

(2)

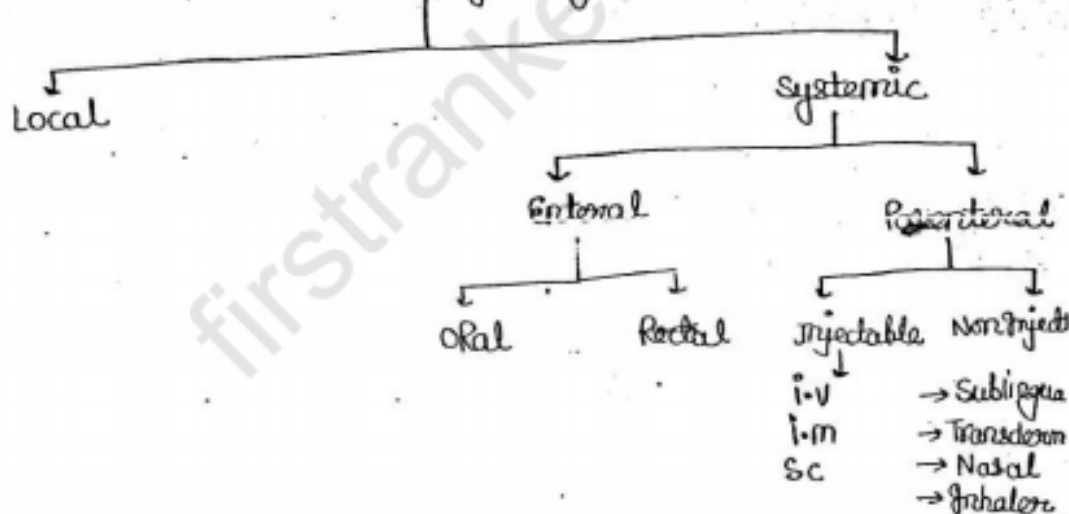
← Pharmacology →

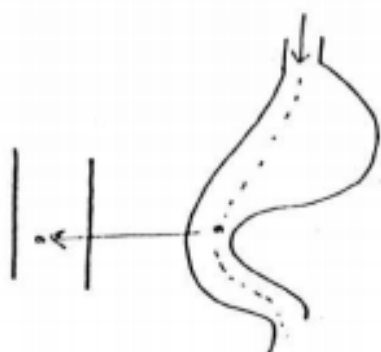
- Pharmacokinetics → effect of body on the drug
- Pharmacodynamics → effect of Drug on the body

Pharmacokinetics

- A → Absorption
- D
- M
- E

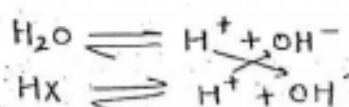
← Route of Drug administration →





Lipid Soluble can cross the membrane & goes in blood

Non Ionised Drug can cross the membrane & goes in blood



Drug	medium	solubility		Cross the memb
• Acidic	A	LS	Non-Ionised	✓
• Basic	B	LS	"	✓
• Acidic	B	WS	Ionised	X
• Basic	A	WS	Ionised	X

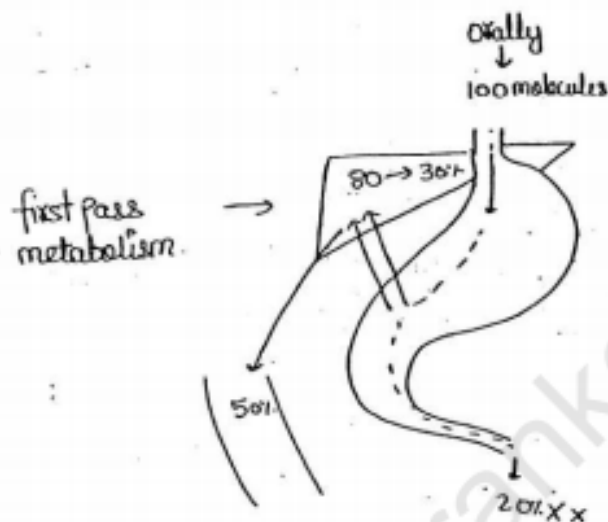
- Nature of the Drug → Acidic/Basic
- PH = ?
- PKa → is that PH 50% of Drug is lipid soluble & 50% of Drug is water soluble

PH	Lipid soluble	water soluble
• 3	99.9%	0.1%
• 4.0	99%	1%
• 5.0	90%	10%
→ 6.0	50%	50%
• 7.0	10%	90%
• 8	1%	99%

> Henderson Hasselbach eqⁿ →
$$pH = pK_a + \log \frac{[Ionized]}{[Non Ionized]}$$

 Tell that How a sub. behave in different medium

φ acidic drug absorb from stomach & basic drug absorb from intestine
 bt most of the drug absorb from intestine b/c → • stay time
 • surface area more



Bioavailability → % of given drug i.e reach in systemic circulation in unchange form.

It depend upon:

- ① absorption → directly proportional to Bioavailability
- ② first pass metabolism → Inversely proportional to Bioavailability
 → Nitroglycerine → given orally → ↑ more absorption → ↓ more 1st pass met. ↓ Bioavailability
 → Nitroglycerine → given sublingual → more bioavailability
- Sublingual routes →
 - ① ↑ bioavailability
 - ② quick action
 - ③ can control the dose (if more split out)
 - ④ Self administrable
 - ⑤ No 1st pass metabolism.

← High 1st pass metabolism →

L → lignocaine

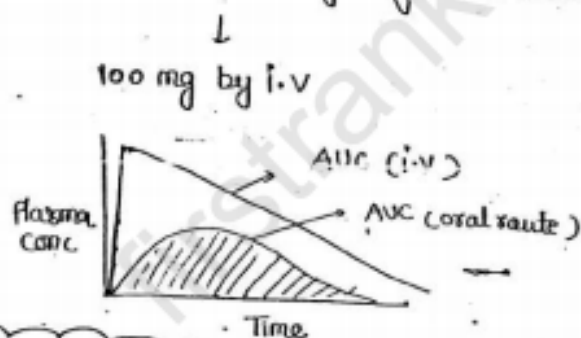
P → Propranolol

G → GTN

∴ How to calculate Bioavailability of Drug →

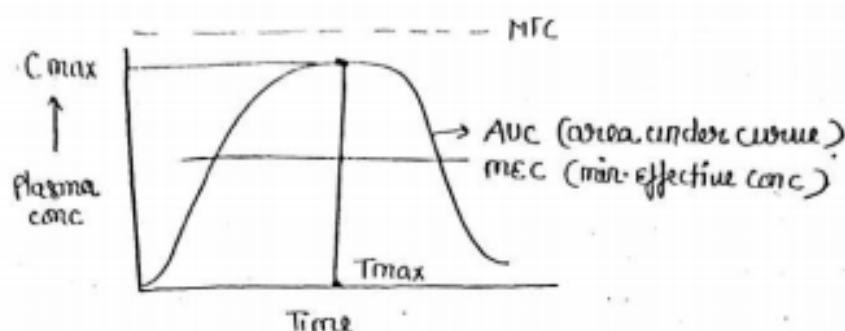
• i.v route → 100% Bioavailability

∴ calculate the Bioavailability by oral route



$$\text{Bioavailability} = \frac{\text{AUC (oral)}}{\text{AUC (i.v)}}$$

(4)

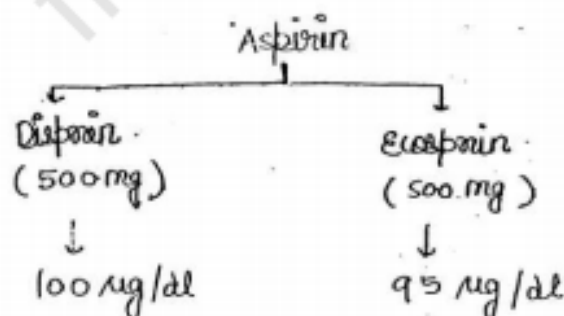


- AUC $\rightarrow$ Tell about extent of absorption.
- Tmax $\rightarrow$ Tell about rate of absorption.
 - Tmax low $\rightarrow$ then use in emergency.
- Cmax $\rightarrow$ always lies b/w two line (MEC & MTC)
- MTC $\rightarrow$ max therapeutic conc

$\longleftrightarrow$ Bioequivalence $\longrightarrow$

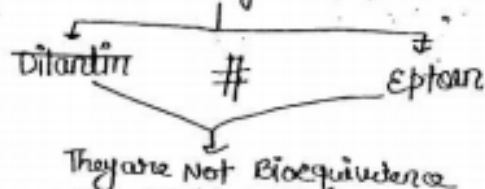
• If Biobility of 2 Brand of same drug is similar then they are said to be bioequivalence (± 20) $\leftarrow$ Not same

EX $\rightarrow$



• Imp

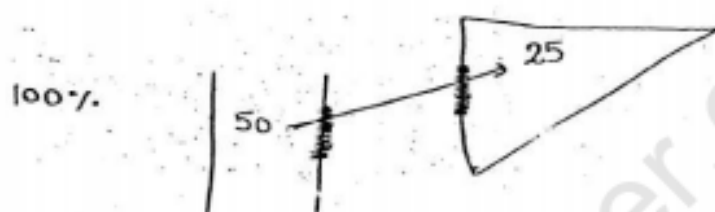
Phenytoin $\rightarrow$ brand are Not bioequivalence



Excipients $\rightarrow$ any things apart from active ingredient of that drugs

Use for $\rightarrow$ • stabilized the drugs
• Improve the taste of drugs.

$\leftarrow$ Distribution $\rightarrow$



• lipid soluble drug have higher distribution

• Plasma protein binding $\propto \frac{1}{\text{Distribution}}$

> Plasma Protein $\rightarrow$ Albumin $\rightarrow$ acidic drug bind to albumin
 α_1 -Acid Gp $\rightarrow$ Bind basic drugs.

sulfonamide $\rightarrow$ 99% plasma protein binding
• Acidic in nature

Displacement rxn $\rightarrow$ when two drug taken & having both drug more plasma protein binding
~~same nature~~
eg $\rightarrow$ warfarin & Sulfonamide

- φ Dilaysis is ineffective those drug having High plasma protein Binding
- φ Dilaysis is Ineffective those drug having High V_d
- φ Dilaysis Effective when drug have $\rightarrow$ low V_d & low PPB.
- $\rightarrow$ PPB $\rightarrow$

- D $\rightarrow$ Displacement $\propto$ n
- D $\rightarrow$ Distribution $\propto$ n
- D $\rightarrow$ Dilaysis Ineffective.

Barriers

φ BBB

Circumventricular organs $\rightarrow$ area of Brain having No BBB

- Eg $\rightarrow$
- Area Postrema
 - Post. pituitary
 - Sub farnical organ
 - Organum vasculosum
 - Lamina Terminalis
 - Chemoreceptor trigger zone (CTZ)
- $\hookrightarrow$ on stimulation cause vomiting

φ antiemetic Drug & antipsychotic drug can not cause vomiting

φ Blood Placental Barrier $\rightarrow$ cause Teratogenicity

Ex $\rightarrow$ Thalidomide

$\hookrightarrow$ Earliest use in morning sickness but now not use

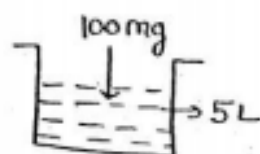
Cause $\rightarrow$ Phocomelia

$\leftarrow$ (See Limbs)

use for $\rightarrow$ multiple myeloma
bt C/I in Pregnancy

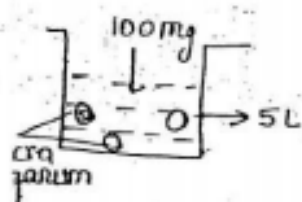
apparent Volume of dist. (V_d)

$$V_d = \frac{\text{Amount of given drug}}{\text{Plasma conc}}$$



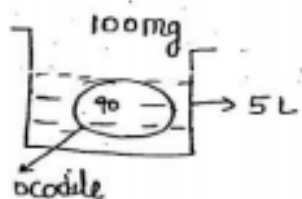
$$P_c = \frac{100}{5} = 20 \text{ mg/dl}$$

$$V_d = \frac{100}{20} = 5 \text{ L}$$



$$P_c = \frac{50}{5} = 10 \text{ mg/dl}$$

$$V_d = \frac{100}{10} = 10 \text{ L}$$



$$P_c = \frac{10}{5} = 2 \text{ mg/dl}$$

$$V_d = \frac{100}{2} = 50 \text{ L}$$

Clinical Imp of $V_d \rightarrow$

Chloroquine $\rightarrow V_d > 1300 \text{ L}$

• max V_d

loading dose $\rightarrow$ Initially higher dose is given to start the effect of drug

$$LD = V_d \times \text{Target } P_c$$

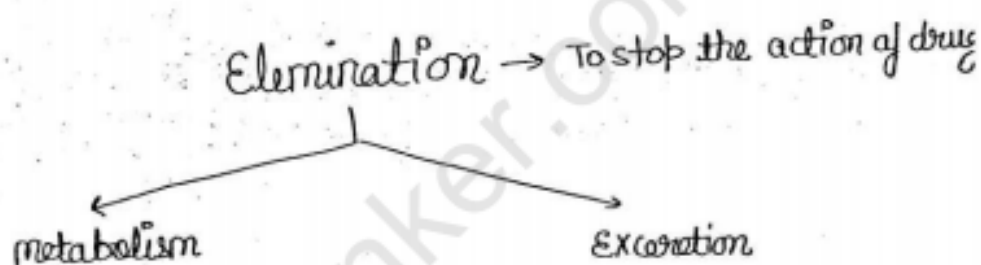
$\rightarrow$ Loading dose depend upon distribution

Φ Maintenance dose →

- Do not depend on distribution

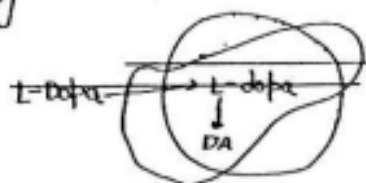
$$MD = \text{clearance} \times \text{Target PC}$$

Maintenance dose depend upon clearance.



