine release → Vasodilation

7. Body Temp. :- ↑se Body temp. (esp. Face & Neck)
- due to ↓se sweating and stimulation of TRC (Thermal regulating centre).

* Atropine :- 0.6-2mg inj IM / IV.
1% Eyedrop/ Eye ointment.
10 µg/kg → childre...

*Other drugs→
→ Hyocine (Buscopan) :- ...mg/1ml - 9nj. S.C. / I.M / I.V.
10 mg Tab.
- Low dose → CNS depression
- High dose → CNS stimulation

✓Special Use :- 1. To relieve Gastro-Esophageal Spasm (Anti-spasmodic) relieve abdomen pain.
2. Motion Sickness :- D.O.C.*
3. Twilight Sleep. :- Sedation & Amnesia during labour.✓
4. Lie detector → during World War-II
- due to sedation & amnesia - subject put Off-guard during sustain Interrogation.

→ Dicyclomine :- 20 mg/2ml → Inj. → Only I.M.

10-20 mg. Tab. Use- Anti-spasmodic. (Abdomen pain)

→ Pirenzapine
→ Propanthaline] - M1 blocker → ↓HCl.

→ Use- Peptic Ulcer ✓

* • Not preffered in current. (↓mucus also).

→ Glycopyrrolate :- 0.2 mg/ml - inj → IM.

↳ do not cross B.B.Br.

↓

only peripheral use

* Use :- Exclusively used as Pre. Anesthetic medication as Anti-secretory.

→ Valethamate Bromide (Epidocin) :- 5 mg/ml. - inj. IM.

• Use :- As cervix dilator during 2nd stage of Labour.

→ Anti-Parkinson :- Benzhexol :- 2-10 mg Tab.
(Tri Hexyphenidyl)

T.B.P → cross B.B.Br. → Central effect.

• Use :- To control tremor & rigidity R/T Parkinsons.

→ Ipratropium Bromide :- M_3 antagonist

↳ Inhalation → Local effect → min. dose, min time, max conc.
(40-80 mcg)

• active inhalation → by self → without affecting other part of body

↳ M.D.I / Rotacap / Respule.

"Meter dose inhalor."

↳ Nebulisation

↳ Passive inhalation

• Relax Bronchial smooth muscles
↓
Broncho-dilation ↑
→ Asthma, COPD as Bronchodilator.

→ Vasicoselective (Bladder Selective)

→ Relax detrussor
↓
Relieve bladder spasm
↓
• Benefit in (Relieve) – Urinary Frequency, Urgency & Incontinence
[Neurogenic bladder, Overactive bladder, Urinary tract infecti

• Flavoxate (Urispas) → 200 mg → B.D.
• Oxybutymin → 2.5-5 mg
• Tolterodine → 1-2mg

→ Midriatic & Cycloplegic:-

• Atropine → 1% Eye drop / Eye ointment
• Potent mydriatic & Cycloplegic

✓ But due to Slow and long-lasting action → Pt. usually handicapp
about a week. [D/E]

• Not suitable For diagnostic use
• Suitable for Therapeutic

** In children below 5 yr, (High Ciliary tone) → weak drug not effective.
↓
Atropine use for diagnosis

→ Homatropine → 1% eye drop
→ 10 time less potent from Atropine.

→ Cyclopentolate:- 1%
→ Potent mydriatic & Cycloplegic
→ Use in children for diagnosis.

→ Transient behaviour abnormality in Children.
Eye → Naso-lacrimal duct → oral → stomach → Brain

→ Tropicamide 0.5-1%.

• weak cycloplegic
- But sufficient For adults
- But insufficien For children

✓ Quickest & briefest action (3-6 hours)
(20-40 min)

✓ Suitable for diagnosis in Adults

Uses of Parasympatholytic :-

1. Anti-Secretory :- (a) as Pre-anesthetic medication :- admn prior G.A
   e.g.- Atropine, Glycopyrolate
   ↓
   • To ↓se secretions during anesthesia.

G.A. ©
↑ secr. → Aspirate → Resp. collapse
Unconscious → Can't spit or ingest.

* Current G.A. like Halothane, not ↑se secretions. → Still Atropine is important to prevent Vaso-Vagal attack & laryngeal spasm during anesthesia. ✓

→ (b). Peptic Ulcer :- Pirenzapine
↳ not preffered in current.

2. Cardiac Vagolytic :- To counter Bradycardia.
↳ Atropine © → 0.5 mg IV

3. Asthma and C.O.P.D. :- Ipratropium Bromide ©
↳ as Bronchodilator

4. Anti-Spasmodic :-
(a) To relieve intestinal, renal and abdominal colic ↑ Smooth muscle spasm pain.
↳ Dicyclomine & Hyocine.

(b) To relieve ↑ Frequency, urgency and incontinence (urinary)
→ Flavoxate

(c) Cervix dilator :- Valethamate Bromide ©

5. Central Uses :-
(a) anti Parkinson :- Benzhexol ©
(b) Motion Sickness :- Hyocine [D.O.C.] ✓
(c) Twilight Sleep :- Hyocine ✓
(d) Lie detector :- Hyocine ✓

6. O.P. Poisoning :- Atropine

7. Mydriatic & Cycloplegic

a) Therapeutic use → Atropin.

↳ in Iritis, Corneal ulcer, Choroiditis, Iridocycl

b) Diagnostic use →

(i) RET (Refraction Error Testing) (दृष्टि दोष)

- Require both mydriasis & Cycloplegia.
- Adult :- Tropicamide ✓
- Child :- Atropin, cyclopentolate ✓ ✓

(ii) Fundoscopy (Retina Examination) {पर्दे का दोष}

[diabetes, glucoma]

- Require only mydriasis.
- Tropicamide (week cycloplegic)
- Phenylephrine (α-agonist)

↳ (only mydriasis)

'Better Option' *

* Side Effects and Toxicity of Atropine / Belladona :-

1. Dry mouth :- difficulty in Swallowing & ~~Bre~~ talking.
2. Dry, Hot & Flushed Skin :- (specially Face & Neck)
3. Dilated Pupil - Photophobia, Blurring of Near Vision. [Cilliary Relax]
4. Palpitation.
5. Difficulty in Micturation & Defecation.

→ On toxicity (High dose) :-

1. Excitement, Psychotic behaviour, disorientation, delirium & Hallucination (visual). → cortical Excitement
2. Hypotension
3. Cardio-Vascular collapse & Resp. depression.
4. Convulsion & Coma.

→ Atropine contraindicated

1. Glucoma (Angle closure)

Mydriasis

2. Elder male ∵ Enlarged Prostate

↓

difficulty in micturation

→ Toxicity Treatment :-

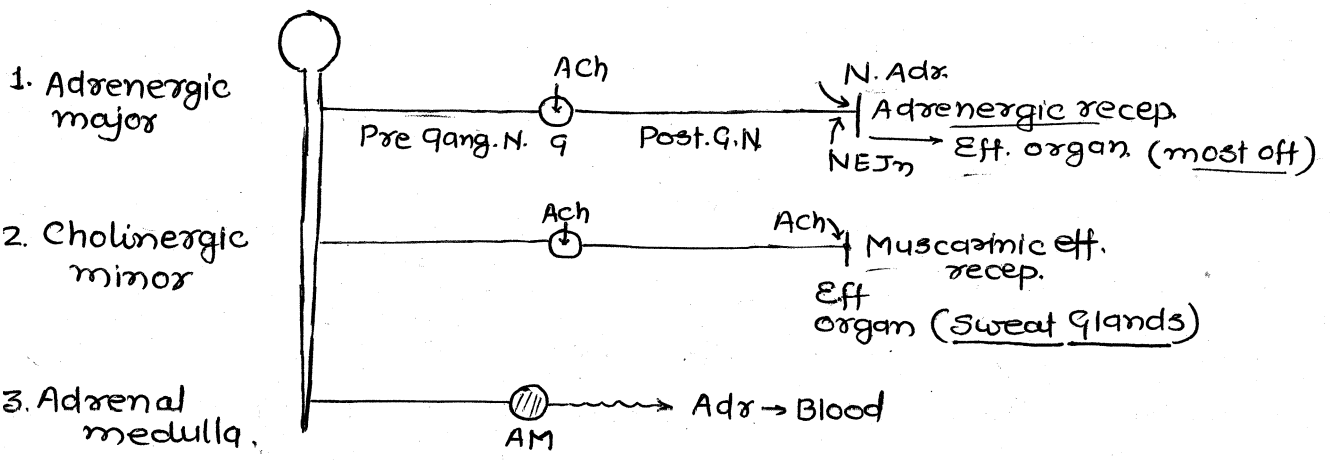
① Gastric lavage → ∵ Tannic acid.

② Pt. kept in dark & quiet room.

③ Cold sponging (Ice Bag)

④ Antidote :- Physostigmine → 1-3mg SC/IV

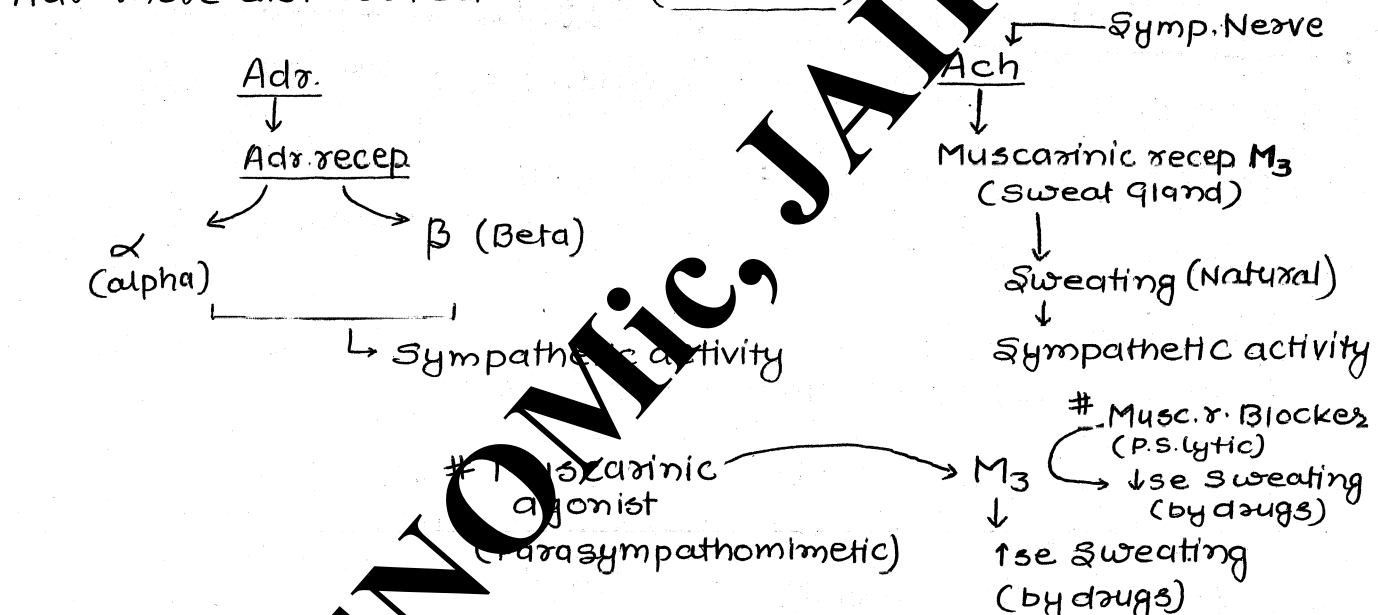
Sympathetic Nervous System :—



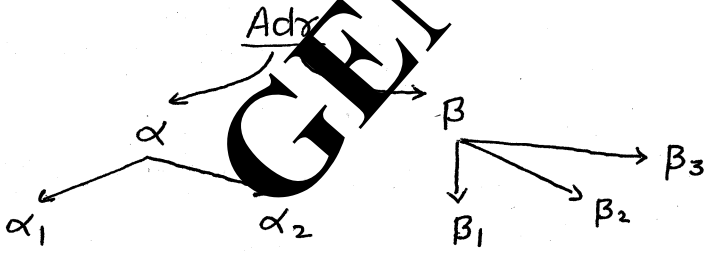
→ Sympathetic activity is mainly bcz of Adrenaline & Nor-adrenaline
(A.M.) (NEJn)

Activity via adrenergic receptor on effector organ

→ ✓ Adr. more distributed action (via Blood)



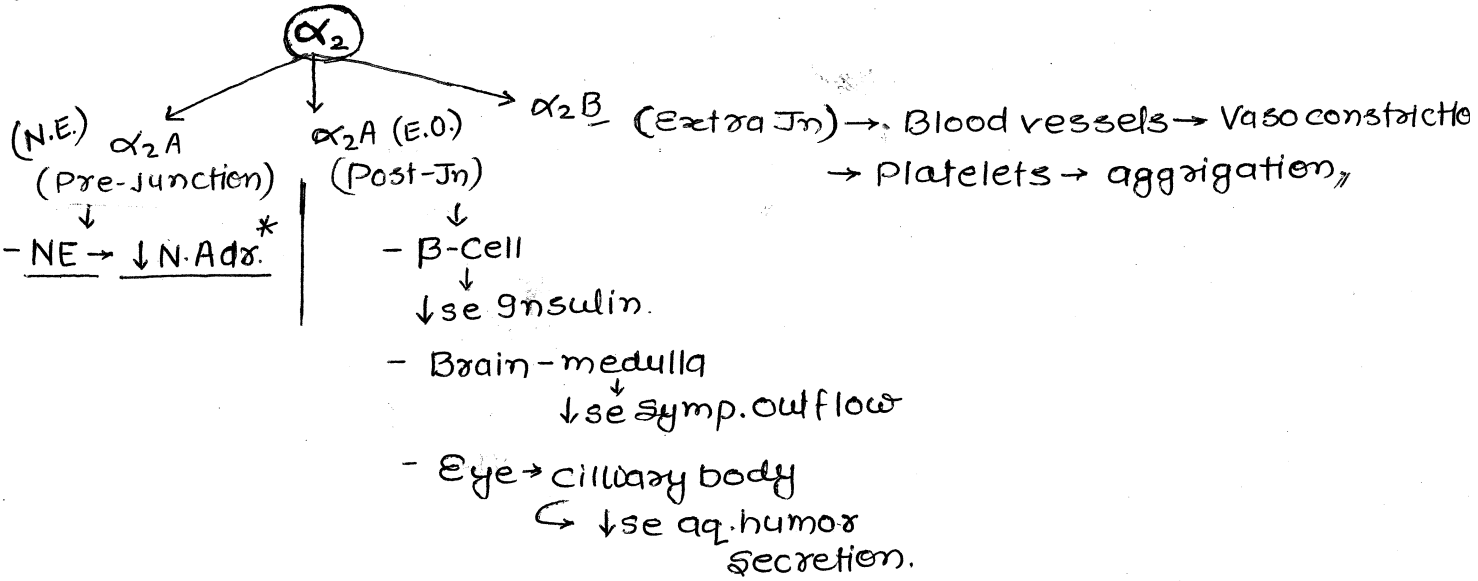
α1-Blocker → Impotence

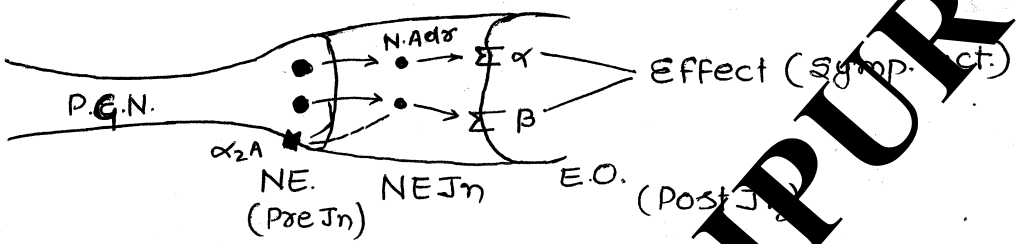


* α-receptor

α_1 = → Excitatory except Gut.
↳ Gut → Relax.
↳ Blood vess. → Vasoconstriction
↳ Eye → Radial (iris) → contriction → Mydriasis.
↳ N.MJn → ↑se Ach
↳ Uterus → contract
↳ Bladder - Trigon → contract
↳ Vas deference → contr. → Ejaculation

α_2 :- Inhibitory except blood vessels.*





* β-Receptor :-

β_1 :- Excitatory
- Heart → ↑se cardiac act.
- J.G cell → ↑se Renin
- Post. Pit → ↑se ADH.

β_2 :- Inhibition
- Gut → Relax
- Bronchi → Bronchodilation
- Blood vessels → Vasodilation
- Uterus → Relax.
- Skeletal muscle → Tremor.
- Ciliary body → ↑se Aq. Humor Secr.
- α-cells → ↑se Glucagon
- detrussor → Relax
- Heart, Liver & Skeletal muscles → Glycogenolysis.

β_3 :- Adipose tissue → Lipolysis
↓ Thermogenesis
↓ Calorigenesis.

Adr

α → Excitatory
β → Inhibitory
'Sym. activity' → Nil

- All body → Excitatory — Inhibitory — Nil
- Gut → Inhibitory — Inhibitory → ↓↓
- Heart → Excitatory — Excitatory → ↑↑

* Nil
  - If α dominancy → Excitatory eff. {overall eff}
  - If β dominancy → Inhibitory eff.

'Sympathetic drugs'

- Sympathomimetic — ↑se Sym. activity
- Sympatholytic — ↓se Sym. activity.

* Sympathomimetic / Adrenomimetic / Adr. recep. agonist / (α-β-agonist) :-

→ Drugs that have action similar to Adr. or Symp. Stimulation.

Pharmacological Action of Adr. (Sympathetic activity) :-

1. Heart - (β_1) → ↑se cardiac activity.
   - ↑se Rate
   - ↑se Force
   → ↑se Cardiac output.

2. Blood vessels
   - α → Vasoconstriction
     - Surface → cutaneous & mucous.
     - (& Renal also)
   - β → Vasodilation
     - Skeletal muscles
     - Liver
     - Coronary

3. B.P. :- • On Adr. I.V. Infusion / S.C.

↓

↑↑se Systolic BP & ↓se diastolic B.P.

[at low conc. → more eff on β_2 ← Adr less " " α] ↓ dom^n

#	V.C.	V.D.
	↑ Resist.	↓ Rest.
press. Falling →	Slow	Fast
गिरावट → {decline in DBP}	less. ↑ DBP	More. ↓ DBP.

β_1 → ↑. Card. act. → ↑↑ C.O. → ↑↑ Sys. B.P.

α → V.C. (less)

β_2 → V.D. (more) → slight net ↓ se (~~vasodilatie~~ Vaso-Resistan → ↓ D. B.P. (Slight).

4. Bronchi (β_2) :- Bronchodilation (Smooth muscles → Rel[illegible])

5. Uterus :-

α → Contract → dominancy in Non-Pregnancy

β_2 → Relax → dominancy in Pregnant.

6. Neuro-muscular Jn. (Skeletal muscles):-

✓ - α → ↑se Ach at N-M Jn.

✓ - β_2 → Skeletal muscle → Tremor.

7. Eye :-

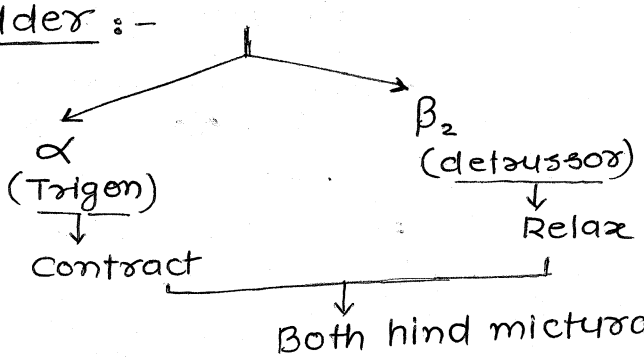
• Radial (α) → contract → Mydriasis.

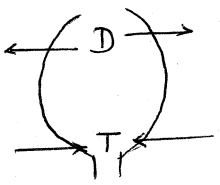
• Ciliary body → α → mainly α_2 → ↓se Aq. Hum. Secretion

• Ciliary body → β → Mainly β_2 → ↑se Aq. Humor. Secr.

8. C.N.S. :- anxiety & restlessness

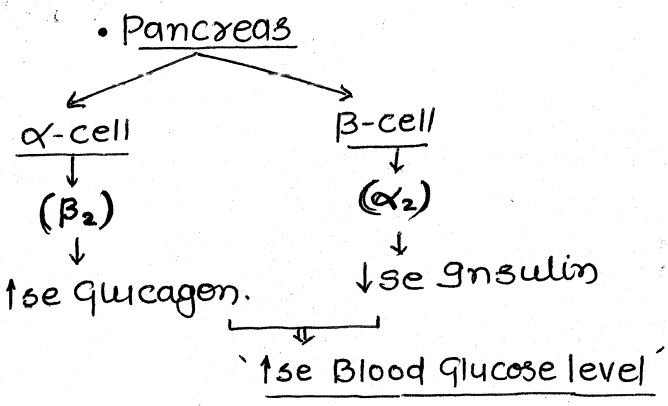
9. Bladder :-

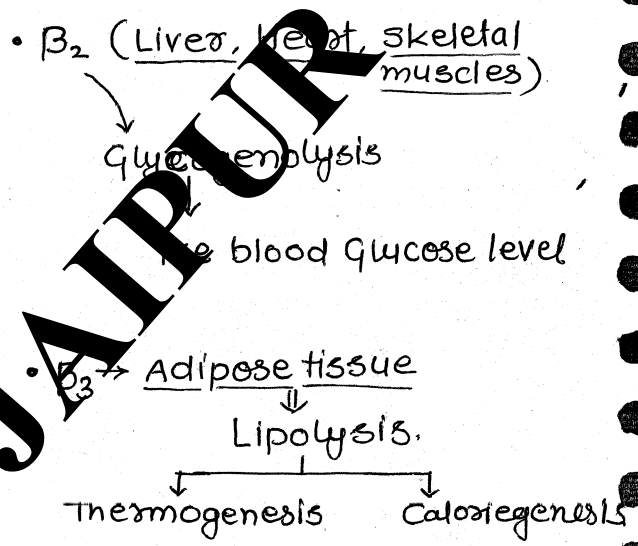




10. Gut :- (α+β) → Relax.

11. Metabolic :-





• Transient Hyperkalemia :- (Liver release K^+)
→ Initially followed by Hypokalemia
(Liver & Skeletal muscles uptake K^+)

Drugs :-

① Cardiac-stimulant :- Adrenaline
- Dobutamine
- Isoprenaline

② Vasopressor → - Nor-Adrenaline
- Phenylephrine
- Ephedrine
- Dopamine
- Methoxamine
- Mephenteramine

③ Bronchodilator :- Salbutamol
- Terbutaline
- Salmeterol
- Formeterol
- Bambuterol

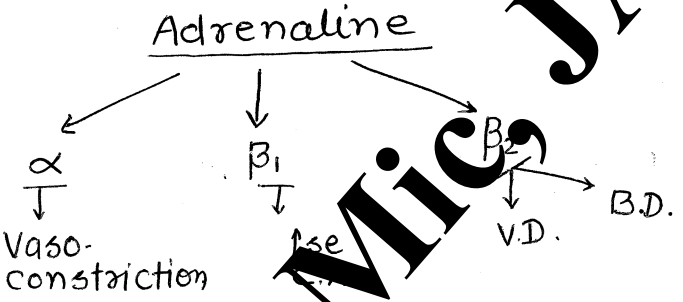
④ C.N.S. Stimulant :- - Amphetamine
- Methylphenidate

⑤ Uterine Relaxant → - Isoxsuprine
(β_2) - Ritodrine

⑥ Anorectics. → - Sibutramine
(apetite suppressants)

⑦ Nasal decongestant → Xylometazoline
- Oxymetazoline

Cardiac Stimulant :-



- Cardiac stimulant (↑CA) & Bronchodilation
  → ↑↑ Syst. B.P & ↓ Diastolic B.P.
  → Surface capillaries (B.V.) → Vasoconstriction (α).
- Adr. inj → (1 mg/ml) → 1:1000 # → SC/IM* → Anaphylactic shock
  → Allergy.- (Ag-Ab rxn.) ↓causes
  • Bronchoconst
  • Vasodilation (due to histamin
  Ant. lateral aspect of ⇑ thigh.* { 0.5 mg ↑ I/M preferred
  SC/IM
  Add 9 ml diluent ⇓ 1 mg/10 ml ⇒ 1:10000 #
  10 µg/kg* ↑ Route of Choice in C.A. → IV
  IV/ET/Intraosseus ↓ Cardiac arrest

- Adr benefit by counter Histamine Effect.

Bronchodilation — Vasoconstriction (cappilaries)

#(Physiological Antagonist of Histamine → Adr.)

Adr :- D.O.C. in Anaphylactic Shock.

- If vasularature not found, then use Endotracheal / Intra-osseus
  - {Children}
    - Humerus,
    - Femur,
    - Tibia.

  in Cardiac arrest.

* Use :- ① In Anaphylactic shock [D.O.C] → IM
② In Cardiac arrest → IV.

- Adverse Effects :- Anxiety, Restlessness, tremor, ~~Palpatations~~.
  - Palpatations.
  - Ventricular tachycardia.
  - Hypertension.

  → on large dose → Angina, M.I.

Contraindication :- Hypertension → (cerebral Haemorrhage)
- Angina → M.I.
- Hyperthyroidism
- with Halothane (Gen. Anasthesia)
  - → it sensitize Heart

Adr. → Arrythemia

- Dobutamine → Dy :- 50 mg / 4 ml
  - ↓
  - β_1 agonist.
    - ↓
    - +ve Inotrophic → ↑se Force
      - → 2-8 ug/kg/min → IV infusion

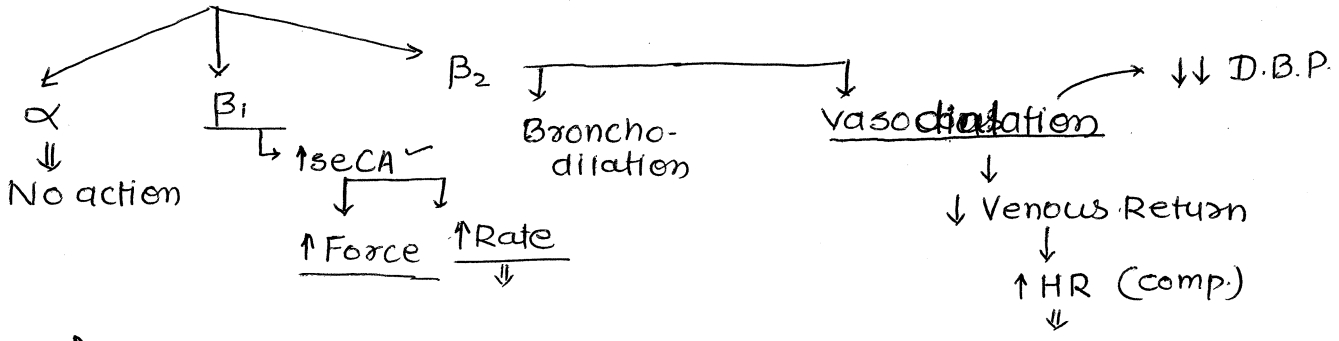
* ↑se Force of Cardiac contraction & output. without
* significant change in Heart Rate & peripheral resistance & B.P.

→ It is used to maintain pumping [to prevent pump failure]
[+ve Inotrophic]

during M.I, Cardiac Surgery & Severe C.H.F.

• Isoprenaline → Inj → 4 mg/2ml.

5-10 µg/min → IV infusion.



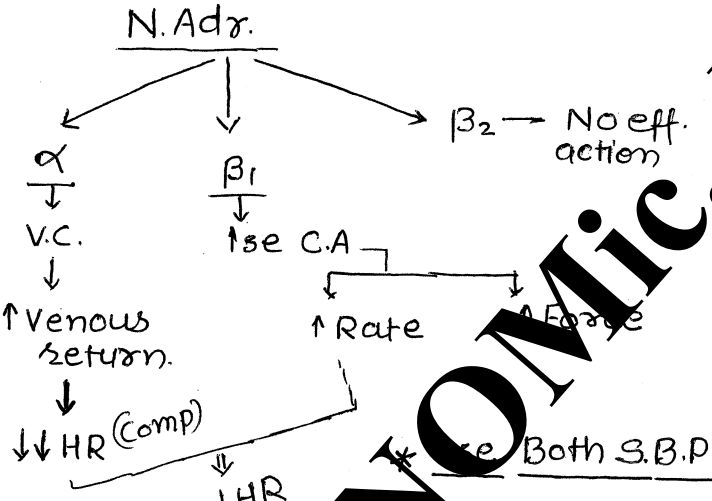
#HR↑↑
#C.O.↑↑
#S.B.P.↑

• ↑se S.B.P. while ↓↓ D.B.P.
• ↑↑ HR. (β_1, β_2)

Use:-
• AV Block

Vasopresser

• Nor-adrenaline → 2mg/2ml inj.
↳ 2-4 µg/min → IV infusion.

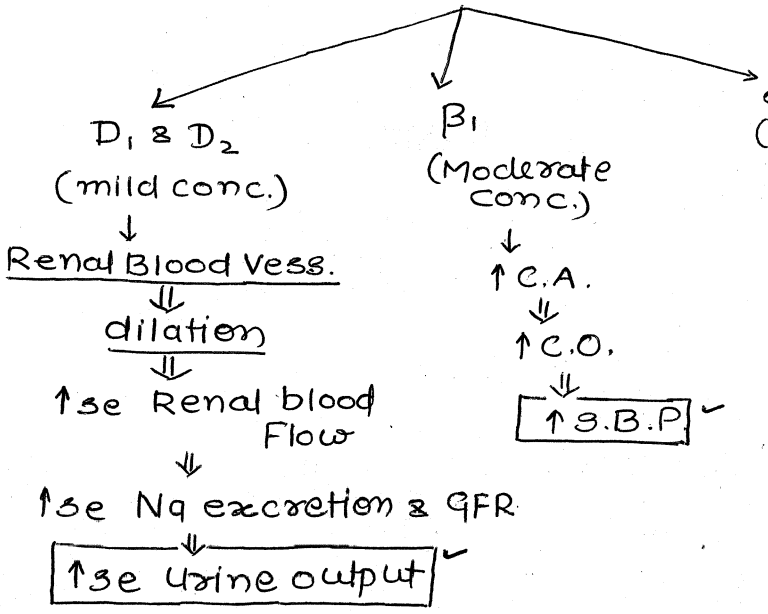


** ↑se Both S.B.P & D.B.P. while ↓se HR.
* Use as Pressure agent in Rx of Hypotension/Shock.

** Never use undiluted. If used → Local tissue Necrosis.
** Do not mix with $NaHCO_3$ → deteriorate (खराब हो जाता है)

• **Dopamine :-** 200 mg / 5 ml inj.

0.2 – 1 mg / min → IV infusion.



* It is used to ↑se SBP & Urine output in Cardiogenic / Septic shock, Severe C.H.F.

• **Ephedrine** → 50 mg / ml inj.
15 mg Tab.
↓
Long acting.

Use :- Postural Hypotension and Hypotension during Spinal anesthesia (Rx)

• **Phenylephrine** → (α-agonist)

- 10 mg/ml inj → Vasoconst. → ↑ BP
  • Use → pressure agent.
- 5-10% ED → Radial → Mydriasis → • Use → Fundoscopy
- 0.25 – 0.5% Nasal drop → constriction of Nasal mucosal capillary → Const. of Nasal mucosa (shrinkage) → Relieve Nasal congestion → • Use → Nasal decongestant.

- Methoxamine → 20 mg/ml
  - similar to Phenylephrine.
  - Use :- Pressure agent.

- Mephenteramine → 15 mg/ml.
  - α + β_1 agonist
  - To prevent / treat → Hypotension / Shock
    ↓ (in)
    M.I., Cardiac surgery & Spinal anesthesia.

Broncho-dilator

β_2 agonist

↓

Inhalation (M.D.I, Rotacap, Respule)
- Active inhalation
- Passive (Nebulizer)

↓

Relax Bronchospasm

↓

Bronchodilation

Local effect →

e.g.-

SABA [Salbutamol 100-200 µg; Terbutaline 250 µg] → Short acting β-agonist → 3-4 time; → 6-8 hr.

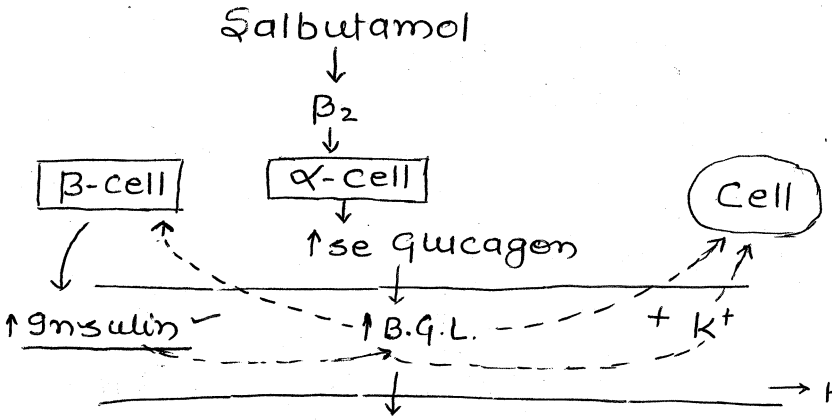
LABA [Salmeterol 25-50 µg.; Formeterol 12 µg] → Long acting β-agonist. → 1-2 time; → 12-24 hr action

Use :- Broncheal asthma & C.O.P.D. as B.D.