← Metabolism →

- Active $\xrightarrow{\text{metabolised}}$ Inactive
- Active $\xrightarrow{\text{metabolised}}$ Active
eg → Diazepam → Oxazepam
- Inactive $\xrightarrow{\text{metabolism}}$ Active
↓
K/a Prodrug
eg → Levodopa





← Pro Drugs →

ALL → ACE Inhibitor (excepted → captopril
Lisinopril)

Prefer → Prednisone

Doing → Dipivefrin

M → methyl dopa, minoxidil, mercaptopurine

D - L- DOPA

In

Clinical → cyclophosphamide, carbimazole

Subject → sulfasalazine

! main purpose of metabolism to make Drug water soluble
! after metabolism all drug are water soluble.



Phase I rxn

Oxidation

Redⁿ

Hydrolysis

Cyclization

Deamination

Phase II rxn

Glucuronide

Glutathione

Acetylation

Methylation

Sulfat

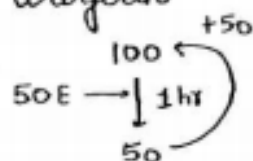
• most of prodrug formed by phase I except minoxidil in phase II rxn.

Enzymes

microsomal
(E.R)

• Can be Induced or Inhibitor

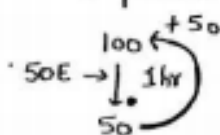
• warfarin



Non microsomal.

• Not Induced or Inhibitor

• Heparin



← Enzyme Inducer →

- G → Griseofulvin (anti fungal)
- P → Phenytoin
- R → Rifampicin
- S → Smoking (Nicotine is Not)
- Cell → CBZ → Polycyclic aromatic Hydrocarbon
- Phone → Phenobarbitone

Enzyme Inhibitors

- it → Valproate
 - < → Ketoconazole
 - in → Cimetidine
 - ues → ciprofloxacin
 - zyme - Erythromycin
 - hibition → INH
- it & are Not Enzyme Inhibitors

CYP (cytochrome P450)

wavelength.

CYP 3A4

↓
Gene
Pigment

↓
Subtype

→ CYP3A4 → m/c Enzyme metabolised the drugs.

→ CYP2D6

↓
Sex HR ↑
Depression

• Beta Block

• Depression Drug →

MAOI

SSRI

SNRI

• antiarrhythmic drug → Except Amiodarone

→ CYP2C9

• Clotting → warfarin

• phenytoin

→ CYP2C19

• Clopidogrel (Prodrug)

⊖
omeprazole.

→ CYP2E1

• Enflurane

• PCM

Drug metabolised by CYP3A4

C - Cyclosporin

T → Tacrolimus

S → statins

C → CAT Drug → C → Cisapride

A → Astemizole

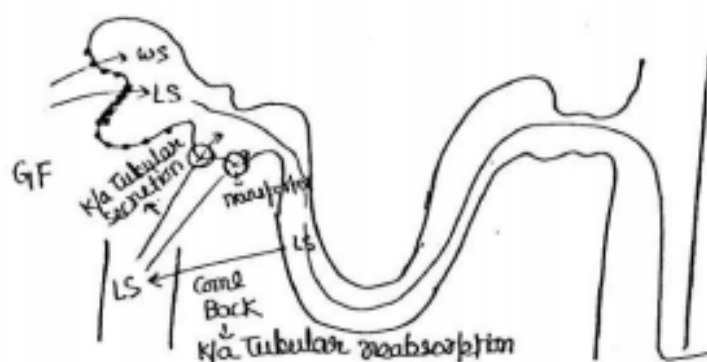
T → Terfenadine

A → Amiodarone

N → NAVIR Last में आये

} → cause
QT
prolongation
So it is
Banned

Excretion



* Lipid soluble drug
Reabsorbed & come back
but w. soluble can
not come back

* water soluble drug
excreted

all the drug can filter by glomerulus b/c lipid soluble can cross the memb & water soluble can cross by pores.

(N) GFR $\rightarrow$ 125 ml/min

Aspirin poisoning $\rightarrow$ NaHCO_3 (make urine alkaline so it can not go to lipid soluble & absorb back)
No any antidote
so +/r give $\rightarrow$ NaHCO_3

Acidic Drugs $\rightarrow$ B $\rightarrow$ Bicarbonates
A $\rightarrow$ Aspirin
M $\rightarrow$ methotrexate

Amphetamine $\rightarrow$ NH_4Cl is given
poisoning

Morphine antidote $\rightarrow$ Naloxone given
Acidic transporter
Basic transporter

Two type of transporter $\oplus$ on Proximal Tube

these tubules are saturable $\rightarrow$ (at a time only one substance can go)
Ex $\rightarrow$ penicillin $\rightarrow$ very low $\rightarrow$ b/c tubular secretion

if clearance is more than filtration the Tubular Secretion must be added.

if clearance is less than filtration the Reabsorption must be @

↳ $V_d = \text{amount given} / PC$

↳ $LD = V_d \times \text{target PC}$

↳ $MD = CL \times \text{Target PC}$

↳ Rate of elimination $\rightarrow$

↳ Clearance $\rightarrow \frac{\text{Rate of elimination}}{PC}$

Half life $\rightarrow$

$$t_{1/2} = \frac{0.693 \times V_d}{CL}$$

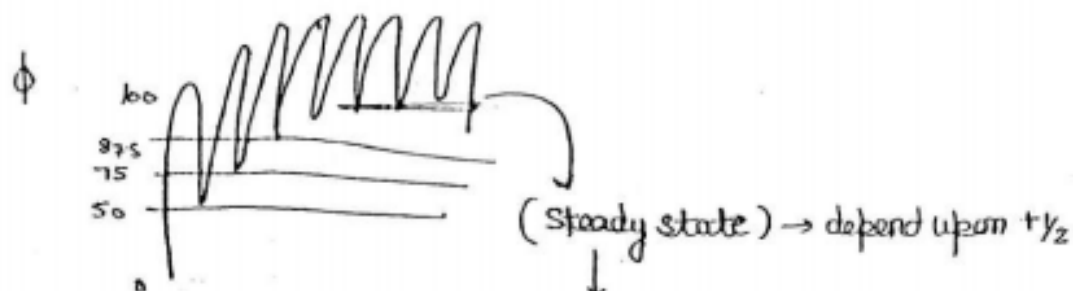
half life can not tell exact dose.

it tell about dosing interval or frequency.

100
↓ $t_{1/2}$
50
↓ $t_{1/2}$
25
↓ $t_{1/2}$
12.5
↓ $t_{1/2}$
6.25

φ $t_{1/2} = 6 \text{ hr}$
after 1 day
Drug remains $\rightarrow$?
↓
after 1 day = $4 t_{1/2}$
ans $\rightarrow 6.25$ remain

φ $T_{1/2} = 6 \text{ hr}$
after 1 day how much is eliminated.
Ans $\rightarrow 100 - 6.25 = 93.75\%$



- * * . Achieved after $4-5 t_{1/2}$
- Conc of steady stat depend upon $\Rightarrow$ dose
- Variation b/w peak & trough $\rightarrow$ depend upon frequency of Dosing Rate.

← ORDER of Kinetics →

First order

- fraction const.

100
↓ 1 hr
50
↓ 1 hr
25
↓ 1 hr
12.5
↓ 1 hr
6.25

- Rate of elimination $\propto [PC]^{\text{order}}$
- Clearance $\rightarrow$ Const
- $t_{1/2}$ (half life) = const

Zero order

- Amount const.

100
↓ 1 hr
80
↓ 1 hr
60
↓ 1 hr
40
↓ 1 hr
20

- Rate of elimination $\rightarrow$ Const.
- clearance $\propto \frac{1}{PC}$
- $t_{1/2}$ (half life) $\propto PC$

Drug following Zero order kinetics

↓
• k_a saturation kinetics

• k_a pseudozero order kinetics

Zero

W - warfarin

A - Alcohol / Aspirin

T - Theophylline

T - Tobutamide

Powen - Phenytoin

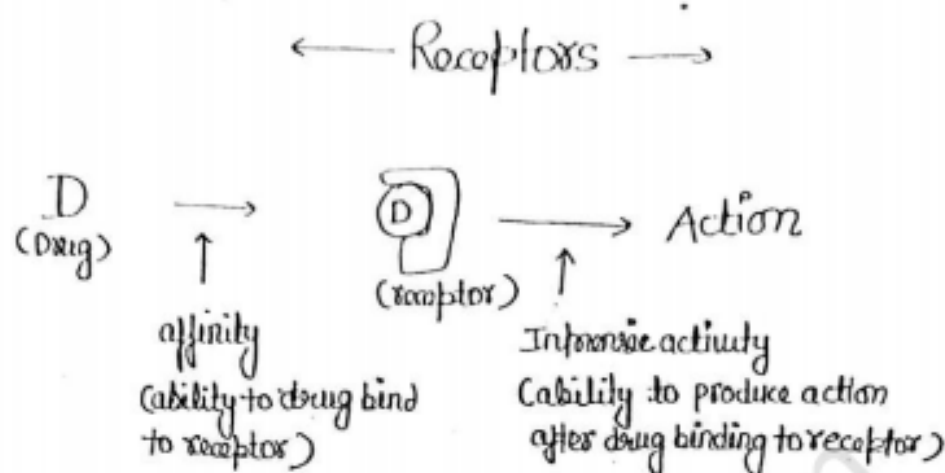
- i) Aspirin → use →
- antiplatelet - 300
 - fever → 600
 - Pain → 900
 - Inflammation 2000
- } Low Dose
↓
it follows
1st order kinetics
- } High dose
↓
it follows
zero order
kinetics
- ii) Zero order kinetics can be convert in 1st order kinetics

← Pharmacodynamics →
Effect of drug on the body.

- φ Physical
- φ Chemical
- φ Enzyme
- φ Receptors.

Enzyme Inhibitors

	K_m	V_{max}
① Competitive ↳ ① reversible But organophosphate are irreversible	↑	—
② Non-competitive ↳ ② irreversible but carbonic anhydrase are reversible	—	↓
③ un-competitive ↓ Ex - lithium -	↓	↓



Agonist → max Intensive activity +1

Partial agonist → sub max Intensive activity 0 to 1

Inverse agonist → have opposite action -ve

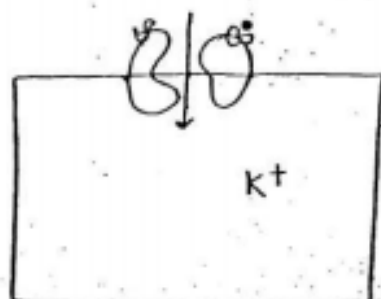
Antagonist → No action/effect 0

us → Partial agonist ?

- ① High Affinity & High IA
- ② Low affinity & Low IA
- ③ Low Affinity & High IA
- ④ High & Low IA

← Signal transduction mechanism →

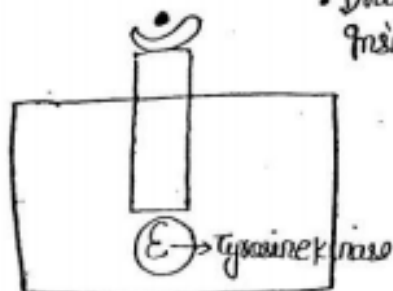
- ① Ionotropic Receptors → • Drug bind gate open. 2 in millise
✓ fastest action.



- EX → • CNS → { GABA_A
Glutamate → NMDA
• NN } Nicotinic
• N1
• 5HT₃

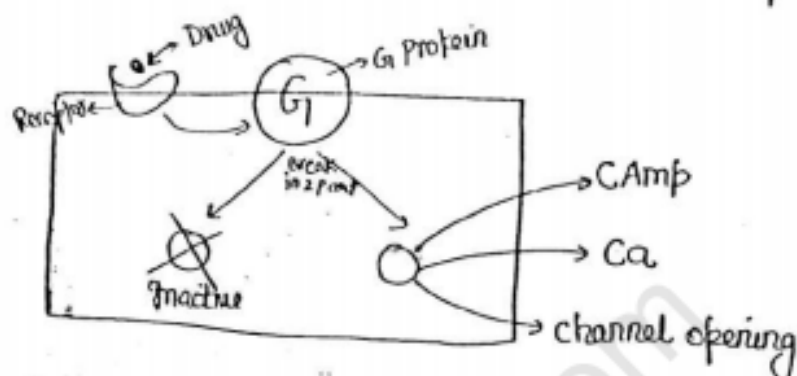
- ② Enzymatic Receptors → k/a Tyrosine kinase receptor.

• Drug bind out side & enzyme active inside



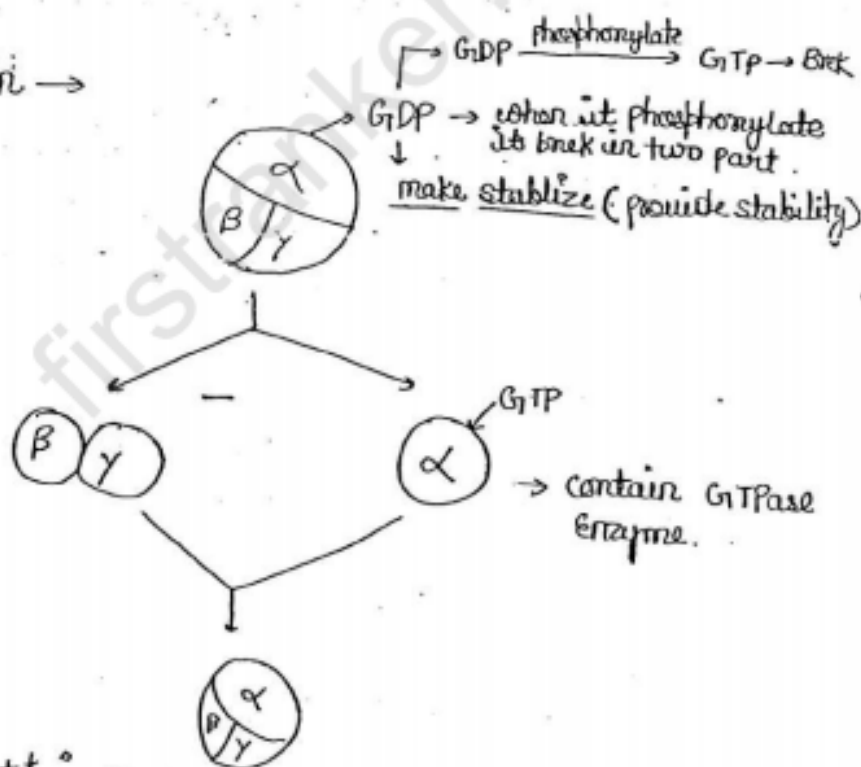
- EX → P → Prolactin
I → Insulin, Not GHRT
G → Growth hormone
C → Cytokine → IL, INF
IGF, IFN

3) G_i-protein coupled Receptor → 99% Drug work
 ↳ this receptor



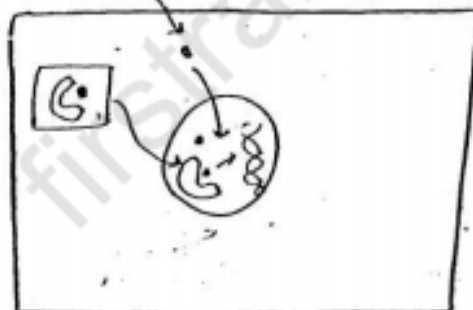
CAMP → stimulate heart.
 & Relaxes other part of body.