- Adverse Effect ⇒ Salbutamol nebulization (continous)
  - → System
    - on Long term use
      - → Hypokalemia
  - Acute
    - Tremor
    - Palpitation

Salbutamol
- → β_2 Skeletal mus. → Tremors
- → β_2 B.V. → V.D. → ↓ VR
- → Weak β_1 agonist

↓ sensitive Heart → Palpitation



- If diabetes mellitus
  ↳ Hyperglycemia. (Insulin↓)

CNS Stimulant → ↑se alertness
↓
↑se Conc.n
⇓
↑ Attention span

- Useg :-
  - Amphetamine :- 5-15 mg
  - Methylphenidate → 5-10mg.

- Use :- ① A.D.H.D. (A Hyperkinetic child)
  ↓
  Methylphenidate S.O.C.
  ② Narcolepsy → [illegible] time sleep attacks.-(hearing-active)
  ↓
  Amphetamine

* No amphetamine after 6.P.M.

Uterine Relaxant → (β_2 agonist)
- Hexasuprine - 5-10 mg
- Relax uterus.
- To postpone labours.

Anorectics (Appetite Suppresant)

↳ Sibutramine → 5-10 mg

- Supress appetite → ↓se Food intake → Wt loss. (3-9 kg ↓)
- β_3 (A.T.) → ↑se Lipolysis → • Calorigenesis (Need of Food Intake ↓)

• Use :- Rx of Obesity.

Nasal decongestant :-

long acting Topical α-agonist ©

Use :- Nasal decongestant

↓

Nasal drop

↓

Shrinkage of Nasal mucosa

↓

Relieve nasal congestion

- Oxymetazole (Nasivion*) ↓ 0.025 – 0.05 % (Ped. – Adult)
- Xylometazoline (Otrivin*) ↓ 0.05 – 0.1 % (P – A.)

* Uses of Sympathomimetics :-

1. Vascular Usage → Hypotension / Shock.
   - Adr → Anaphylactic shock (d.o.c.)
   - Dobutamine, dopamine] – Cardiogenic shock
   - Ephedrine → Postural Hypotension → Hypotension during spinal anesthesi
   - N.Adr. → Shock.

(b) Along ∈ Local anesthesia.

↓ Adr + Lignocaine

V.C. (1 : 100000)

↓

- ↓se. L.An. absp
- [↑se L.A. duration of action]

(c) To control local bleeding:-

e.g. Epistaxis. → Adr, Ephedrine (1%) [1:10000]

↓

cotton

↓

Nasal compression

↓

Arrest Nose bleed

(d) Nasal decongestant :-

- To relieve nasal congestion → in cold, rhinitis, Sinusitis, blocked nose or eustachian tube.

Topical α-agonist

↳ xylometazoline

2. Cardiac Usage:-

(a) Cardiac arrest (Resuscitation of failing heart)

↳ as Cardiac stimulant ⇒ Adr. → I/V. [R.O.C.] ✓

(b) C.H.F. → dobutamine

→ dopamine

(c) AV Block → Isoprenaline

3. Broncheal Asthma & C.O.P.D → as bronchodilator

β_2 agonist (Inhalation) → Salbutamol. ✓

4. Allergy:- Adr. [D.O.C.] - IM

5. Mydriatic → in Fundoscopy → Phenylephrine

{DIE}

↳ only mydriasis

No cycloplegia ⇒ suitable for diagnosis.

6. Uterine Relaxants :- β_2-agonist → Isoxsuprine
(To postpone labour)

7. Central Uses :-

a) Narcolepsy :- Amphetamine

b) ADHD :- Methylphenidate [D.O.C**].
(Hyperkimetic Child)

c) Obesity :- Sibutramine.

* Anti-Adrenergic / Sympatholytic / Adrenergic receptor blocker / Adr.-receptor antagonist :—

→ Drugs that antagonise receptor action of Adrenaline.
(↓se Symp. activity).

→ These drugs block α or β or both (α & β).

Sympatholytic
- α-Blocker
- β-blocker
- (α+β) blocker.

• α-Blocker → Drugs that antagonise α-receptor effect of Adr.
Cont affecting β-effect.

* ↓se symp. activity of α-receptor.
* ↓se α-effect of Adr.

- Drugs :-

1. Non-selective α-Blocker (α_1+α_2 blocker)
e.g:- Phenoxybenzamine
- Phentolamine

2. α_1-selective Blocker.
e.g:- Prazocin
Terazocin
Doxazocin
Alfuzocin
Temsulocin

Phaxmacological action of α-Blockers:-

1. Relax vascular smooth muscles
↓
Vasodilation → ↓ Renal blood Flow → ↓ GFR → Fluid retention

- Vasodilation → ↓ BP
  - → Rx of HTN
  - → Adv. effects ⇓ - postural Hypotension ⇓ (Dizziness & Syncope on standing)
- Vasodilation → ↓ Venous Return ↓ ↓ Mean Arterial pressure ⇓ ↑ HR. (Reflex Tachycardia)
- Vasodilation → dilate both Artery & Vein → ↓ Preload
  - ↳ ↓ afterload ⇓ Benefit in C.H.F.

Vasodilation

2. Dialation of Nasal mucosal capillary ⇒ Nasal congestion.

3. Diarrhea (↑se motility)

4. Miosis (Relax Radial muscles)

5. Contraction of Vas deferens → inhibit
↓
Inhibition of Ejaculation/ 'Retrograde Ejaculation'
↓
'Impotence'

*6. ↓se tone of smooth muscles of Trigon, prostate & sphincter (Bladder base)
↳ (due to blockage of α₁) ↓
dialate urinary way
in B.P.H. (Bladder Hypertrophy of prostate)
⇓
↑se urine flow in B.P.H. Pt.
↳ 'Benign Prostatic Hypertrophy'

• B.P.H.
⇓
↑ Prostate size
⇓
Narrowing of urine way
⇓
- Pain during micturition & ↓se urine Flow.

*Drugs →

• Non Selective α-Blockers :-

1. Phenoxybenzamine ($\alpha_1 + \alpha_2$ blockers)

↳ 50 mg/ml Inj. → IV infusion.

① → Pheochromacytoma → To ↓BP (By inducing Vasodilation).

↳ Adrenal Gland Tumor

↓

↑se ~~Nor~~ Adr

↓

↑se B.P.

⇓

'Hypertensive crisis.'

② → Secondary shock → Benefit due to vasodilation.

↳ Shock due to reflex vaso-constriction.

③ → PVD (Peripheral Vascular disease) → benefit due to V.D.

Eg. ↳ Raynauds disease

↓

V.C. (extremities)

⇓

(Cold Feet & Hand)

2. Phentolamine (α_1 & α_2 blocker) :-

↳ Short acting

→ 5 mg I.V. → ↓S.B.P. (>35↓) & DBP. (>25↓)

Use :- Diagnosis of Pheochromacytoma.

- Pre & operative management of pheochromacytoma.
- To control B.P. in cheese rxn & chlonidine withdrawl

• α_1 Selective blocker :-

1. Prazocin.

$\alpha_1 A$ (Bladder bass) ⇓ dilate urinary way in B.P.H. Pt. ⇓ ↑se Urine flow in BPH Pt. → Rx of B.P.H.

$\alpha_1 A$ (B.V.) ↓ V.D. → ↓B.P. → Rx of HTN

** 9n current, not preffered in B.P.H. due to Vascular Side effects.

– Dose → Start - 0.5 mg H.S.
→ Later - 2.5 - 5 mg.

• Ist dose → Hypotension (postural) – dizziness & fanting on standing.

To avoid this, Stard c low dose at bedtime.

→ Use :- ① HTN.
② PVD.
③ C.H.F.

2. Terazocin → 1-2 mg → Similar to H Prazocin.
• Use → in HTN.

** ↑se Apoptosis of prostate cell. ⇒ ↓se size.
↳ Programmed cell death.#
↳ Benefit in B.P.H.

3. Doxazocin → 1-2 mg → Similar to Prazocin.
• Use → HTN.

4. Alfuzocin → 10 mg., Use → HTN.

5. Tamsulocin → 0.4 mg H.S.
↳ $\alpha_1 A$ selective Blocker.
↓
≈ ↑se Urine outflow in B.P.H. Pt.

• Use → ** B.P.H. [DOC]
↳ No vascular side effects.

* Uses of α-Blocker:-

1. Pheochromacytoma
   - Diagnosis & I.O.M. ⇓ Phentolamine
   - Therapeutic ⇓ Phenoxybenzamine
2. HTN → Prazocin
3. P.V.D. → Prazocin, Phenoxybenzamine
4. Cheese rxn. → Phentolamine
5. Sec. Shock → Phenoxybenzamine
6. B.P.H. → Temsulocin.
7. C.H.F. → Prazocin

* Side-Effect of α-Blocker :-

1. Reflex. Tachycardia (Palpitation)
2. Nasal Congestion
3. Miosis
4. Diarrhea
5. Postural Hypotension.
6. Inhibition of Ejaculation / Retrograde Ejaculation (Impotence)
7. Fluid Retention.

Beta Blocker :- Drugs that ↓se β-receptor effect of Adr.
- ↓se symp. activity of β-receptor.
- ↓se β-receptor effect.

① Non Selective β-Blocker:-

(a) $\beta_1 + \beta_2$ blocker :- propranolol
Sotalol,
Timolol,
Pindolol.

(b) $\alpha + \beta$ Blocker :-
- Labetalol
- Carvedilol.

② β_1 - Selective Blocker (Cardio-selective) :-
- Atenolol
- Metaprolol
- Bisprolol
- Esmolol
- Betaxalol
- Acebutalol
- Celiprolol
- Nebivolol.

Pharmacological action of β-blocker (Propranolol) {Propranolol}

1. Heart :- ↓se Cardiac activity
↓se Rate & ↓ Force (on High dose)
⇓
↓se C.O.
⇓
↓se B.P. → Rx of HTN.

→ ↓ CA
⇓
↓ O_2 demand
- M.I.
- Classical Angina.

• Rx :-

→ ↓CA
⇓
depress conduction System & SA Node.
⇓
• Rx → Arrythemia

→ By ↓ Symp. Act. on Heart
⇓
Prevent Remodeling of Heart.
⇓
Arrest disease progression
⇓
↓se mortality in C.H.F. (Survival benefit in C.H.F.)
⇓
{on long term use after Pt. Stabilize}

* C.H.F.
↓ CO
↑ SA (comp). β-B
Remodeling of Heart
worsening of CHF.
↑ Mortality.
↑ CO

• β-Blocker
⇓
In C.H.F.
- Initially (Not use)
⇓
Worsening
- Later (use)
⇓
Survival

* β-blocker is not used initially in C.H.F.

⇓

↓se Force in CHF

⇓

↓se C.O. in C.H.F. → 'worsening'

2. Blood Vessels → β_2 ⇒ Vasoconstriction

β_1 Blocker
(Atenolol)
⇓
↓CA
⇓
↓CO
⇓
↓ B.P.
(From initial use)

$\beta_1+\beta_2$ blocker
(Proprenolol)

β_1 + β_2
⇓ ⇓
↓CO VC
⇓ ⇓
↓ BP ↑ B.P.

- So initial use → Reduction in B.P. not as much.
- # But on continous use, later due to const. ↓se in C.O., ↓se in vascular resistance also → ↓se B.P.

3. Bronchi (β_2) → Bronchospasm in Asthmatic.

- ($\beta_1+\beta_2$) blocker → Contraindicated in Broncheal Asthma & C.O.P.D. #
  (propranolol)
- β_1 Blocker → can be used in Broncheal asthma, C.O.P.D
  (Atenolol)
  ⇓
  *If possible, then also avoid in Bronc. Asth & COPD.
  ⇓
  Loss of receptor-selection action on High dos

4. Eye :- Ciliary body → β_1 + β_2
(less) (More)
⇓
↓se Aq. Humor Secr.
↳ Rx → Glucoma (To ↓ I.O.P.)

5. C.N.S. :- Relieve anxiety

- ↑se dreaming, nightmares & Forgetfullness.

6. Skeletal Muscles → (β_2)

↳ Supress Tremors.

*# Only $\beta_1 + \beta_2$ blocker (Propranolol) Supress tremor,

– β_1 blocker not effective in tremors.

→ Due to inhibition of Glycogenolysis & Vasodilation in Skeletal muscles, that require during exercise, (S.A)

S.A. → Adr → β_2 (SM) → V.D. → O_2 ↑

(during Exercise) → Glycogenolysis → Glucose

•β_2 blockage (Skeletal Muscles) ↳ ↓se exercise capacity & ↑se Tiredness.

* with Non Selective ✓, not with β_1-selective ✗ Blocker.

7. Metabolic → (β_2)

→ Abnormal lipid profile (↑ LDL & ↓ HDL)

✓ ∈ Non-selective β-blocker, not ∈ β_1-Blocker

* → Hypoglycemic attack in D.M. Pt. ∈ Non-selective β-blockers (Propranolol), So Propranolol contra-indicated in D.M. & propranolol also block alarming sign of Hypoglycemia.

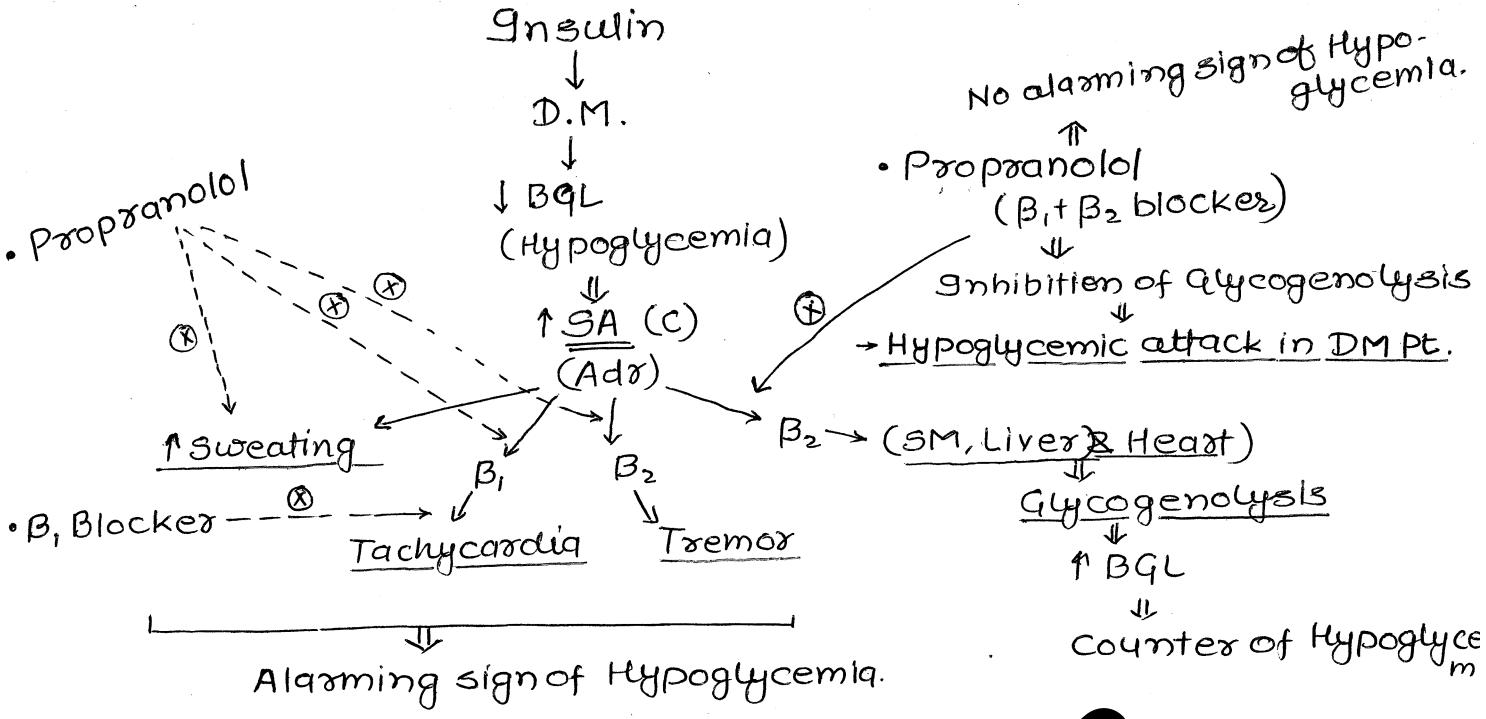
↳ (all signs) → sweating, Tremor, palpitations.

** → No ~~glu~~ hypoglycemic attack with β_1-blocker in D.M Pt. ~~of~~ & only block ~~also~~ tachycardia & alarming sign of Hypoglycemia.

So β_1-blocker is safe & can be used in DM Pt.

** → No hypoglycemic attack in normal individual ∈ any β-blockers.

*



Propranolol :→ 40-160 mg.

- Side effects & Contra-indications of β Blocker :-

1. Bradycardia.
   ↳ C.I. in sick sinus and AV Block
2. Bronchospasm in Asthematic → Non-selective β-blocker C/I in A Broncheal asthma & C.O.P.D.
3. Hypoglycemia attack in DM
   ↳ Non-selective β-blocker C/I in D.M.
4. Abnormal Lipid profile (Non-selective β-Blockers)
5. ↓se exercise capasity & Tiredness. (Non selective)
6. β-Blocker C/I in Varient Angina (due to coronary spasm)
   ↳ do not prevent coronary spasm, even worsen it.
7. Sudden withdrawl of β-blocker → precipitation of Angina & M.I.
8. Cold Feet & Hands & worsening of P.V.D. (Non-selective β-B)
   ↳ C/I in P.V.D.
9. G.I.T. disturbance
10. Forgetfullness, Nightmares, Lack of drive

11. Sexual distress in Men.

12. Propranolol contra-indicated in pregnancy
↳ ↓se placenta size.

Other β-Blocker :-

- Sotalol → 40-80 mg
  # → K⁺ channel blocker also.

- Pindolol → 5 mg
  # → $\beta_1 + \beta_2$ blocker & Intrinsic Sympathomimetic activity.
  ↳ prefer in those who are in risk of Bradycardia.
  (Less chance of Bradycardia).

- Timolol → 0.25 - 0.5 %
  (Eye drop) → $\beta_1 + \beta_2$ blocker
  ↓
  ↓se Aq. Hum. Secr. → ↓se IOP.
  # → Naso-Lacrimal duct
  ⇓
  Oral cavity
  ⇓
  absp.
  ⇓
  • Bronchospasm in asthmatic.

  • Use :- # First line drug in Rx of Glaucoma.
  # ↳ C/I in Glaucoma Hs Asthematicus

→ β_1-Selective blocker (Cardioselective) :-

✓• No Hypoglycemic attack. → Safe in D.M.
✓• Less / No chance of Cold feet & Hand.
✓• No abnormal Lipid profile.
✓• Less / No chance of Bronchospasm.
✓• Do not compromise exercise activity & tiredness.
✓• Safe during pregnancy.
✓• Not effective in Tremors.

1. Atenolol :- 25-100 mg.
2. Metoprolol :- 25-100 mg.
   ↳ ** Prefer in DM Pt.

③. Bisprolol :- 5 mg ⇒ Long acting.

④ Acebutalol :- 200 mg

↳ # Partial agonist activity → Less chance of Bradycard

⑤ Esmolol :- 100 mg / 10 ml – inj.

⇓ ⇓

Short acting. I/V infusion.

⑥ Betaxalol :- 0.5% Eyedrop

↓

β_1-blocker

↳ ↓se aq. Hum. secretion.

⇓

↓I.O.P. #

• Use :- In Glaucoma initially

& in Glucomatus asthematicus.

⑦ Caliprolol :- 100-200 mg

↳ NO donor (Nitric oxide) & Partial β_2 agonist

⇓ ⇓

Vasodilation • Safety promise in C.O.P.D &

Broncheal asthma.

⑧ Nebivolol :- 2.5-5 mg.

↳ N.O. donor → Vasodilation.

* α + β Blocker :-

↓ ↳ ↓se. C.O.

V.D.

⇓

↓se. B.P.

• Labetalol :- Start → 50 mg B.D. Tab.

Later → 100-200 mg B.D. / T.D.S.

↳ Choice of Pill. (1st line drug in Rx of HTN during Pregnanc

↳ 20 mg / 4 ml → Inj. → 20-40 mg I/V infusio

(dil. ⊂ N.S. → 100 ml) ↓ ②

1 ampule.

↳ Rx of Emergency HTN.

• Carvedilol

↳ {3.125-25 mg Tab}

Uses of β-blocker :-

1. HTN.
2. Classical angina (C/I in Varient Angina.)
3. C.H.F. → Not used initially
   → Survival benefit on Later use.
4. Arrythemia
5. M.I. (a) during M.I. → To limit infarct size or To prevent/ treat arrythemia.

   (b) Post M.I. → To prevent re-infarction. (secondary prophylaxis of M.I.)
6. Pheochromacytoma.
7. Disecting aorlic ancurryem → benefit by ↓ contractile force & Aortic pulsation.
8. Anxiety :- Propranolol.
9. Tremor :- Propranolol.
10. Glucoma :- Timolol, belaxalol.
11. ✓Migraine :- Propranolol. (For prophylaxis)
    → Naproxin
    → Somatriptin
12. Thyrotoxicosis → Propranolol → by ↓se Symp. activity
    ↓
    ↑ Thyroid function
    → Sweating, palpitation, anxiety, nervousness, tremors. (All-Symp.)
    S/S.
    ↓
    • Symptomatic benefit in thyrotoxicosis by supress anxiety, palpitation, Sweating, nervousness, Tremor.

* Also ↓se thyroid function. by Inhibit conversion of $T_4 \rightarrow T_3$.
   T_4 ↓ less active
   T_3 ↘ More active.

✓Lipid insoluble β-blocker → Atenolol, Sotalol. (No centralause)

Membrane stabilizing β-blocker → Propranolol (Non-selec.), Acebutalol (B_1-B)

β-blocker ≅ K^+ channel blocker propesty → Sotalol.

β-blocker ≅ Intrinsic Sympathomimetic activity → Pindolol ($B_1 + B_2$) (Partial agonist)
→ Acebutalol (B_1)

β-blocker c̄ vaso-dilator property

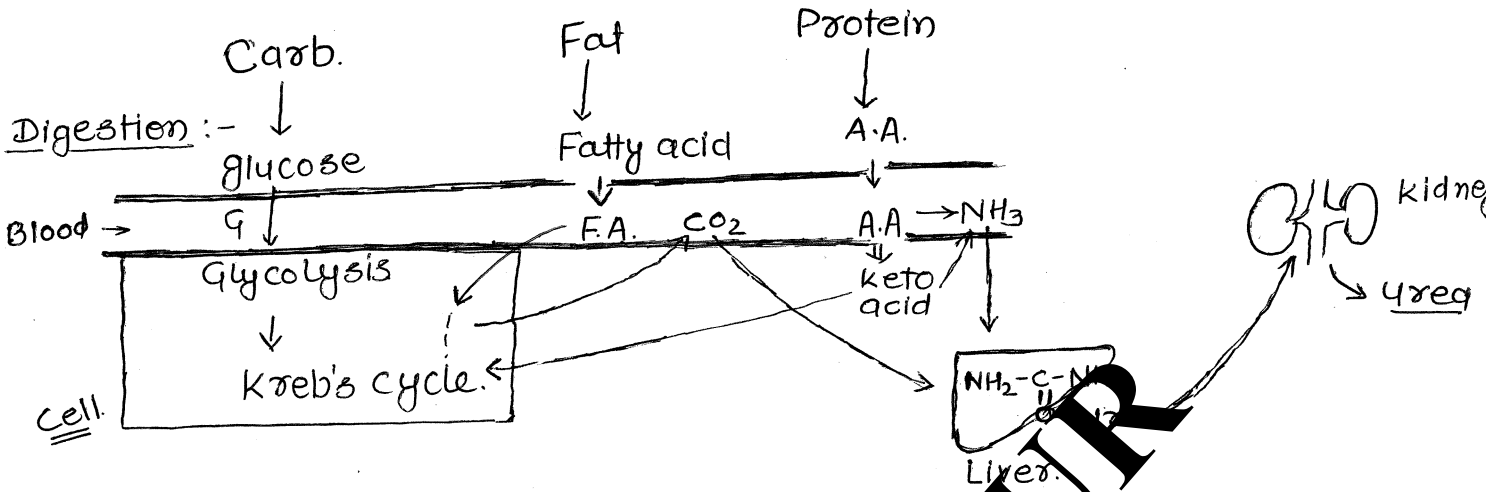
- → Celiprolol
- → Nebivolol] N.O. donor

- → Labetalol
- → Carvedilol] α+β blocker

July, 15, 2022.

'Drugs acting on Kidney'

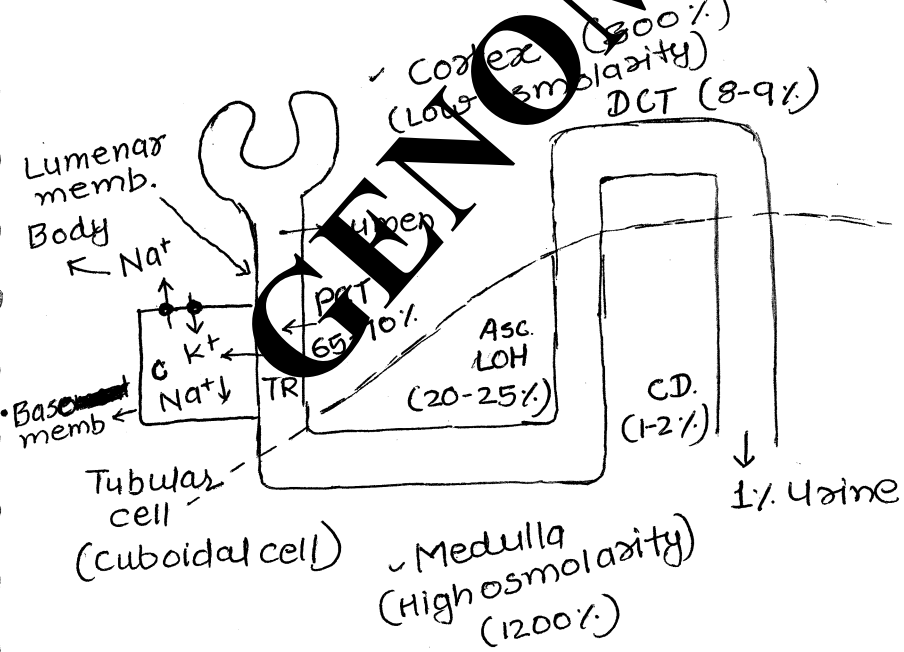
- Diuretic (↑ Urine output)
- Antidiuretic (↓ Urine volume)



- Urine = G.F + T.S. − T.R.
  - G.F (125 ml/min) {180 L/D.} 1500 ml/day
  - T.S. 100 ml
  - T.R. (99%) {175.5 L/D.} 99 ml
  - Urine = 1 ml/min.

- Most of the diuretics act by use Tubular reabsorption #

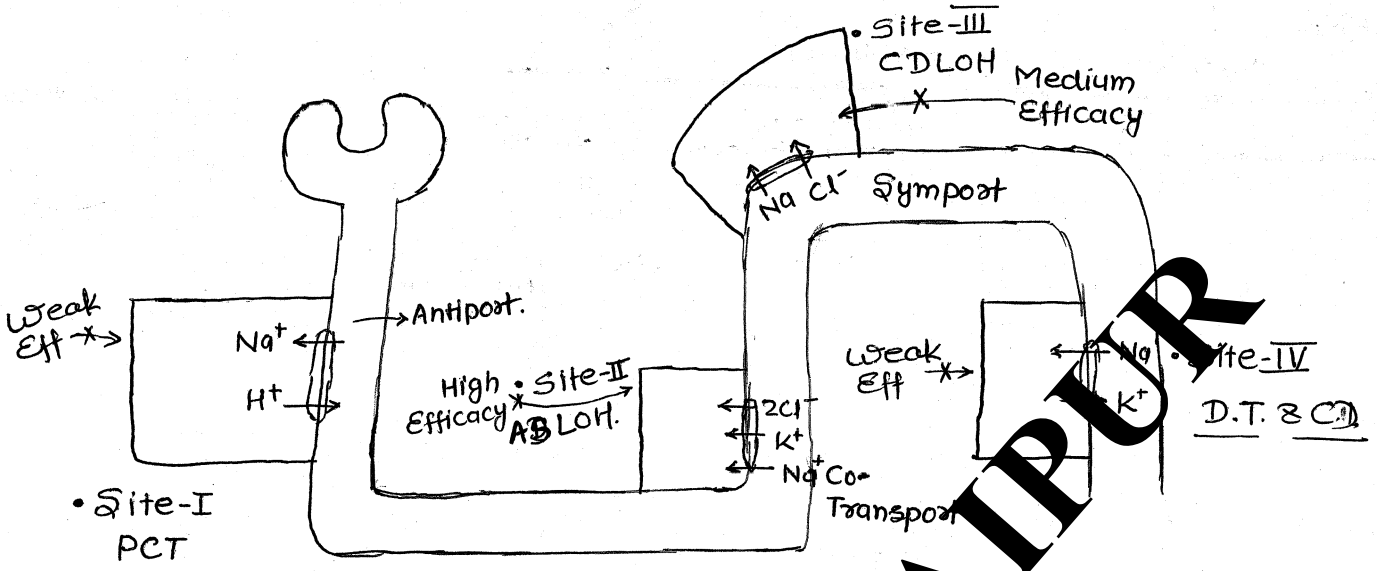
Tubular Reabsorption

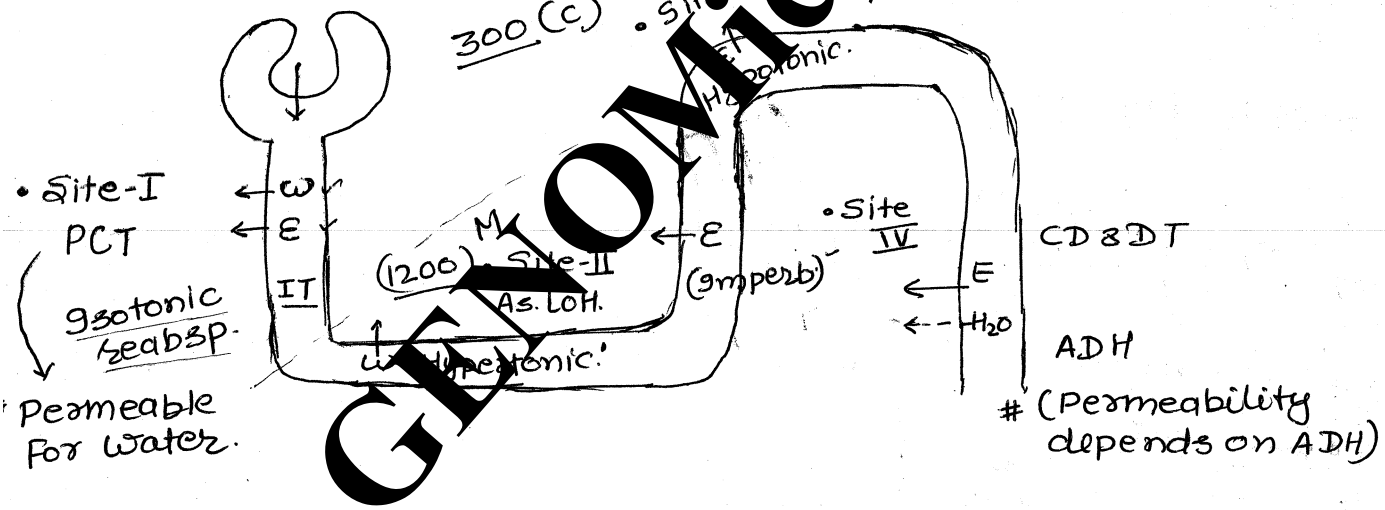


Nephron
(Renal tubule)

Coz
→ Na^+-K^+ ATPase pump ⊕nt on Basolateral membrane of Tubular cell in entire length of Nephron → Na^+ deficit in Tubular cell, that makes entire length tubular cell curious to pick up Sodium from lumen.

• Sites of Tubular Reabsorption:-





1. P.C.T. :- Site-I :- Channel :- $Na^+ - H^+$ antiport ✓

↳ Water permeable → Inhibited by Weak Efficacy diuretics (Carbonic Anhydrase Inhibitor)

2. Site-II :- Ascending Loop of Henley :-

Water Imperbeable Channel :- $Na^+ - K^+ - 2Cl^-$ cotransport ✓

→ Inhibit by :- High Efficacy diuretics.

3. Site-III :- Cortical Diluting Segment of LOH :-

{W.I.P}

- Channel :- $Na^+ - Cl^-$ Sympost ✓

→ Inhibit by :- Medium Efficacy diuretics.

4. Site-IV :- DT & CD :-

- Channel :- $Na^+ - K^+$ Antiport.

→ Inhibit by :- Weak Efficacy diuretics (K^+ Sparing diuretics)

Diuretic.

↓

By act on their relavant site by inhibit channel ↓se tubular reabsorption.

- High ⇓ Site-II ($Na^+ - K^+ - 2Cl^-$ Co-transport) ⇓ ↑↑↑ Urine output
- Medium ⇓ Site-III ($Na^+ - Cl^-$ Sympost) ⇓ ↑↑ Urine output.
- Weak
  - Site-I ($Na^+ - H^+$ Antiport) ⇓ ↑ U.O.
  - Site-IV ($Na^+ - K^+$ Antiport) ⇓ ↑ U.O.

* Diuretic :- Drugs that are used to ↑se Urine output.

→ Drugs that cause nett loss of Na^+ & water in Urine

All diuretic → 'Natriuretic'

⇓

↑se Na loss in urine [Natriuretic]

⇓ ⇓

'Hyponatrimia' 'Hypernatriurea'

Kaliuretic → ↑se K^+ ion in urine

⇓ ⇓

High & medium diuretics, Carbonic anhydrase inhibitor (weak). Hyperkaliurea [kaliurea]

⇓

Hypokalemia

Calciuretic → ↑se Ca^{+2} ion in urea.

⇓ ⇓

High efficacy diuretics. Hyper calciurea. → Calc urea

⇓

Hypocalcemia

Saluretic → ↑se Na^+ - Cl^- ion in urine

⇓ ⇓

High & Med. Eff diuretics Acute saline depletion.

Calcisaving (Ca⁺ retaining) diuretics → ↓se Ca^{+2} loss in urine

⇓ ⇓

(Med. Eff. diuretics) Hypocalciurea

⇓ ⇓

Thiazide 'Hypercalcimea'

Kalisaving (K^+ sparing) diuretics → ↓se K^+ loss in urine

⇓ ⇓

K^+ sparing diuretic. Hypokaliurea

⇓

'Hyperkalemia'

Loss

	Na^+	K^+	Ca^{++}
→ High Eff.	↑	↑	↑
→ Medium eff.	↑	↑	↓
• Weak			
→ C.A.I.	↑	↑	—
→ k^+ Sparing	↑	↓	—

Drugs:-

1. High Efficacy diuretics:-
   - Frusemide
   - Torsemide
   - Bumetanide
2. Medium Efficacy diuretics.
   - (a) Thiazide diuretic :- Hydrochlorothiazide
   - (b) Thiazide like :- Chlorthalidone, Xipamide, Metolazone.
3. Weak Efficacy diuretics →
   - (i) Carbonic Anhydrase inhibitor :- e.g:- Acetazolamide
   - (ii) K^+ Sparing diuretic :-
     - (a) Aldosterone antagonist ⇒ Spironolactone
     - (b) Inhibitor of Na^+ channel ⇒ Amiloride, Triamterine
   - (iii) e.g. Osmotic diuretic ⇒ Mannitol, Glycerol, Isosorbide

High Efficacy diuretics:—

(High Celling diuretics / Loop diuretics)

↳ act on 'Loop of Henley'.

* ↑se urine output upto 10 L/day. (High Celling)

– Act on Site-II – 'Ascending loop of Henley'

⇓

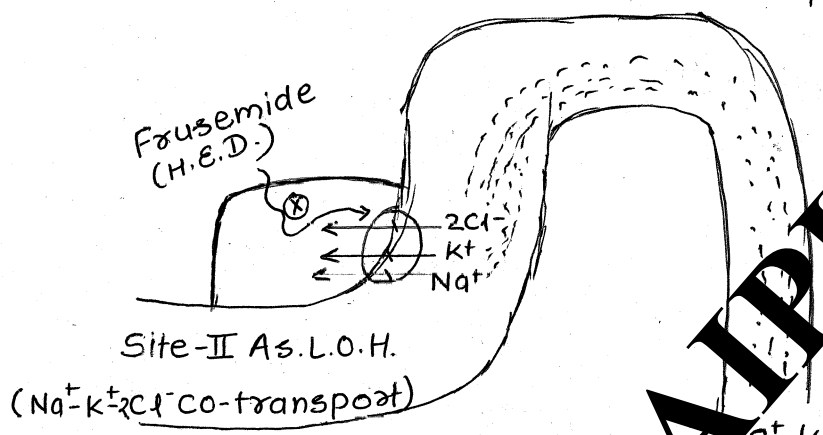
- By inhibit Na^+-K^+-$2Cl^-$ cotransport.

⇓

↓se tubular reabsorption

⇓

↑↑↑ urine output.



Na^+ K^+ Cl^-

⇓

↑urine output.

High Efficacy diuretic

⇓

↑se, Na^+ - K^+ - Cl^- & Ca^{++} in urine

Loss of

Hyponatremia ← * Natriuretic

Hypokalemia ← * kaliuretic

* Salyretic ↓ Saline depletion

* Calciuretic ↓ Hypocalcemia

Eg:-

* Frusemide (La[illegible])
  - 20 mg/2 ml [illegible] → IM / IV
  - 40 mg Tab
  - Onset :-

IV ↓ 2-5 min.

IM ↓ 10-20 min

Oral ↓ 20-40 min.

- Duration :- 3-6 hours. # → Suitable for acute use (emergency)

↳ Rapid onset.

* Usual dose :- 20-80 mg OD. → Morning. B.H.U. 2017
* Pulmonary Edema :- 40-80 mg IV.
* Renal Insuffiency :- upto 200 mg every 6 hourly IV.

→ Torsemide (Dytor) →
- 10 mg Tab.
- 10 mg/ml. Inj.

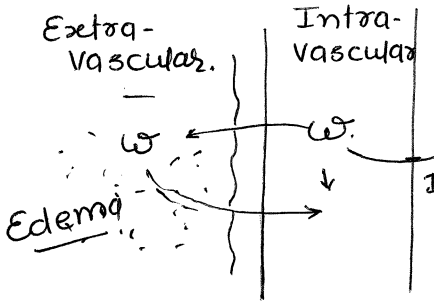
→ Bumetanide :- 'Most potent diuretic' → Specially used in * Pulmonary Edema
- 1 mg Tab.
- 0.25 mg/ml Inj.

* Uses of High Efficacy diuretic :-

① HTN :- Only in Emergency.

diuretic → ↑ Urine output → ↓ plasma volume → ↓ B.P.

*② Edema → Irrespective to etiology of Edema - Cardiac, Cirrhotic & Nephrotic



** C.H.F. → preferred for Rapid mobilization of Edema fluid (in C.H.F.

** In Nephrotic & Resistant Edema ↳ Drug of CHOICE.*

③. Pulmonary Edema :- Following M.I. & L.V.F. (Left Ventricular failu

M.I. / L.V.F. ⇓ pumping (Heart) ⇓ Pul. Edema ⇓ Breathing difficulty - (Cardiac asthma) ↓ Auscultation → Krakle sound *

E.C.G. ⇢ P.E.

Frusemide (I.V.)
- V.D.
- saluretic

↓ Venous return ⇓ 'Benefit in Pulmonary Edema'

④ Cerebral Edema → Along ⊂ Mannitol [To ↑se mannitol effect]

⑤ Along ⊂ Blood Transfusion in Severe Anemic
⇓
To prevent Vascular Overload.

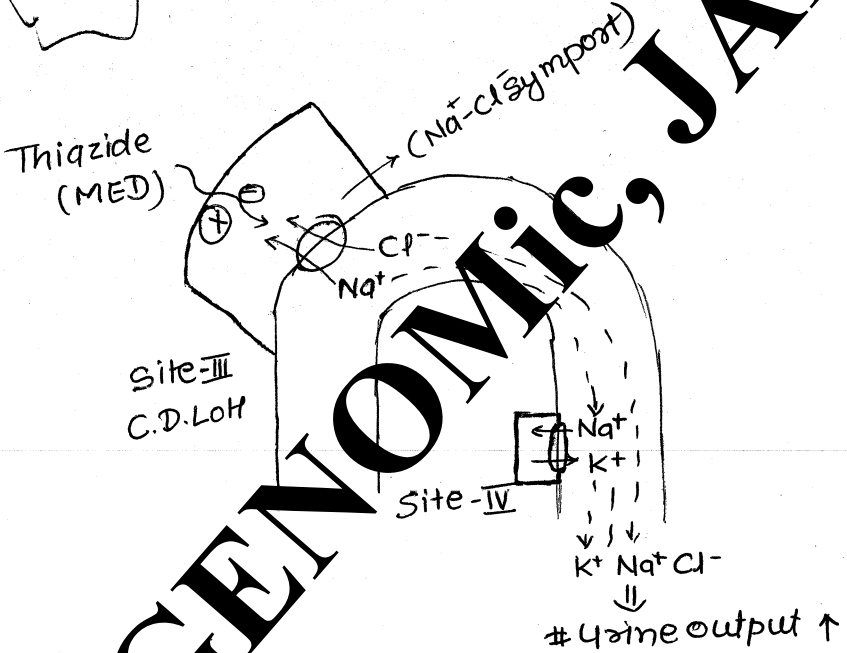
⑥ HyperCalcemia & Renal Calcium stone.
⇓
{Benefit by ↑se loss of Ca in Urine.} MED

⇓ Lasix + Fluid.
⇓
{Flush the stone ⊂ brisk diuresis.}

Stone
High → Remove
Medium → Prevent.

Medium Efficacy diuretics :-

⇒ Act on site - III (C.D.LOH)
⇓
⇒ By inhibit Na^+-Cl^- Symport.
⇓
↓se tubular reabsorption
⇓
↑↑se Urine output.



→ Due to inhibition of Site-III by Med.E.d.
⇓
↑se loss of Na^+, K^+, Cl^- in Urine.

- Natriuresis → Hyponatremia
- Kaliuresis → Hypokalemia
- Saluresis → Saline depletion.

** Due to inhibition of Site-III, more Na^+ reaches at Site-IV.

⇓

Na^+ exchange ⇄ K^+ at Site-IV

(Retain) (loss)

⇓

↑se K^+ loss in urine

** Thiazide ↓se Ca^{++} loss in urine.

⇓

Hypocalciurea

⇓

Hypercalcemia

⑤ Thiazide like → HCTZ (Hydrochlorthiazide)

- 12.5-100 mg (Tab)
- onset ⇒ 1 hr.
- duration ⇒ 5-15 hr.

→ Suitable for chronic use. (Long duration)

⑥ Thiazide like → Chlorthalidone → 50-100 mg

Metolazone → 5-20 mg

Xipamide → 20-40 mg

* Uses of Medium-Eff. diuretics

① HTN → First line drug.

② Edema → only for maintainance.

③ Diabetes insipidus → ↓se urine volume. (in D.I. Pt, Thiazide act like anti-diuretic.)#

④ Ca Stone

⇓

Hypercalciurea → Recurrent Ca Stone :-

** Thiazide by ↓se Ca^{++} loss in urine, benefit in Hypercalciurea

Complications of High & Medium Eff Diuretics →

1. Hypokalemia → Most significant

↳ Specially focus on :- post-MI, digoxine & anti-arrythematic recieving pt.

(below 3.5 mg/dl)

2. Dilutional Hyponatremia.

3. Acute Saline depletion.

4. G.I.T. & C.N.S. disturbance.

5. Hypocalcemia & Hypercalcemia.
(High) ↑ (Medium) ↑

6. Hyper Uricaemia → ↑se serum Uric acid level
avoid in Gout.

7. Allergic Manifestation → Sulpher drugs can cause allergy
(diuretics) ↑

8. Hearing Loss → due to High Efficacy diuretics
⇓
Ototoxic.
⇓
{damage Hair cell} Inner Ear.
⇓
convert mechanical vibrations into Electrical signals → Brain.

9. Hyperglycemia & Hyperlipaemia → Metabolic disturbances.

Interaction of High & Med. eff. diuretics :-

#① Potentiate anti-hypertensive action of other anti-hypertensive drug.

② High Efficacy diuretic (Frusemide) + Aminoglycocide (streptomycin) → Additive Ototoxicity.
⇓ ⇓
{damages Hair cells} {damages auditory nerve}

③. Due to Hypokalemia, ↑se digoxine toxicity. (in CVS).

④ Indomethacin (NSAIDs) ⇓ ↓ Antihypertensive action of High & Med. eff. diuretics.
** ↓se Prostaglandin
⇓
↓se afferent arteriole dilation
⇓
↓se Renal Blood Flow

⑤ High and med. efficacy diuretic
⇓
↑se lithium reabsp (PT)
⇓
↑se serum lithium & level ⇒ Lithium toxicity

** H & M.E. diuretics
⇓
Hyponatremia
⇓
#compensatory tubular reabsp. of Na^+ ↑se at PCT.
(Li^+ absorb along c Na^+ via Na^+ channel)
⇓
↑sed Li^+ absp. at PCT
⇓
↑sed serum Li level ⇒ Lithium Toxicity.

** High Na diet, along c Lithium to ↓se Lithium reabsorption (or ↑se excretion of Li)

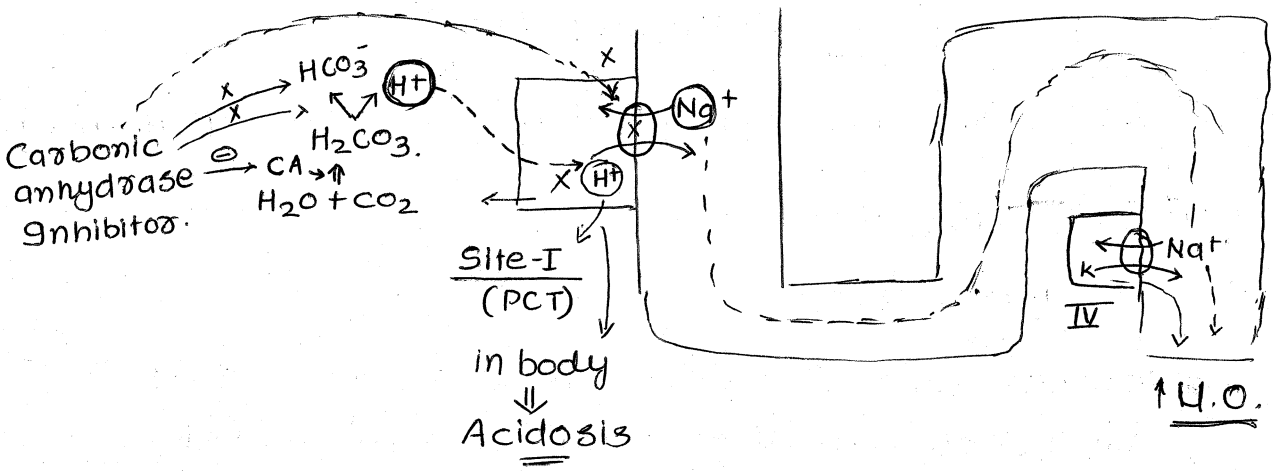
* Hyponatremia ⇒ ↑se Lithium reabsp ⇒ ↑se Toxicity
(Low Na diet)
Hypernatremia ⇒ ↓se lithium reabsp ⇒ ↓se "
(High Na^+ diet)

** Diuretics → Contraindicated during pregnancy
⇓
↳ compromise placental / Fetal Circulation.
⇓
Miscarriage / Abortion.

Weak-Efficacy Diuretics:-

1. Carbonic Anhydrase inhibitors

e.g:- Acetazolamide :- 250 mg → OD / B.D.
⇓
Action site-I (PCT)
⇓
by inhibit carbonic anhydrase enz.
⇓
↓ availability of H^+ to exchange c Na^+
(Inhibit Na^+-H^+ antiport)
⇓
↑se loss of Na^+ in Urine & retain H^+ in body.
⇓
↑se Urine output ⇓ acidosis



*Carbonic-anhydrase inhibitor:- ↑se loss of Na^+ & K^+ in urine → due to site IV

→ Hyponatremia

→ Hypokalemia

→ Retain H^+ in body → Acidosis

→ ↑se loss of HCO_3^- in urine ⇒ alkaline urine.

*Uses:-

⊛ due to hypokalemia & acidosis, not preferred as diuretic.

1. Glucoma :- To ↓se I.O.P.

C.A.I. → ↓se availability of HCO_3^-

↓se aq. humor production

↓se aq. humor secretion

↓se I.O.P.

** HCO_3^- ⇒ Major constituent of Aq. Humor & C.S.F.

2. Epilepsy → absence seizures

↑CO_2 in brain & acidosis.

Sedation and Elevation of seizure threshhold.

(↓se possibility of seizures)

3. To alkaline urine. (HCO_3^- urine) → pH ↑

4. Acute mountain sickness:- benefit by ↓se C.S.F.

↳ High altitute ⇒ ↓se Atm. pressure

⇓

Expansion of C.S.F.

↓se partial pressure of O_2. → Headache, nausea, vomiting, vertig dizziness.

* Adverse Effects →

✓ 1. acidosis.
✓ 2. Hypokalemia
✓ 3. drowsiness.
✓ 4. Fatigue
✓ 5. Abdominal discomfort.
✓ 6. Fever & rashes.

* Contra-indicated in Liver disease.

↳ ~~of use~~ Hepatic Coma.

alkaline urine
⇓
↓ NH_3 in urine
⇓
Liver ⊗ → No process of NH_3 (↑ in Blood)
↙ Brain
Encephalopathy

2. K^+ Sparing diuretic →

(i) Aldosterone antagonist:-

e.g:- Spironolactone :- 25-50 mg. BD/~~OD~~. QID

→ act on site-IV :-(DT & CD)

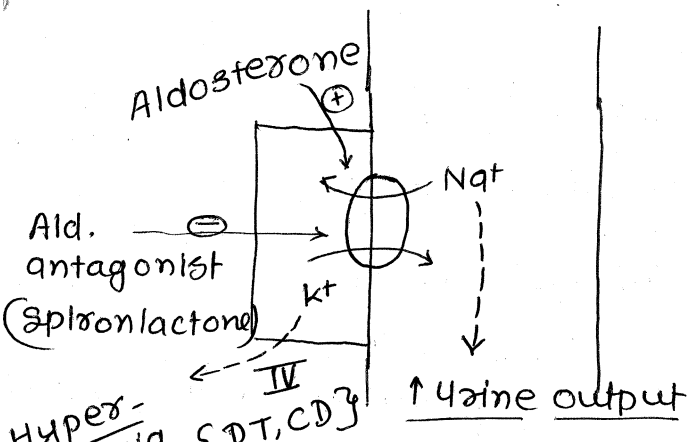
↳ by aldosterone antagonism

⇓

Inhibit Na^+-K^+ antiport.

↙ Retain K^+ in body ⇓ Hyperkalemia

↘ ↑ loss of Na^+ in urine ⇓ ↑ urine output



* Uses :-

1. Edema → well effective in Nephrotic & Cirrhotic Edema, due to aldosterone antagonism.

Nephrotic Cirrhotic
↘ ↙
↑se Aldosterone level
(Hyperaldosteronism)
⇓
{Edema} ⊖→

2. C.H.F.

↓ Mortality. (survival benefit)
{by prevent remodeling}
due to aldosterone antagonism.
↳ Arrest disease progression.

CHF
⇓
Aldo. Level
⇓
Remodeling of Heart
⇓
worsening of C.H.F.

3. Along c High & Med eff. diuretic to prevent Hypokalemia

* Adverse effects :-

- → Hyperkalemia
- → drowsiness
- → confusion
- → Abdominal discomfort

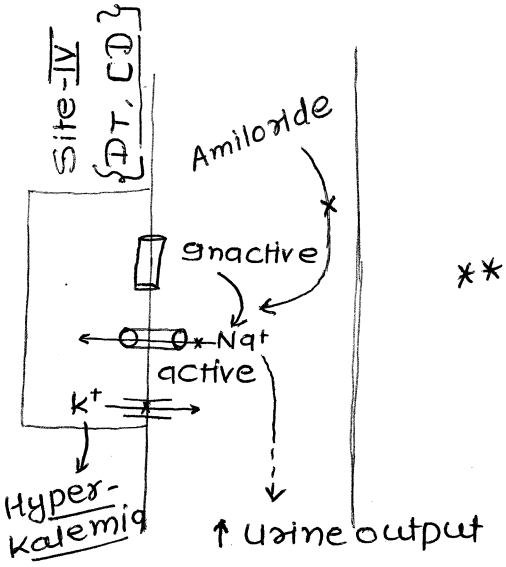
→ Hirsutism → abnormal hair growth
→ Gynaecomastia
→ Impotence.
] → due to anti-androgenic effect.

*→ Aldosterone antagonist never use along c K+ Supplement.
↳ can lead to dangerous Hyperkalemia

(ii) Inhibitor of Renal Epithelial Na^+ channels:-

→ act on site - IV (DT, CD) → by inhibit Na^+ channel.

- ⇓ Retain K^+ → ⇓ Hyperkalemia
- ⇓ loss Na^+ → ↑ Urine output

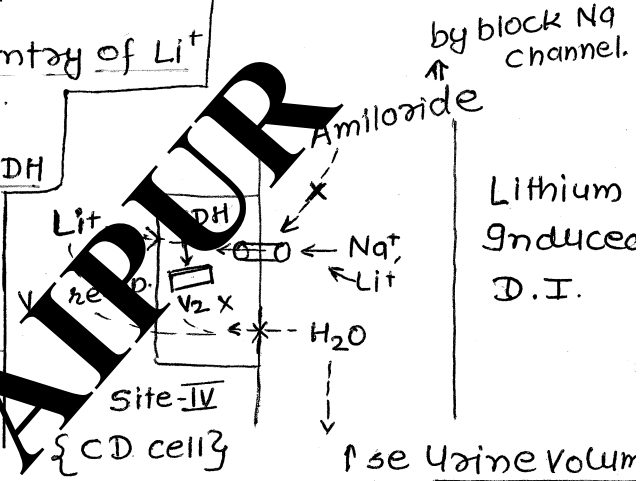


- Amiloride :- 5 mg
- Triamterene :- 50-100 mg.

** Amiloride D.O.C. for Rx of Lithium induced D.I.

↓

by inhibit Na^+ channel
⇓
Prevent Entry of Li^+ in CD cell.
⇓
Prevent ADH dysfn.
⇓
Mitigate Li induced DI.



3. Osmotic Diuretics →

→ Mannitol ⇒ 10-20% → I/V infusion

↳ Non-electrolyte, pharmacologically inert.

→ Low molecular weight

→ Hypertonic solution

⇓

do not enter in cell

↑se plasma [EC] Osmolarity → Hyperosmolar

- Mannitol
  - ⇓ IV.
  - ⇓ ↑ Plasma osmolarity (Expand E.C.F.)
  - ⇓ ↑ GFR (Mannitol Freely Filter)
  - ⇓ More water, Electrolyte ē Mannitol in PCT.
  - (Mannitol not reabsp) → ⇓

Mannitol retain water osmatically in lumen

⇓

82% at PCT.

Retain Na^+-Cl^- in PCT → Isotonic reabsp at PCT. (W+E) ↘x ↘x

↓

↑ Urine output

** Mannitol encourage movement of water from Brain, Parenchyma & aqueous humor, & C.S.F. (by Osmotic action).

↓ IOP ✓ ↓ ICP ✓

Uses:-

♣. Mannitol never uses to treat chronic edema or as. & natriuretic.

1. To ↓se ICP & IOP, before & after brain & occular surgery.
2. In Glaucome (↑IOP) & Head injury (↑ICP) to ↓se. level.
3. To maintain GFR and Urine output in impending Renal Failure. like, Cardiac Surgery, Hemolytic Rxn, Severe trauma & Shock.

If Renal Failure already set, then not used.

4. To counter low osmolarity of Plasma. due to Rapid Hemodialysis/ Peritoneal dialysis.

Contra-Indications:- ✓ ① Acute tubular necrosis
② Anuria
③ Pulmonary Edema
④ Left ventricular fail. (acute)
⑤ C.H.F.
⑥ Cerebral Haemorrhage

* 1. Due to Hyponatremia → Headache, behaviour changes. (Rx :- 3% NaCl)

2. Mannitol in winter → Needle shape Crystal. (dissolve at room temp)

✓ 3. Assessment of mannitol effect in Head injury Pt. → by check Pupil size {if ICP ↓sed, then Pupil respond}

* Isosorbide
* Glycerol
→ oral. (0.5-1.5 gm/kg.)

Anti-diuretic :—

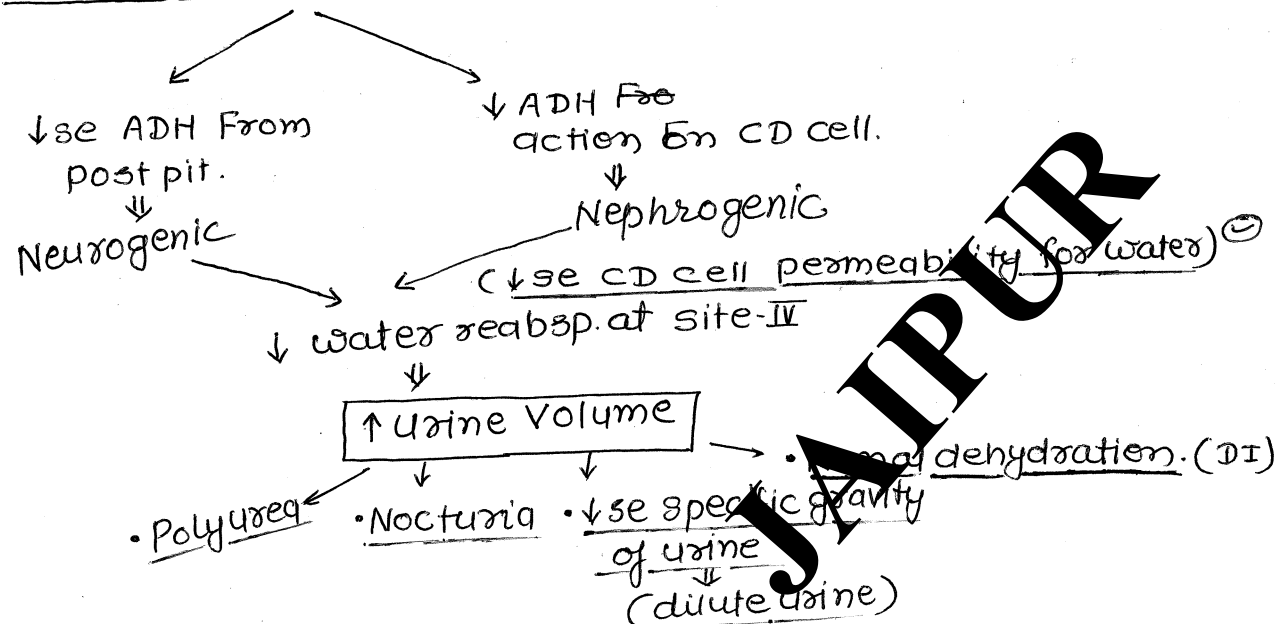
- Drugs that are used to ↓se urine volume and particularly indicated in Diabetes insipidus.

① Anti-diuretic hormone & desmopressin.

② Thiazide (HCTZ), Amiloride

③ Indomethacin, Carbamazapize.

* Diabetes insipidus :-



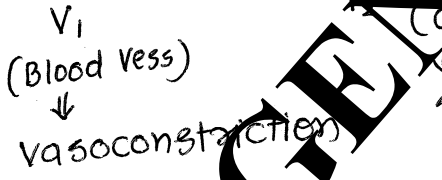
Drugs :-

I. 1. ADH (Vasopressin)

Post. Pit. → Osmoreceptors — Plasma osmolarity.

(⊕) (↑) → Fluid in body ↓ {conc. blood} ⇓⊕ ADH Secr. ↑

P.O. ↓ → ADH. ↓



(CD cell)

↑ Permeability For water.

↓ Urine Volume

→ conc. urine ✓

→ ↑ specific gravity of urine ✓

⇒ Fluid retention ✓

⇒ Hyponatremia ✓

* SIADH → ↑ ADH → Fluid retention
↑ ADH → conc. urine / ↕ Spec. gravity / ↓ urine vol.
↑ ADH → Hyponatremia
Rx ↓
Demeclocycline# ↳ ↓ ADH action on CD cell.

2. Desmopressin → only act on V_2 recep. (CD cell)
↓
↓ urine volume.

Uses :- (182)

1. Diabetes Incipidus. (Neurogenic) → D.O.C. ⇒ Desmopressin*
↓
{10-4 µg / day, Nasal drop}

2. Nocturia in Adult → desmopressin.

3. Bed-wetting in Children → 'Nocturnal Enuresis'
↳ Desmopressin.
↳ 5-10 µg / bed time.
↳ Nasal drop.

* During desmopressin use, fluid restriction → 1 hour before & 8 hr after admn.

4. Bleeding Esophageal varices. → Vasopressin [v.c.]

** Vasopressin used as last option to use B.P.
↳ 10 IU/ml inj.}

Adv. Effect :- ① Hyponatremia*
② Fluid retention*
③ Nasal irritation.
④ Epistaxis
⑤ Backache in female. → uterine contraction.

II. Thiazide diuretic (HCTZ) →

↳ act as antidiuretic in DI Pt.

Thiazide

⇓

Hyponatremia

⇓

Compensatory tubular reabsp. ↑ at PCT

⇓

{Isotonic reabsp. → Wt E}

⇓

↑ water reabsp. at PCT. (1)

⇓

less water reaches at Site-IV

⇓

↓ Volume of water at Site-IV that is available for loss in D.I. Pt.

⇓

↓ Urine volume in D.I. Pt.

Use:-

① Neurogenic and nephrogenic DI

- Amiloride → D.O.C. in Lithium induced nephrogenic D.I.

III • Carbamazepine :- ↑ ADH (Post pit.) → Neurogenic D.I.

• Indomethacin → (NSAID)

⇓

↓ PG

⇓

↓ Afferent arteriole dilation

(By BP ↓)

↓ GFR

⇓

↓ Urine volume

Rx :- Nephrogenic DI

↓ Proteinuria

Rx :- Nephrotic Syndrome

* Nocturnal Enuresis

I Line drug

Desmopressin → more effective

↓ Urine Vol. → Hypo-natremia

⇓

delayed bladder filling

⇓

micturation after wake up

Imipramine (T.C.A) → cardiotoxic

(Above 5 yr. only)

⇓

↓ delta (δ) wave sleep

(deep sleep ↓)

⇓

more chance of wake up for micturition at night.

July 26, 2022

Drugs acting on C.V. System

→ Anti HTN
→ Angina
→ MI
→ CHF
→ Arrythemia

• Cardio Vascular Drugs :-

* **Anti-Hypertensive drugs** :— Drugs that are used to lower down elevated B.P. to Normal.

HTN ⇒ Elevated BP.

	Systolic	Diastolic
• Normal →	< 120	< 80
• Pre HTN →	120-139	80-89
• HTN-I →	140-159	90-99
• HTN-II →	160 & above	100 & above
• HTN-U/E →	above 180	above 120.

urgency / Emergency
↓ ↘ End organ damage.
No damage

* **ISH** (Isolated Systolic HTN) :- when only Systolic BP in HTN range

→ **HTN** → Very common disorder of past middle age.
→ It is not a disease itself, but a very imp. risk factor for cardio-vascular morbidity & mortality.

↳ Silent death → Eye ⇒ Ratinopathy (Blindness)
- Heart (CV) ⇓ CHF, MI
- Brain ⇓ Stroke
- Kidney ⇓ Chronic Renal disease C.K.D.

HTN

Primary
Idiopathic
[Essential]

For the requirement of Body! →

↳ maybe Sympathetic or RAAS overactivity.

↳ over 95% cases.

↳ R_x :- Life time reduction of B.P. by drugs.

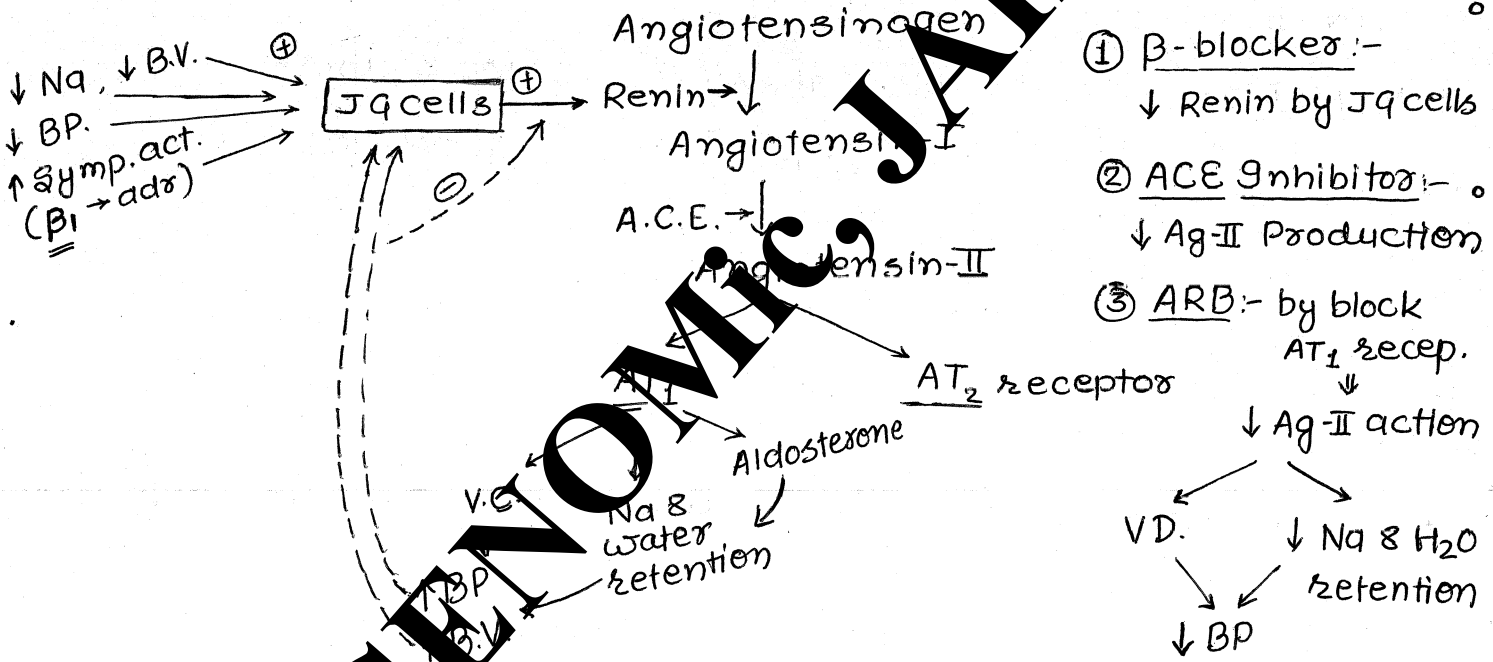
Secondary
↓
disease condition.