• G_i-protein →



↳ CAMP & Ca⁺⁺ is Second messenger.

⊕ Intracellular Receptor → • Only lipid soluble can cross & bind on these Receptor
• Slowest acting receptor



Ex → Nuclear Receptor

Sex → Hormone → Estrogen
Progesterone
Testosterone

A → Vit A

T → I_3 , I_4

cytoplasmic Receptor

C → Corticosteroid

D → Vit-D
Glucocorticoids → Mineralocorticoids

⊕ if asked Nuclear Receptor Superfamily then both cyto & Nuclear Receptor

Qus → Nuclear Receptor ?

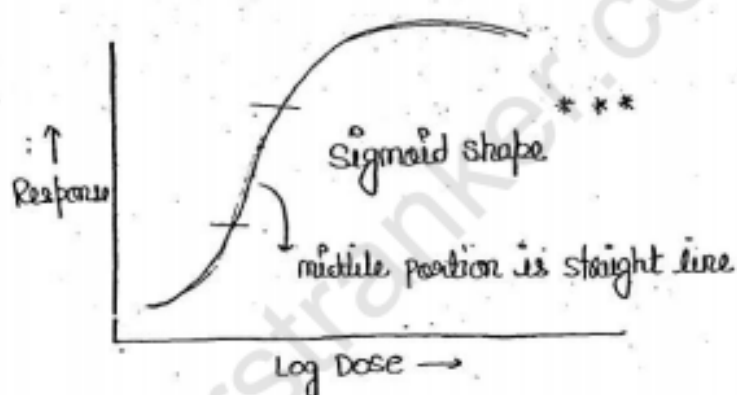
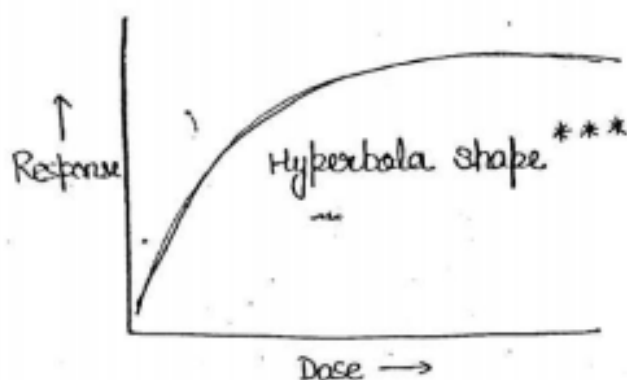
- ① Aldosterone.
- ② calcitriol
- ③ Thyroxine
- ④ all of these

Qus Nuclear mechanism

- ①
- ②
- ③
- ④ all of these

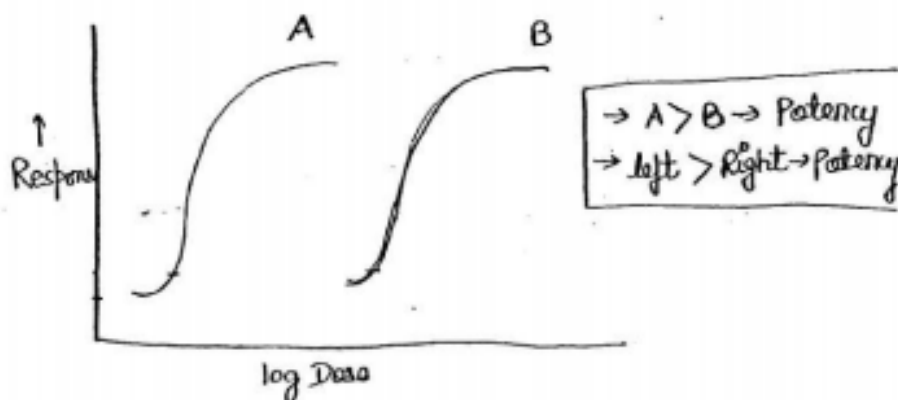
firstRanker.com

← Dose Response curve →

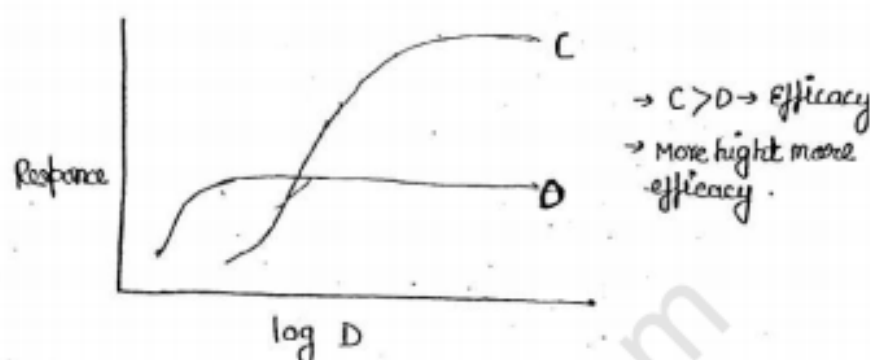


φ log DRC →

→ Potency → (Power) →



↳ Efficacy



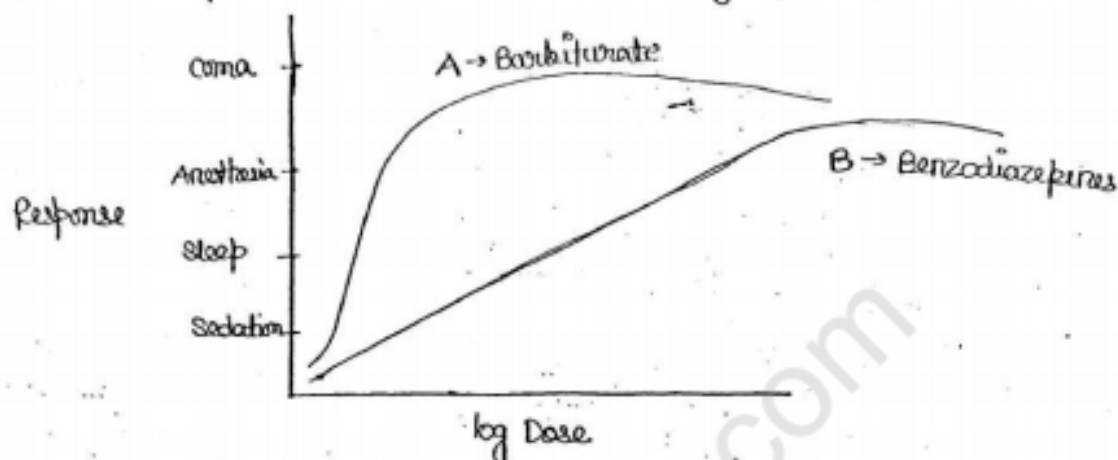
↳ Efficacy is clinically more important than potency.

↳ Efficacy vs Effectiveness
 ↓ ↓
 (under control condⁿ) under clinical condⁿ

↳ graph se efficacy bat sakte h. Not effectiveness

(15)

φ SLOPE → Tell about safety of Drugs

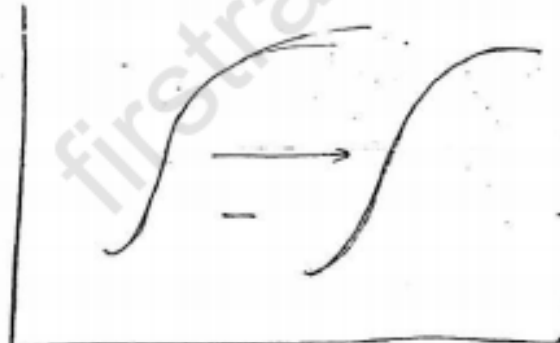


φ if steeper slope → unsafe

φ if less steeper → safe. B safe than A

Effect of competitive & Non competitive on DRC curve

① competitive Inhibitors



φ in competitive Inhibitors → Potency ↓

φ Non competitive Inhibitors → Efficacy ↓

***** ← Therapeutic Drug monitoring →

- adjusting the dose of drug according to plasma conc. is TDM
- TDM is never done for →
 - ① antihypertensive drug
 - ② antidiabetic drug
 - ③ anticoagulant drugs.

penicillin is very safe drug so TDM never done for penicillin

Therapeutic Index →

TDM is in small therapeutic index.
TDM is not done in large therapeutic index.

TDM Done in →

- 1) Narrow therapeutic index.
- 1) can not check response.
- 1) Drug so variation in conc.



(16)

φ TDM is done for →

A → Aminoglycosides

Drug → Digoxin

Possessing → Phenytoin (all antiepileptic drug)

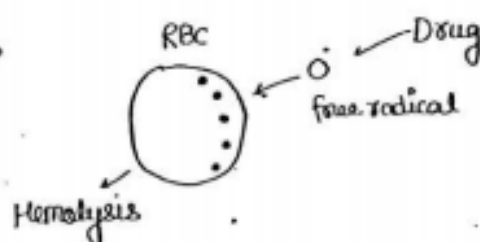
Low → Lithium

Therapeutic → TCA

Index → Immunosuppressant → cyclosporin
Tacrolimus

***** ← Pharmacogenetics →

1) G6PD deficiency →



- Primaquine
- Sulfonamide / Dapsone
- Nitrofurantoin
- Furazolidone

} these Drugs cause Hemolysis in those pt G6PD Deficiency

2) Acetylation → (N-acetyl transferase)

↑ high acetylation → less effective

(N) - INH - 300 mg

↓ → Peripheral neuropathy
(slow acetylation)

→ Drug metabolised by Acetylation →

S → Sulfonamide / Dapsone

H → Hydralazine

I → INH

P → Procainamide

} they also cause SLE



③ Sch Induced apnea →

↓
Succinyl choline → muscle relaxant

⊙ shortest acting (< 5 min)

↓
b/c it metabolised by pseudocholinesterase enzyme
these are ⊕ in large amount in plasma.

⊙ used for ET Tube Intubation.

↓
Time for ET Intubation → 5 Sec.

Some people atypical pseudocholinesterase enzyme deficiency
↓ (T_{1/2} > 1/2 hr)

work slowly

↓
Sch can't break

↓
It will affect other muscle

Diaphragm & Intercostal muscle

↓
Diaphragm & I. muscles relax

↓
cause Apnea

***** ← Clinical trials →

→ it is Testing the drug in human beings

→ Licence authority → DCGI / US-FDA

• Drug controller
 • General of India
 • Headquarter → Delhi
 • Rofecoxib → like aspirin
 • Not cause peptic ulcer
 • b/c cause MI

→ Investigational New Drug Application (INDA)

Phase I → • Done in Healthy Volunteer. (b/c see for side effect)
 • Can not know efficacy of Drug.
 • K/a Dose finding study.
 • measure Maximum Tolerable Dose → main aim of Phase I
 • Safety also known

Phase II → • Done in pt. (20-100 pt. takes)
 • Know the efficacy & safety of the drugs.
 *** Indication of efficacy

Phase III → • Done in pt. (up to 5000 pt.)
 • pt. taken from multiple center.
 • Know efficacy & safety of drug → **** confirmation of efficacy

Phase IV → • NDA (New Drug application)
 • Seen Rare side effect → $< 1/20,000$
 • Seen also long term side effect.
 • max no of pt (volunteer)

← Phase 0 (zero) →

- Done in Healthy volunteers.
- its Not Mandatory
- given very small dose (microdosing study)

↓
attache a radio labeled in drug & seen
where the drugs goes (can see pharmacokinetics
of Drug)

← Placebo →

- Control Blinding
- Single Blind study → • Done in phase II
• only subject are blind
- Double Blind study → • Done in phase III
• both Investigator & subject are blind
- phase I is open study

Pharmacovigilance

- Study of adverse effect is pharmacovigilance
- Detection
- assessment
- understanding
- Prevention



⌀ Adverse event → any thing wrong in pt taking drug

← Pharmacovigilance programme of India →

↓
AMC → • ADR Monitoring center.

• Name of software → VigilyLow ***

↓
Data record in

• NCC → National co-ordinating centre)

• Indian Pharmacopoeia commission → Gaziabad

International co-ordinating center → Upsala monitoring center → Sweden

← ORPHAN DRUG →

• Drug use for rare disease - (< 200 000 pt worldwide)
Expenses can not be met by selling the drugs
↓
K/A rare disease
• in developing country some common Disease Drugs
are also orphan Drugs.