Eg:- Pheochromacytoma
[Tumor of adrenal gland]

↳ few cases. (<5%)

↳ R_x :- Reduction of B.P. required till cause removed.

→ Anti-hypertensive drugs ↓se BP by acting on:-
- Heart (↓ cardiac output)
- Blood vessels (Vasodilation)
- Kidney (↑ Urine output → ↓ Blood vol:)



① β-blocker :-
↓ Renin by JG cells

② ACE Inhibitor :-
↓ Ag-II Production

③ ARB :- by block AT_1 recep.
↓
↓ Ag-II action
↓
VD. ↓ Na & H_2O retention
↓
↓ BP

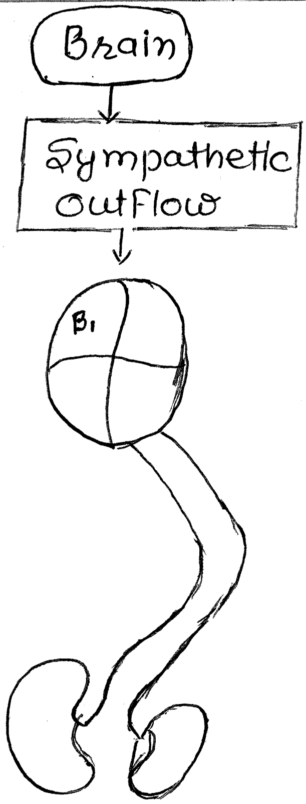
4. α+β blocker:-
e.g:- Labetalol
V.D. + ↓CO ⇒ ↓BP

5. Ca channel blocker:-
e.g:- Amlodipine.
V.D. ⇒ ↓BP.

8. ACE Inhibitor:-
e.g:- Lisinopril.
↓ Ag-II

9. Angiotensin receptor blocker →
eg:- Losarton.
↓ Ag-II action.

⇒ Both (8) and (9)
⇓
by ↓ Ag-II level/action
V.D. ⇒ ↓ Na⁺ & water retetion
↓BP



1. Central Sympatholitic
e.g. Methyldopa
↓ Symp. outflow ⇒ ↓ BP.

2. β-blocker:-
e.g:- Atenolol.
↓ Cardiac activity ⇒ ↓CO ⇒ BP

3. α- blocker:-
e.g:- ~~Rz~~ Prazocin.
Vasodilation ⇒ ↓BP.

6. Vasodilator :-
e.g:- Sodium nitroprusside
VD ⇒ ↓ BP.

7. Diuretic
e.g:- Frusemide, HCTZ
↓CO → ↓ BV ⇒ ↓ BP.

1. ACE Inhibitor:- by inhibit A.C.E.
⇓
↓ Ag-II Production
→ Vaso-dilation
⇙ Artery + Vein dilation
↓ After-load
↓ Pre-load
⇓
• Rx ⇒ CHF
↳ Maintain pumping ☺
→ ↓ Vascular resistance → ↓BP
→ ↓se Na & water reabsp.
↓ vascular load (↓BV) → ↓BP
⇓
• Rx of HTN
→ less cardiac work.
MI/ High Cardio-vascular risk

→ By Prevent Hyperconstriction of Efferent arteriole,
↓
prevent diabetic nephropathy

Ag-II ↓
↓
EAdil.

D.M.
↓
↑ Blood Glucose level
↓
↑ Plasma osmolarity.
↓
Eff. arteriole hyperconstriction.
↓
Hyperfiltration
↓
Proteinurea ⇒ diabetic Nephropathy.

Eg:- Captopril ⇒ 25-150 mg
Lisinopril ⇒ 5-40 mg
Enalapril ⇒ 2.5-40 mg
Ramipril ⇒ 1.25-10 mg

Uses →
① HTN
② CHF
③ M.I. → Prevent remodeling & Subsequent CHF.
④ High Cardio Vasc. Risk (↓ cardiac work)
⑤ Diabetic nephropathy.

Adverse Eff:-
① Hypotension :- Specially on initial use.
↓
- Start at low dose at bedtime.
② Hyperkalemia → ↓ ALDOSTERONE
③ Dry cough.
④ Angiodema
⑤ Dysgeusia → Reversible loss of taste sensation. (mainly ⊂ Captopril)
⑥ Fetopathic → Fetal Growth Retardation.

C|I :- ① Pregnancy
② Renal Artery Stenosis. (worsening due to efferent arteriole dilation).

** Avoid in Hyperkalemia & Azotemia (↑BUN)
↳ Blood urea nitrogen.↑
↓
(worsening due to efferent dilation)

2. Angiotensin Receptor Blocker (ARB) ⇒

By block AT_1 receptor
⇓
↓ Ag-II action
↙ vasodilation
↘ ↓ Na & water retention.

E.g:-
→ Losartan ⇒ 25-50 mg
- Telmisartan ⇒ 20-80 mg
- Valsartan ⇒ 80-160 mg
- Olmisartan ⇒ 20-40 mg
- Candisartan ⇒ 8 mg

#Uses :- ① HTN
② CHF
③ MI
④ Diabetic Nephropathy

Adverse Effect :- Headache
- dizziness
- Angiodema
- Fetopathic

C/I :- (i) Pregnancy
(ii) Renal artery stenosis
(iii) Avoid in Hyperkalemia & Azotemia

→ ACE-I / ARB + K^+ Supplemant / K^+-Sparing diuretic # AIIMS Jodhpur 201
⇓
'dangerous Hyperkalemia'

3. α-Blocker :- Prazosin
⇓
Vasodilation ⇒ ↓ BP.

4. β-blocker → Atenolol
⇓
↓ Cardiac activity ⇒ ↓ C.O. ⇒ ↓ B.P.

5. α + β-blocker → Labetalol
⇓
V.D. ↓ C.O.
⇓
↓ BP.

6. Diuretic → ↑ Urine output ⇒ ↓ Plasma Vol. ⇒ ↓ BP.
High :- Frusemide → Emergency HTN
Med. → HCTZ → First line drug in Rx of HTN (Reduce salt intake Inste of MFDu)

④ Central Sympatholytic ⇒

- Clonidine → 100 μg OD
- Methyldopa (pro drug) → 250-500 mg BD / TDS.

Methyldopa ↓ α-methyl. N. Adr.

Clonidine and α-methyl. N. Adr. → α_2A α_2 Agonist (Brain → medulla)

⇓

↓ Sympathetic outflow

⇓

↓ BP.

* Adverse effect:
  ↳ Sedation & Lethargy

* Methyldopa is First line drug in Rx of HTN during Pregnancy.

⑤ Vasodilator → By relax Vascular smooth muscles

⇓

Vasodilation

⇓

↓ BP

(a) Arteriolar → mainly dilate artery.

e.g.:- Hydralzine :- 25-50 mg.
↳ (by Nitric oxide → Relax Vascular smooth muscles)

* In History, **DOC** For Rx of Emergency HTN. during Pregnancy.
* Due to tachycardia, can precipitate Angina in old age Pt.
* Systemic Lupus Erythematus (SLE) → caused by Hydralzine.

- → Diazoxide → 50-100 mg ⇒ K^+ channel opener
- → Minoxidil ⇒ K^+ channel opener
  - In current, used in Rx of alopecia. (Topical) (2-5%) — 'Mintop'
  - → Hirsutism :- adverse effect of minoxidil

(b) arteriolar + Venular ⇒ 'Sodium nitroprusside'

⇓

by nitric oxide N.O.

⇓

Relax vascular smooth muscles.

50 mg vial dilute in 500 ml NS.

⇓

'IV infusion'
↳ onset → seconds.
↳ duration → 3-5 minutes.

⇒ Use :- In Emergency HTN.
- CHF, LVF, MI.

⑨ Ca^{+2} Channel Blocker ⇒ Relax Vascular smooth muscles

⇓

Vasodilation

↓ BP
Rx :- HTN

mostly dilates Artery
↓ AFterload
⇓
↓ Cardiac work
⇓
↓ O_2 demand
⇓
Rx :- Classical Angina

coronary art. dilation
⇓
↑ coronary blood flow
⇓
↑ O_2 supply
⇓
Rx :- Variant Angina

C.C.B.

D.H.P.
(Di Hydro pyridine)
e.g:- Amlodipine → 5-10 mg
Nifedipine → 5-20 mg
⇓
Vasodilation
↓ BP.
↓ Mean arterial pressure
⇓
Reflex tachycardia
⇓
↑HR *

Use :- ① HTN
② Classical Angina
③ Variant Angina

Adverse Eff :- (i) Palpitation (Reflex tachycardia) ↑
(ii) Flushing ⇒ Redness of Face
(iii)* Ankle Edema
(iv) Headache
(v) Hypotension
(vi) drowsiness.

* can be used ± β-blocker - DHP
(↓HR) (↑HR)

** DHP (espl → Nifedipine) ⇒ ↑HR ⇒ ↑ O_2 demand
⇓
Short acting
↳ Not used / Avoid in Post MI Pt.

Other than DHP
→ Diltiazam ⇒ 30-60 mg
→ Verapamil ⇒ 40-160 mg
Vasodilation & depress SA Node
⇓ ⇓
↓ BP ↓ HR

Use :- ① HTN.
② Classical Angina
③ Variant Angina
④ Arrythemia.*

Adverse Eff → Nausea
→ Constipation
→ Bradycardia

** Not used ± β-blocker :- D/V
(↓HR) (↓HR)
⇓
*Severe Sinus depression

** Can be used in Post-MI Pt., if when β-blocker not in use

* CCB as antihypertensive.
  ↳ (safe in pregnancy, elder, asthematic, diabetic)
  ↳ prefer in Post-Stroke (do not compromise cardiac output)
  ↳ do not alter lipid profile
  ↳ do not male sexual functions.
  ↳ don't ↓se Renal perfusion.
  ↳ and not compromise Exercise capacity.

Rx of HTN :-
- No treatment required in Pre-HTN.
** → If History of MI, Sh Stroke, CKD and DM, (compelling indication) then Rx also required in Pre-HTN.

Treatment start ē one drug is Stage-I HTN.

* Selection of First-line drug :- (Normal :- < 140mmHg).

	Preferred	Avoid
1. Diuretic	- Obese, - Elder, - Low cost - ISH (Isolated Systolic HTN)	- Pregnancy - Gout
2. ACE Inhibitor/ ARB.	- Young. - Left ventricular Hypertrophy Gout dyslipidemia	- Pregnancy (Fetopathic) - Renal artery Stenosis. - Hyperkalemia - Azotemia
3 Beta blocker	- Young, - anxiety - Tachycardia - Migraine - Low-cost	- Asthma, - COPD - Sick-sinus - AV block - Peripheral vascular disease
4. C.C.B. -	- Elder, - ISH. - Pregnancy, - DM, - Asthma, PVD	- Post-MI → DHP - CHF & Sick-sinus (diltiazem, verapamil)

* Stage-II HTN → Rx start ē 2 drugs.

If no proper response, then change the combination.

Afterward, use three drug combination.

** If no proper response ē 3 drug (full dose), 'Resistant HTN' ⇒ use 4 drug Combination

Combination (+ second drug)

Prepare/ Suitable
- different class
- different action
- complement action
  - ↓ HR ①
  - ↑ HR ②

Avoid
- Same class
- Same action
- ↑ Rate ① ↑ Rate ②

#

Pregnancy

Avoid
- diuretic
- ACE Inhibitor
- ARB
- Propranolol ($\beta_1 + \beta_2$ blocker)
- Na Nitroprusside

use
- Methyldopa] I st line drog
- Labetalol] (choice of pill)
  - (Slightly preferred)
- Ca Channel blocker (Nifedipine) ↓
  - β_1 agonist
  - Hydralazine

discontinue before labour ↓ To induce labor
- uterine relaxant
- Tocolytic

Emergency HTN

① Na Nitroprusside
② Glyceryl trinitrate
③ Labetalol
④ Frusemide
⑤ phentolamine
⑥ timolol

Aug. 4, 22.

Anti-Anginal drugs.

→ drugs that are used to prevent, terminate or abort attacks of Angina.

Angina Pectoris :- It is pain syndrome due to Ischemia of Myocardium.

* It is crying of Heart due to lack of O_2 in myocardium. (due to imbalance b/w supply & demand of O_2 of MC.)

→ ↑ demand of O_2 of Myocardium

↓ Supply of O_2 of myocard.

Myocardial Ischemia
(lack of O_2 in myocardium)
⇓
Anerobic Glycolysis
⇓
↑ Lactic acid
⇓
Irritate nerve ending
⇓
Ischemic Pain in Pectoral Region
↳ Angina Pectoris

← Classical Angina

Stable Angina / Effort " / Common "

→ attack precipitate during ↑ed demand situation. like → Exercise, Emotion, Eating & Coitus.

** Due to atheroma, supply ↓se, not ↑se in respect of ↑ed demand; cause of attack.

Rx:- ↓se demand (↓se cardiac work)

Variant Angina

Uncommon Angina, Spastic Ang. - Prinzmetal's Angina

⇒ Attack during @ rest / sleep.
⇒ due to sudden coronary spasm
⇓
↓se coronary Blood Flow
⇓
Cause :- ↓se Supply.

Rx:- ↑se supply (coronary dilation)

* Unstable Anging ⇒ due to rupture of atheroma
⇓
Thrombus Formation C Coronary spasm.
⇓
occlusion of coronary artery.
⇓
(↓↓Supply) ← ↑se Severity of attacks.

Cause:- thrombus + spasm.

* Rx of Unstable Angina ⇒ Antiplatelet / Anti coagulant + Coronary dilator.
or

1. Nitrates.
2. β-blocker
3. CCB.
4. K^+-channel opener
5. Others.

1. Nitrates. → Relax vascular smooth muscles (by Nitric oxide)

⇓

Vasodilation

⇓

Dilates both Arteries & Veins (mostly)

⇓

↓ After load

↓ Need of Force to pump blood

⇓

Relieve/prevent ⇒ CHF (Maintain Pumping)

⇓

Rx of CHF *

↓ Pre load.

↓ Cardiac work

⇓

↓ O_2 demand.

⇓

Rx of Classical Angina *

↓ BP.

(Rx :- HTN) *

Coronary dilation.

Relive/prevent Coronary Spasm.

⇓

maintain ⇒ Coronary Blood Flow.

⇓

↑/maintain ⇒ O_2 supply.

⇓

Rx of Variant Angina *

Rx of M.I.

** By relax smooth muscles.

↙ Relieve Esophageal Spasm.

↘ Relax Sphincter of Oddi

⇓

Relieve billiary cholic (Pain due to ↑ed press in HPD, CBD & G.B).

E.g:- Nitroglycerine (Glycrine Tri-nitrate)

↙ Sublingual (0.5 mg)

duration → 10-30 min

↳ Used in Emergency (S.O.S) → To abort/terminate attack

↘ Oral (5-15 mg)

→ 4-8 hrs.

↳ Chronic Prophylaxis → For prevention (Routine)

⇒ Oso Sorbide dinitrate (ISDN)

5-10 mg

⇓

Sublingual

duration :- 20-40 min

⇓

Emergency / SOS

⇓

To abort / terminate attack

Oso Sorbide Mono Nitrate (ISMN)

20-40 mg.

⇓

Oral.

⇓

duration :- 6-10 hrs

⇓

(Routine) Chronic prophylaxis

e.g. BD.

⇓

To prevent attack.

Adv. Effect:

① Hypotension.
② Fullness in Head
③ Headache (Tolerance) → disappers ∝ time → develops tolerance
④ Flushing.
⑤ Weakness, Sweating, Palpitation

** G.T.N ⇒ Subling. Tab.

⇓

* If dizziness & Fainting

⇓

Indication of Hypotension. (Over effect)

discard the unabsorbed Fraction of Fraction

⇓

"spit the drug"

lay down in Supine Pos.

* If there is no stinging sensation below tongue after Sub-ling admn. of drug ⇒ drug potency ↓ed.

Uses:-

① Classical Angina ② Variant Angina ③ M.I.
④ Acute Coronary Syndrome (Unstable Angina)
⑤ Emergency HTN.
⑥ LVF / CHF.
⑦ Esophageal Spasm.
⑧ Billiary cholic.
⑨ Cyanide Poisoning (↑ Excr. of Cyanide in Urine)

2. β-blocker ⇒ Atenolol ⇒ ↓ Cardiac activity ⇒ ↓ O_2 demand
⇒ Rx of Classical angina.

** Contraindicated in Variant Angina.
Coz :- β-blocker do not prevent coronary Spasm, Even worsens it.

3. Ca Channel blocker ⇒ Amlodipine, Nifidipine
⇓
Vasodilation
⇓
arterial dilation → ⇓ AL ⇒ ↓ O_2 demand → ⇓ Rx :- Classical Angina
coronary dilation → ⇓ ↑ O_2 supply. → ⇓ Rx :- Variant Angina

4. K^+ Channel opener :- Nicorandil ⇒ 5-20 mg. (NICORAN)
↓
↑ K^+ outside ⇓ (Hyper-Repol) by Relax Vascular Smooth muscles.
Slow depol.
⇓
Vasodilation. → Coronary dilation ⇒ ↑ O_2 Supp. ⇒ Rx ⇒ VA
→ A+V dilation ⇒ ↓ Cardiac work ⇒ ↓ O_2 demand
Rx :- CA

5. Others.
→ Ranolazine ⇒ 500 mg ⇒ ↓ Ca^+ overload in myocardium
⇓
↓ Cardiac work.

→ dipyridamol ⇒ Not preferred in current. ⇒ cause coronary Steal
↓
divert coronary blood flow from ischemic to non-ischemic zone.
↙ coronary dil. ↘ Anti-Platelets.

overdose → Blue vision.
↑
→ GTN + Sildenafil → Severe Hypotension
↓ (Viagra) ⇓ M.I ⇒ death.
VD ⇓ (Vasodilation)

*Sildenafil ⇒ Phospho-diesterase inhibitor.
(V.D)
⇓
Use :- Pulmonary HTN. in (ICU)
& Penile erection dysfn

Drugs used in M.I.

M.I. ⇒ Ischemic necrosis of a portion of myocardium.

- Sudden occlusion of a branch of coronary artery (due to thrombus formation)

⇓

↓↓ O_2 supply

⇓

Severe Myocardial Ischemia

⇓

↑↑ Anerobic glycolysis

⇓

↑↑ Lactic acid

Cell death
- programmed → 'Apoptosis'
- accidental → 'Necrosis'

Pain

Acidosis (↓PH) in the portion.

⇓

Inhibition of Glycolytic Enzymes.

⇓

Inhibition of Glycolysis.

⇓

No Energy Production

⇓

Myocardial - Ischemic Cell death

⇓

Myocardial Ischemic Necrosis

⇓

'Myocardial Infarction'

① Pain, anxiety & apprehention ⇒ (Morphine) Narcotic Analgesic

* Morphine relieve - ① Pain, anxiety & apprehention (All) in M.I.

⇓

↓se Symp. activity that ↑se due to above (P, A, A)

⇓

↓ cardiac activity

⇓

↓ Cardiac load

⇓

↓ O_2 demand

* If asked any of them, then Pain gets priority

Histamine release
② Vasodilation
⇓
↓ cardiac load
also relieves Pulm. edema
Beneficial in Cardiac Asthma*

* {Ultimate Goal :- To ↓ O_2 demand.}

Cardiac Asthma :
Breathing difficulty due to Heart failure associated Pulmonary edema

2. Oxygenation ⇒ administer O_2 / assist respiration.

3. Maintainance of Blood Volume & Tissue Perfusion ⇒
⇓
Slow I/V Saline. To prevent SHOCK.

** But try to avoid Vascular overload.

4. Correction of Acidosis ⇒
$NaHCO_3$ I/V infusion.

5. Treatment & Prevention of Arrythemia ⇒
I/V Infusion of Esmolol. (β-blocker)*

6. Prevent/ Pump Failure ⇒
Relieve

- Diuretic ⇓ Frusemide (I/V) ⇓ V.D. + ↑U.O. ⇓ ↓ Venous Return. ⇓ Relieve:- Pulmonary Edema
- Inotropic ⇓ Dobutamine/ Dopamine ⇓ ↑ Force ⇓ ↑ C.O.
- Vasodilator ⇓ Nitroprusside / NTG. ⇓ [A+V] dilation ⇓ ↓ Need of Force to pump Blood.

7. Prevention of thrombous Extension :-
Antiplatelets ⇒ Aspirin
Anticoagulant ⇒ Enoxaparine.

8. Thrombolytic ⇒ Break down thrombus.
Eg:- Alteplase.

9. Prevention of Subsequent C.H.F. & Remodeling :- ACE-I. / ARB.

10. Prevention of further attacks :- ① Anti platelet ⇒ Aspirin.
② β-blocker ⇒ Atenolol
③ Hypolipidemic ⇒ Atorvastatin

'Anti-Arrythemic Drugs'

- Drugs that are use to treat or prevent irregular cardiac rhythm.

• Arrhythmia ⇒ Irregular Cardiac Rhythm.

- Myocardial ischemia, neurogenic, drugs, pH & electrolyte imbalance, Stretching & mechanical injury.

Ion channel of cardiac fibre ⟹ Abnormal ion movement.

⇓

alteration in Electro-Physiology of Cardiac Fibres.

⇓

abnormal automaticity & impaired conduction OR BOTH.

{Enhanced/ectopic automaticity} ⇙

⇓

Irregular cardiac Rhythm ⇒ 'Arrhythemia'

⇓

(Rate, Ratio, timing of cardiac events disturbed)

• Arrhythemia ⇒ Uncontrolled Ectopic discharge of Ions*

Rx ⇒ Controlled ion movement. ⇒ Ion channel Suppression

- Drugs :-

• Class-I :- Na^+ channel blocker.

- Quinidine
- Disopyramide
- Procainamide
- Lignocaine
- Mexiletine.
- Propaphenone
- Flecainide

- Class-II :- β-blocker

  propranolol, Esmolol, Sotalol.

- Class-III :- K^+ channel blocker

  - Bretylium
  - Amiodarone ✓

- Class-IV :- Ca^{+2} channel blocker

  - diltiazam - Verapamil. (Anti-arrhythmic)*

Class-I

* Na^+ Channel Blocker :— aka 'Myocardial depressant
* aka 'Membrane Stablizing agent'
* Local anesthetic action.
* Limit conductance of Na^+ ( ) across biological membrane.

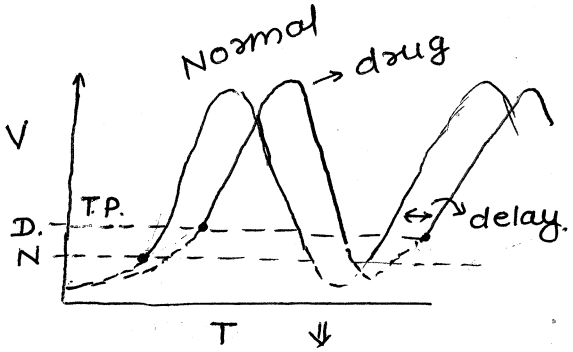
⇒ Delay Na^+ channel opening.

- Moderate (I-A) (1-10s)-
  - Quinidine ✓
  - disopyramide ✓
  - procainamide ✓
- little (I-B) (<1sec)-
  - Lignocaine ✓
  - Mexiletine ✓
- marked (I-C) (>10s).-
  - Propafenone ✓
  - flecainide ✓

→ Na^+ channel blocker ↑e

* Threshold potential.

→ ↓se $\frac{dV}{dt}$ by Class-I



impulses below new threshold won't be effective & limits the no. of impulses ⇒ delays Electro-cardiac activity

Class-II :- β-blocker.

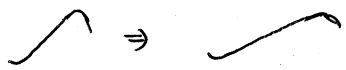
⇒ Propranolol ⇒ Class-IA also.

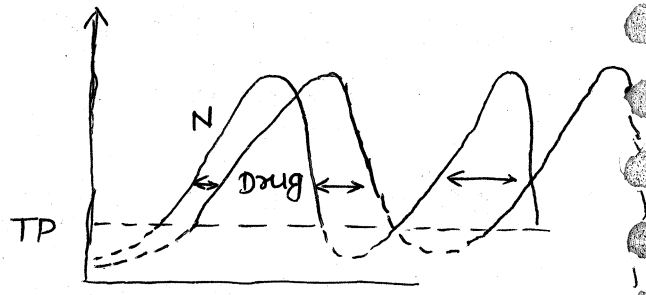
⇒ Esmolol ⇒ IV infusion

⇒ Sotalol ⇒ class-III also (K^+ channel blocker also)

* depress SA Node & conduction System

Eta ⇒ delay threshold Potential.
⇒ decrease Slope of Phase-IV



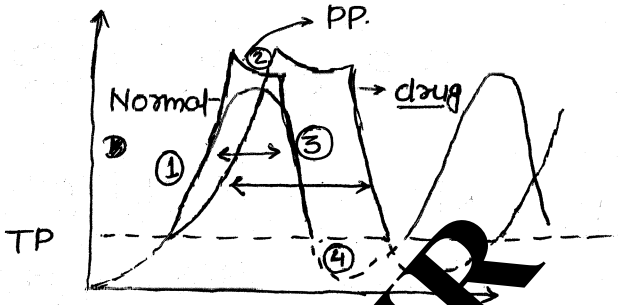


Class-III K^+-Channel blocker.

* Agent widening action potential duration.

- Bretylium
- Class-II also.*

- Amiodarone ⇒
  - 100-200 mg Oral
  - 150 mg Injection I/V



* Broad Spectrum anti-arrhythemic.
⇓
Blocks Na^+, K^+, Ca^{++} Channels.*

*Iodine containing drug
↳ can lead to Hyperthyroidism {Rarely}

* Inhibit conversion of T_4 to T_3 (More active) →
↓ Less active
*Hypothyroidism (M/C.)

* Avoid amiodarone (Not used) in Thyroid Pt. ⇒ Thyroid Profile
*
** ⇒ On long term use, Pulmonary alveolitis / fibrosis & Corneal deposition.* PFT, Eye Examn.

⇒ 2 dose ⇒ Loading dose ⇒ I/V bolus ⇒ 150 mg (1 ampule) ⇒ 10 min → 15 mg/min.
⇒ Maintainance dose ⇒ I/V infusion,
900 mg in 24 Hrs. (6 amp)
Total dose = 1050 mg.

any infusion < 30 min Kla Bolus.

First 6 hrs.
⇓
360 mg in 360 min
1 mg/min

later 18 hrs.
⇓
540 mg
⇓
0.5 mg/min.

PABLO

Class-IV Ca+2 Channel Blocker :-

- Diltiazam
- Verapamil

⇒ depress SA Node & conduction system.

⇒ ↓se slope of Phase-IV

⇒ delay ~~act~~ threshold potential

mech. same as class-II

Special Points ⇓

* All anti-arrhythemic drugs are Pro-arrhythemics. (Before admn, confirm the type of arrhythmia. → can cause arrhythm)
* Class-I-C ⇒ Most dangerous class of anti-arrhythemics.
* Ventricular Tachycardia (VT) → IOS. ⇒ blocks Na channel.
  - acute ⇓ Lignocaine
  - Chronic ⇓ amiodarone.

** Note :- But in current, amiodarone preferred in both acute & chronic VT.

* AFI ⇒ atrial flutter & AF ⇒ Atrial Fibrillation. ⇒ ** Esmolol ~ I/V infusion ↳ Short acting.
* AV-Block.
  - Atropine# (Anticholinergic)
  - Isoprenaline# (Sympathomimetic)
* PSVT (Paroxysmal Supraventricular Tachycardia) ⇒ adenosine ⇓ 6-12mg (IV) Fast ⇓ Raise Hand after admn. ⇒ Fast acting ⇒ In order to make drug reach to Heart.
  - D.O.C for Termination
  - & Verapamil ↘ *. D.O.C for both Termination & Prevention
* Digitalis. use to control Ventrical rate in PSVT, AFI & AF.
* Vent. fibrillation ⇒ DC Shock.

Sept. 5,

'Cardiac Glycosides & Drugs for C.H.F. / C.C.F / H.F.

HF / CHF / CCF :- ↓se ability of Heart to pump blood efficiently throughout of the body c̄ congestion of fluid.

HF ⇒ ↓ Pumping ⇒ congestion of blood in vessels
⇓
↑ Hydrostatic Press.
⇓
↑ fluid leakage
⇓
Edema

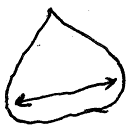
Intravasc. → Extravasc.

HF / CHF
- (R.V.F) Right Sided
  - Fluid backs up in vessels ⇓ Edema in Lower extremities & Abdomen
- Left Sided (L.V.F.)
  - → Systolic failure (no proper ejection)
  - → diastolic failure (no proper filling)
  - ⇓ ↓ cardiac output ⇓ Tissue Hypoxia (Forward Failure)
  - Pulmonary Edema (Breathing difficulty) → Right Sided — Backward Failure.

⇒ Generally, Starts c̄ Left & on progression Right involved. ✓ Maybe possible, both in same time.

HF
- Class - I ⇒ Mild ⇒ no limitation of Physical activity.
- Class - II ⇒ Mild ⇒ Slight limitation of Physical act.
- Class - III ⇒ Moderate ⇒ marked limitation "
- Class - IV ⇒ Severe ⇒ Symptoms even at rest.

HTN
⇓
Pathological Hypertrophy of ventricle (Left)
⇓
{↑se Ventrical Size but ↓se Force} ↑ Heart Size
⇓
Hypodynamic Heart
⇓



Froglike Heart

↓ Stroke
⇓
↓ Cardiac output (↓ pumping)
• Heart Failure •

HF :- ↓se ventricular Force of Contraction.

Rx of CHF :-

Rx

Rx of low output Symptoms ↑se Cardiac Output (Improve pumping)

↑ Force
⊕ve inotropic*

↓ need of Force for pumping.
(Arterial dilator)

Arrest / Reversal of disease
(↓ mortality)
By prevent Remodeling.*
{β-blocker, ACE-inhibitor, ARB, Aldosterone-antagonist}

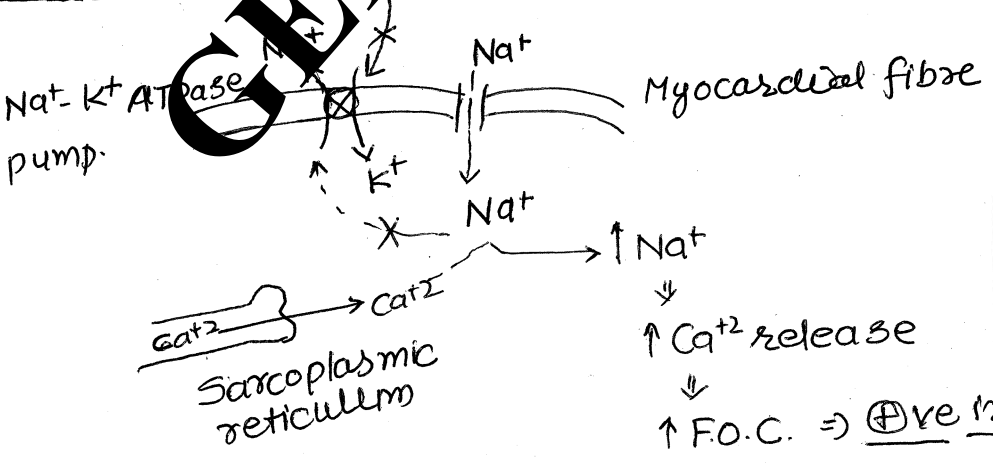
** Diuretic & Venodilator
⇓
by ↓se venous Return (↓ Preload)
⇓
benefit in pulmonary Edema (RVF).

1. Cardiac Glycosides
⇓
Natural
-obtained From Digitalis Plant. (Fox Glove Plant)
E.g :- digoxin & digitoxin.

**↑se Force of cont. but Significant change in O_2 consumption

Cardiotonic

Mechanism of digoxin :-



• Digioxin ⇒ by inhibit Na^+-K^+ ATPase of Myocardial fibre

⇓

↑se Na^+ dependent intracellular Ca^{+2} release

⇓

↑ Force of contraction (+ve Inotropic)

** By ↑se Vagal tone, depress SA Node & ↓se Sympathetic activity

⇓

↓se HR. (Bradycardia)

(-ve Chronotropic effect)

* depress conduction System (-ve dromotropic effect)

** ↓ Systole time & ↑↑ diastolic time (more)(less)

⇓

↑ Cardiac Cycle time.

⇓

↓ Heart Rate.

** Systole Shorten

(Same Force in less time)

⇓

↑ Inotropicity

⇓

↑ Stroke ⇒ ↑ C.O.

Bottle

• Adverse effect → Nausea, Vomiting, anorexia,
- abdominal pain
- Bradycardia (Not used when HR < 60) **
* Xanthopsia (Yellow vision)
* arrhythmia → almost all types

- Tachyarrhythmia → Rx ⇒ KCl
- Brady-arrhythmia (AV Block) → Rx ⇒ Atropine
- ventricular arry. → Rx - Lignocaine
- Supra-ventricular arrythmia → Propranolol

** Stop digoxin before defibrillation. (↑se Risk of arrythemia** if not stopped.)

Contra-indication

1. Hypokalemia / High & med. Efficacy diuretics.
⇓ ⇓
↑se toxicity. ←———— Hypokalemia.

** Hypokalemia → Conformational changes in Na^+-K^+ ATPase Pump (Rotates & comes in Front of digoxin)
⇓
Digoxin Tightly Bound this Pump
⇓
↑se Toxicity*

2. Hypercalcemia
⇓
↑se Toxicity

3. M.I.
4. AV-Block {Partial}
5. Acute Myocarditis.
6. Thyrotoxicosis. (Peak of Hyperthyroidism)
7. Myxodema. (Severe Hypothyroidism)

- Digoxin ⇒ [0.25-0.5 mg I.V. / Oral. Tab.]
  - Emergency & maintainance drug.

- [Digitalitation] {digoxin admission} → Oral → Slow - Prefer; Fast - Not prefer.
  → I.V. → only in Emergency.

- (5/7) ⇒ 5 or 7 days. → 2 days for removal (← Dr.)

- Serum Therapeutic level ⇒ [0.5-1.4 ng/ml] *

- Toxicity ⇒ (>2 ng/ml) *
  Rx ⇒ ① Stop digoxin
  ② KCl
  ③ digoxin antibody ⇒ (Digibind / Digifab)

* Digoxin well absorbed orally from Stomach*
(↑se peristalsis → ↓ absp. while ↕peristalsis ⇒ ↑ absp)

** It is vice-versa for other drugs. that absorbed from intestine.

* Digoxin excreate in urine in unchanged form
do not require reduction of dose in liver pt.*

** ↑se toxicity of digoxin in old age / Renal Pt.
* Renal clearance ↓se c age. ← coz
* Digoxin ↑se urine output.
* Digoxin ↓se Heart size to Normal that ↑ed in CHF,

digoxin toxicity
- acute → Hyperkalemia
  - due to inhibition of Na^+-K^+ ATPase
- Chronic → Hypokalemia
  (↑se K^+ loss in urine)

2. Inotropic
→ dobutamine
→ dopamine
] ⇒ ↑ Force ↑ C.O.
(Sympathomimetic)

3. Diuretic - Frusemide, bumatanide ⇒ ↑ U.O. & vasodil.
↓
↓ venous return
↓
Relieve pulmonary edema

4. β-blocker - Pindolol
- on long term use ⇒ survival benefit. ⇒ ↓se mortality
- after stabilizing Pt.*

5. Aldosterone antagonist ⇒ Spiralactone

Survival benefit ⇒ ↓se mortality }

- by antagonise aldosterone, prevent remodeling.

6. Vasodilator ⇒

(a) arteriolar ⇒ CCB, Hydralazine

↓

Arterial dilation ⇒ ↓ After load ⇒ benefit in C.H.F

- ↓se need of Forse to pump blood.

(b) Venodilator ⇒ ISDN, NTG, ⇒ Veno dilation ⇒ ↓ Preload

↓

Relieve Pul. Edema

(c) A+V dilator ⇒ ACE Inhibitor, ARB, α-Blocker, Na Nitroprusi

↳ dilate both A+V ⇒ ↓se both Al

III

7. Phospho-diesterase-inhibitor ⇒ Amrinone

Milrinone

* Inodilator

↓

↑ Cyclic AMP

↑ Force ✓ Vasodilation ✓

↓

Benefit in C.H.F. ✓

8. Neprilysin inhibitor ⇒ Sacubitril

By inhibit neprilysin

↓

Prevent degradation of B.N.P.

↓

↑ BNP

Natriuresis Vasodilation

↓

Benefit in C.H.F.

** ARNI ⇒ ARB + Neprilysin inhibitor

{Valsartan + Sacubitril} ⇒ ↓se the risk/chance of Hospitalization in C.H.F. Pt.

9. Synthetic BNP ⇒ Nesiritide *

Natriuresis — V.D.

10. V_2 Receptor blocker/antagonist ⇒ Tolvaptan.

↓se ADH action on CD-cell (V_2) site-4/kidney

⇓

↑ Urine Volume

* Use to relieve fluid in C.H.F. Pt.
(Removal of excess fluid in body of CHF Pt.)

** Use in S.I.A.D.H. ⇒ benefit by ↓se ADH effect

Syndrome of Inappropriate ADH.

Diuretic & Venodil. → Slow → Relieve Pulmonary edema

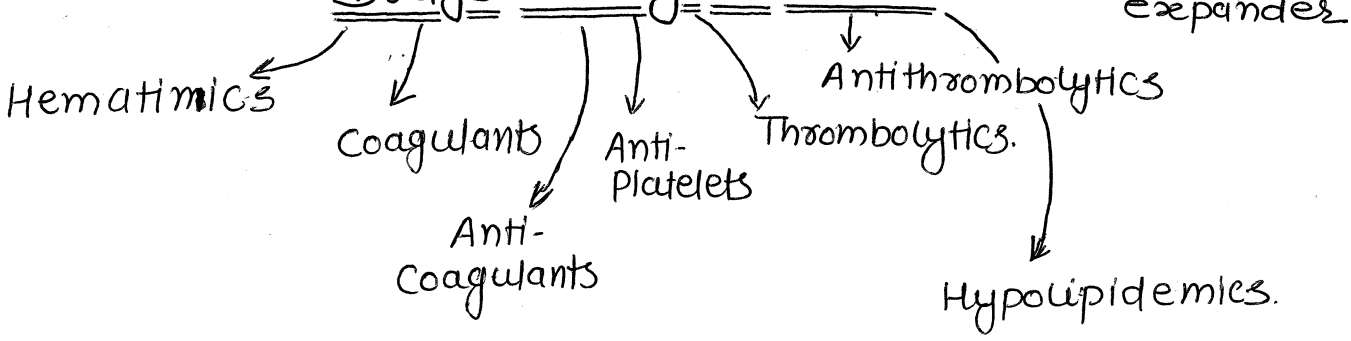
System ← Heart (RV) → Lungs → Heart → System

Inotropes & Art. dil.

Fast

↑ C.O.

Drugs acting on Blood



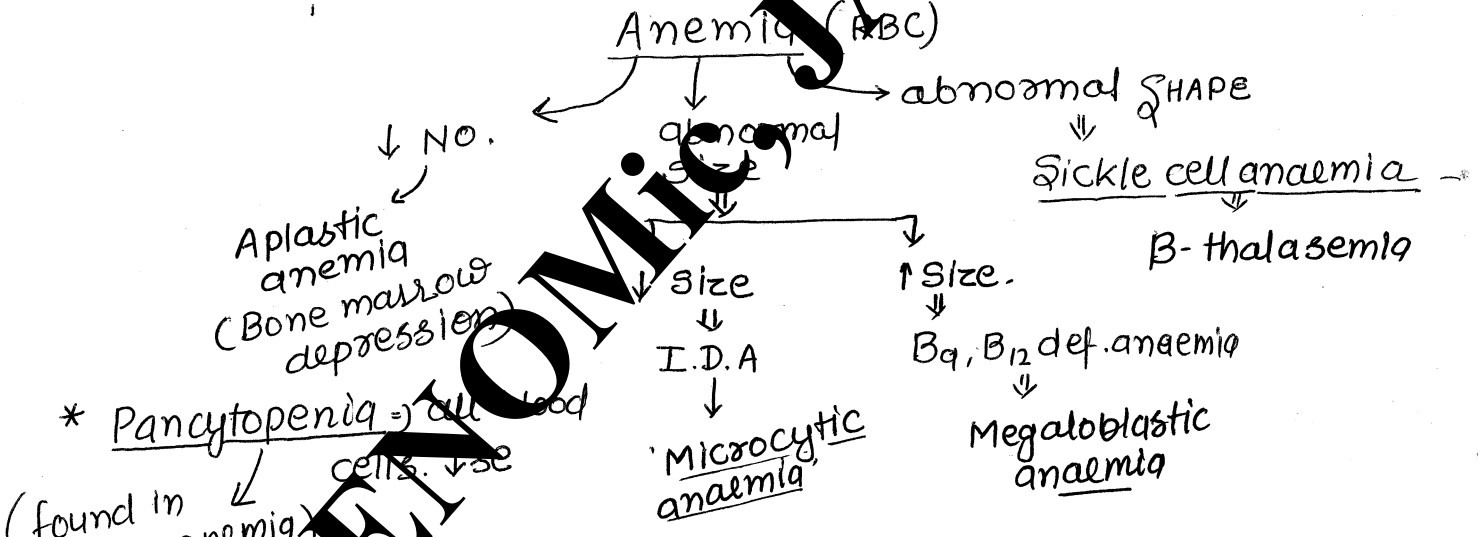
Hematimics

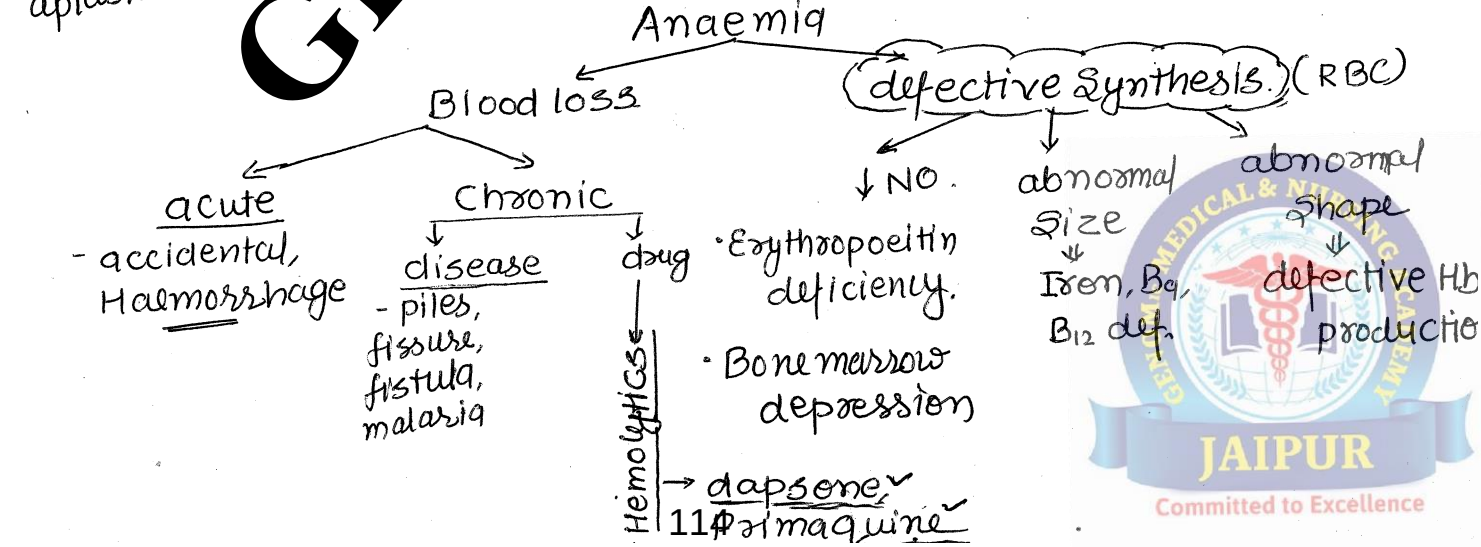
Blood Forming substances.

- Indicated in the Rx of Anemia.

① Iron
② B_9
③ B_{12}
④ Erythropoietin

→ * deficit RBC functioning in terms of O2 carrying. ⇒ Anemia ☹





• **Hematinics:—**

* **Iron ⇒**

Prep.

- **Oral**
  - Tab. ⇓ Ferrous Sulfate
  - Caps. ⇓ Carbonyl Iron → Autrin
  - Syrup ⇒ Ferric ammonium Citrate → dexorange
- **Parentral** (Prior required AST)* ⇓ Allergy sensitivity test
  - IM (deep) ⇓ 'Jectofer' (Iron Sorbitol)
  - IV ⇓ Iron sucrose ⇓ 100 mg / 5 ml (IV infusion) ⇓ dilute c NS. ⇓ ⊙ FCM (Ferric Carboxy maltose) 500 mg / 5 ml 100 ml NS., 2 inj. in ~~gat~~ 1/2 hr.

• **Coagulant** ⇓

C.F ⇒ 13
Exact ⇒ 12.
VI ⇒ abst.

Ca^{+2} = IV th C.f.

• Vit. K. ⇒ Physiological Coagulant ⇒ produces ↳ 2, 7, 9, 10 C.F.

Intrinsic Pathway (Slow)

XII → XII^a
XI → XI^a
IX → IX^a
X → X^a

• APTT ⇒ (26-32 sec)

Extrinsic fast

VII → VII^a

• PT (12-14 sec)

Common Pathway ⇒

X^a + V → Prothrombin → Thrombin
Fibrinogen → Fibrin (soluble) ↓ Thrombin
Fibrin (insoluble) Clot

INR ⇒ Therapeutic value / Standard value

⇓

aPTT / PT.

• Heparin in body ⇒ Mast cells, me - in Lungs.

⇓

mucopolysaccharide acid

↳ strongest organic acid in body

G.I.T. drugs.

* Affective Disorders :-

⇒ (Affective Psychosis) ⇒ Mood disorders

Mania + Depression

⇓

Bi-Polar disorder (Manic-depressive Psychosis)

~~Attachment~~ Affection

⇓ ⇓

Emotional Attachment

⇓

Emotion

⇓

Feeling

⇓

Mood

upswing → Mania

swing → depression

⇓

B.P.D.

* Anti-depressants (Mood Elevator)

• Depression :- ↓ N.Adr. & 5HT levels / activity (in brain)

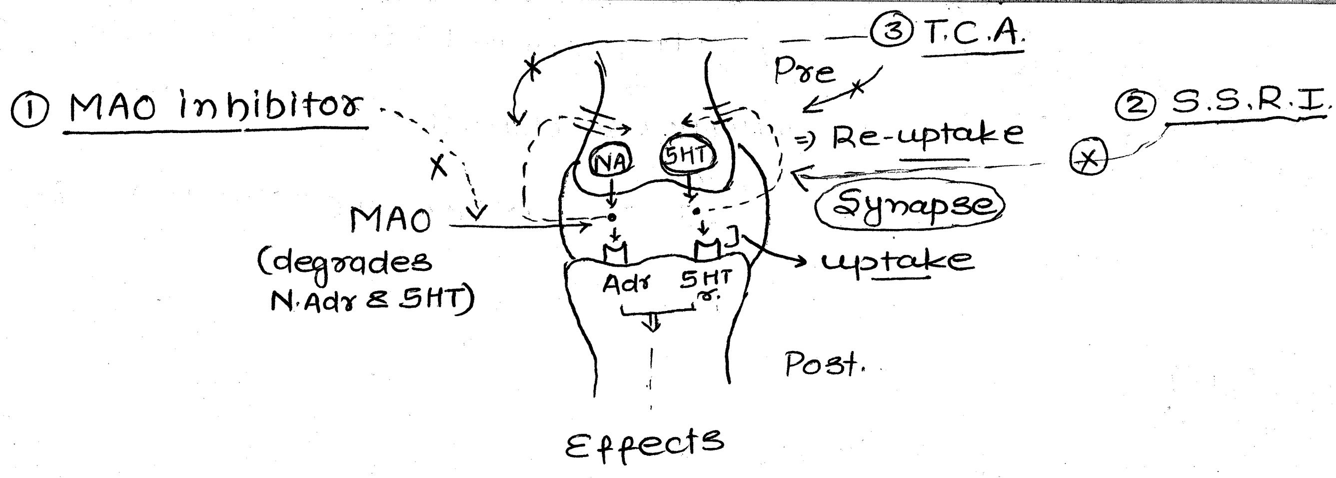
⇓

↓ Effort making.

• Rx. :- ↑ NAdr. & 5HT level / activity in brain ⇒ ↑se Effort making

⇓

depression retorted.



1. T.C.A :- inhibit re-uptake of N.Adr. & 5HT.
⇓
↑ activity / level. ⇒ Rx of depression.
⇓
Eg. ↑ Effort making.

2. S.S.R.I. :- ↑ 5HT level | activity.

3. MAO-A inhibitor ⇒ ↓ N.Adr. / 5HT degradation ⇒ ↑ level | activity

• CHEESE Reaction ⇒ dairy products & beverage + MAO Inhibitor
(cheese, Paneer) (Beer)
⇓ ⇓
Rich in Tyramine ← ⊖ MAO
⇓ ⊕
N.Adr.
⇒ ↑ N.Adr. ⇒ HTN.
'Hypertensive Crisis'
⇓
Rx :- Phentolamine #

* Avoid dairy products & beverages in Pts that are on MAO-inhibitor.
(Avoid Tyramine rich foods)

4. Atypical Antidepressants.
(New class)

* Anti-Manic / Drugs For B.P.D. 'Mood Stabilizers' (M.D.P.)

→ Mania :- ↑ Dopamine, N. Adr. & 5HT.

* Drugs :— Lithium Carbonate. (300 mg tab)
- daily 600-1200 mg in 2-4 doses. (C meal)
- Therapeutic response ⇒ 1-2 WKS (7-10 days)

Adverse Effects ⇓
→ Nausea, Vomiting, diarrhea..... etc.
→ on long term use → diabetes incipidus (ADH dysfn)
→ If use during preg^{n} → ① Foetal Goiter

Lithium interferes C Iodine utilization. (↓ Iodine availability)
⇓
↓ T_3, ↓ T_4
⇓
↑ TSH → Thyroid Enlargement.

⇒ Lithium contra-indicated in preg^{n}.

② Ebstein Anomaly → Tricuspid valve defect in fetus.
'Cardiac anomaly'

Serum Therapeutic Level of Lithium ⇒
- Normal :- 0.5 / 1.1 / 1.2 meq/L
- Bi Polar disorder :- 0.5-0.8 meq/L (prophylaxis)
- Mania :- 0.8-1.1 / 1.2 meq/L (Therapeutic)

→ Toxicity starts at 1.5 meq/L
→ Hemodialysis above 4 meq/L

Toxicity
- Mild: 1.5 mEq/L — -Lethargy, - Tremor
- Mod.: 1.5-2.5 meq/L — - motor incoordination
- Severe: >2.5 meq/L ⇓ - nystagmus

# General Anaesthetic	# Local Anaesthetics
- Area ⇒ Whole body	- Particular area
- act through ⇒ C.N.S.	- P.N.S.
- Consciousness - altered	- unaltered.
- Major Sx :- Prefer.	- not preferred
- minor Sx - not prefer	- Preferred.
- Poor Health - Risky	- Safe

*Stages of G.A. :-

• G.A. → CNS. → Inhibition of conduction & Transmission.

I. Stage :- Analgesia :- pain disappear, dream like state
- Starts from G.A. inhalation ⟶ end at loss of consciousness.
- Conscious → can listen & see.
* amnesia developes at the end of stage
- minor operations can be done

II. Stage :- Delirium :- loss of consciousness to begining of normal resp.
- apparent excitement
- Pt. Hold breath, Jerky breathing, Shout, Struggle,
(↑) fluctuating B.P. & HR, micturition & defecation & vomiting.
mydriasis (Reflex activity ↑)
- no use even cut short by the use of induction G.A.

III. Surgical :- onset of regul resp. to cessation of breathing.

IV 4 planes ① - Rolling eyeball
② - Loss of corneal & laryngeal reflexes
③ Loss of Light reflex & pupil starts dilating
④ - Shallow abd. resp. / Intercoastal paralysis

Mostly Surgeries ← [②, ③]
occasionally reach ← ③
never attempt ← ④

⇓

IV. Medullary Paralysis → cessation of breathing, circ. fail. & death.

* Ketamine :- (dissociative / Child anaesthesia) ⇒ 1·5 mg/kg.

dissociation.

Own body ← → Surrounding

⇓

Sensory loss.

(feels like body is Freely dancing)

⇓

* Rave parties.

- Conscious, light sleep, immobile amnesia, analgesic
- Choice :- Head & neck Sx, bleeding, asthematic & Hypotensive Pt.
- during recovery, Hallucination & delirium.
- ↑se all pressure (BP, ICP, IOP)
- C/I in psychosis., Glaucoma.

Local Anaesthetics

Local Anaesthetic

⇓

act on Na^+ Channel (Nerve & Nerve-ending)

⇓

By block Na^+ channel

⇓

Block conduction

⇓

Loss of sensation in a particular area where applied.

LA → Na^+ → depol^n → conductio

Lignocaine

- Injection
  - Infiltration anaesthesia (2%)
  - Spinal anaesthesia (5%)
- Surface (0·5-2%)
  - Oral gel (mouth Gel sore)
  - Gelly ⇓ Catheterization
  - Spray ⇓ for sustained penile Erection.
  - Ointment ⇓ in piles, fissur fistula

* Epidural anaesthesia :- analgesia / multiple dose via catheter

- Thorasic ⇒ Thorasic & upper abdominal Sx. ✓
- Lumbar ⇒ Similar to spinal anaesthesia. ✓
- Caudal ⇒ Sacral canal ⇒ Vaginal & ano-rectal Sx ✓

↳ pudendal nerve ⇒ affect.

Vertebral column anaesthesia

Epidural An.

→ Epidural space

→ Entire length of Vertebral column :- Thorasic, Lumbar, Caudal

→ nerve ~~m~~ expose

→ multiple dosing (catheter)

→ analgesia in various regions

→ more skill required than Spinal.an.

– more risk of injury to spinal cord @ Thorasic region.

Spinal an.

→ Sub-arachnoid space

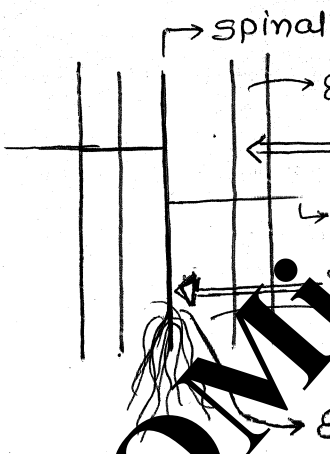
→ L_3-L_4 or L_4-L_5] End of Spinal cord

→ Spinal cord expose

→ Single dosing

→ To anaesthasise lower limb.

– due to pt. position & specific gravity, spinal anesthesia, not move upward C.C.F.



Morphine (Natural) ⇒ 10 mg/ml.

- Histamine release
  - ↙ Vasodilation.
    - ↙ Hypotension
    - ↘ Benefit in L.V.F. (cardiac asthma)
  - ↘ Bronchospasm. (C/I in bronchial asthma)

- ↑se Billiary spasm.
  ⇓
  Worsening of Billiary colic.
  (C/I in Pancreatitis)

* Non-Narcotics | NSAIDs | Non-Opoids | Aspirin like
  ⇓

Cell
⇓
Phospho-lipid ← Steroid
⇓ ← Phospholipase A_2
Arachidonic acid
NSAIDs (COX inhibitor) ⊗ → Cyclooxygenase
⇓
↓ PG Synth. → PG → Inflamm. / Pain / Fever
⇓
Relieve:- pain, fever, inflamm.

COX-I	COX-II	COX-III
⇓	⇓	⇓
PG.	PG. Localised	P.G.
Routine PG.	(Pain & inflamm.)	(Hypothalamus)
(Mucus)		⇓
		Fever.

1 Non Selective COX inhibitor → ~~Ret~~ Inhibit all COX.

↳ Relieve Pain, fever & inflamm.

But ↓ mucus also ⇒ can lead to Peptic ulcer (Gastric Side-Effects)

That's why omez. is given c most.

2. COX-II Inhibitor ⇒ Inhibit only COX-II.

- Relieve pain & inflamm.
- no risk of Peptic ulcer.

3. Cox-III inhibitor ⇒ Relieve fever & pa[illegible] ⇒ no risk of peptic ulcer.

E.g. Paracetamol.

* Aspirin. :- Irreversible Cox inhibitor.

⇒ AP, AI & [illegible] Analgesic

⇓ ⇓

Antipyretic anti-inflammatory

- but in current use as anti-Platelet. (75-150 mg)

* Adv. Eff :- Ti[illegible]tus (Tingling sensation of in Ear)

↳ Sign of Salicylism. (salicylate ↑)

- Toxicity :- Resp. alkalosis & metabolic acidosis

(I)-Early. (II)-Later ⇓ compensatory

↳ children (noticed later)

Toxicity

Ⓒ Aspirin antidote :- $NaHCO_3$.

- Aspirin in Preg^n ⇒ Low Birth Wt. Baby Ⓒ

(Early) Ⓒ (Later) → Pre closure of ductus arteriosus.

Endocrine

Hypothyroidism

Thyroid origin

Primary :- ↑TSH & ↓ T_3, T_4.

Sec. :- ↓TSH & ↓ T_3, T_4.

Tertiary :- ↓TRH & ↓ T_3, T_4

Pit. origin

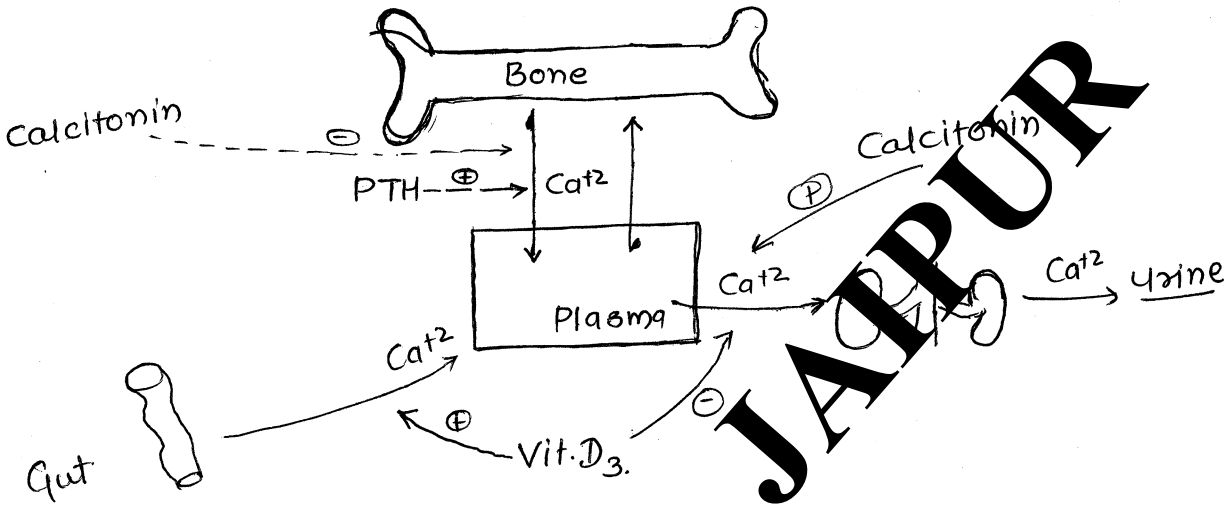
Hypothalamic origin.

Hyperthyroidism

↓ TSH & ↑ T_3, T_4 Pri

↑ TSH & ↑ T_3 T_4 Sec

↑ TRH & ↑ T_3 T_4 Ter.



1. DRUGS AFFECTING BLOOD

(A) HAEMATINICS –

Blood forming substances indicated in treatment of anemia

1. Iron

Total body iron 2.5 to 5 gram (avg. 3.5 gram)

Ferrous sulphate, Ferrous Gluconet tablet

Iron sucrose injection, Iron Sorbitol injection

USE: - Iron deficiency anemia

Adverse effect- Epigastric Pain, Nausea, Vomiting, Heart Burn, Metallic Taste, Constipation & Staining of Teeth

Acute iron poisoning- Abdominal Pain, Haematemesis, Diarrhea, Lethargy, Cyanosis, Dehydration, Acidosis, Convulsion & Shock

Treatment-Desferrioxamine IM/IV

2. Folic acid-(vit.B-9)

Rubifol tab- 5 mg

USE: -magaloblastic anemia

NTD

Mouth ulcer

3. Cynocobalamine (vit.B-12)
Tablet & Injection

USE: -Magaloblostic / Pernicious anemia

Neuropathy

4. ***Erythropoietin-***
   2000-4000 IU/ml SC/IV
   promote erythropoiesis

   uses-

   Anaemia of chronic renal failure
   Cancer chemotherapy
   To increase blood production pre operative
   AIDS patient on Zidovudine

(B) COAGULANT –

Agent that promote blood coagulation

Indicated in hemorrhagic state

Whole blood/plasma provide all factors- best therapy

1. Vit.K(10mg/ml)
   Physiological Coagulant

   Antidote- oral anticoagulant

USES–

To control bleeding, oral anticoagulant toxicity, dietary deficiency, newborns. Liver disease, prolonged anti microbial therapy, Obstructive Jaundice

2. Ethamsylate
   250-500mg- tab/ inj
   Anti hyaluronidase action- improve capillary wall stability

3. Rutin
   60 mg tab

4. Anti haemophillic factor
   5-10U/kg iv infusion

5. Fibrinogen
   500 mg iv infusion

(C) ANTI COAGULANTS: -

Drugs used to reduce coagulability of blood.

1. In vitro-

Sodium citrate, Sodium oxalate, E.D.T.A.

2. In vivo-

A .Parenteral- Heparin, Enoxaparin sodium

b. Oral Anti Coagulant- Warfarin Sodium, Acenocoumarol, Dicumarol

Phenindione

In vitro-

Sodium citrate- 1.65 g/350 ml blood- Blood transfusion
Sodium edetate- 2mg/ml – Laboratory investigation
Sodium oxalate- 10 mg/ml– Laboratory investigation

In vivo-

A. Parenteral-

Heparin-Natural, HMW, Mucopolysacharide

Mechanism- activate antithrombin-III that bind to active form of factor X, II, IX, XI, XII, & XIII and inactive them

Onset- Immediate

Duration- 4-6 Hour

1000- 5000 U/ml - IV/SC

Adverse effect- Bleeding, thrombocytopenia, Alopecia, Osteoporosis

Contra indication-bleeding disorder, severe hypertension, chronic alcoholics, aspirin

Anti dote- Protamine sulphate 50 mg/5 ml

Enoxaparin sodium (LMWH)

(20-40mg)- injection- SC

b. Oral Anti Coagulant-

Warfarin sodium 8-12mg

Acenocoumarol 1-4 mg

Dicumarol 50 mg

Phenindione- 200mg

Onset- Delayed (1-3 Days)

Duration- 3- 6 days

Mechanism- decrease biosynthesis of factor II, VII, IX & X

Adverse effect- Epistaxis, Haematuria, Bleeding in GIT, intra cranial or other internal

Antidote- Vit. K

USES of anti coagulant-

Deep vein thrombosis & pulmonary Embolism
Myocardial infraction
Unstable angina
Atrial fibrillation
Cerebrovascular disease.
Vascular Surgery & Prosthetic heart valves

(D) ANTI PLATELET/ANTI THROMBOTIC –

Drugs that prevent platelets aggregation by interfere platelet function and are useful in prophylaxix of thromboembolic disorder.

DRUGS-

Aspirin(75 to 150mg),

Clopidogrel(75mg),

Dipyridamole(150- 300mg)

Ticlopidine (250 mg)

USES-

Coronary artery disease (Angina &M.I.)

Cerebrovascular disease

Peripheral vascular disease

Venous thromboembolislm

Coronary angioplasty

Stents

Bypass implants

Prosthetic heart valves

(E) TROMBOLYTIC/FIBRINOLYTIC/PLASMINOZEN ACTIVATOR

Drugs that are use to lyse thrombus/ Clot to recanalize occluded blood vessels

Mainly coronary artery

Curative rather than prophylactic

ACTION-

Convert Plasminogen (inactive) to Plasmin (active) that convert Fibrin (insoluble)/ thrombus to fibrin (soluble)/ dissolution of clot.