(1)

← Drug label →

- Name of the Drug $\left\{ \begin{array}{l} \text{generic name} \\ \text{Brand Name} \end{array} \right.$
- Abbreviation → IP → Indian pharmacopia
BP → British pharmacopia
USP → US pharmacopia.
BNF → British National formulary
- Expiry date → JUNE 2016 → means 30 June के बाद use नहीं कर सकते
- Schedule H / OTC →

↓
only take
Dr prescription

↓
over the counter
take without Dr. prescription
- frozen → -20°C
- cold → $2-8^{\circ}\text{C}$
- cool → $8-25^{\circ}\text{C}$
- ⊕ Shelf life → Total period of drug (जब से बना और जब expired किया)

← Drug Promotional Literature →
(DPL)

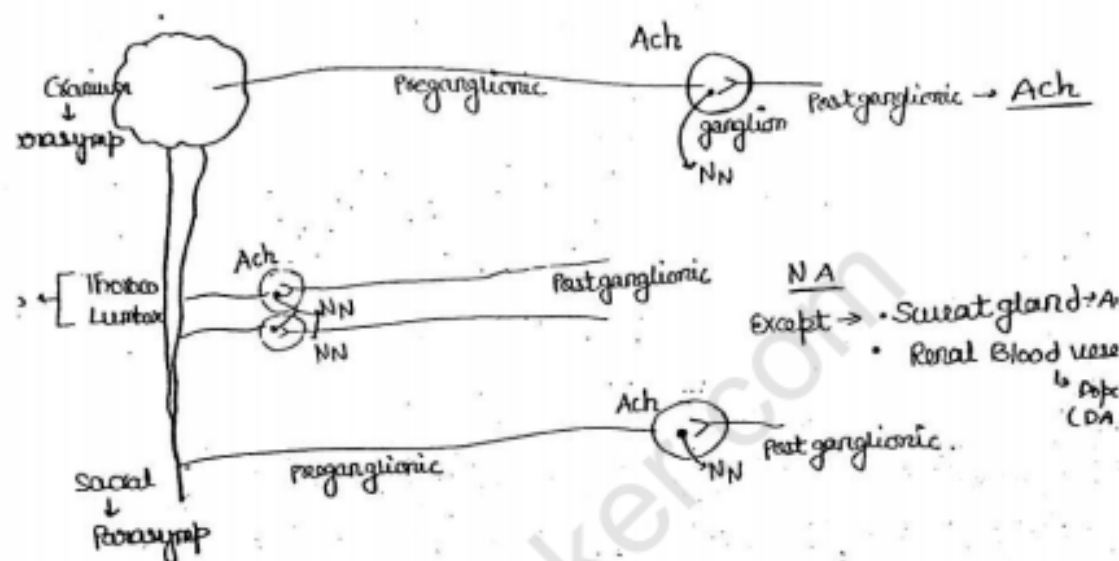
• Name of Drug (generic Name)

Not > 3:1 size of generic & brand name
1 3

Expiry date is not required

S/E ⊕

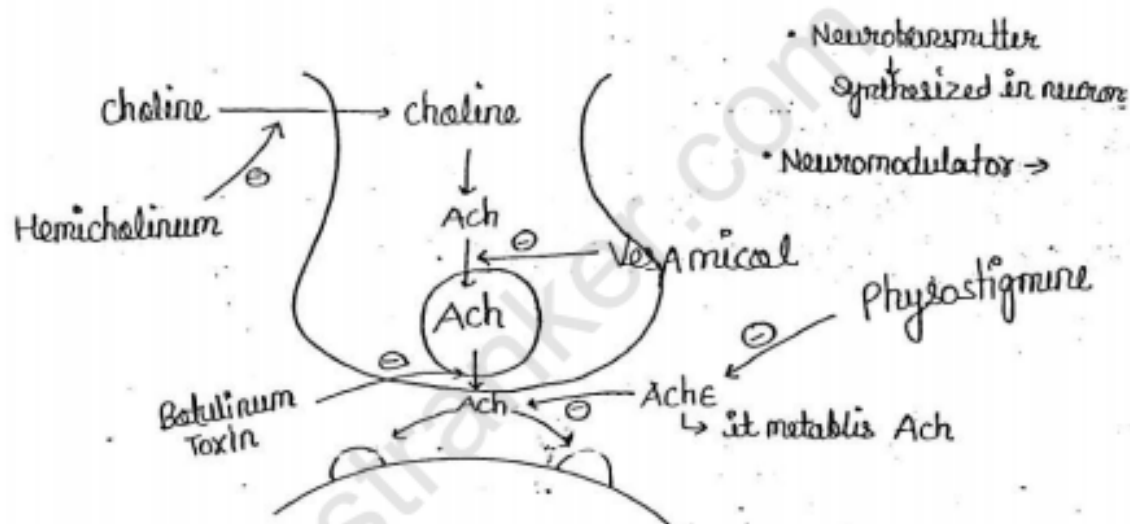
← Autonomic Nervous System →



	Parasympathetic	Sympathetic
Heart	depressed ↓↓ rate & conduction ↓ Not contractility	stimulate +++ Rate cond ⁿ contract
Stomach	↑	↓
Bronchus	Bronchoconstriction	Bronchodilation
Int. IT	Diarrhea	constipation
Bladder	↑ out flow	↓ out flow
Salivary gland	↑ secretion	↓ secretion (except sweat ↑)
Pupil	Miosis	mydriasis

Parasympathetic

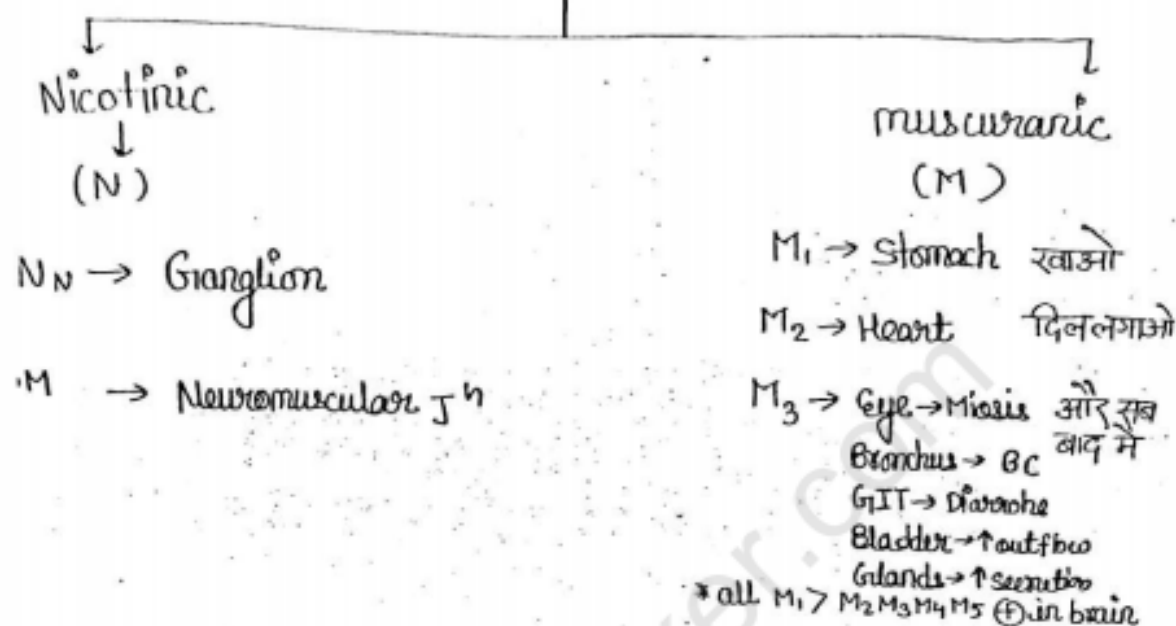
- origin from Cranio Sacral out flow
- Cranial → 3, 7, 9, 10
- Sacral → S2, S3, S4
- preganglion are long & post ganglion - short.



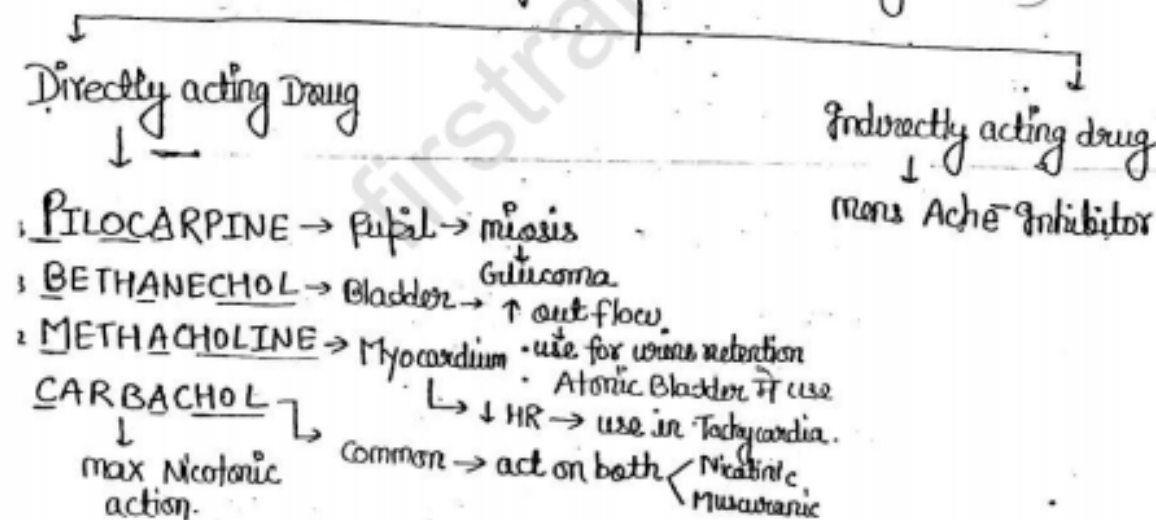
- rate limiting steps → uptake of choline / entry of choline
- Hemicholinium Inhibit the entry of choline in neuron.
- VesA micol → Inhibit the entry of Ach in vesicle.
- Botulinum toxin → Inhibit the release of Ach.
- Physostigmine → Inhibit the AChE



Receptors



Parasympathomimetic drugs





(2)

Indirectly acting Parasympatholytic

↓
AChE Inhibitor

Reversible

Lipid soluble

Physostigmine

- Cross GI memb
- Eye memb cross
- BBB cross
- use → Eye (Glaucoma)
- Atropine poisoning

Water soluble

Neostigmine

- Not cross
- Not cross
- Not cross

Irreversible

↓
• Organophosphate

• Malathion

• Parathion

• Carbamates

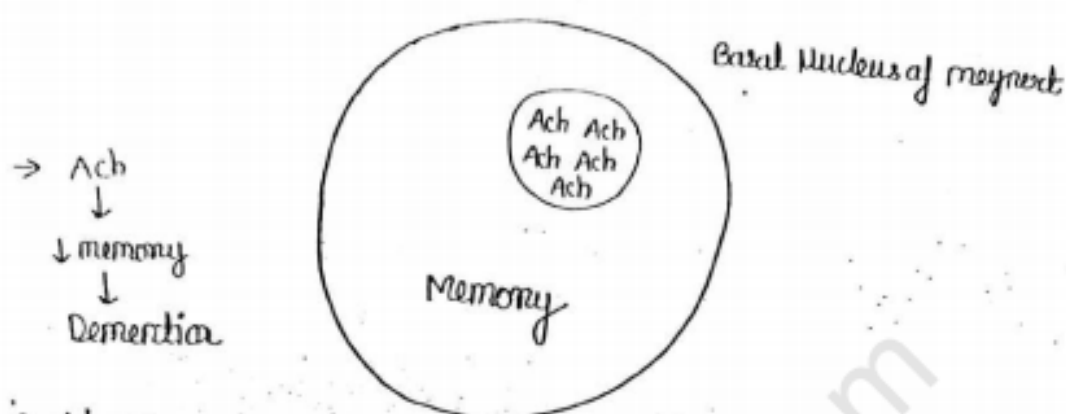
• Carbaryl

• Propoxur

Atropine poisoning → Atropine lipid soluble

- it is muscarinic blocker → M₁ #
- M₂ #
- M₃ #

• Physostigmine is DOC for Atropine poisoning

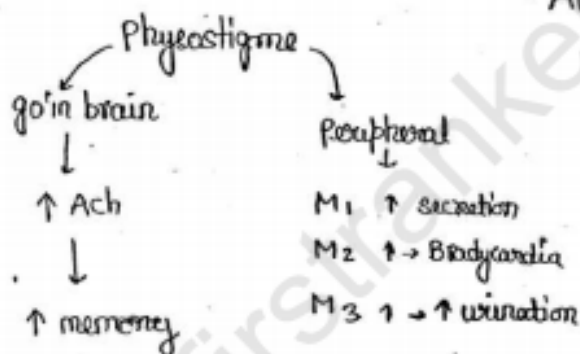


in old age → loss of memory → k/a Senile dementia

• Alzheimer's > 60 yrs

↓
DOC

D → Donepezil
R → Rivastigmine
G → Galantamine



‡ TACRINE → • almost 99% goes in brain
• it just like physostigmine
• short acting

‡ Donepezil
Rivastigmine
Galantamine } • Hepatotoxic.
• lipid soluble like Tacrine
• Long acting
• Not Hepatotoxic

- φ Neostigmine
- Pyridostigmine
- Edrophonium

Myasthenia gravis

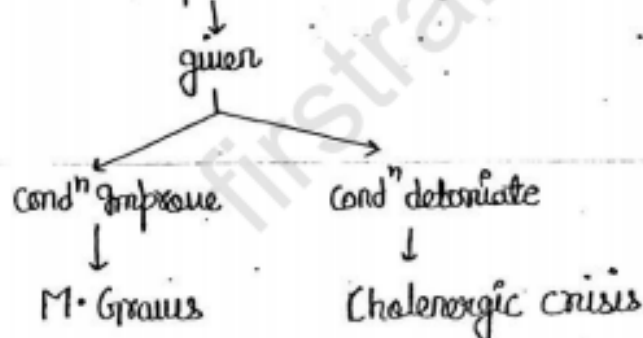
- φ Autoimmune ds.
- φ NM receptor के against antibody बन जाती है।

Symptoms → muscle weakness, ptosis

• Levator palpebrae superioris (LPS) → m/c muscle involved in M. Gravis

φ Cholinergic crisis → ↑ NM → muscle weakness.