DRUGS-

Streptokinase- 7.5-15 lac IU

B-streptococci-C, Antigenic & fever

Urokinase- 2.5- 10 lac IU

Obtain from urine, not antigenic but cause fev

Alteplase (rt-PA) – 50 mg inj

Tenectaplase (rt-PA)

Retaplase (rt-PA)

* rt-PA- Similar to human TPA (tissue plasminogen activator)- prepared from Human Tissue culture

USES—

Acute M.I – Alternative First line approach to Emergency Percutaneous Coronary Intervention-thrombolysis favored with in 1-2 hours of onset of MI

Deep vein thrombosis- l leg, Pelvis & Shoulder- up to 60% Treated

Peripheral arterial occlusion-Recanalise 40% limb Artery occlusion (if uses in 72 hours)

Stroke- Alteplase with in 3 hours

Pulmonary embolism- Indicated for large life threatening pulmonary embolism

(F) ANTI FIBRINOLYTIC-

Drugs which inhibit plasminogen activation and dissolution of clot

EACA(Epsilon Amino Caproic Acid)

5 gram/20 ml inj

500 mg tab

Tranexaemic Acid

100 mg/ml inj

500 mg tab

Uses-

Overdose of PA

To prevent recurrence of GIT & Subarachnoid haemorrhage

PPH

Abruptio placenta

Menorrhagia

Epistaxis

Peptic ulcer

Occular trauma

Tonsillectomy

Prostate Surgery

(G) HYPOLIDMICS -

Drugs that are use to lower down level of lipids &lipoproproteins in blood.

DRUGS-

a. **H.M.G. co-a reductase inhibitor-**
   Atorvastatin(10-40 mg)
   Simvastastin(5- 20 mg)
   Lovastatin (10- 40 mg)
   Rosuvastatin (5- 20 mg)

   Decrease cholesterol synthesis
   Adverse effect- Headache, Nausea, Bowel upset, Sleep disorder, Myopathy.

b. **Fibric acid derivative**
   fenofibrate(200mg)
   Gemfibrozil (300 MG)
   Increase activity of lipoprotein lipase- increase destruction of VLDL
   Adverse effect- Skin rashes, Body ache, Myopathy

c. **Resins-**
   Cholestyramine (4-16 g)
   Decrease cholesterol by decrease bile acid absorption

d. **Niacin (B_3)-**
   Nicotinic acid(2-6 g)
   Decrease production of VLDL
   Adverse effect- cuteneous vasodilation, flushing & itching

e. **Other-**
   Ezetimibe (10 mg)
   Decrease cholesterol absorption

USES-

As Antihyperlipidmics (coronary artery disease)

(H) PLASMA VOLUME EXPANDERS

Drugs that are use to expand plasma volume by retain fluid in vascular compartment through exerting osmotic pressure.

- Human Plasma
- Human albumin (20% solution 100 ml)
- Degraded gelatin polymer (3.5 % in 500 ml)
- H.E.S (Hydroxy ethyl starch) (6% Solution)
- P.V.P (Poly vinyl pyrrolidone) (3.5% solution) – not prefer
- Dextran- 40 & 70

*Human plasma & Human Albumin- Natural- Best option- But not preferred as PVE due to high coast

*All other PVE- Also Known as Synthetic colloids

USES-

PVE use in such conditions where plasma Volume deficient or lost like-
Burn, hypovolemic &endtoxic shock, severe trauma, extensive tissue damage.

Temporary use in whole blood loss till blood arrange.

CONTRA INDICATION-

Severe anemia, Cardiac failure, renal insufficiency, pulmonary edema.

2. GASTROINTESTINAL DRUGS

(A) EMETICS-

Drugs use to induce vomiting.

DRUGS-

Ipecacunha (Emetine)

Syrup- adult – 15- 30 ml, children- 10 -15 ml

Irritate GIT mucosa & CTZ- Vomiting

Onset- 15 min

Apomorphine –injection

6mg- SC/IM

Stimulate C.T.Z.- Vomiting (Within 5 minutes).

USES-

Induction of vomiting when undesirable (toxic/overdose) ingested.

CONTRA INDICATION-

Morphine poisoning, Corrosive material, C.N.S stimulant, Unconscious patient & Kerosene poisoning

(B) ANTI EMETICS-

Drugs that are use to prevent & suppress vomiting.

DRUGS-

1. **Anticholinergics-**Hyoscine, Dicyclomine
2. **Antihistaminics-**Diphenhydramine, Promethazine, Cinnarizine, Cyclizine, Meclozine, Doxylamine
3. **5-HT_3 antagonist-**Ondensetron, Grainesetron
4. **Gastro Kinetic(prokinetic)-**Metaclopramide, Domperidone, cisapride, mosapride
5. **Neuroleptic-**Prochloperazine, chlorpromazine
6. **Adjuvant antiemetics-** Dexamethasone, Benzodiazepines, Cannabinoids

Anticholinergic-

Hyoscine

0.2- 0.4 mg- ORAL/IM

DOC- Motion sickness

Antihistaminics- Safer & Prefer For long term use

Promethazine (highly sedative) 25mg tab

Cinnarizine (Anti vertigo) 25- 75 mg

Cyclizine (50 mg) Meclozine (25 mg)- Sea sickness

Doxylamine (10 mg) use along with Pyridoxine in morning sickness

5-HT_3 antagonist- Chemotherapy induce vomiting.

Ondensetron- 2mg/ml- inj, 4-8 mg tab

Grainesetron-1mg/ml-inj, 1-2 mg tab

Adverse effect- Headache, Abdominal discomfort

GastroKinetic (prokinetic) - Speeden Gastric emptying.

Metaclopramide(Reglan)

10 mg tab/ inj

Adverse effect-sedation, dizziness, loose stools, Muscle Dystonias

On long term use- Parkinsonism, Galactorrhoea and Gynaecomastia

Domperidone 10-30 mg tab 10 mg/ml drop

Cisapride 10- 20 mg

Mosapride 5 mg tab

Neuroleptic-vertigo associated vomiting

Prochloperazine (stemetil) 5-25 mg tab, 12.5 mg/ml inj

Adverse effect- Muscle dystonia & EPD

Adjuvant antiemetics-

Dexamethasone 8- 20 mg IV

Benzodiazepines- Diazepam

Cannabinoids- Tetrahydrocannabinol- Dronabinol & Nabilone

(C) DRUGS FOR PEPTIC ULCER-

Peptic ulcer-Occurs in the part of GIT which is exposed to HCl and pepsin

DRUGS-

***1. Reduction of* gastric acid secretion-**

a. H_2 –blocker- Ranitidine, Famotidine, Roxatidine

b. Proton pump inhibitor– Omeprazole, Pantaprazole, Rabemeprazole, Esomeprazole, Lansaprazole

c. Anticholinergic-Propanthaline

***2.* Neutral Gastric acid (Antaacids)-**

Systemic-Sodium bicarbonate

Non systemic- Magnisium hydroxide, Calcium carbonate,Aluminium hydroxidegel

3. .Ulcer protective–

Sucralfate, colloidal bismuth subcitrate

4. Anti H-pylori drugs-

Amoxycillin, Metronidazole,Tinidazole, Clarithromycin, Tetracycline

1. Reduction of gastric acid secretion-

a. H_2 –blocker-

Ranitidine 150- 300 mg

Famotidine 20-40 mg

Roxatidine 75- 150 mg

Advesrse effect- Headache, Diziness

Uses-

Duodenal ulcer – 8 Weeks- 70 to 95%

Gastric ulcer- 8 Weeks – 50 to 75 %

Stress ulcer

Zollinger-Ellinson Syndrome

GERD

Prophylaxis of aspiration Pneumonia

b. Proton pump inhibitor–

Omeprazole 20- 40 mg

Pantaprazole 40 mg

Rabemeprazole 10- 20 mg

Lansaprazole 15- 30 mg

Esomeprazole 20- 40 mg

Adverse effects- loose stools, Abdominal pain, Muscle & joint pain &Diziness

Uses-

Duodenal ulcer – 2 to 4 Weeks

Gastric ulcer- 4 to 8 Weeks

Stress ulcer

Zollinger-Ellinson Syndrome

GERD

Prophylaxis of aspiration Pneumonia

Neutral Gastric acid (Antaacids)-

Sodium bicarbonate- **Systemic action**

Magnisium hydroxide- fast action- laxative nature

Aluminium hydroxidegel- Slow action- Constipation nature & decrease phosphate absorption

Calcium carbonate- Potent & Rapidly acting

Megaldrate (hyroxy magnesium aluminate)

3. .Ulcer protective– Sucralfate—

protective coating on ulcer10 ml TDS

Colloidal Bismuth Subcitrate- Increase Mucous, Coating & anti H.pylori action

120 mg tab

4. Anti H-pylori drugs-

H-pylori bacteria(gram-ve bacilli) produces ulcer&anti H-pylori drugs kill H-pylori bacteria.

Amoxycillin, Metronidazole,Tinidazole, Clarithromycin, Tetracycline

(D) DRUGS FOR CONSTIPATION

(Laxatives/ Purgatives/Cathartics)

Drugs that promote evacuation of bowel

Laxative or aperients- milder action soft and formed stools

Purgative or cathartics- strong action more fluid evacuation

Constipation- Infrequent production of hard stools requiring straining to pass or sense of incomplete evacuation.

DRUGS-

1. **Bulk luxative-**Isapghulla Methyl cellulose, Dietary fibre; Bran
2. **Stimulant purgative-** Bisacodyl, Senna, Sodium picosulphate, Castor oil, Tegaserod
3. **Stool softner-** Docusates, Liquid parafin
4. **Osomotic purgative-** Lactulose

Bulk luxative- Increases stoolswater content & bulk

Isapghulla- Psyllium- Natural colloidal mucilage- Absorb water- Gelatinous mas

3-12 gram

Methyl cellulose 4-6 gram semisynthetic, colloidal, derivative of cellulose

Dietary fibre; Bran- Unabsorbed cell wall & cellulose, pectins, glycoproteins

Stimulant purgative- irritates GIT mucosa- increase intestinal motility- promote evacuation of bowel

Bisacodyl 5 mg

Senna- Cassia

Sodium picosulphate 5mg/5ml

Castor oil 15-25 ml

Tegaserod 6mg tab

Stool softner-

Docusates- emulsify colonic content.

100- 400mg

Liquid parafin- by lubricant action.

15- 30 ml

5. **Osomotic purgative-**Retains water osmotically in intestine

Lactulose

Uses of Purgative-

a. Functional constipation-

Spastic- Dietary fibre or Bulk laxative

Atonic- Bulk forming, Senna, Bisacodyl

b. Bedridden patient- MI, Stroke, Fracture, post operative
Lactulose, Bisacodyl

c. To avoid straining at stools- Hernia, CVD, Eye surgery
Bulk forming, Lactulose

d. preparation of bowel for surgery-
Saline purgative, Bisacodyl

e. Food/drug poisoning-
Saline purgative

Laxative CI

in undiagnosed abdominal pain, colic or vomiting

Secondary constipation due obstruction in Bowel, hypothyroidism, Hypercalcaemia, malignancies and drugs like- Opiates, Sedative, Anticholinergics, Antiparkinson, Antidepressant, Antihistaminic oral Iron and laxative abuse.

(E) TREATMENT OF DIARROHEA

Passage out of to frequent unformed (poorly formed) watery stools.

Management of diarrhoea-

1. **Treatment of fluid depletion, shock & acidosis**
2. **Drug therapy**
3. **Maintenance of Nutrition**

1. ***Maintenance of water electrolyte balance (rehydration)*** - Treatment of fluid depletion, shock &acidosis

   a. O.R.T. (oral rehydration therapy)- Mild (5-7%) to moderate (7.5-10% BW)

   b. I.V.R.T. (intra venous rehydration therapy)- Severe (>10 % BW)

2. Drug therapy-

a. Non specific anti diarroheal-

Absorbant- Isapghulla

Anti secretory-

Sulfasalazine 500 mg

Mesalazine 400 mg

Atropine

Racecadotril 100 mg

Antimotility drugs (opoids)-

Loperamide- Opiate analogue
CI below 4 year child

Dipnenoxylate- Synthetic opoid
CI below 6 year child

b. ***Specific Antimicrobial drugs***-G.I.T. infection associated diarrhoea

Norfloxacin
Ciprofloxacin
Ofloxacin
Metronidazole
Tinidazole
Ornidazole

3. **Maintenance of Nutrition-** Breast milk, Boiled potato, Banana

3.RESPIRATORY SYSTEM DRUGS

(A) DRUGS FOR COUGH

Cough-protective reflux

It is of two types:-

Useful- productive/wet cough

Useless- non productive/dry cough

DRUGS-

(I) **Pharyngeal demulcents-**

Sooth the throat- symptomatic relief from cough.

Ex-lozenges, glycerine, cough drops.

(II) Expectorants (mucokinetics)-

Expel out cough

By increase bronchial secretion or reduce its viscosity- facilitate its removal by coughing

Useful in productive (wet) cough

a. Bronchial secretion enhancer-

Sodium orPotasium citrate, Potassium iodide,Vasaka,Guainphenesin, Ammonium chloride

b. Mucolytic-

Bromhexine, Ambroxol, Acetyl Cysteine

(III) Antitussives (cough centre suppressants)-

Useful in non productive (dry cough) or use to suppress over coughing in wet cough also

a. Opoids-

Codeine, Pholcodeine

b. Nonopoids-

Dextromethorphan, Noscapine

c. Antihistaminics-

Promethazine, Chlorpeniramine, Diphenhydramine.

(IV) Adjuvant antitussive (bronchiodilatar) -

Ex- Salbutamol, Terbutaline

(B)DRUGS FOR BRONCHIAL ASTHMA-

BRONCHIAL ASTHMA-

Narrowing of air tube (bronchoconstriction), increase Bronchial secretion & mucosal edema resulting in congestion of respiratory air way that leads to difficulty in breathing (Dyspnoea), Wheezing & cough.

Bronchial Asthma- Inflammatory condition

COPD- progressive disease with emphysema & bronchial fibrosis

Approaches to treatment-

Prevention of AG:AB

Neutralization of IgE

Suppression of inflammation & bronchial hyperactivity

Prevention of release of mediators

Antagonism of released mediators

Antagonism of constrictor neurotransmitter

Agonism of dilator neurotransmitter

Directlyacting bronchodilator

1. Bronchodilators-

***A. Sympathomimetics*(B$_2$-agonist)-**

Ex- Salbutamol, Terbutalin, Salmeterol, Formeterol

***B.Anti cholinergic*(m$_3$ antagonist).-**

Ex-Atropine methonitrate, Ipratropium bormide

C. Methyl xanthines-

Ex-Theophyline, Aminophyline, Doxophyline

2. Corticosteroid-

Decrease bronchial hyperactivity & inflammation

Ex-Hydrocortisone 100 mg- IV

Fluticasone 50-100 mcg

Budesonide 100-400 mcg

Beclomethasone 50-200 mcg

3.Monoclonal antibody-

Omlizumab- SC/IV

4. Leukotriene antagonist-

Ex- Montelukast, Zafirleukast

5. Mast cell stabilizer

Sodium chromoglycate 1mg MDI

Ketotifen 1-2 mg tab

Add. – H_1 blocker also

Mild episodic asthma- B_2 agonist

Seasonal Asthma- inhaled steroid and B_2 agonist

Mild chronic Asthma- inhaled steroid and B_2 agonist

Moderate Asthma- inhaled steroid and B_2 agonist

Severe asthma- Inhaled steroid + B_2 agonist + Oral LT antagonist/Theophyline

Status Asthmaticus- Hydrocortisone –IV & Salbutamol nebulization

4.DRUGS ACTING ON C.N.S

(A) SEDATIVES & HYPNOTICS

Sedatives- Calm down body but do not induce sleep.

Hypnotics- Induce & maintain sleep.

Both depress C.N.S on Low dose- Sedative & on high dose-hypnotic

DRUGS-

1.Barbitutates-

(a)Long acting - Phenobarbitone

(b) Short acting- Pentobarbitone

(c) Ultra short acting- Thiopentone sodium

2. benzodiazepines-.

Ex- Diazepam Alprazolam, Clonazepam, Lorazepam, Nitrazepam, Clobazam, Chlordiazepoxide, Flurazepam

3. Newer nonbenzodizepine hypnotics-

Ex- Zopiclone, Zolpidem, Zaleplon

Barbitutates- Having low therapeutic index so higher toxicicity.

(a)Long acting - Phenobarbitone- anti epileptic

(b) Short acting- Pentobarbitone

(c) Ultra short acting- Thiopentone sodium- General anaesthetic

Benzodiazepines- Having higher therapeutic index lesser toxicity a specific antagonist also develop (flumazenil) that can be use on over dose so they are more safer than barbiturates.

Ex- Diazepam Alprazolam, Clonazepam, Lorazepam, Nitrazepam, Clobazam, Chlordiazepoxide, Flurazepam

USES-

Anti Anxiety, Muscle Relaxant, Sedative, Hypnotic, Anti Convulsant, General Anaesthetic.

Newer nonbenzodizepine hypnotics-

Ex- Zopiclone, Zolpidem, Zaleplon

B. ANTI PARKINSONIAN DRUGS

Drugs that have therapeutic effect in Parkinsonism.

Parkinson disease-Extrapyrimidalmotor disorder Characterized by Rigidity, Tremor, Hypokinesia With secondary manifestation like defective posture & GAIT, Mask like face &Sialorrhoea, Dementia may accompany.

If untreated- several years- end stage disease- patient rigid unable to move unable to breath properly- chest infection

PD- progressive degenerative disorder

Cause- Deficiency of dopamine in Striatum (Due to degeneration of neronesin Substantia Nigra &Nigrostrital Tract)

Treatment- Increase dopamine & Decrease acetylcholine.

DRUGS-

A. Increase dopaminergic activity

Dopamine precursor-Levodopa (100 mg)

Peripheral Decarboxylase Inhibitor-Carbidopa (10 or 25 mg)

Dopamine Facilitator-Amantidine (100 mg)

Dopamine agonist-Bromocriptine(1.25-2.5 mg)

MAO-B inhibitor-Selegiline (5-10 mg)

COMT Inhibitor-Entacapone(200 mg), Tolcapone(100-200 mg)

B. Decrease cholinergic activity

Ex-

Central anticholinergic-Benzhexol(2-10 mg), Biperiden(2-10 mg)

Antihistaminic- Orphedrine(100-300 mg), Promethazine(25-75 mg)

Anticholinergic mainly benefit in tremor

Increase Dopaminergic activity is main therapeutic approach in PD for this purpose levodopa is First line drug.

Levodopa use along with Carbidopa to increase Levodopa effect

Dopamine precursor-Levodopa (100 mg)

Peripheral Decarboxylase Inhibitor-Carbidopa (10 or 25 mg)

ADEVERSE EFFECT-

Nausea, Vomiting, Postural hypotension, Alteration in taste sensation, Abnormal Movements, Behavioural effects (Psychosis).

None of the above drug alters the basic pathology of PD

Disease continue to progress

Drugs only provide symptomatic relief and give 3-6 years of productive life.

C. DRUGS USED IN MENTAL ILLNESS

(PSYCHOTROPIC DRUGS / PSYCHOPHARMACOLOGICAL AGENT)

Drugs are those having primary effects on psyche and are used for the treatment of psychiatric disorders.

PSYCHIATRIC DISORDERS-

Psychosis- severe psychiatric illness with serious distortion of thought&behaviour with delusion & hallucination (unable to recognise reality and of perception) there is inexplicable misperception &misevaluation patient unable to meet ordinary demand of life.

a. **Cognitive disorder-** Delirium & Dementia
b. **Functional disorder-** Schizophrenia & Paranoids States

Affective disorder- Mania & Depression

Neuroses- anxiety, Phobic states, OCD, Hysterical

PSYCHOTROPIC DRUGS-

1. Antipsychotic- Psychosis
2. Antimanic(mood stablizer) – Mania & B.P.D.
3. Anti depressant – Depression, Phobia, OCD & GAD
4. Anti anxiety – anxiety & phobia

5. **Psychomimetic/Psychedelic/Psychodysleptic/Hallucinogen- Produce psychosis like state- cannabis**

ANTIPSYCHOTIC-

Having salutary therapeutic effect in psychosis

Psyschosis- Dopaminergic over activity in limbic system

DRUGS-

A. TYPICAL (Dopamine Antagonist)- D_2 Blocker action- Decrease dopamine activity of Psychosis.

Chlorpromazine-(100-800mg/day)-Power full anti emetic also

Haloperidol- (2-20mg/day)- High potency- Also use in treatment of Acute mania

Pimozide- High potency- (2-6 mg)

Flupenazine- High potency- (1-10 mg)

Thioridazine- Low potency-(100- 400 mg)

Flupenthixol- 3-15 mg

Loxapine- 20-200mg

B. Atypical antipsychotic- Minor D_2 Blocker& major 5-HT_2 antagonist Action.

Clozapine-(50-300mg/day)

Olanzepine-(2.5-10mg/day)

Quetipine- (50-400 mg/day)

Ziprasidone-(40-160mg/day)

Risperidone-(2-12mg/day)

PHAMACOLOGICAL ACTIONS -

Reduce irrational behaviour, agitation and aggressiveness and controls psychotic symptomatology. Disturbed thought & behaviour normalized, anxiety is relieved. Hyperactivity, delusion and hallucination are suppressed.

USES-

Schizophrenia, Organic brain syndrome, Mania, Anxiety, Antiemetic.

ADVERSE EFFECT-

Drowsiness, Lethargy, Mental confusion, Develop Seizures
Increase Appetite & Weight gain
Postural Hypotension
Dry Mouth, Blurring of vision & constipation
Galactorrhoea, Gynaecomastia, Amenorrhoea & Infertility

Extra Pyramidal Disturbances-Dose limiting more with high potency Typical (Haloperidol, Pimozide, Fluphenazine) & less with low potency Typical (Thioridazine) & Atypical (except Risperidone)

a. **Parkinsonism**
b. **Acute muscular dystonias-** Bizarre muscle spasm

c. **Akhathesia-**

d. **Malignant neuroleptic syndrome-** Rigidity, Tremor, Immobility, Semiconciousness, Fluctuating BP & HR

e. **Tardive dyskinesia**

HYPERSENSITIVITY REACTIONS-

Cholestatic jaundice, skin rashes, urticaria, Agranulocytosis, Myocarditis.

ANTI ANXIETY-

Drugs that are used for the treatment of anxiety.

Anxiety- Emotional state, associated with uneasiness, discomfort &concern or fear about future threat.

Cause- Stress (it is stimulus that can be physical, social, biological etc.)

Two types-

1. Acute stress- Anxiety 2. Chronic Stress- Depression

Treatment- Mild C.N.S. depressant.

DRUGS-

Benzodiazepines-

Alprazolam(0.25-1mg), Diazepam (5-30mg), Chlordiazepoxide(20-100mg). Lorazepam 91-6 mg)

ADVERSE EFFECT-

Sedation, psychomotor slowing and cognitive impairment, light headedness, vertigo, increase appetite.

Azapirones- Buspirone (5-15 mg) – partial agonist of 5-HT_{1A} Receptor

Antihistaminic(sedative)-Hydroxyzine(50-200mg)

B-blocker- Propranolol. (10-40 mg)

ANTI DEPRESSANT

Drugs that are used for the treatment for the depression.

Depression- Characterized by sad mood, loss of interest and pleasure, low energy &guilt.

Cause- Decrease 5-HT &N.Adr. level/activity in brain.

Treatment- Increase 5-HT &N.Adr. level/activity in brain.

DRUGS-

A. **Tri Cyclic Anti depressant- I*nhibit reuptake of NAdr. & 5-HT***

Imipramine(50-200mg/day), Amitriptyline(50-200mg/day), Doxepine(50-150mg/day)

Clomipramine(50-150mg/day)

Desipramine(50-150mg/day), Nortriptyline(50-150mg/day)

Increase N.Adr.& 5-HT Level /Activity in brain-depression retorted

B. **Selective Serotonin Reuptake inhibitors(SSRI)-**

Fluoxetine(20-50mg/day), Sertraline(50-200mg/day), Escitalopram(10-20mg/day)

Paroxetine (20-50 mg)

Increase 5-HT level/activity in brain-depression retorted.

C. **MAO-A Inhibitor-** Chlorgyline, Moclobemide (150-300 mg)

Prevent neuronal degradation of Noradrenalin& Serotonin by inhibiting MAO thus N.Adr. &Serotonin Level /Activity increase in brain-depression retorted.

CHEESE REACTION

D. **Atypical Antipsychotic-**

Trazadone (50-200 mg)

Mianserine (30-100 mg)

Mitrazepine (15- 45 mg)

Duloxetine (30-80 mg)

Venelaflaxine (75-150 mg)

USES-

Major depression (Endogenous Depression)- Response in 2 to 3 weeks

OCD & Phobia

Neuropathic pain

Enuresis (Bed wetting in children)

Anxiety disorder (GAD)

Panic Disorder

Social Phobia

Migraine- Amitriptyline

Pruritus- Doxepine

ADHD- TCA (Imipramine, Nortriptyline)

ADVERSE EFFECT-

Sedation, Mental confusion- ***Mainly with TCA specially Amitriptyline (and also with Trazadone)***

Blurring of vision, Dry mouth, Bad taste, Constipation- **TCA**

Increase appetite & Weight gain- **TCA & Trazadone**

Postural hypotension, Cardiac arrhythmia- **TCA**

Sweating & Fine tremor- **TCA**

Rashes Jaundice- **Mianserine**

ANTI MANIC/MOOD STABILIZERS-

Drugs that are use for the treatment of mania& BPD

DRUGS-

Lithium carbonate (300mg tab) – 600 to 1200 daily in divided dosage

Therapeutic Response -1 to 2 weeks

ADVERSE EFFECTS-

Nausea, vomiting, diarrhea

Thirst, Polyurea

Fine tremors & rarely Seizures

Coarse tremor, Gidiness Ataxia, Motor incoordination, Nystagmus, Mental confusion, Slurred speech, Drowsiness, Delirium, Coma & Convulsion.

vomiting, Diarrhea, Albuminurea& Arrhythmia.

On long term use- Diabetes Incipidus

If use during pregnancy- foetal goiter.

Lowtherapeutic index, higher toxicity so serum monitoring required on prolonged use.

Serum level maintained in-

Bi Polar Disorder- 0.5- 0.8 meq/L

& In

Mania- 0.8- 1.1/1.2meq/L

Toxicity starts at 1.5 meq/L

and on 2.0 meq/L toxicity symptoms are Coarse tremor, Gidiness Ataxia, Motor incoordination, Nystagmus, Mental confusion, Slurred speech, Drowsiness, Delirium, Coma & Convulsion.

Vomiting, Diarrhea, Albuminurea& Arrhythmia.

Treatment- Osmotic diuretics & Sodium bi carbonate

Haemodylysisabve 4 meq/L

Lithium CI during pregnancy

Interaction- high & medium efficacy diuretics- increase plasma lithium level- lithium toxicity

Tetracycline/A.C.E. inhibitors/ NSAIDS- increase lithium retention- lithium toxicity

Lithium increases sulfonyl urea & insulin action- hypoglycemia.

USES-

Acute Mania

Prophylaxis in BPD

OTHER DRUGS

Carbamazepine- **Mania & BPD**

Sodium valproate- **Acute mania (first line)**

Lamotrigine- **BPD**

Atypical Antipychotic (Olanzapine, Risperidone &Quetipine)- **Acute mania**

Olanzapine- **Maintenance therapy of BPD**

Typical Antipsychotic (CPZ/Haloperdo- INJl)- **Rapid control of acute mania**

D. ANTI CONVULSANT/ANTI EPILEPTIC

Epilepsies- Group of C.N.S. disorder characterized by Paroxysmal cerebral dysrhythmia, manifesting as episodes of loss or disturbance of consciousness, with or without characteristic body movements (convulsion).

Most of cases idiopathic (primary)

Some may be secondary to Trauma/Surgery on Head, Intracranial Tumour, Tuberculoma, Cysticercosis & Cerebral Ischemia

Cause- Uncontrolled ectopic discharge of ions.

Seizures- Brief episodes of epilepsies.

Types of Seizures-

A. **Generalized seizures-** whole body involve

Generalized tonic-clonic(Major epilepsy/grand mal epilepsy)

Absence Seizures(Minor epilepsy/petit mal epilepsy)

Atonic Seizures

Myoclonic Seizures

B. **Partial seizures (focal seizures)-** Partial body involve.

Simple partial seizures

Complex partial seizures (TPL)

Secondary generalized

C. Unclassified Seizure-

Infantille Spasm

Febrile Seizure

Treatment- suppression of uncontrolled ectopic discharge of ions.

MECHANISM OF DRUG ACTION-

A. Drugs acting on Na^+ channels (Prolongation of Channel inactivation)-

Phenytoin, Carbamazepine, Valproic acid, Zonisamide Lamotrigine Topiramate, Lacosamide

B. Calcium channel (Inhibition of t-Type)

Ethosuximide, Valproic acid, Zonisamide

C. Chloride Channel (Facilitation of GABA mediated opening)-

Barbiturates, Benzodiazepines, Valproic acid,Gabapentine, Vigabatrin, Tigabine

D. Inhibition of GLUTAMATE Synapse-

Phenobarbitone, Phenytoin, Valproic acid, Lamotrigine, Topiramate, Lacosamide, Lavitiracetam

DRUGS-

1. **Barbiturates-** Phenobarbitone(60-180mg/day)

Sedation, sudden withdrawal- convulsion

2. Benzodiazepines-Diazepam(0.2-0.3 mg/kg), Clonazepam(0.5-5 mg/kg), Clobazam(10- 20 mg), Lorazepam(0.1 mg/kg)

3. Carbamazepine (200-400mg)

Sedation, Dizziness, Vertigo, Diplopia, Ataxia, Leucopenia, Water Retention & Aplastic Anaemia

4.Valproic acid (200-600mg)

Anorexia, Heart Burn, Vomiting, loose Motion, Alopecia, Liver Damage, Agranulocytosis, Tremor, Epigasric Pain, PCOD, Obesity & Rash

5. Ethosuxumide (250 mg/5ml)

Gastrointestinal intolerance

6. Phenytoin (100 mg Tab/Inj)

Cleft palate, Gum hypertrophy, Hirsutism, Osteomalacia, Megaloblastic Anaemia, Vit, K Deficiency, Decrease Insulin Release, Lymphadenopathy, Ataxia & Arrhythmia.

6. **Gabapentine**(300 mg)
   Enhance GABA release

7. **Zonisamide**(25- 100 mg)

   Renal stone, Sommolence& Metabolic Acidosis

8. **Lamotrigine** (25-100 mg)

   Sleepiness, Diplopia, Ataxia

9. **Vigabatrin** (500- 1500mg)

   Visual Field Contraction, Alteration of colour vision,Behavioural changes

10. **Topiramate** (25-100 mg)

    Weight Loss, Renal stone

11. **Levitiracetam** (500-1000 mg)

    Irritability, Aggression

12. **Lacosamide**(50-200 mg)

    Ataxia, Vertigo, Diplopia & Tremor

13. **Tigabine** (4-16 mg)

    Sedation, Nervousness, Asthenia & Amnesia

USES-

a. Generalized tonic-clonic seizures-

Valproic acid, Lamotrigine,Carbamazepine

b. Partial seizures-

Carbamazepine, Lamotrigine, Valproic acid

c. Absence Seizures-

Valproic acid, Ethosximide

d. Myoclonic-

Valproic acid, Topiramate

e. Atonic-

Valproic acid, Lamotrigine

f. Febrile seizures-

Diazepam

g. Status epilepticus-

Lorazepam, Diazepam

h. Infantile Spasm-

ACTH, Cortticosteroid

i. Eclamptic Seizure-

Magnesium Sulphate

** Folic Acid (second & third trimester) Use along with antiepileptic during pregnancy to minimise Neural Tube Defects.

** Vitamin K (last month) to minimise Risk of Bleeding.

** Valproate- Most Teratogenic

** Lamotrigine- Prefers during Pregnancy

E. ANAESTHETICS-

Drug that are use to induce reversibe loss of sensation.

Two types-

(a) General anesthetics- Effects on Whole body

(b) Local anesthetics- Effects on Particular area

(a) GENERAL ANAESTNETICS –

Drugs that are use to induce General Anaesthesia

GA-

Loss of all sensation specially pain

Immobility & Muscle relaxation

Abolition of Somatic & Autonomic Reflexes

Deep Sleep (Unconscious) & Retrograde Amnesia

Stages of GA-

I- Analgesia- Pain abolish, dream like state

II- Delirium-Loss of consciousness to beginning of normal respiration

Apparent excitement

III- Surgical- onset of regular respiration to cessation of breathing

a. Roving Eyeball
b. Loss of reflexes(corneal & laryngeal)
c. Loss of light reflex & pupil starts dilating
d. Dilated pupil & shallow abdominal Respiration

IV- Medullary Paralysis-Cessation of breathing, failure of circulation & death

DRUGS-

1. Inhalation-

a.Gases-

Nitrous oxide

Given along with O_2 (70+30)
Laughing gas
Good analgesic but poor muscle relaxant
Onset quick & smooth and fast recovery

b.Volatile liquid-

Halothane-(0.5-4 %) potent anaesthetic but not good analgesic or muscle relaxant

Ether-now preferred in current

Isoflurane (1-3%)- Neurosurgery

Desflurane

Sevoflurane

2.Intravenous-

a. Inducible-Fast onset & short duration.

Ex-**Thiopentone sodium** 3-5 mg/kg (Onset-15 to 20 sec & Duration- 6 to 10 min)

Propofol 2mg/kg (Onset-15 to 45 sec & Duration- 5 to 10 min)

b. Slower-Onsetslow,but duration long.

Ex- Diazepam (0.2-0.5 mg/kg)

Midazolam(1-2.5 mg)

Lorazepam(2-4 mg)

ketamine (dissociative /child anesthesia)-1.5 mg/kg

Fentanyl (2-4 mcg/kg)

Complication of G.A-

Respiratory depression, salivation, laryngospam,nausea,vomiting**.**

Preanaesthetic medication administered to avoid complication of G.A(to make anaesthesia safe and less unpleasant)

Ex- Diazepam, Atropine, Metoclopramide, Ranitidine etc.