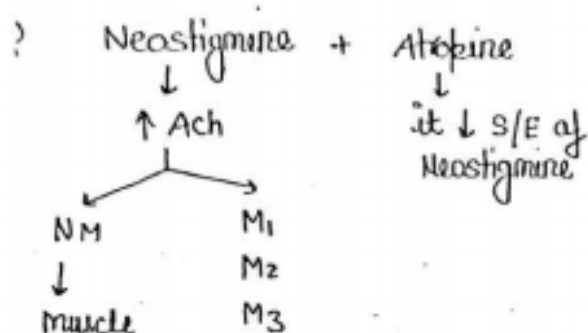
→ Edrophonium → (< 10 min)



φ Edrophonium is DOC for Diagnosis of M. Gravis
market Name Tensilon Test

→ Neostigmine } T/T of M. Gravis
→ Pyridostigmine }

φ Neostigmine + Atropine

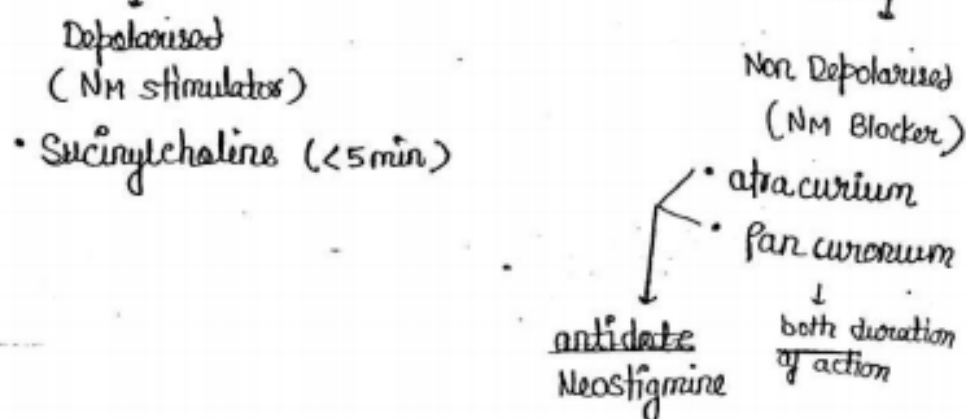


Atropine is not use in treatment of M. Gravis, becoz it use for ↓ S/E of Neostigmine

← Cobra Bite →

- φ symptom jst like m. gravis
- φ T/T of choice → antivenom
- φ T/T → Neostigmine + Atropine

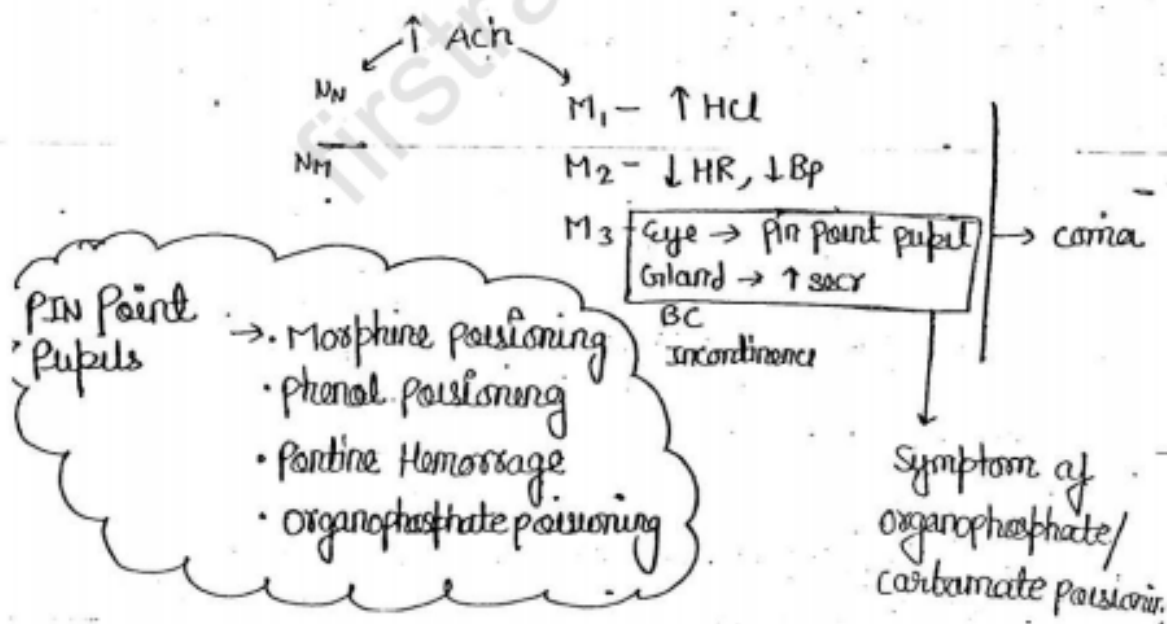
← Reversal of muscles Relaxant →



- ① M. Gravis
 - ② Cobra Bite
 - ③ Reversal of muscle relaxant
- } → Nicotinic use
Neostigmine + Atropine
- ④ Post operative paralytic ileus → M₃ → Neostigmine only.
 - ⑤ Post operative urinary retention → M₃ → Neostigmine only.

Irreversible

- Organophosphates → • malathione
 - parathion
 - Carbamates → • Carbaryl
 - Propoxur
- } → Highly lipid soluble.



⚡ In OP poisoning → when NN stimulate then BP & HR ↑ but it is rare

† organophosphate poisoning

→ Doc Atropine → given i/v route.
• every 5 min

φ Sign of atropinization → mydriasis (dilate)

↓ m/c use.
it also m/c sign of
Brain death.

• ↓ Secretion → most reliable
• most specific sign

• HR ↑ > 100 (Tachycardia)

p → Atropine can not reverse → Muscle weakness

↓
i.e Nicotin receptor

← AChE Reactivators →

↓
oximes

• Pralidoxime (PAM)

• DiAcetylmonoxime (DAM)

1) Oximes are Not Doc



Oxime



only for



OP poisoning

Not for carbamates.

PAM Does Not enter in brain bt DAM Enter in brain

Aging of Enzyme

So start the oxime as early as possible
b/c after ageing enzyme oxime can not Reverse..

← Parasympatholytic Drugs →

① Stomach → M₁ → Peptic ulcer
↓
• Pirenzepine } M₁ Blocker → use in peptic ulcer
• Telenzepine
φ Atropine is C/I in peptic ulcer

2) Heart $\rightarrow$ $M_2 \rightarrow$ Atropine is Doc in Bradycardia & AV Block

- Bradycardia
- AV Block

③ Bronchus (M₃) $\rightarrow$ Ipratropium
Tiotropium $\rightarrow$ use in B. Asthma
COPD

④ Bladder $M_3 \rightarrow$
 $\downarrow$
 $\uparrow u_0$

S/E of anticholinergic $\rightarrow$ urinary retention
C/I $\rightarrow$ BPH
use $\rightarrow$ overactive bladder.

S - Solifenacin
O - oxybutynin
F → flavoxate
T - Tiotropium
Bladder → Darifenacin

use for T/T
of overactive bladder

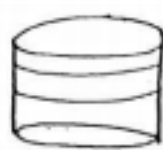
- Dorefonacin
- Sotefonacin

} → most varicoselective

→ oxybutylin → max S/E

→ Tolterodine → Can not cross BBB

Smooth muscles $\rightarrow$ M_3 $\rightarrow$ contraction of smooth muscle
K/a $\rightarrow$ Colic pain



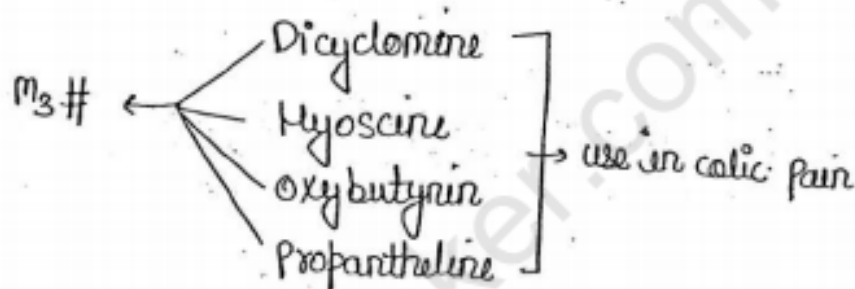
Colon



Ureter



Bladder



glands $\rightarrow$ M_3 $\rightarrow$ Block
 $\downarrow$ $\downarrow$
 $\uparrow$ secretion $\downarrow$ secretion

S/E - Dryness

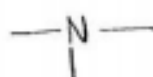
Hyperthermia

$\downarrow$
so Atropine c/I in children

$\rightarrow$ Atropine uses pre anesthetic medication

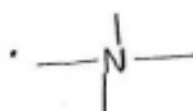
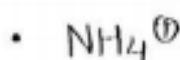
use in hyper secretion $\left\{ \begin{array}{l} \phi \text{ Glycopyrrolate} \rightarrow \text{can not cross BBB} \\ \phi \text{ Atropine} \end{array} \right.$

Tertiary amine



• lipid soluble

Quaternary Amine



• water soluble

⑦ Eye → M3 → block cause mydriasis

- So c/I in Glaucoma
- use for funduscopy

Anticholinergic M3

block

- Loss of accommodation
- Cause cycloplegia

cause blurring of vision

• use in Refraction Testing (by ophthalmologist)

use Drug → • Atropine → strongest cycloplegic drugs bt duration of action > 7da
• Homatropine
• Cyclopentolate
• Tropicamide → Doc for Refraction Testing in adult

⑧ CNS → Hyoscine (Scopolamine)

• use for motion sickness at high altitude.

• Motion due to vestibular system

• use for Prophylaxis of motion sickness NOT T/T

↓
Vestibular
vomiting center
↓
Vomiting

→ • ↓↓ CNS (depress the brain)

• use in Lie detector / Truth Serum
give i-v route

• Now a days Not use in Lie detector b/c Mortality rate is High

Mountain sickness

- at very high altitude (Hypoxia)
- DOC Acetazolamide

D Poisoning $\rightarrow$ OP carbamates Early mushroom poisoning } Doc Atropine

→ DOC for belladonna poisoning → Physostigmine

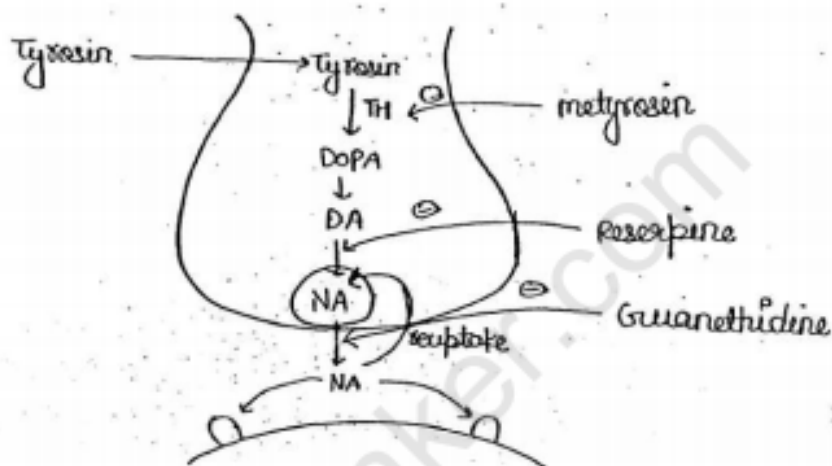
ϕ Atropine
 ϕ Datura
 ϕ belladonna

} Poisoning $\rightarrow$ Doc $\rightarrow$ Physostigmine

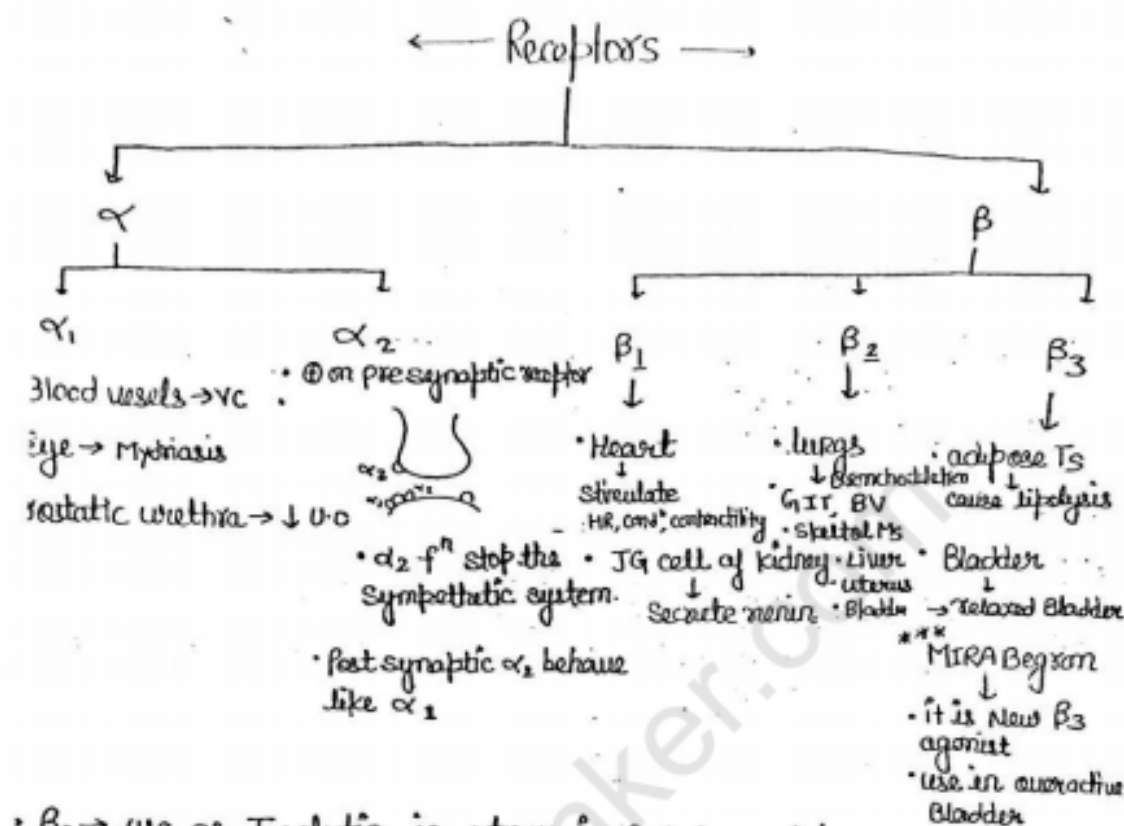
(27)

Sympathetic Nervous Syst →

- origin - Thoracolumbar outflow.



- rate limiting steps → Tyrosine $\xrightarrow{\text{Tyrosine Hydroxylase}}$ DOPA
- mettyrosin Inhibit Tyrosine Hydroxylase (competitive inhibitors)
- Reserpine
- Guanethidine
- cocaine Imipramine } they Inhibit reuptake of NA



- β₂ → use as Tocolytic in uterus in post term labour
- use as Vasodilation in Blood vessels
- But α₁ cause vasoconstriction in Blood vessels



- β₂ is more in → Heart & Spinal Muscles
- Blood vessels of skin - α₁ → Vasodilation
- No change in CNS supply
- Sympathetic over activity cause → Tremor
- B/c of β₂

Hypoglycemia → activation of Sympathetic system

β₁
↓
Stimulates
↓
↑ HR
Palpitation

β₂
↓
Tremor

Ach
↓
Sweating

} warning symptom of Hypoglycemia

β_2 stimulate $\rightarrow$ Liver $\rightarrow$

- Glycogenolysis $\oplus$ Stimulate
- Gluconeogenesis $\oplus$ stimulate
- Glycogenesis $\ominus$ Inhibit

 $\rightarrow$ $\uparrow$ Blood sugar

ϕ Hypoglycemia $\rightarrow$ Blood sugar < 60 mg/dl

So β_2 cause Reversal of Hypoglycemia

ϕ β Blocker mask the warning symptom of Hypoglycemia

ϕ But Sweating is only symptom $\oplus$ in Hypoglycemia when pt Taking β -Blocker.

ϕ β -Blocker is contraindicated in Diabetic Patient

Sympathomimetic Drugs

Directly acting

Indirectly acting

① Reuptake Inhibitor

A. Cocaine $\rightarrow$ local anesthetic

it is only L-Anest cause

vasoconstriction but all L-Anest

cause vasoconstriction

B. Imipramine $\rightarrow$ antidepressant Drug

TCA

② Displacement $\rightarrow$ Tyramine

Nasal decongestant [Ephedrine
Pseudoephedrine]

Tachyphylaxis $\rightarrow$ rapid development of Tolerance

Due to Displacement

Chess contain Tyramine

Ephedrine is Doc as Vasopressor in Pregnancy

Amphetamine $\rightarrow$ can cross BBB $\rightarrow$ $\downarrow$ sleep

$\downarrow$ Highly addictive Drug $\uparrow$ Attention

K/a RAVE DRUG

Φ MDMA → methylene, Dioxy methamphetamine

K/A → RAVE DRUG

• Amphetamine → use in Narcolepsy → ↑ sleep attack

DOC → MODAFINIL

• Attention Deficit Hyperkinetic Disorder (ADHD) → T/T Amphetamine

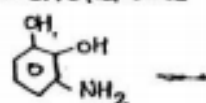
• DOC → Methylphenidate

• T/T of choice → Methylphenidate

but old time Behaviour Therapy are use

Directly acting Sympathomimetic Drug

↓
Catecholamine



Non Catecholamine

COMT → ⊕ in large quantity in GIT

• it break catecholamine

• so catecholamine do not given orally

Catecholamine

Indogenous

Dopamine

Adrenaline

Nor Adrenaline

Exogenous

Dobutamine

fenol Dopam

Isoprenaline

(Isoproterenol)



← Dopamine →

- $D_1 \rightarrow < 2 \rightarrow D_1$ in Blood vessels $\rightarrow$ cause Vasodilation
 $\downarrow$ max Renal Blood vessels
 $\beta_1 \rightarrow (2-10 \mu\text{g/kg/min}) \rightarrow$ use in CHF $\rightarrow$ Intermediate dose
 $\alpha_1 \Rightarrow > 10 \rightarrow$ it cause vasoconstriction

• use in shock $\rightarrow$ High dose Dopamine given

Shock + oliguria (renal failure) $\rightarrow$ DOC $\rightarrow$ Dopamine
 $\downarrow$
High Dose

φ जिस Drug में Dopa आयेगा वो D_1 में work करेगा, अगर नहीं है Dopa Name में तो D_1 में work नहीं करेगा।

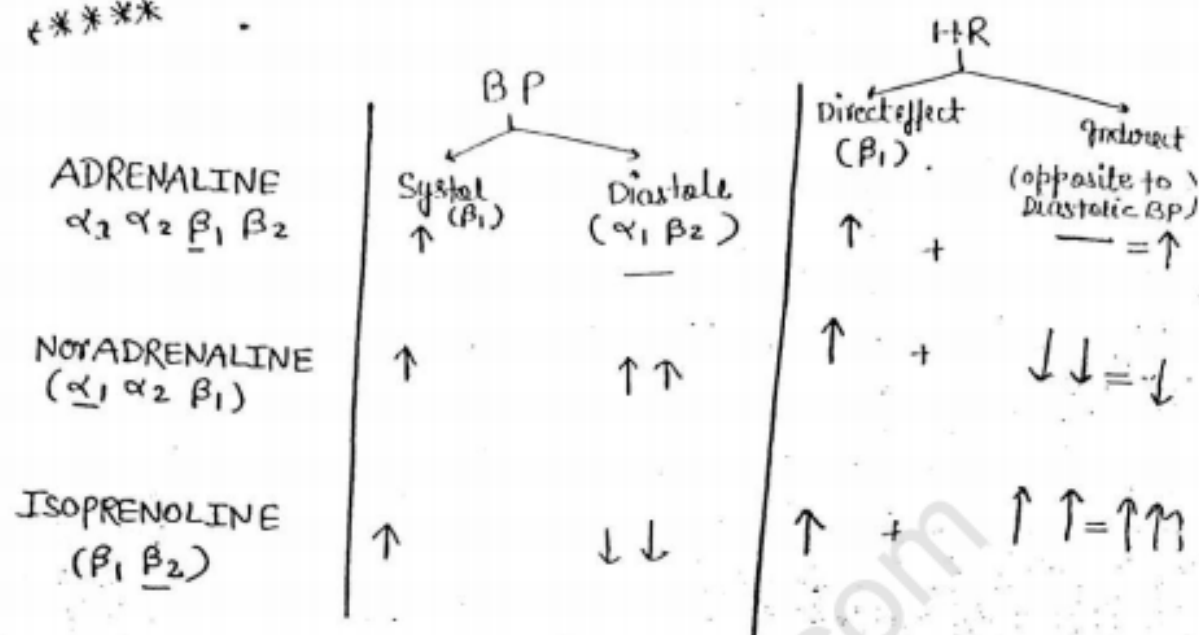
φ Dobutamine $\rightarrow \beta_1$ में work करेगा
• use in T/T of CHF

φ Fenoldopam $\rightarrow$ act only on D_1 receptor
• use in T/T of Hypertension emergency b/c it given i.v Not orally

φ Adrenaline $\rightarrow$ all the receptor में work करेगा, $\alpha_1, \alpha_2, \beta_1, \beta_2$
($\alpha_1, \alpha_2, \beta_1, \beta_2$)

φ Noradrenaline
($\alpha_1, \alpha_2, \beta_1$)

φ Isoprenaline
 β_1, β_2



Isoprenaline → Increase pulse pressure. (PP = systolic - Diast)

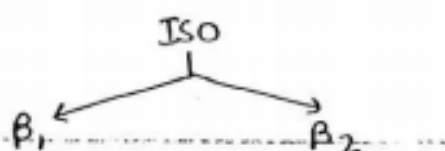
effect of Noradrenaline in (N) person → Bradycardia.

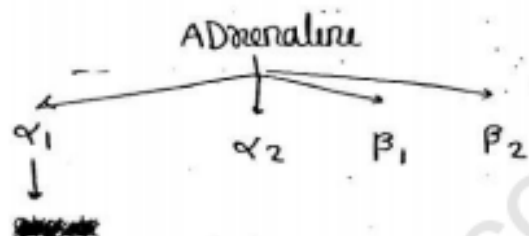
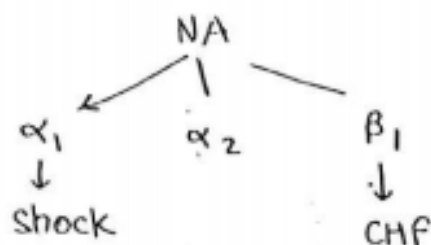
" " " Heart transplant person → only direct effect come

effect of Noradrenaline in (N) person & Atropinized → Tachycardia.

		HR
Noradrenaline	(N)	↓
	Transplant	↑
	Atropinized	↑

only direct effect
Tachycardia.





φ adrenaline → • DOC for anaphylactic shock (↑ both ↑ GPs
Bronchodilation)

• route of choice → i.m > S.C

• i.v is never done

• Conc of choice → 1:1000 solⁿ

• Adrenaline repeats when pt Not relive $\bar{c}$ in 10 min
(as soon early possible)

— • if 2 time Adr. given & not relive → then i.v given
↓
diluted then given (1:10000)

φ Cardiac Arrest → • Adrenaline give

• route → i.v (1:1000)

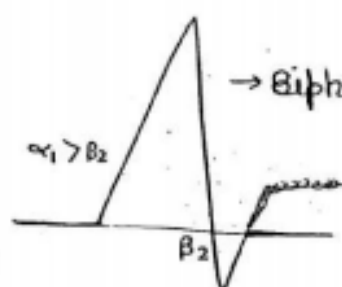
• i.v > Intraosseous (tibia में inject कर देते हैं)

• i.v > Intraosseous > Endotracheal

• Intracardiac adrenaline Never done

← Vasomotor reversal of Dale →

- (A) High dose $\alpha_1 \rightarrow$ strong
(Low dose) $\beta_2 \rightarrow$ sensitive



→ Biphasic effect of Adrenaline

BP पहले से भी ज्यादा कम हो जाता है।

when given high dose

↓
both α_1 β_2 activate

↓
Net effect Vasoconstriction

↓
↑ BP

↓
But after some time

↓
Dose metabolised

↓
Dose ↓

↓
Vasodilation (b/c of β_2)

↓
↓ BP

↓
after some time

↓
BP corrected
(b/c whole dose of drug metabolised)

Pheochromocytoma
↑ BP

Adrenaline
($\alpha_1, \alpha_2, \beta_1, \beta_2$)

↓
BP - 180

↓
α #

• BP ↓ much more

• Pt go in shock & die → b/c ~~Biphasic~~ Vasomotor reversal of Dale.

• So alpha blocker alone never given → in Adrenaline pheochromocytoma

Noradrenaline
($\alpha_1, \alpha_2, \beta_1$)

Non catecholamines

- ① α_1 Stimulator $\rightarrow$
- Phenylephrine $\rightarrow$ use in eye drop
 - cause mydriasis without cycloplegia
 - Atropin $\rightarrow$ mydriasis + cycloplegia
 - Methoxamine
 - Mephenteramine
 - Miodrine
- } use in t/t of shock & out oliguria.

- Xylometazoline
 - Oxymetazoline
 - Naphazoline
- } use in Nasal drop
↓
Nasal decongestant

- ② α_2 Stimulator $\rightarrow$
- Clonidine
 - Methyldopa $\rightarrow$ producing
- } use in HTN

• Clonidine Never suddenly stoped b/c it cause Rebound Hypertension

- Dexmedetomidine $\rightarrow$ New α_2 stimulator/agonist
 - K/A - SABA
 - use $\rightarrow$ mainly Sedation produce.

- ③ β_2 Stimulator $\rightarrow$
- (SABA) SHORT acting
 - Salbutamol
 - Terbutaline
 - (LABA) Long acting
 - Salmeterol
 - Formoterol
- } by Inhalation route
↓
in asthma

- * Salmeterol $\rightarrow$ slow acting K/A LABA
- Formoterol $\rightarrow$ fast acting $\rightarrow$ so it use both acute attack & prophylaxis
- SABA $\rightarrow$ use in acute attack of asthma
- LABA $\rightarrow$ for prophylaxis in asthma



Salbutamol → use in t/t of Hypokalemia

↓
Insulin can also be used

Ritodrine }
Isoxsuprine } → β_2 agonist → uterus relax
करने के लिए

↓
Tocolytics

Sympatholytic Drugs

α Blockers

α_2 # $\rightarrow$ Yohimbine
IDazoxan } Selective α_2 blocker.

$\alpha_1 + \alpha_2$ #
(Non Selective)

α_1 #
(Selective)

• use in Hypertension.

• Non selective blockers are use in severe Hypert.

$\alpha_1 + \alpha_2$ # $\rightarrow$ $\uparrow$ HR by α_2 blocking (Presyn) $\rightarrow$ K/a Tachycardia.

$\alpha_1 + \alpha_2$ #

Reversible

• Phentolamine

• Talazoline

• Cheez xcn $\rightarrow$ by tyramine

clonidine withdrawal $\rightarrow$ Rebound HTN $\rightarrow$ DOC

Phentolamine & Talazoline

Irreversible

$\rightarrow$ Phenoxybenzamine

use $\rightarrow$ pheochromocytoma.

ϕ cheez xcn $\rightarrow$ due to tyramine

• in this condⁿ
BP $\uparrow$

• DOC $\rightarrow$ Phentolamine
& Talazoline

MAO $\rightarrow$ Tyramine
Intestine

α_1 # (zosin)

- ① Prazosin
- ② Terazosin
- ③ Doxazosin
- ④ Alfuzosin

use
HTN
+
BHP/BPH } Doc these drugs

S/E ← Postural Hypotension/orthostatic Hypotension / first dose Hypotension

⌀

• due to α_1 #

• So α_1 # given at Bed time

α_1

α_{1A}

⊕ on prostate

α_{1B}

⊕ on Blood vessels

- Tamsulosin
- Silodosin

} they are selective
 α_{1A} #

• Doc for BPH

• They don't cause Postural Hypotension

α_1 # → Cause miosis

φ Floppy iris syndrome → occurs in pt. w/ cataract
 Sx who is on α_1 blocker for BPH

β #

$\beta_1 + \beta_2$ #
 (first generation) } Non selective β blocker.