*** Balance anaesthesia- Inhalation + IV*

*** Concious sedation-supplemented with LA- Monitored state of altered consciousness(Diazepam, Midazolam, Fentanyl)*

(b) LOCAL ANAESTHETICS-

Act on local area

Consciousness unaltered

Mechanism-block nerve conduction by block Sodium channel

DRUGS-

a.Injectable-

Low potency-Procaine

Intermediate potency-Lignocaine, Prilocaine

High potency- Bupivacaine, Dibucaine, Tetracaine, Ropivacaine

b.surface-

Cocaine, Lignocaine, Tetracaine, Benzocaine, Oxethazaine

USE-

Surface Anaesthesia-Topical application

InfilterationAnaesthesia- Minor surgery

Anti arrhythmic- Xylocard

Conduction block (Nerve Block & Field block)

Epidural anaesthesia-Epidural Space (Thoracic, Lumbar & Caudal)

Spinal anesthesia-Subarachnoid space (below the lower end of spinal cord0

Complication of Spinal Anesthesia-

Respiratory paralysis, Hypotension, Headache, Nausea, Vomiting

F. ANALGESICS-

Drugs that are used to reduce or relieve pain

Two types

1. Narcotic 2. Non narcotic

(i) NARCOTIC/ OPOIDS/ MORPNINE LIKE

Drug that obtain from opiumor it's semisynthetic and synthetic derivatives.

- Act on C.N.S.
- Produce dependence
- High degree analgesia(relieve visceral pain)
- Induce respiratory depression(on high dose death

DRUGS-

Morphine 10 mg/ml

Codeine

Diacitylemorphine(heroin)

Dextroprophoxyphene

Tramadol

Fentanyl

Pethidine

Pentazocin

USES-

Analgesics

Anaesthetics

Antitussive

Left ventricular failure

CONTRA INDICATION-

Bronchial asthma

Head injury (because it increase I.C.P. &induce vomiting)

Hypotension

Hyporthyroidism.

(ii) NONE NARCOTIC/NSAID'S/NON OPOIDS/ASPIRIN like

- Relieve moderate/weak intensity pain
- Primarily act on peripheral pain mechanism
- Do not produce dependence & C.N.S. depression

MECHANISM-

Act by inhibiting cyclo-oxygenase (COX) enzyme threw this they inhibit prostaglandin synthesis which is responsible for pain, fever & inflammation.

DRUGS-

Aspirin

Ibuprofen

Naproxen

flurbiprofen

Aceclofenac

Piroxicam

Ketorolac

Indomethacin

Mephanamic acid

Diclofenac sodium

Nimesulide

Etoricoxib (cox-2 inhibitor)

Paracetamol,

USES-

As analgesic- headache, backache, myalgia, joint pain, toothache, neuralgia, dysmenorrhoea, post traumatic & post operative.

Anti inflammatory- rheumatoid arthritis, osteoarthritis, acute gout, ankylosing spondylitis

Antipyretic

Post M.I. & post stroke

Patent ductus arteriosus closure.

ADVERSE EFFECTS-

Epigastric pain, nausea,vomiting,peptic ulcer, headache, dizziness & rashes

(G) C.N.S. STIMULANT

Drug that are use to stimulate C. N. S. (specific area of brain) & having resuscitative value in coma & fainting.

DRUG-

- Amphetamine, Methylphenidate, Modafinil - ADHD& narcolepsy
- Caffeine, theophylline- As anti asthmatic
- Doxapran – As analeptic (respiratory stimulant)

(H) SKELETAL MUSCLE RELAXANTS-

Drugs that are use to relax skeletal muscles are known as skeletal muscles relaxant (S.M.R.)

Three categories

(A) Neuromuscular blocker (N.M.B.)

(B) Directly acting

(C) Centrally acting

DRUGS-

A.NEURO MUSCULAR BLOCKER – Act on neuron muscular junction

d-Tubocurarine,Pancuronium bromide
Atracurium, Vecuronium

Mivacurium
Succinyl choline, Decamethonium

B.CENTRALLY ACTING – Act on medullary region & medullary centre

Chlorzoxazone, diazepam, Baclofen, Tizanidine, Thicolchiocoside

C.DIRECTLY ACTING –Directly act on muscle end plate

Dantrolene

USES-

(i) N.M.B. **–**Adjuvant to G.A., Endotracheal intubation, laryngoscopy,Bronchscopy, ECT, Assisted ventilation, Tetanus, Status epilepticus

(ii) Centrally Acting**–**Acute muscle spasm**,** Backache, Tetanus**,** E.C.T., orthopedic manipulation

(iii) **Directly acting-**Malignant Hyperthermia & MMS

5.AUTOCOIDS & RELATED DRUGD

DRUGS FOR TREATMENT OF GOUT

CLASSIFICATION

1. ***On basis of action-***
   a. Xanthine oxidase inhibitor-
      e.g. allopurinol
      Act by inhibiting synthesis of uric acid.
   b. Uricosuric –
      e.g. Probenecid, Sulfinpyrazone.
      Act by increasing excretion of uric acid through uirne
2. ***On basis of condition of use***
   a. For acute gout – NSAID, Colchicines, Steroid (prednisolone).
      Relieve pain & inflammation
   b. For chronic gout – Allopurinol, Probenecid, Sulfinpyrazone
      Decrease uric acid

DRUGS FOR TREATMENT OF RHEUMATOID ARTHRITIS

CLASSIFICATION

1. Drugs suppressing (modifying) the disease- disease modifying drugs (DMARDs)-

   Immunosuppressant: Methotrexate, Azathioprine, cyclosporine.

   Gold

   d-penicillamine

   HCQS

   Sulfasalazine

   Leflunomide

2. Biological response modifier-

   Ex- Infliximab

   Adjuvant drugs- corticosteroids

   Ex- Prednisolone

   use to relieve pain & inflammation

3. NSAIDs –

Ex- Indomethacin
use to relieve pain & inflammation

ANTIHISTAMINICS

H_1 Receptor antagonists (H_1 -antihistamines)

CLASSIFICATION-

a. 1st generation – Hydroxyzine(Atarax-25mg), Diphenhydramine, Promethazine (phenargan), Pheniramine meleate (Avil 4-mg), Meclizine, Chlorpheniramine Cyclizine,
Higher Sedation & anticholinergic effects.

b. 2nd generation – Fexofenadine (Allegra), Loratidine, Cetrizine
Lesser sedation

ADVERSE EFFECTS:

Dryness of nose, mouth and eyes, sedation and drowsiness.

USES :

To treat and prevent allergic reaction, in blood transfusion, anti emetics, Cough, Cold, itching, asthma, anti anxiety.

6.DRUGS ACTING ON ENDOCRINE SYSTEM

ANTERIOR PITUTARY HORMONES-

Secretion:-contolled by

- 5 releasing and 2 inhabiting hormones of hypothalamus

Name of hormone	stimulation by	inhabitation by
Growth hormone (GH,somatotropin)	GHRH	GHIH(somatostatin)
TSH (thyrotropin)	TRH	GHIH(somatostatin)
FSH	GnRH	-
LH	GnRH	-
Prolactin	PRH	PRIH(Dopamine)
ACTH	CRH	-
Melanocyte Stimulating hormone	CRH	Dopamine

GH deficiency-Dwafism – treatment by GH/analogs

Ex-Somatropin, Somatrem

GH excess- Gigantism &Acromegly- treatment by somatostatin/analogs

Ex-Somatostatin, Octreotide.

Gonadotropins

Anterior pituitary hormones regulating ovarian and testicular fuctions.

Luteinizing hormone (LH)

LH is responsible for the stimulation of the interstitial cells of the testis (leyding cells) which lead to the production of the testosterone. In the female, is stimulate secretion of progesterone.

Follicular stimulating hormone (FSH)

FSH is responsible for stimulation of follicles secretion of estrogen from follicles in female & in male support spermetogenesis.

Uses of Gonadotropins-(FSH+LH)

1. Amenorrhoea& infertility
2. Hypogonadotrophic Hypogonadism in male
3. Cryptochism

SyntheticGnRH- Increase release of LH & FSH

EX- Gonadorelin

GnRH agonist- Initially increase Gn but after 1-2 week decrease Gn

Ex-Nafarelin, Triptorelin, Goserelin, Leuprolide

Uterine fibroid, Endometriosis, Assisted reproduction

GnRh Antagonist- Quick GnSupression

Ganirelix, Cetrorelix

Human Chorionic Gonadotropin (HCG)

It is produced in large amount throughout pregnancy.

Prolactin-

Induce milk synthesis

TSH-

Stimulate Thyroid

ACTH-

Promote Steroidogenesis in Adrenal cortex

ADRENO CORTICAL STEROIDS (CORTICOSTEROIDS)

Disorders of adrenocortical function:

a. hypofunction of adrenal cortex- addison's disease.

b. hyperfunction – cushing's syndrome – deposition of fat on the face and back(moon face, buffalo hump), hyperglycemia and hypertension.

GLUCOCORTICOIDS

Examples

Natural- hydrocortisone (cortisol), Cortisone and Corticosterone.

Synthetic- Dexamethasone, Prednisolone, Mehylprednisolone, Triamcinolone, Deflazacort, Fluticasone & Budesonide

PHARMACOLOGICAL ACTIONS

a. Hyperglycemic

b. Osteoporosis

c. Anti-inflammatory-(by inhibiting phospholipase A_2& decrease capillary permeability)

d. Anti – allergic action.

e. suppression of immunity – used as immunosuppressant.

ADVERSE EFFECTS:

a. causing's syndrome- characterized by moon face, buffalo hump

b. Sodium retention and edema

c. weighty gain due to fluid retention and fat deposition

d. Glycosuria

e. osteoporosis, peptic ulcer, increase susceptibility to infection

f. Muscle wasting (protein catabolism)

USES-

Anti inflammatory, anti allergic, organ transplantation, gout, arthritis, asthma, auto immune disorder.

ANDROGENS

Most important androgen is testosterone.

25 mg IM

ACTION-

Spermatogenesis, growth of prostate, secondary sexual characters in male, epiphysis closure.Skeletom muscle (anabolic), & Erythropoiesis

ADVERSE EFFECT-

Virilization, Acne, Cholestatic Jaundice, Early closure of epiphysis, Gynaecomastia,

CI- Prostate cancer & Male breast cancer.

USES-

Testicular failure

Hypopituitarism

AIDS related muscle wasting

Ageing

ANABOLIC STEROIDS

Derivatives of testosterone having poor androgenic & more anabolic effects.

Ex- Nandrolone, Oxymethalone, Stanozolol

USE-

Osteoporosis

To enhance physical ability in athletes.

IMPEDED ANDROGENS/ ANTIANDROGEN

Danazol- Decrease Gn secretion

Uses- Endometrisis, Fibrocystic Breast disease

Cyproteron Acetate- Decrease LH

Flutamide- Anti androgenic

Use- Prostate cancer

Bicalutamide- Anti androgenic

Use- Prostate cancer

5-ALPHA REDUCTASE INHIBITOR-

Finasteride, Dutasteride

Use- BHP

ESTROGENS & PROGESTINS-

USES OF ESTROGEN-

To control menopausal symptoms

Senile vaginitis, Dysmenorrhea, Acne

(Estradiol 5 mg IM Dienestrol Cream 0.01%)

Anti Estrogen- Clomiphene citrate

SERM- Tamoxifen Citrate, Raloxifene

Aromatase Inhibitor- decrease Estrogen

Letrozole, Anastrozole- Breast cancer

USES OF PROGESTRON-

Progesterone 10-100 mg IM

As oral contraceptive.

HRT, Treatment of threatened & habitual abortion, uterine bleeding, Endometriosis.

ANTIPROGESTINE-

Mifepristone

CONTRACEPTIVE

Drugs that are use to prevent conception

MECHANISMS-

Inhibit- spermatogenesis, ovulation, maturation of ovum & implantation, inhibit release of hormone.

Preparations-

Combined pill= Ethinyl estradiol + Norgestrel(MALA-D)

Phase pill= Ethinyl estradiol + Levonorgestrel(TRIQULAR)

Mini pill= Norgestrel

Post coital Contraception= Levonorgestrel

GOSSYPOL- orally effective male contraceptive(inhibit Spermetogenesis)

CENTCRHROMAN (SAHELI)- Nonsteroidal contraceptive.

Mifepristone (progesterone antagonist)- terminates very early pregnancy (use along with misoprostol)

THYROIDS & ANTITHYRIODS

THYROIDS-

Thyroixin(T_4)& tri iodo thyronine(T_3)- iodine containing derivatives of tyrosine

Deficiency of these hormones leads to-

hypothyroidism that leads to Cretinism, Myxoedema(Emergency Hypothyroidism), Goiter

DRUGS-

Thyroxine Sodium Tablet

USE-

Treatment of Hypothyroidism, Cretinism, Myxoedema, Nontoxic goiter

ANTI THYROIDS

Drugs used for the treatment of hyperthyroidism

DRUGS-

Inhibit Hormone synthesis-

Propylthiouracil, methimazole,Carbimazol

Inhibit Hormone release-

Iodine

Destroy thyroid tissue-

I^{131}

Uses- Hyperthyroidism, preoperative preparation, Thyroid storm, Thyrotoxicosis

DRUGS AFFECTING CALCIUM BALANCE

Increase resorption by-corticosteroid,PTH, Thyroxin, Loop diuretic, Alcohlism& PGE_2

Decrease resorption by- Androgen, Estrogen, GH, Calcitonin, Biphosphonate, Fluoride &Thizide

PARATHYROID HORMONE (PARATHARMONE PTH)

By chief cells of parathyroid gland.

Acton – increase plasma calcium level

On high con.(continuous)-Osteoclast activity dominant-increase bone resorption- increase plasma calcium level

On intermittent exposure (low con.) Ostoblast activity dominant- increase bone formation

Hypoparathyroidism-Lower plasma calcium level, Tetany, Convulsion, Laryngospasm,Cataract & Psychiatric changes.

Hyperparathyroidism-Hypercalcaemia, Decalcification of bone, Renal Stones Metastatic calcification, Muscle weakness, Constipation, Deformities & fractures.

** Teriperatide- Recombinant PTH- use in treatment of severe osteoporosis

CALCITONIN-

100 IU/ML

Lowers plasma calcium level by blocking PTH induce bone resorption (decrease osteoclast activity)

Uses-hypercalcaemic state,Post menopausal women, Paget's disease

VITAMIN- D

Increase Plasma Calcium Level by increasing absorption of calcium from gut & renal tubules.

D_1 - Mixture of substances found in food

D_2 – Calciferol- yeast, fungi, bread & milk

D_3 – Cholecalceferol- synthesized in the skin

Caclitriol- Active form of vit D_3

Uses- Vit D Deficiency, Rickets, Osteoporosis, Hypoparathyroidism & Fanconi syndrome

Biphosphonates-increase apoptosis of osteoclast

Alendronate 5-10 mg OD

Zoledronic acid 4 mg INJ

Use- Osteoporosis, hypercalcaemia of malignancy, Paget's disease

ANTI DIABETIC DRUGS

DM- *metabolic disorder characterized by hyperglycemia, glycosuria, hyperlipaemia, negative nitrogen balance and sometimes ketonemia.*

DM- high blood glucose level- increase glycosylation of tissue protein- pathological changes- Thickening of capillary basement membrane, lumen narrowing, atherosclerosis, neuropathy, retinopathy & nephropathy

Diabetes Mellitus- Two types

1. IDDM- circulating insulin low or very low, more prone to ketosis, less common, low degree of genetic predisposition & low level of c-peptide
2. NIDDM- insulin in circulation low, normal or even high over 90% cases, high degree of genetic predisposition

   *Abnormality of glucoreceptor

   *Insulin restence

   * Excess hyperglycemic hormone/obesity

INSULIN

1921- Banting & Best

51 AA- Two chain

A-chain-21 AA & B-chain- 30 AA

Insulin is a polypeptide hormone secreted by beta cells of pancreas in response to arise in blood glucose level.

- Insulin lowers blood sugar level by glycogenesis, lipogenesis & entrap glucose in to cell
- Diabetes mellitus occurs due decrease insulin secretion or it's action.

ACTION OF INSULIN:

hormone of anabolism-storage of fuel/energy.

a. Stimulation of –glycogen synthesis.
b. Lipogensis
c. Uptake of glucose by muscles

Route – ineffective orally –given by S.C.injection

ADVERSE EFFECT

a. Hypoglycemia – coma and convulsions
b. Lipodystrophy – at site of injection.
c. Allergy- rashesh

- **PREPARATIONS OF INSULIN:**
  a. **Short acting –** Human insulin Soluble(0.5-1, 2-4, 6-8 h)
     Insulin Zinc suspension(semilente)-Amorphous
  b. **Intermediate acting** – Human insulin Isophane(1-2, 8-10, 20-24 h)
     Human insulin Biphasic, Insulin zinc suspension(lente)
  c. **Long acting –**Insulin glargine (2-4, 8-12, 24)
     Protamine zinc insulin, Insulin zinc suspension(ultralente)-Crystalline

** Rapid acting insulin- Insulin Lispro, Insulin Aspart (0.2-0.4, 1-2, 3-5)

INSULIN DOSE

Type-I 0.4 – 0.8 U/KG/DAY

Type-II 0.2 – 1.6 U/KG/DAY

ORAL HYPOGLYCEMICS

Drugs lower blood glucose leveland are effective orally.

Insulin sensitizer- Increase action of insulin by improve it's binding with receptor

1. **Biguanides**

Ex-Metformine

Long use of biguanides result in development of lactic acidosis and megaloblastic anemia (due to deficiency of vitamain b_{12})

2. **Thiazolidinediones**

Ex- piogitazone

Insulin secretogogues-Increase insulin secretion

a. **Sulfonylureas**

Ex- Chlorpropamide, Tolbutamide, Glimepiride, Gliclazide, Glipizide

b. **Meglitinide analog**

Ex-Repaglinide

Alpha glucosidase inhibitor- Inhibit conversion of disaccharide to monosaccharide

Ex- Acarbose, miglitol

DPP-4 Inhibitor- Increase insulin & decrease glucagon

Ex-Sitagliptin, Teneligliptin

SGLT-2 inhibitor- Decrease glucose reabsorption in renal tubule- Glycosuria

Ex- Dapagliflozin

UTERINE STIMULANTS (OXYTOCICS, ABORTIFACIENTS)

These drugs increase uterine motility, especially at the time of labour.

PP Hormone-Oxytocin (2 IU/ML)

Induction of labour, PPH, Uterine inertia, Breast engorgement

Ergot- Ergometrine, Methylergometrine

PPH

Prostaglandins- PGE_2, $PGF_{2\alpha}$, Misoprostol (PG analog)

Cervix ripening

Others-Ethacridine

UTERINE RELAXANT (TOCOLYTICS)

These drugs use to decrease uterine motility to postpone labour

B_2- agonist- Isoxsuprine,Ritodrine

CCB-Nifedipine

Magnesium sulphate (1gram/2ml- inj)- Pre eclampsia &Eclampsia

Loading Dose-

4 gram (20%) –IV over 5 min

Follow by-

10 gram (50%) – IM

If convulsion occurs in 30 min then-2 gram(20%)- IV over 5 min

Maintenance dose-

5 gram (50%) – IM every 4 hour

Focus on- RR(16/min), Patellar Reflux & Urine output (30 ml/hour)

If RR drop Use antidote –Calcium Gluconate

Normal plasma level- 1.5- 2 mEq/L or 1.8- 2.4 mg/dl

Therepeutic- 4-8mEq/Lor 4.8- 9.6mg/dl

ECG changes- 5-10mEq/Lor 6-12mg/dl

Decrease deep tendon reflex & Respiratory depression – 10mEq/Lor 12mg/dl

Respiratory Arrest- 15mEq/Lor18mg/dl

Cardiac arrest-above 20mEq/Lor 24mg/dl

7.ANTI MICROBIAL DRUGS

ANTI MICROBIAL DRUGS

Drugs that are designated to inhibit/kill the infecting organism

CHEMOTHERAPY- Treatment of any systemic infection or neoplasm by the help of chemical agent is known chemotherapy.

CHEMOTHERAPY- Treatment by chemotherapeutics agents.

Two types-

1. Anti microbial drugs (only systemic)
2. Anti neoplastic agent

(1) Anti microbial drugs/Anti infective (use in infection)

(i) Topical (ii) Systemic

It includes use of-

a. Antibiotics

Ex- Penecillin, cephalosporines

b. Others

Ex- sulfonamides

Anti microbial can be-

Antibacterial – Amoxycillin

Antifungal- Griseofulvin

Antiviral – Acyclovir

Antiprotozoal - Metronidazole

Antihelminthic - Albendazole

(2) Anti neoplastic/Anti cancer- use in cancer

It includes

a. Antibiotics — Ex- doxorubicin

b. others — Ex- methotrexate

ANTIBIOTICS-

Chemical agents that are obtained from microorganism and are use to kill or inhibit the microorganism / host defective cell.

Classification of antimicrobial-

A. according to spectrum of activity-

(a) Broad spectrum

Ex- Chloramphenicol

(b)Narrow spectrum

Ex- Streptomycin

B. mechanism of action-

(a) Inhibit cell wall synthesis-

Ex- Penicillins, Cephalosporines

(b) Inhibit protein synthesis-

Ex-Tetracyclines, Chloramphenicol

(c) Inhibit DNA gyrase-

Ex- Ciprofloxacin

(d) Cause misreading of m-RNA codone-

Ex- Streptomycin

E. Type of action-

(a) Primary bacteriostatic-

Ex- Tetracycline, Chloramphenicol

(b) Primary bacteriocidal-

Ex- Penicillins, Cephalosporines

ANTI MICROBIAL

(A) SULFONAMIDES

SULFONAMIDES- First antimicrobial agent effective against pyogenic bacteria.

DRUGS

Sulfadiazine, sufamethoxazole, sulfadoxime, silver sulfadiazine, sulfacetamide etc.

ACTIVITY-

Primary bacteriostatic on high dose bactericidal,effective against gram positive & gram negative bacteria.

Mechanism – Sulphonamide compete with PABA for bacterial folate synthetase by inhibit folate synthase inhibit folic acid synthesis

ADVERSE EFFECT-

Allergic reactions, Thrombocytopenia, hypothyroidism, goitre, kernecterus(neonatal jaundice), S J reaction, Crystalurea

USES-

Ulcerative colitis,U.T.I., Meningococcal meningitis, Conjunctivitis,Malaria etc.

COTRIMOXAZOLE

It is fixed dose combination of ofTrimethprim + Sulfamehoxazole in 1:5 ratio.

cotrimoxazole(Trimethprim 80mg+ Sulfamehoxazole 400mg) Mar. Pr[illegible] Septran

it is bacteriocidal

uses & adverse effect similar to sulfonamides.

(B) QUINOLONES

Synthetic antimicrobial having quinolone structure

1. Nalidixic acid 0.5 gram

   Effective against gram (-) bacteria

   Use- urinary antiseptic

2. FLURO QUINALONES-

Synthetic antimicrobial agent

DRUGS-

FIRST GENERATION-

Norfloxacin 400mg

Ciprofloxacin 500mg

Ofloxacin 200-400mg

SECOND GENERATION-

Levofloxacin 250-500mg

Gatifloxacin 200-400mg

Sparfloxacin 200-400mg

Moxifloxacin 400 mg (0.5% e/d)

ACTIVITY-

Mainly effective against gram negative aerobic bacteria.

Mechanism- act by inhibiting bacterial D.N.A. gyrase enzyme which is required for DNA replication thus by inhibiting this inhibitDNA replication.

USES-

U.T.I., Typhoid,Bacterial gastroenteritis, Tuberculosis, Meningitis, Respiratory infection

Conjunctivitis (Eye drop- Ciplox)

ADVERSE EFFECTS-

Nausea, vomiting,dizziness,headache,photosensitivity, cartilage damage, prolong QT interval.

C./I.- In children (Ciprofloxacin) & during pregnancy(all FQ).

(C) BETA LACTAMS ANTIBIOTICS

Antibiotics that contain B-lactame ring

Four categories

1.PENICILLINS ***2. CEPHALOSPORINES***

3. MONOBACTAMS ***4. CARBAPENEMS***

1. PENICILLIN

It is the first natural antibiotic that was discovered in 1928 byAlexenderfleming& used clinically first in 1941.

DRUGS-

- **Natural –Ineffective orally&narrow spectrum of activity**
  Benzyl penicillin (penicillin-G)- 0.5-5 mu – I.M.
  Benzathine penicillin (penidureinj 12 mu) –I.M.
- **Semi Synthetic-Effective orally & broad spectrum of activity**
  Amoxycillin(500mg), Cloxacillin(500mg), Ampicillin(500mg), Piperacillin(1-4 gram), Ticarcillin, Nafcillin, Methicillin
  Clavulanic acid(125mg), Sulbatum (250-500mg), Tazobactum (250-500mg)
  I- betalactamase inhibitor

ACTIVITY-

NATURAL-

Mainly effective against gram (+) cocci & bacilli & gram (-) cocci bacteria.

SEMISYNTHETICeffective against gram (+) cocci & bacilli & gram (-) cocci & bacilli (also) bacteria.

Mechanism- Act by inhibiting bacterial call wall synthesis

USES-

Pharyngitis, Otitis media(streptococcal infection), Pnemonia, Meniningitis(meningococal)

Gonorrhoea,Diphtheria, Syphilis, RTI,UTI

Amoxycillin combined with clavulanic acid to increase activity.

ADVERSE EFFECTS-

Local irritancy, hypersensitivity, superinfection

2. CEPHALOSPORINES-

DRUGS-

First generation-more- gram (+) weak gram(-)

Cephalexin 250-500mg

- DOC – UTI during pregnancy

Second generation- more gram(-) & anaerobes

Cefuroxime 200mg

- Not effective against pseudomonas

Third generation-more effective against gram negative enterobacteriaceae& pseudomonas but less effective against gram positive cocci & anaerobes

Cefixime(200mg oral), Cefotaxime (250- 1000 mg), Ceftriaxone (250- 1000 mg), Ceftazidime (250- 1000 mg), Cefoperazone (250- 1000 mg) Cefpodoxime (200 mg oral)

Fourth generation- similar to third but high resistant to beta lactamase

Cefpirome 1000mg IM/IV
cefepime 1000mg IV

- Indicated in serious hospital acquired infection

***MECHANISM*-Bactericidal,** act by inhibiting cell wall synthesis.

USES-

AS alternative to penicillin, R.T.I., U.T.I., Meningitis, Syphilis, Septicemia, Typhoid, Gonorrhea, Surgical prophylaxis

ADVERSE EFFECT-

I.M. injection painful, diarrhea, hypersensitivity, nephrotoxicity.

3. MONOBACTAMS

Aztreonam 0.5-2 gram IM/IV

Effective against gram negative enteric bacilli, H. influenza & pseudomonas

4. CARBAPENEMS

Imipenem (with cilastin) 500 mg IV (degrade by dehydropeptidase-I)- Renal tubule

- Can cause seizure

Meropenem 0.5–2 gram slow IV

- effective against gram positive and gram negative bacteria (both aerobes and anaerobes)
- More gram negative aerobes less gram positive cocci
- Reserve drug for nosocomial infection like septicaemia & febrile neutropenia

Faropenem 200 mg tablet

- Indicated in respiratory, ENT & genitourinary infection

(D) AMINOGLYCOSIDES-

DRUGS-

Sterptomycin(first line drug T.B.),Amikacin(250-500mg), Tobramycin(eye drop),Gentamycin(injection & Cream),Neomycin(Cream),Kanamycin(second line drug TB), Sisomicin, Netilmicin,Spectinomycin, Framycetin

ACTIVITY-

Mainly effective against most aerobicgram negative bacilli.

Mechanism-Inhibit protein synthesis by bind several sites of 30 & 50s ribosome cause misreading of m-RNA code.

- Netimicin- For serious infection only& least ototoxic
- Spectinomycin -Gonorrhoea in penicillin allergic patient
- Amikacin, Gentamycin & Tobramycin- Gram negative with pseudomonas
- Neomycin- oral- Gut sterlization

ADVERSE EFFECT-

Nephrotoxicity,Damage to VIII Cranial nerve(Auditory nerve), Neuromuscular Blockage.

USES-

U.T.I., Gastroenteritis, Conjunctivitis, Skin infection,etc.

(E) MACROLIDE ANTIBIOTICS

DRUGS-

Erythromycin,Azithromycin(250-500mg), Clarithromycin, Roxithromycin(150-300mg), Spiramycin.

ACTIVITY-

Effective mainly against Gram Positive bacteria& few gram negative bacteria.

Mechanism- Inhibiting protein synthesis by acting on 50’S ribosomes.

*Clarithromycin- Rx of Mycobacterium avium complex & also for h. pylori induced peptic ulcer.

* Spiramycin- DOC for Rx of Toxoplasmosis in pregnancy.

* Erythromycin- in infant- Risk of hypertrophic pyloric stenosis.

ADVERSE EFECT-

Epigastric pain, hypersensitivity, hepatitis

USES-

As an alternative to penicillin, U.R.T.I., Whooping Cough, Chancroid, Skin infection etc.

(F) BROAD SPECTRUM ANTIBIOTICS–

1. ***TETRACYCLINES***
2. ***CHLORAMPHENICOL***

1. TETRACYCLINES

DRUGS -

Tetracycline(250-500mg), Oxytetracycline(250-500mg), Doxicycline(100mg), Demeclocycline(150-300 mg), Mincocycline(100 mg),.

It is broad spectrum antibiotic

EFFECTIVE AGAINST:

All Gram(+)ve and gram(-)ve cocci

most gram (+)ve bacilli and

Some gram (-)ve bacilli and

Also effective against- Spirochedes, Rickettsia, Mycoplasma, Entamoeba histolytica &Plasmodia..

Mechanism of action:-

Bacteriostatic, Inhibit protein synthesis by acting on 30s ribosome.

ADVERSE EFFECT-

Liver damage, Kidney damage, Photo toxicity, In children's discoloration (yellowish) of bones &teeth, if pregnant women then Suppression of bone growth in foetus, increase intra cranial pressure, Antianabolic effect, Diabetes incipidus, hypersensitivity, suprinfection.

USES-

Mixed Injection, Cholera, Chlamydial Infection, Atypical Pneumonia, Cholera, Plague, Brucellosis, Rickettsial fever, Acne, Malaria

2. CHLORAMPHENICOL

It is broad spectrum antibiotic

EFFECTIVE AGAINST:

Gram(+)ve and gram(-)ve cocci

most gram (+)ve bacilli and

Some gram (-)ve bacilli and

Also effective against- Spirochedes, Rickettsia, Mycoplasma.

Mechanism of action-

Bacteriostatic, inhibit protein synthesis by acting on 50 s ribosomes.

DOSE- 250-500mg.

ADVERSE EFFECT-

Bone Marrow Depression,Hyper Sensitivity,Gray Baby Syndrome(Due to Deficiency of Glucuronide Enzyme).

USES-

Entericfever(typhoid),Anaerobic infection, Halicobacter influenza(Pyogenic Meningitis), UTI, Intraocular infection, Conjunctivitis & External ear infection.

(G) OTHER ANTIBIOTICS-

1. Lincosamide-Antibiotic

Inhibit protein synthesis by acting on 50 s ribosomes

Similar to macrolide

Additional-Anaerobes &aerobic gram negative bacilli

Ex-Clindamycin, Lincomycin

2.Glycopeptide- Antibiotic

Inhibit cell wall synthesis

MRSA & gram positive cocci

Ex-Vancomycin, Teicoplanin

3. Oxazolidinone- Synthetic

Inhibit Protien synthesis

VRSA

Linezolid

4. **Mupirocin**- Antibiotic

   Gram positive

5. **Fusidic acid-** Steroidal Antibiotic

   Gram positive.

6. **Pleuromutilns-**

   Inhibit Protein synthesis

   Retapamulin- topical treatment of impetigo

7. **Glycylcyclines-**

   Tigecycline- Broad spectrum

8. **Streptogramins-Bacteriocidal**

   Quinpristine-Dalfopristin

9. **Polypeptide antibiotic- Bactericidalbut high toxicity**

   Polymyxin B and Colistin

   Detergent like action, effective against gram negative bacteria

   Bacitracin

   Inhibit cell wall synthesis, effective against gram positive bacreria

** Neosporin powder-

Neomycin + Bacitracin + Polymyxin-B

ANTI TUBERCULAR DRUGS

Drug that are used in the treatment of tuberculosis.

Tuberculosis- very slowly progressive infection

Caused by- mycobacterium tuberculosis/ bovis (gram positive bacilli).

Mainly effects to lungs (pulmonary tuberculosis)

Combination of more than one drug is given in the treatment of T.B. to prevent emergence of resistance

Classification

a. **First line- More effective lesser toxic**
   Ex-Isoniazid, Rifampicin,Pyrazinamide, Ethambutol, Streptomycin.

b. **Second line- lesser effective more toxic**
   Ex-kanamcyin, Amikacin, PAS,Thaiacetazone,Ethionamide,Cycloserine, Ofloxacin, Levofloxacin etc.