β_1 # → Second generation

β_2 # → Butoxamine } selective β blocker

φ $\beta_1 + \beta_2$ # → • Asthma
 DM
 Peripheral vascular ds } C/I $\beta_1 + \beta_2$ #
 b/c β_2 #

← $\beta_1 + \beta_2$ # (first generation) →

① Cardioselectivity → (β_1 #) or 2nd gen β #

New → Nebivolol → most cardioselective

Beta → Betaxolol

Block → Bisoprolol

act → Acebutolol

Exclusively → Esmolol → Shortest acting β #

at → Atenolol

myo → metoprolol

carotid → Celiprolol

Safe in asthma
 DM, PVD



② Intrinsic sympathomimetic Activity (ISA) → Partial agonist

Advantage → • Does Not cause severe bradycardia.
• but it has less efficacy.

Contain → Celiprolol

Partial → Pindolol

Agonistic → Alprenolol

Activity → Acebutolol

③ Membrane stabilizing property →

- means having Na^+ channel blocking property
- Na^+ channels # = Local anesthetic property

• it is C/I in Glaucoma.

advantage → Use in arrhythmia

Posses → Propranolol (max)

Memstab → Metoprolol

Local → Labetolol

anesthetic → Acebutolol

property → Pindolol

Note → Acebutolol has cardioselective, mem stabilizer
& Intrinsic symp activity present



④ Water soluble β #

• it is C/I in Renal-failure

Ex $\rightarrow$ A Atenolol

N Nadolol $\rightarrow$ longest acting β -Blocker

S Sotalol

⑤ 3rd Generation β # $\rightarrow$ [β # + Additional cv advantage + VDe dilati

$\downarrow$

β/c it also block α #

• LABETALOL
• CARVEDILOL $\rightarrow$ they block β & α both.

$\downarrow$
carvedilol $\rightarrow$ Ca^{+2} channel #

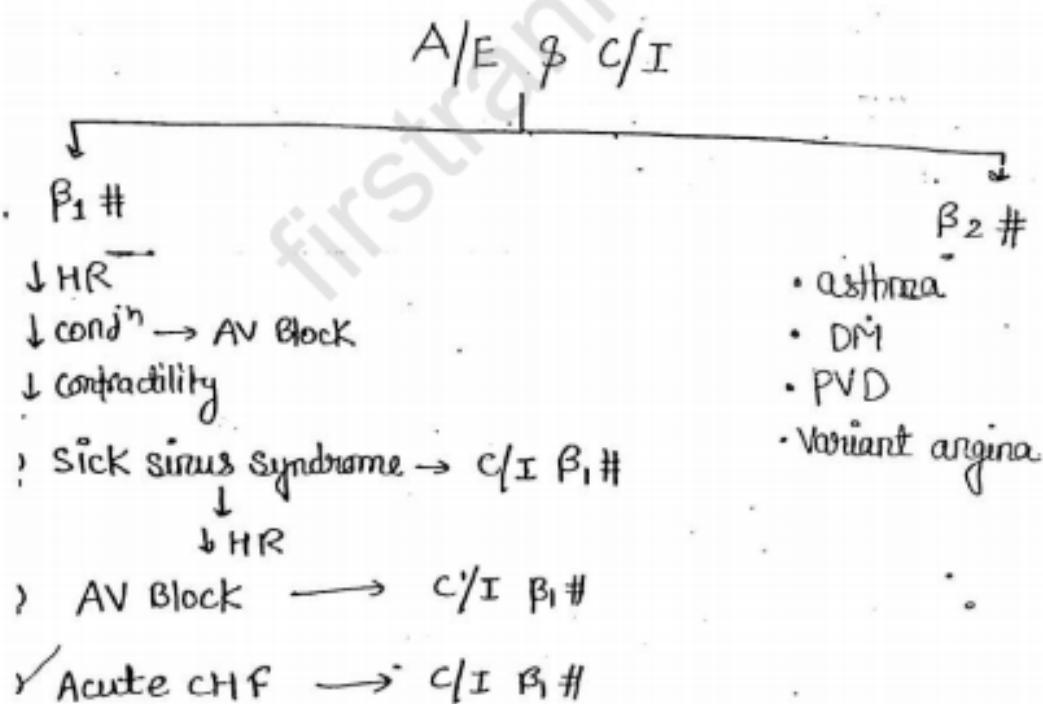
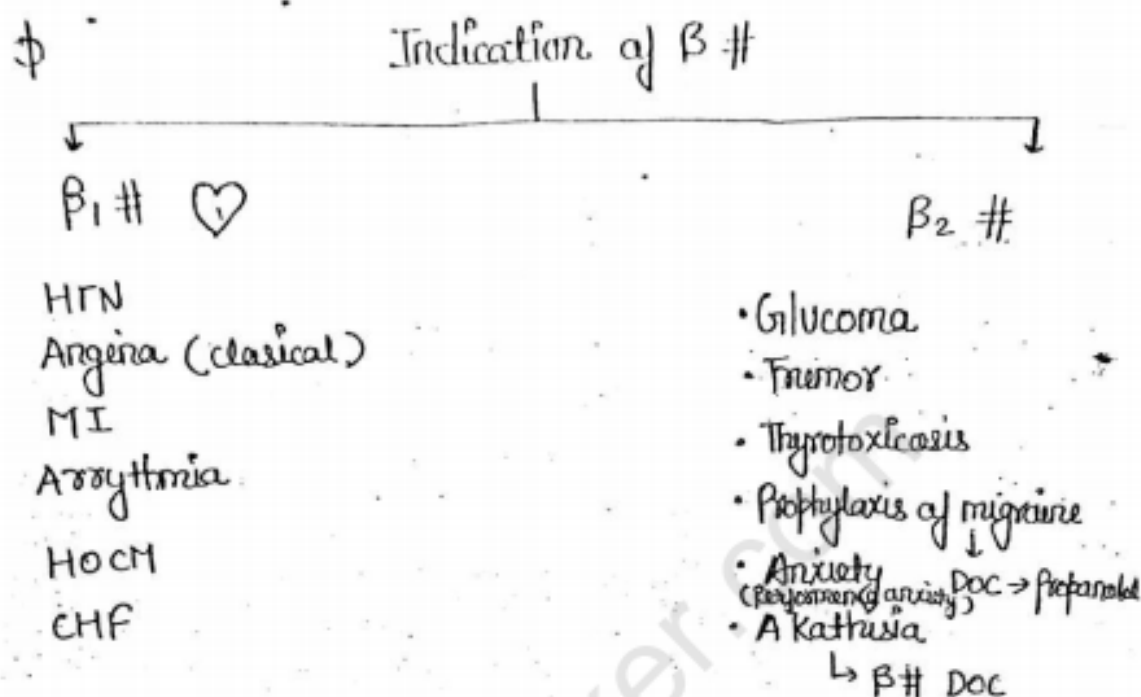
• Antioxidant property

$\rightarrow$ Nebivolol $\rightarrow$ 3rd gen β #

• it release NO (Nitrous oxide) $\rightarrow$ cause VD

$\rightarrow$ K^+ opener $\rightarrow$ Tilisolol $\rightarrow$ cause VD

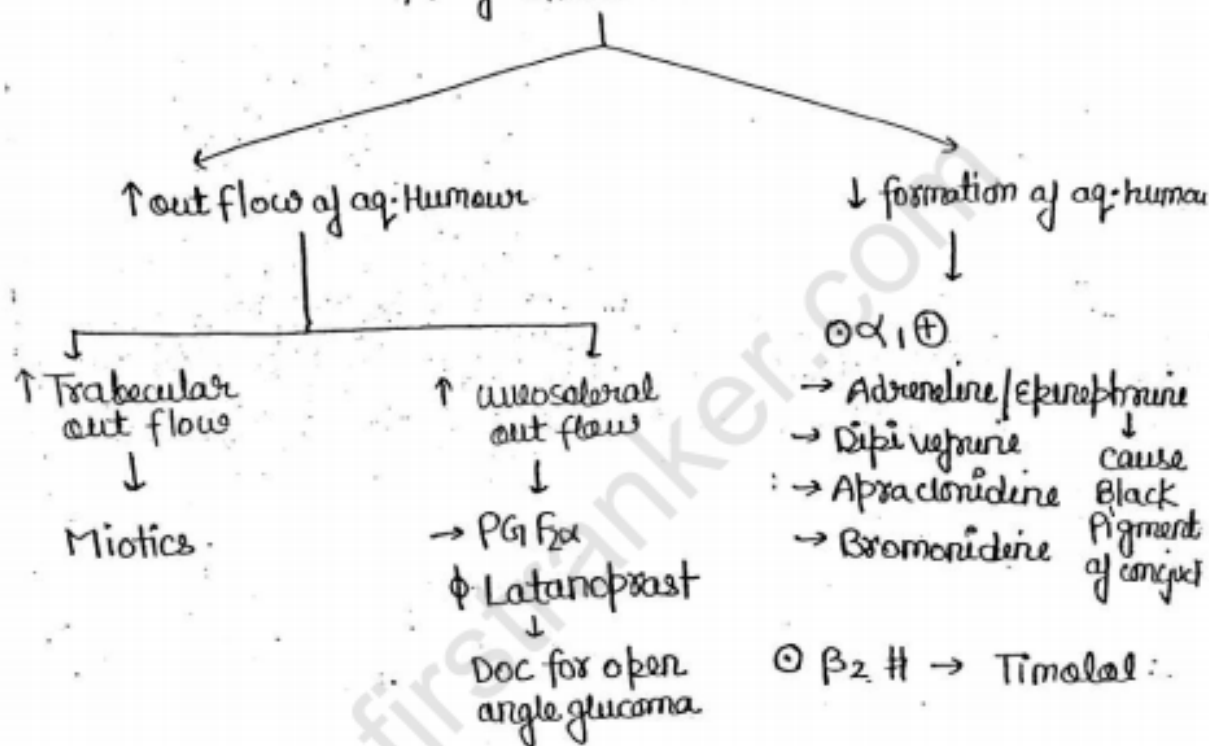
$\rightarrow$ β_2 agonist $\rightarrow$ Celiprolol $\rightarrow$ cause VD



← GLAUCOMA →

→ ↑ IOP due to ↑ Aq. Humour

T/T of Glaucoma



→ Adverse effect of Miotics → stenosis of Nasolacrimal Duct
cataract

→ Adverse effect of Prostaglandin → (PGF₂α)
Latanoprost

P • Pigmentation of Iris (Heterochromia Iris)

G • Growth of Eye Lashes → (Hypertrichosis)



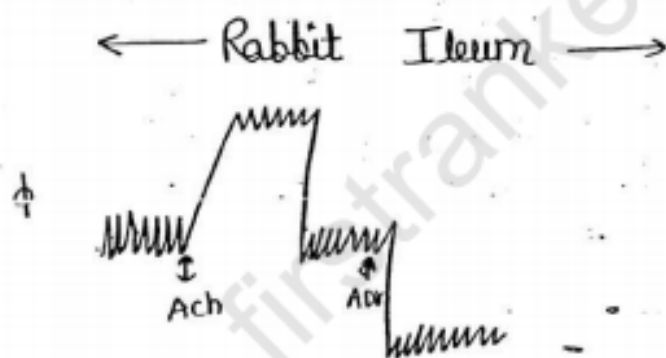
- ϕ Apraclonidine $\rightarrow$ Cause LID retraction
- ϕ Brimonidine $\rightarrow$ Cause Brain depression
 - So it CI < 2 yr children
 - also cause Iridocyclitis

firstranker.com

♂ wt of Rabbit $\rightarrow$ 1.5 to 2.5 kg (AIIMS)
 • 4-6 month old Experiment करो है
 Scientific Name $\rightarrow$

$\rightarrow$ Eye $\rightarrow$

	Pupil	Light Rn	Corneal Rn
Adrenaline	$\uparrow$ (mydriasis)	$\checkmark$ $\oplus$ nt	$\checkmark$
Ach	$\downarrow$ (miosis)	$\checkmark$ $\oplus$ nt	$\checkmark$
Atropine	$\uparrow$ (mydriasis)	$\times$ (absent)	$\checkmark$
Lignocain	-	$\checkmark$ $\oplus$ nt	$\checkmark$



$\rightarrow$ Stimulant Drugs

① Receptor $\rightarrow$ Ach

② Directly $\rightarrow$ CaCl_2 (CaCl_2)

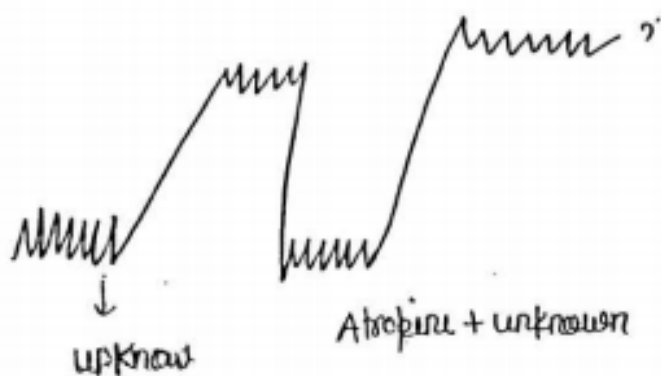
$\rightarrow$ Depressant

① Receptor $\rightarrow$ Adrenaline

② Directly $\rightarrow$ KCl.