- Isoniazide- Peripheral neuritis, Enzyme inhibitor
- Rifampacin- Orange red colour urine
- Ethambutol- Potical neuritis
- Streptomycin- Aminoglyocoside

- All first line cidal except Ethambutol
- H, Z, E – inhibit mycolic acid synthesis
- R- inhibit DNA dependent RNA synthesis
- H, R, Z –Hepatitis
- H- Rapidly growing
- Z- Slow growing
- R- Spurters
- H, R, E- Both intra & extracellular
- Z- intracellular
- S- Extracellular
- Maximam sterilizing action- Z
- Maximum CSF penetration- Isoniazise
- Minimum CSF penetration- Streptomycin

- S- CI during pregnancy
- Pregnancy-HRE (india)
- Children- HZR
- To prevent latent infection- children- 9 month –H (if HIV then 12 month)
- Mono drug resistance TB- Single First line drug resistance except rifampacin
- Poly drug resistance TB- two or more first line drug resistance both H & R
- MDR TB- Both H & R resistance

ANTI LEPROTIC DRUG

- Drugs that are use in the treatment of leprosy.
  Causative agent – mycobacterium laprae
- It is very slowly progressive bacilli gram(+) ve.
- It mainly affects to – skin,nerves.

DRUGS

I. Sulfones:
   Ex.dapsone- LAMPRISTIC
   Dose- 25-100
   Similary action with sulfonamide (Inbition of PABA)
   HaemolyticAnaemia
   CI- G6PD deficiency

II. PHENAZANINE devivative:-
   Ex.clofazimine- Reddish black colur of skin
   Dose -50-100 mg

III. Antitubercular drugs:
   Ex- Rifampin, Ethionamide

IV. Antibiotics-
   Ex-Claritromycin, Ofloxacin, Mincocycline

- Multi bacillary leprosy- 12 month- RCD
- Paucibacillary leprosy- 6month- RCD

ANFTIUNGAL DRUGS

Classification
Topical antifungal- Clotrimazole, Miconazole
Systemic antifungal- Fluconazole
According to mechanism of action-

- ***a.*** Drugs acting on cell membrance -.ketoconazole, Amphotericin B, Terbinafine,fluconazole, Itraconazole
- ***b.*** Drugs affecting cell division(microtubules)- Griseofulvin
- ***c.*** Drugs affecting nucleic acid synthesis - 5-FC(5-fluorocytocine)

ANTI MALARIAL

CLASSIFICATION-

1. Drugs effective against Pre &Exoerythrocytic phase (Tissue schizontocide)- Primaquine
2. Drugs effective against Erythrocytic phase (Erythrocytic schizontocide) -Chloroquine, Artemisinin, Quinine, Mefloquine, Pyrimethamine
3. Gamatocide- Primaquine
4. Antibiotics- e.g. tetracycline

- chloquine acts by inhibiting polymerization of hemoglobin to form hemozoin
- primaquine causes hemolythicanemia patients of G6– PD
- Casual prophylaxis- target preerythocytic phase- Primaquine
- Suppressive prophylaxis- Erythrocytic phase- CQ, MQ & Doxycycline
- Clinical cure-Erythrocytic schizontocide-Q, CQ, Sulfonamide, Doxycycline
- Radical cure- Exoerythrocytic phase(Vivax)- Primaquine
- Gametocide- Primaquine
- Vivax- CQ + PQ
- Vivax –CQ resistance- Q + D + PQ
- Falciparum-CQ + PQ or Sulp + Pyre + PQ
- Falciparum CQ resistance- Q + D or Arte +Sulp + Pyre or Arte + Lume

ANTI AMOEBIC

CLASSIFICATION-

1. Luminal
   Ex- Diloxanide furoate, Tetracycline
2. Tissue Amoebicide-
   a. Extraintestinal- Choloquine
   b. both intestinal and extra intestinal- Metronidazole, Tinidazole, Secnidazole, Emetine

- Metronidazole shows disulfiram like action with alcohol
- Metronidazole- Cacinogenic
- Metronidazole- Also effective in anaerobic bacterial infection
- Soidiumstilbogluconate- Kalaazar
- Pentamidine- Kalaazar

ANTIVIRAL DRUGS

Classification

Anti-HerpesDrugs

Ex- Idoxuridine, Acyclovir, Famiciclovir, Ganiciclovir, Foscarnet

- Anti-herpes Drugs- Inhibit viral DNA
- Acyclovir- Effective against Herpes simplex-I & II & Varicella zoster
- Ganciclovir- DOC -CMV

Anti Influenza Drugs

Ex- Amantadine, Rimantadine, Oseltamavir, Zanamavir

- Amantidine&Rimantidine- Prevent uncoating of Influenza-A virus (Decreaseduration of symptoms of influenza)

- Oseltamavir&Zanamavir- Prevent virion release- Effective against both Influenza-A & Influenza-B

Anti-HepatitsDrugs

Ex- Ribavirin, Lamivudine, Entecavir, INF

- Anti-Hepatits Drugs- Effective against Hepatitis-B & Hepatitis-C virus

- INF α- Use in Rx of chronic Hepatitis-B virus infection
- INF α + Ribavirin- Acute & Chronic Hepatitis-C virus infection
- Entecavir- DOC- Chronic Hepatitis-C virus infection

Anti-retroviral Drugs

a. NRTI- Zidovudine (AZT), Stavudine, Lamivudine,Abacavir, Tinofovir
b. NNRTI- Nevirapine, Efavirenz, delavirdine,
c. PI- Ritonavir, Saquinavir, Lopinavir, Indinavir
d. ENTRY Inhibitor-Ibalizumab
e. INTEGRASE Inhibitor- Raltegravir, Dolutegravir

- Reverse transcriptase inhibitor-Competitive inhibitor (NRTI), Non-competitive inhibitor (NNRTI)
- PI- Inhibit maturation of infectious virion
- ENTRY Inhibitor- Prevent entry/ Fusion
- INTEGRASE Inhibitor- prevent viral DNA integration in nuclear genome

- ART- 2NRTI + 1NNRTI/II or 2NRTI + 1PI

- Infant prophylaxis- Z + N for 6 weeks

- PEP- T + L + PI for 28 days (start within 72 hours)

- Nevirapine- Use to prevent vertical transmission better option Zidovudine

ANTI HELMINTHIC DRUG

Drugs that either kill (vermicide) or expel (vermifuge) infesting helminths.

Ex- Albendazole, Mebendazole, Thiabendazole, Praziquental, Ivermectine, Niclosemide, Piperazine, Pyrental pamoate, Levimisole, Diethyl carbemazine

Effective against various worms belonging to Nematodes,Cestodes& Trematodes.

Nematodes-

Round worm (Ascaris)-Albenda, Mebenda

Hook worm (Ancylostoma)- Pyrantel,Albenda, Mebenda

Thread worm (Enterobious)-Pyrantel,Albenda, Mebenda

Whip worm (Trichuris)-Albenda, Mebenda

Filaria (Wucheria- DEC) (Burgia- Ivermectin)

Cestodes-

Tape worm (Taenia- Praziquental) (Neurocysticercosis-Albendazole)

Trematodes-

Flukes (Scistosoma)-Praziquental

DEC- Use in Rx of Eosinophilia

Ivermectin (6 mg)- Orally effective drug in scabies

8. ANTI CANCER DRUGS

ANTI CANCER DRUGS

1. **Cytotoxic drugs:**
    a. ***Alkylating agent-Drugs that kill fast dividing cells by alkylation (DNA)***
        Ex-Cyclophosphamide, Chlorambucil, thio-TEPA, Ifosfamide, Melphalan, Busulfan, Procabazine
    b. ***Antimetabolites- Affect nucleic acid synthesis***
        Ex-Methotrexate, 6-MP, 5-FU, 6-TG, Azathioprine
    c. ***Plant derivatives- Interfere in cell cycle***
        Ex- vincristine, vinblastine, paclitaxel, docetaxel, Etoposide.
    d. ***Antibiotics-Interfere with DNA template function***
        Ex- Doxorubicin, Bleomycin, Mitomycin-C, Actinomycin-D, Daunorubicin
    e. ***Others-***
        Ex- Cisplatin, carboplatin (Cross linking of DNA) Imatinib (tyrosine kinase inhibitor)

- Acute leukaemia- Vincristine, 6-MP, Cyclophosphamide
- Chronic lymphatic leukaemia- Chlorambucil, Cyclophosphamide
- Chronic Myeloid leukaemia- Busulfan, Imatinib
- Hodgkin's disease- Vinblastine, Dacarbazine
- Multiple Myeloma- Melphalan, Prednisolone, Cyclophosphamide
- Wilms Tumour- Actinomycin-D, Vincristine
- Cancer lung- Cyclophosphamide, Vincristine, Doxorubicin
- Carcinoma Cervix- Mitomycin, Cisplatin
- Osteogenic Sarcoma- MTX, Doxorubicin
- Haemorrhagic cystitis- Cyclophosphamide, Ifosfamide Rx- Mesna
- Cyclophosphamide- Alopecia & SIADH
- Busulfan- Pulmonary fibrosis, adrenal insufficiency & hyperpigmentation
- Cisplatin- Emesis, nephrotoxicity & Ototoxicity
- Procarbazine- Most leukemiogenic
- 5-FU- Hand & foot syndrome
- Bleomycin-Pulmonary fibrosis
- Doxorubicin&Daunorubicin- Cardiotoxic

2. **Drugs affecting hormonal balance:**

Prednisolone- Acute childhood leukaemia & breast cancer
Ethinylestradiol- Prostate carcinoma
Tamoxifen- Breast carcinoma
Letrozole-Breast carcinoma
Anastrtazole-Breast carcinoma
Flutamide- Prostate Carcinoma
Bicalutamide- Prostate Carcinoma
Finasteride- Prostate Carcinoma
Nafarelin- Prostate/Breast carcinoma
Hydroxyprogesterone- Endometrial carcinoma

- All cancerous drugs are highly toxic – effect on all rapidly dividing and normal cells

ADVERSE EFFECT

a. Bone marrow toxicity – Anaemia& Granulocytopenia
b. Alopecia – baldness
c. Live, kidney, skin toxicity etc.
d.

A. TABLE OF CHOICE OF DRUGS

Disease	Drug of choice
Chloramphenicol resistant typhoid	Ciprofloxacin
Whooping cough,diphtheria	Erythromycin
Mycoplasma infection	Erythromycin
Cholera prophylaxis	Doxycycline
Plague	Streptomycin
Genital prophylaxis	Acyclovir
Kala-azar	Pentamidine
Syphills	Penicillin G
Cellulities	Nafcillin (or) oxacillin
Actinomycosis	Penicillin G
Leprosy	Dapsone
Ascariasis	Albendazole
Hook worm infection	Mebendazole
Giardiasis, vaginitis	Metronidazole
Cutaneous candidiasis	Nystatin powder (or) cream
Systemic fungal infection	Amphotericin B
Malaria	Quinine + doxycycline
Plamodiumfelciperum	Artesunate

B. TABLE OF IMPORTANT SIDE EFFECT

Drugs	**Important side effect**

Sulfonamides	Crystalluria
Ciprofloxacin	Affects bone and cartilage
Pencillins	Anaphylaxis
Erythromycin	Cholestatic jaundice
Clindamycin	Pseudomembroanous colitis
Streptomycin	Ototoxicity, neuromuscular blockade
Tetracyclins	Fanconi like syndrome, photo sensitivity, dental and bone effect
Chloramphenicol	Gray baby syndrome, bone marrow depression
Ketoconazole	Heptotoxicity
INH	Peripheral neuritis
Rifampicin	Hepatotoxicity, orange red coloured secretions
Ethmbutol	Optic and peripheral neuritis
Metronidazole	Metallic taste, nausea
Anti cancer drugs	Bone marrow depression, GIT ulceration, perforation
Phenytoin	Gum hypertrophy, hirsutism
Morphine	Respiratory depression, addiction
Aspirin	Salicylism, GIT ulceration
Paracetamol	Hepatotoxicity
Phenylbutazone	Bone marrow depression
Halothane	Malignant hyperthermia
N_2o	Diffusion hypoxia
Barbiturates	Respiratory depression, dependence
Atropine	Dry mouth
Alpha blockers	Reflex tachycardia
Minoxidil	Hirsutism

C. DRUGS INTERACTION WITH ANTIBIOTIC

Antibiotic	Interacting drug	Drug reactions
Metronidazole	Warfarin	Potentiation of anti coagulation
Griseofulvin	Alcohol	Dilsulfiram reaction
Metronidazole	Alcohol	Dilsulfiram reaction
Rifampicin	Warfarin	Diminished effects of warfarin
Tetracycline	Penicillin	Inhibits of action of penicillin
Tetracycline	lithium	Increase lithium retention
Chloramphenicol	Warfarin	Potentiation of anti coagulation

D. MECHANISM OF ACTION OF IMPORTANT ANTIBIOTICS

Drugs	Mechanism of action
Poly mixins, bacitracin,amphotericim B	Alter cell wall permeability
Pencillin, cephalosporins, vancomycin	Inhibit cell wall synthesis
Tetracycline, chloramphenicol erythromycin	Inhibit protein synthesis
Rifampicin,metronodazole	Interface with DNA function
Aminoglycosides, streptomycin	Misleading of m-RNA
Anti viral drugs	Interfere with DNA synthesis
Fluroquinolones-ciproflaxacin	Inhibit DNA gyrase

E. ANTI DOTE OF SOME RUGS

Poison	**Antidote**
Paracetamol	N-acetyl cysteine
Mercury/arsenic	BAL (british anti lewisite)
CO	Oxygen
Cynide	Amylnitrate
Opioids	Naloxone
Atropine	Physostigmine
Oraganophosphates	Antropine, pralidoxime
Benzodiazepines	Flumazenil
Fluorides	Milk
Iron	Desferroxime
Methtrexare	Leucovorine
Heparin	Protamin sulphate
Lead	BAL, Dimercaprol
Benzodiazepines	Flumazenil
Opoids (morphine)	Naloxone
Vit. K	Oral anti coagulant
Methnol	Ethenol, fomepizole
Organophosphate	Atropine, pralidoxime
LSD	Phenothiazine
Histamine	Adrenaline
Atropine	Physostigmine

EMERGENCY DRUGS

Salbutamol	Treatment of an acute asthma attack
Diphenhydramine	Treatment of allergic reaction
Epinephrine	Treatment of cardiac arrest, anaphylaxis, or acute asthma attack
Glucose, oral (usually in a tube)	Treatment of hypoglycemia
Nitroglycerin	Treatment of an acute anginal attack
Oxygen	Treatment of emergency situations in which pt. is having difficulty breathing
Atropine	Increase in cardiac rate
B-Blockers	Reduction in blood pressure
Dextrose 50%	IV solution for hypoglycemia; when pt. can't swallow
Diazepam/alprazolam	Initial treatment of status epilepticus
Glucagon	Management of severe hypoglycemic reactions
Hydrocortisone	Treatment of allergic reactions, anaphylaxis, or adrenal crisis
Morphine	Opioid analgesic used to treat the pain associated with MI
Spirits of ammonia	Treatment of syncope
Bretylium	Treatment of arrhythmias
Procainamide	Treatment of arrhythmias
Verapamil	Treatment of arrhythmias
Lidocaine	Treatment of arrhythmias
Flumazenil	Treatment of benzodiazepine overdose
Naloxone	Treatment of opioid overdose

1. AMINOPHYLLINE- Antiasthmatic& COPD Preparations

Loading dose: 5 mg/kg (ideal body wt). Maintenance: 0.5 mg/kg/hr.

2. AMIODARONE HYDROCHLORIDE-Ventricular and supraventricular arrhythmias.
   Dosage: 200 mg 3 times/day

3. ATROPINE SULFATE- Bradycardia 500 mcg every 3-5 mins, Organophosphorus poisoning pre anesthetic medication

4. CALCIUM GLUCONATE- Hypocalcaemia 10-50 mmol/day. Acute hypocalcaemic tetany 2.25 IV infusion. Antidote in severe hypermagnesaemia; Severe hyperkalaemia 10 mL of 10%

5. CAPTOPRIL-ACE Inhibitors-HTN, Heart failure, MI. HTN in diabetic nephropathy.

6. CLONIDINE- Antihypertensives- HTN, Migraine prophylaxis.

7. DIAZEPAM- relief of anxiety, agitation & tension due to psychoneurotic states & transient situational disturbances
   Dosage: 10mg/2ml

8. DIGOXIN-Inotropics-Cardiac failure accompanied by atrial fibrillation; management of chronic cardiac failure where systolic dysfunction or ventricular dilatation is dominant; management of certain supraventricular arrhythmias, particularly chronic atrial flutter & fibrillation.
   Dosage: 5mg/2ml

9. DIPENHYDRAMINE-antihistamine-Hay fever, urticaria, vasomotor rhinitis, angioneurotic edema, drug sensitization, serum & penicillin reaction, contact dermatitis, atopic eczema, other allergic dermatoses, pruritus, food sensitivity, parkinsonism, motion sickness.Dosage: 50mg/ml

10. EPINEPHRINE-Acute asthmatic attacks, Advanced cardiac life support
    Dosage: 1mg/ml

11. FUROSEMIDE- loop diuretics- edema, hypertension
    Dosage: 20mg/2ml

12. HYDRALAZINE HYDROCHLORIDE- antihypertension- For hypertensive patient
    Dosage: 20mg/ml

13. HYDROCORTISONE SODIUM SUCCINATE- endocrine, hematologic, rheumatic & collagen disorders, dermatologic, ophth, GI, resp & neoplastic diseases, edematous states, control of severe incapacitating allergic conditions, TB meningitis w/ subarachnoid block or impending block when used concurrently with appropriate anti-TB chemotherapy, shock secondary to adrenocortical insufficiency or shock unresponsive to conventional therapy when adrenocortical insufficiency may be present
    100 mg/ 2 mL, 250 mg/ 2 mL

14. ISOSORBIDE-5- MONONITRATE- prophylactic treatment of angina pectoris.
    Dose-30 mg, 60 mg

15. ISOSORBIDE DINITRATE- unresponsive left ventricular failure secondary to acute MI, severe or unstable angina pectoris
    Dose: 10 mg/10mL

16. MAGNESIUM SULFATE- anticonvulsant- prevention & control of convulsions in patients w/ preeclampsia or eclampsia, control of HTN,
    Dosage: 250 mg/10 mL

17. MEPERIDINE HYDROCHLORIDE -relief of moderate to severe pain, pre-op medication, support of anesth&obstet analgesia
    Dosage: 100 mg/ 2mL

18. METOCLOPRAMIDE- antiemetic & anti-spasmodic
    Dosage: 10 mg/ 2mL

19. MIDAZOLAM HYDROCHLORIDE-hypnotics & sedatives- Dosage: 5mg/5mL

20. MORPHINE SULFATE- Relief of moderate to severe pain not responsive to non-narcotic analgesics. Premed. Analgesic adjunct in general anesthesp in pain associated w/ cancer, MI & surgery. Alleviates anxiety associated w/ severe pain. Hypnotic for pain-related sleeplessness.
    Dosage: Adult 5-20 mg IM/SC 4 hrly.

21. NICARDIPINE HYDROCHLORIDE- IV infusion Dilute to 10-20 mg/100 mL (conc of 1.01-0.02%). Indication: Hypertensive emergencies or urgencies, peri-op & post-op HTN,

22. NTG PATCH-Prevention of angina pectoris due to coronary artery disease
    Dosage: Starting dose: 0.2-0.4 mg/hr. Dosing schedule: Daily patch-on period of 12-14 hr&

daily patch-off period of 10-12 hr.

23. PARACETAMOL-Analgesics (Non-Opioid) & Antipyretics
Dosage: Adult &childn ≥10 yr 2-3 mL, ≤10 yr 1-2 mL. Depending on severity of case, dose may be repeated 4 hrly. In severe cases, dose may be administered by IV very slowly

24. PHENYTOIN- Dosage: Adult Initially 100 mg tid. Maintenance: 300-400 mg daily. indication: Tonic-clonic& complex partial (psychomotor, temporal lobe), prevention & treatment of seizures occurring during or following neurosurgery

25. TERBUTALINE- Indication: For reversible airways obstruction, in asthma, COPD. Decreases uterine contractility & may be used to arrest premature labor

26. VERAPAMIL HYDROCHLORIDE-, chronic coronary insufficiency, angina pectoris, paroxysmal supraventricular tachycardia, tachyarrhythmias, long-term treatment after MI.

27. IPRATROPIUM INHALATION- Bronchodilator for treatment of bronchospasm associated w/ COPD, including chronic bronchitis, emphysema and asthma- 0.5 mg/2 mL

28. FENOTEROL/IPRATROPIUM BROMIDE-prevention and treatment of symptoms in chronic obstructive airway disorders with reversible bronchospasm

29. BUDESONIDE-regular treatment of asthma where use of a combination (inhaled corticosteroid and long acting beta 2 agonist) is appropriate

30. TERBUTALINE SULFATE- Indication: relief of bronchospasm in obstructive airway diseases-Dose: Adult 5-10 mg, Children 2-5mg

31. HEPARIN SODIUM- Anticoagulants, Antiplatelets & Fibrinolytics (Thrombolytics)
Dosage: 5000 iu/1 mL, 25000 iu/1 mL
treatment and prophylaxis of thromboembolic disorders
Have on hand protamine sulfate, specific heparin antagonist

32. ESMOLOL HYDROCHLORIDE-Beta blockers- supraventricular tachycardia; post-operative tachycardia or hypertension; non-compensatory sinus tachycardias; intra-operative tachycardia or hypertension; unstable angina, non ST segment elevation MI
Dosage: 100mg/10ml

33. D- 50%
    Indication: for hypoglycemia

34. POTASSIUM CHLORIDE
    Dosage: 40 meqs/20 ml
    Indication: for hypokalemia, acute MI

35. SODIUM BICARBONATE- metabolic acidosis, systemic or urinary alkalinization, antacid, cardiac arrest
    Dosage: 10mEq/10ml; 50mEq/50ml

36. DOPAMINE- shock and hemodynamic imbalances, hypotension
    Dosage: 40 mg/Ml; 80 mg/mL; 160 mg/mL

37. DOBUTAMINE- increased cardiac output in short term treatment of cardiac decompensation caused by depressed contractility
    Dosage: 12.5 mg/mL

38. LIDOCAINE -Local anesthetic, ventricular arrhythmias caused by MI, cardiac manipulation or cardiac glycosides
    Dosage: 2% - 5%
39. MANNITOL- test dose for marked oliguria or suspected inadequate renal function, oliguria, to reduce intraocular or intracranial pressure, diuresis in drug intoxication
    Dosage: 5% , 10%, 15%, 20%, 25% in 500cc/1,000cc

40. DEXTROSE 5% IN WATER (D5W) SOLUTION- fluid replacement and caloric supplementation in patients who can't maintain adequate oral intake or are restricted from doing so- Dosage: 250ml bottles (5g dextrose/100ml water)

USE OF DRUGS DURING PREGNANCY

The safety of approximately 50 % of medications for the mother and fetus remains unknown

FIVE CATEGORIES

Class A

No risk in controlled human studies
Examples
Acetaminophen
Pyridoxine (Vitamin B6)

Class B

No risk in controlled animal studies

Examples
Amoxicillin
Cephalosporin antibiotics

Class C

Small risk in controlled animal studies
Examples
1. Codeine
2. Dicloxacillin

Class D

Strong evidence of risk to the human fetus
Examples
Rifampicin
Fluoroquinolones
Aminoglycosides

Class X

Never to be used in Pregnancy
Very high risk to the human fetus
Examples
Thalidomide
Oral contraceptive pills
Misoprostol

LIST OF COMMONLY USED DRUGS IN PREGNANCY AND THEIR CATEGORIES

Drugs	**Category**
Analgesics and Antipyretics	B and C
Acetaminophen	B
Phenacetin	B
Aspirin	C

Drugs	Category
Antiemetics	B and C
Doxylamine	B
Meclizine	B
Cyclizine	B
Dimenhydrinate	B
Antibiotics	B, C and D
Penicillin, Ampicillin, Amoxycillin,	B
Cloxacillin Cephalosporins	B
Erythromycin	B
Gentamicin	C
Amikacin	C/D
Streptomycin	D
Sulphonamides	B/D
Tetracyclines	D
Amoebicides	B
Metronidazole	
Anthelmentics	B
Piperazine	
Mebendazole	
Antimalarials	C
Antifungals	C
Anti TB Drugs	B and C
Ethambutol	B
INH	C
Rifampicin	C
Pyrazinamide	C
PAS	C
Vitamins	
B,C,D,E,folic acid	A
Hormones	
Thyroxin	A
Androgens	X
Estrogens	X
Progestogens-	
Hydroxyprogestrone	D
Medroxyprogestrone	D
Norethindrone	X
Norgestrel	X

Drugs	Category
Bronchodilators	C

MEDICATIONS CONTRAINDICATED IN PREGNANCY

Drug	Comments
Vitamin A and its derivatives including isotretinein, accutane and etretinate.	Significant risk of spontaneous abortion and risk of many significant anomalies
ACE inhibitors	May cause kidney damage in the fetus when used in II and III trimester, decrease in the amount of amniotic fluid and deformities of face, limbs and lungs
Anticoagulants- warfarin	Use during I trimester produces defects like nasal hypoplasia and a depressed nasal bridge, named as Fetal warfarin Syndrome. Use during II and III trimesters is associated with increased risk of fetal malformation.
- Heparin	Safe but if taken for long time osteoporosis and decrease in number of platelets in pregnant women occurs
Estrogen and Androgens	Genital tract malformations
Thyroid preparations-	
Methimazole	Overactive and enlarged Thyroid gland
Carbimazole	Overactive and enlarged Thyroid gland
Radioactive iodine	Underactive Thyroid gland in fetus
Propylthiouracil	Safe
Anticonvulsants-	
Carbamazepine	Risk of birth defects
Phenytoin, Phenobarbitone	Bleeding problem in the newborn which can be prevented if pregnant woman takes Vit. K by mouth every day for a month before delivery or if the newborn baby is given an injection of Vit. K soon after birth
	Risk of birth defects.
Trimethadione	Increased risk of miscarriage in the women
Sodium valproate	Increased risk of birth defects in fetus; including a cleft palate and abnormalities of the heart, face, skull, hands or abdominal organs
Antidepressants- Lithium	Birth defects (mainly of the heart), lethargy, decreased muscle tone, underactivity of Thyroid gland and nephrogenic diabetes insipidus in the new born. Ebstein's anomaly (tricuspid valve malformation) has been reported in a number of foetuses exposed to this drug

Drug	Comments
NSAIDs	
Aspirin and other Salicylates	Delay in start of labor, premature closing of ductus arteriosus, jaundice, brain damage in the fetus and bleeding problems in the woman during and after delivery and in the newborn
Antibiotics- Tetracycline	Slowed bone growth, permanent yellowing of the teeth and increased susceptibility to cavities in the body
Chloramphenicol	Gray Baby Syndrome
Ciprofloxacin	Possibility of joint abnormalities (seen in animals)
Kanamycin and Streptomycin	Damage to fetus's ear resulting in deafness (risk of ototoxicity)
Sulfonamides	Jaundice and brain damage in newborn
Antineoplastic agents-	
Busulfan	Birth defects such as less than expected growth before birth, underdevelopment of lower jaw, cleft palate, abnormal development of skull bones, spinal defects, ear defects and club foot.
Chlorambucil	
Cyclophosphamide	
Methotrexate	
Oral Hypoglycemic drugs	A very low level of sugar in the blood of newborn. Inadequate control of diabetes in the pregnant woman
Chlorpropamide	
Tolbutamide	

List of some of the drugs whose use is contraindicated during pregnancy along with the harmful damaging effects they may produce on the fetus

USE OF DRUGS DURING BREAST FEEDING

Drugs safe to take in usual doses

NAME OF DRUG	*USE*
Acetaminophen	Used for pain relief
Acyclovir and valacyclovir	Antiviral for herpes infections

Antacids	Used to treat upset stomachs
Bupivacaine	A local anesthetic
Caffeine	A stimulant
Cephalosporins	Antibiotics for lung, ear, skin, urinary tract, throat, and bone infections
Clotrimazole	Used to treat yeast and fungal infections
Contraceptives (progestin-only)	Used for birth control
Corticosteroids	Used to treat inflammation of joints and other conditions
Decongestant nasal sprays	Used to treat stuffy noses
Digoxin	Used to treat heart problems
Erythromycin	Used for skin and respiratory infections
Fexofenadine	Antihistamine for allergies and hay fever
Fluconazole	Used to treat yeast infections
Heparin and LMW heparins	Used to stop blood from clotting
Ibuprofen	Used for pain relief
Inhalers, bronchodilators, and corticosteroids	Used for asthma
Insulin	For diabetes; dosage required may drop up to 25 percent during lactation
Laxatives, bulk-forming and stool softening	Used to treat constipation
Lidocaine	A local anesthetic
Loratadine	Antihistamine for allergies and hay fever
Low molecular weight heparins (enoxaparin, dalteparin, tinzaparin)	Anticoagulants
Magnesium sulfate	Used to treat preeclampsia and eclampsia
Methyldopa	Used to treat high blood pressure
Methylergonovine (short courses)	Used to prevent or control bleeding after childbirth
Metoprolol	A beta-blocker used to treat high blood pressure
Miconazole	Used to treat yeast infections
Nifedipine	Used for high blood pressure and Raynaud's syndrome of the nipple
Penicillins	Used to treat bacterial infections
Propranolol	A beta blocker used to treat heart problems, and high blood pressure
Theophylline	Used to treat asthma and bronchitis
Tretinoin	Cream used for acne
Thyroid replacement	Used to treat thyroid problems
Vaccines (except smallpox and yellow fever)	
Vancomycin	An antibiotic

Verapamil	Used for high blood pressure
Warfarin	Used to treat or prevent blood clots

Drugs probably safe in usual doses

Little is known about the effects of these drugs on a breastfeeding infant, but if there is an effect, it will probably be mild. In rare cases, a child has an allergic reaction.

NAME OF DRUG	***USE***
ACE inhibitors	Used to treat high blood pressure
Anticholinergic agents	Used to treat intestinal and gall bladder spasms; may reduce milk supply
Anticonvulsants	Used for seizures and mood disorders
Antihistamines	May reduce milk supply and cause infant drowsiness or fussiness
Antituberculars	Used to treat tuberculosis
Azathioprine	Used to suppress the immune system following organ transplants
Barbiturates (except phenobarbital)	For sedation and tension headaches
Bupropion	For depression
Clindamycin	Used to treat abdominal and vaginal infections
Oral decongestants	Used to treat congestion associated with colds or allergies; often reduces milk supply
Ergonovine (short course)	Used to treat uterine bleeding. May reduce milk supply.
Fluconazole	Antifungal
Gadolinium	Contrast agent for MRI studies
Haloperidol	Used to treat psychosis
Histamine H2 blockers	Used to treat stomach problems
Labetalol	Used for high blood pressure; caution with preterm babies
Hydrochlorothiazide (low doses)	Diuretic for high blood pressure
Lorazepam	Used to treat anxiety
Methimazole	Used for hyperthyroidism; less than 20 mg/day is probably safe
Metoclopramide	Used for gastrointestinal problems and to increase milk supply
Midazolam	Sedative used in anesthesia
Naproxen	Used for pain relief; okay if baby is at least 1 month old
Oxazepam	Used to treat anxiety

Paroxetine	Used to treat depression
Phenothiazines	
Propofol	Sedative used in anesthesia
Propylthiouracil (PTU)	Used to treat hyperthyroidism
Quinidine	Used to treat heartbeat irregularities
Quinolone antibacterials	Treatment of urinary tract infections
Salicylates (occasional use)	Used for pain relief
Sertraline	Used to treat depression
Spironolactone	Used to treat high blood pressure
Sumatriptan	Used to treat migraines
Tetracyclines < 14 days	Used to treat acne and urinary tract infections
Trazodone	Used for depression and sleep
Tricyclic antidepressants (avoid doxepin)	Used to treat depression, nortriptyline preferred
Verapamil	Used for high blood pressure

CONTRAINDICATED DRUGS IN LACTATION

1. ***Medications that decrease milk production***
    1. Bromocriptine
    2. Diuretics
2. ***Chemotherapeutic Medications***
    1. Cyclophosphamide
    2. Cyclosporine
    3. Doxorubicin
    4. Methotrexate
    5. Gold salts
    6. Propylthiouracil
    7. Methimazole

3. ***Radioactive Chemicals used in Nuclear Medicine***
    1. Gallium-67 (in Breast Milk up to 14 days)
    2. Indium-111 (in Breast Milk up to 20 hours)
    3. Iodine 131 (in Breast Milk up to 14 days)
    4. Radioactive Sodium (in Breast Milk up to 96 hours)
    5. Technetium-99m (in Breast Milk up to 3 days)
4. ***Cardiovascular medications to avoid in Lactation***
    1. Avoid Atenolol and use other Beta Blockers only with caution
    2. Avoid Acebutolol
    3. Avoid Amiodarone

5. Miscellaneous Medications

1. Dextroamphetamine
2. Ergotamine
3. Lithium
4. Metronidazole
5. Chloramphenicol
6. Potassium iodide
7. Phenindione (Anticoagulant)

6. Drugs of Abuse

1. Amphetamine
2. Cocaine
3. Heroin
4. Marijuana
5. Nicotine
6. Phencyclidine