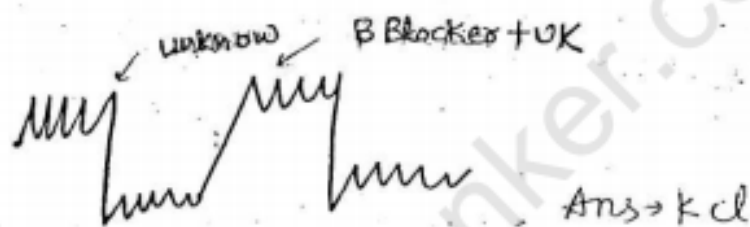
Qus

①



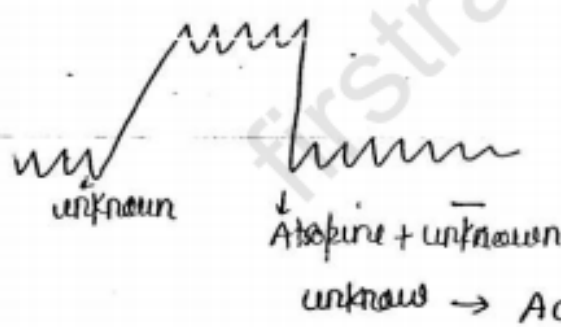
Ans unknown $\rightarrow$ CaCl_2

②



Ans $\rightarrow$ KCl

③

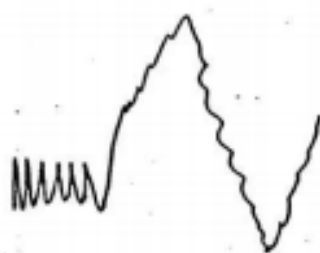


unknown $\rightarrow$ ACh



(37)

Effect on Dog Bp $\rightarrow$



NA (Noradrenaline)

← CVS →

CHF $\rightarrow$ Rt sided failure $\rightarrow$ Accumulation of blood in Lower limb

Hepatomegaly & ↑ JVP

It-Sided-failure

Inotropic $\rightarrow$

D β_1 stimulators $\rightarrow$ DA $\alpha_1 \beta_1 \alpha_2$
Dobutamine $\beta_1 \rightarrow$ Preferred Inotropic Drugs.
ISO $\beta_1 \beta_2$
NA $\alpha_1 \alpha_2 \beta$

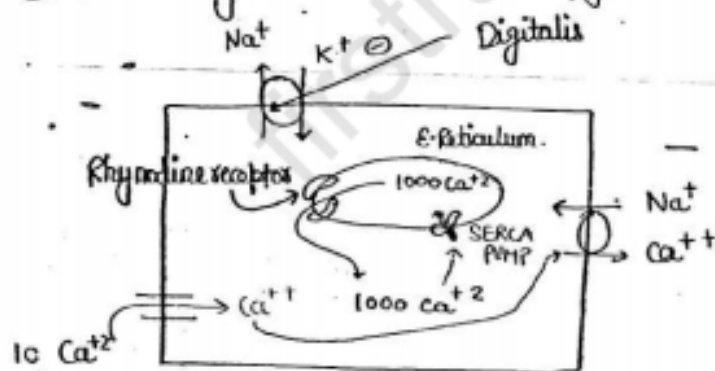
1) Phosphodiesterase Inhibitors $\rightarrow$

• Phosphodiesterase $\xrightarrow{\ominus}$ CAMP

fⁿ of CAMP $\rightarrow$ $\begin{cases} \uparrow \text{HR} \\ \uparrow \text{card} \\ \uparrow \text{contract} \end{cases}$

• EX $\rightarrow$
• Amrinone
• milrinone
• levosimendan. } these drug are k/a Inodilators
: b/c both action $\oplus$ Inotropic & Vasodilator.
 $\rightarrow$ Ca^{++} sensitizing agent

3) Cardiac Glycosides $\rightarrow$ k/a Digitalis (slow acting)



$\rightarrow$ Digitalis inhibit Na^+/K^+ pump $\rightarrow$ $\uparrow$ Na^+ Intracellularly

$\downarrow$
 $\text{Na}^+/\text{Ca}^{++}$ Exchanger Not work
So Ca^{++} Not go out
 Ca^{++} goes in SR/ER (1000+10)
more contraction



φ Digitalis can cause arrhythmia →

- Mechanism of Action of Digitalis →
- ① $\text{Na}^+ - \text{K}^+$ blocker
 - ② $\downarrow \text{Na}^+ - \text{K}^+$ exchanger
 - ③ $\uparrow \text{Ca}^{++}$ in endoplasmic reticulum

→ Digitalis have Vagomimetic property

$\downarrow$
 $\downarrow \text{HR}$
 $\downarrow \text{conduction}$

→ Atrial fibrillation → atrial rate 400-500/min (bpm)

$\downarrow$ MoA Digitalis → $\downarrow$ conduction (atria to ventricle)

Digoxin

C/I → Renal failure

Digitoxin

Liver failure

φ m/c S/E of Digitalis →

- Nausea
- Vomiting

} → m/c & earliest S/E

② arrhythmia → m/c arrhythmias → Ventricular bigeminy
 most specific → NPAT ∇ AV Block
 (not paroxysmal atrial tachycardia)

→ arrhythmia Not present →

- ① Atrial flutter
- ② Mobitz Type 2 Heart block

③ Gynecomastia.

$\left. \begin{array}{l} D \\ I \end{array} \right\} \text{Digitalis}$
 S - spironolactone
 C - cimetidine / Ketoconazole
 O - oestrogens.

→ they cause gynaecomastia

④ yellow vision → xanthopsia (digitalis S/E)

Risk of ↑ Toxicity of Digitalis

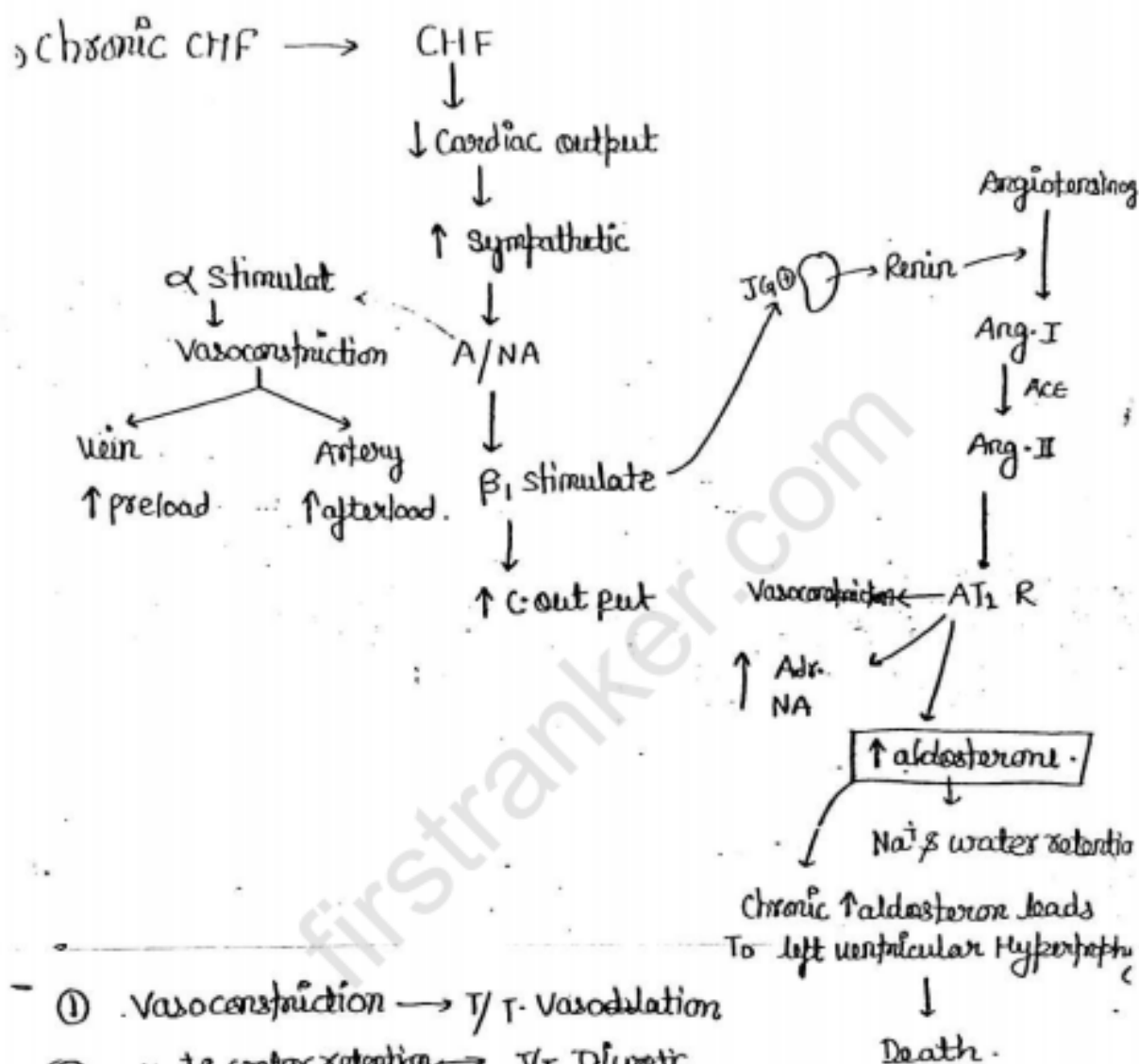
↓ K^+	Quinidine	• Renal failure → Digoxin • Liver failure → Digitoxin
↓ Mg^{+2}	Verapamil	
↓ Ca^{+2}	Amiodarone	
	Thiazide	

• Lignocaine is DOC → for Digitalis Induced ventricular arrhythmia

• DIGIBIND → It is indicated only in severe Digitalis Induced ventricular arrhythmia
 ↓
 it gives when Lignocaine not work

Istaroxime → • It is New drug
 • it is just like Digitalis
 • Not approved till now
 • it stimulate SERCA

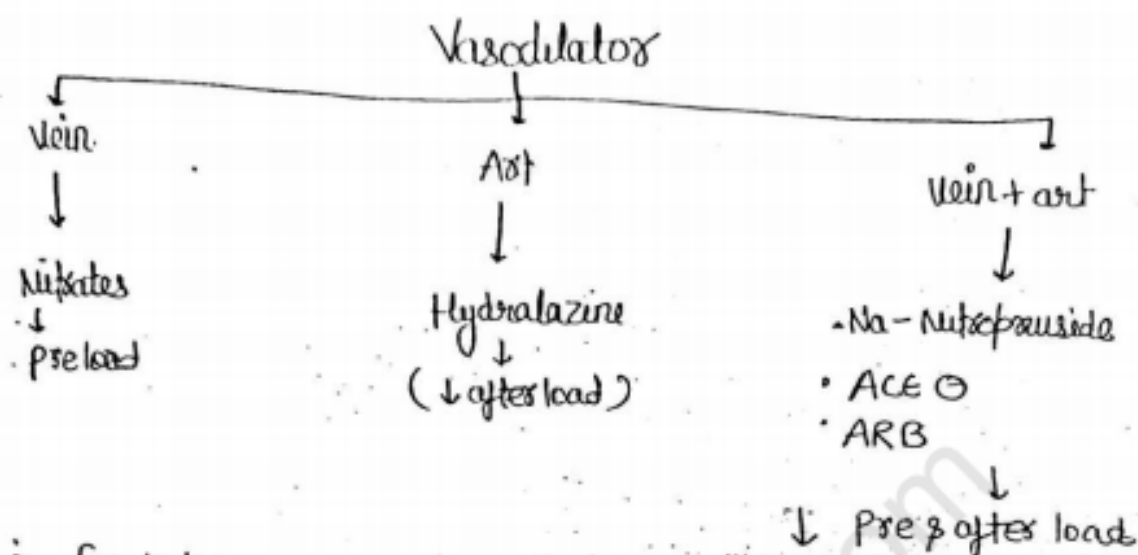
(40)



① Vasoc constriction → T/T. Vasodilation

② Na⁺ & water retention → T/T Diuretic

③ LVH → ⊖ RAAS



for LVH →

- ① β #
- ② ACE I
- ③ ARB
- ④ Aldosterone

} use in ↓ mortality in CHF.

β -Blocker → it is c/i in acute CHF.

- r/o c β # carvedilol.
- ↓ mortality ~~chronic~~
- chronic CHF में देते हैं ठीक स्लोली

ARB } they also ↓ CHF mortality
ACE I }

Spironolactone → can ↓ mortality in CHF

← New Drug in CHF →

① BNP (Brain Natriuretic peptide) → • $\downarrow$ Na^+ in urine
• Vasodilation

→ BNP metabolised by NEP (Neutral endopeptidase)

EX → NESIRITIDE → (it is recombinant BNP)

- Not given orally
- It given i.v
- short acting

② NEP Inhibitors → • ECADOTRIL
• SACUBITRIL → New Drug

③ Vasopeptidase Inhibitors → they inhibit NEP & ACE

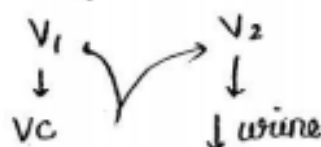
→ OMAPATRILAT

→ SAMPATRILAT

② Vasopressin / antidiuretic Hormone (VP/ADH)

↓
Vasoc constriction

↓
urine ↓



oral → • TolAVAPTAN

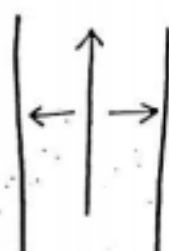
i.v → • ConIVAPTAN

→ they inhibit V_1 & V_2 receptors

← Hypertension →

$\geq 140/90 \text{ mmHg}$

BP ↓ by →



• ↓ Volume
• ↓ Na^+ } Diuretics

- ① Diuretics
- ② Vasodilators
- ③ Sympathetic syst. Block
- ④ RAAS block

→ Diuretic → Thiazides are DOC for Hypertⁿ

→ Vasodilators →

① NO → ↑ cGMP → VD → ↓ BP

EX → Nitroprusside
Hydralazine } fast action
use in Hypert Emergency

- Short acting
- so it given by infusion (i.v)
- it is sensitive to light
- Very fast action so when it given
- then syst. BP < 160 then stop given

• it metabolised to form CN^- so it can NOT given > 72 hr (C/I)

• MICRODRIP set

• C/I in Emergency



Hydralazine →

- fast acting
- Safe in pregnancy
- it is also K^+ channel opener.
- it metabolised by Acetylation
- S/E → SLE

② D_1 agonist → Fenoldopam (i.v.)
↓
given for HTN emergency

③ K^+ opener →

- Minoxidil
- Diazoxide
- Hydralazine

M
D
H

- minoxidil is pro drug
- metabolised by Phase II en
- use in Alopecia.

S/E → O. hirsutism → so c/I in young female

→ Diazoxide →

- It decrease Insulin
- S/E → Hyperglycemia → so c/I Diabetes.
- it use for T/T of Insulinoma

4) Ca^{+2} Blocker

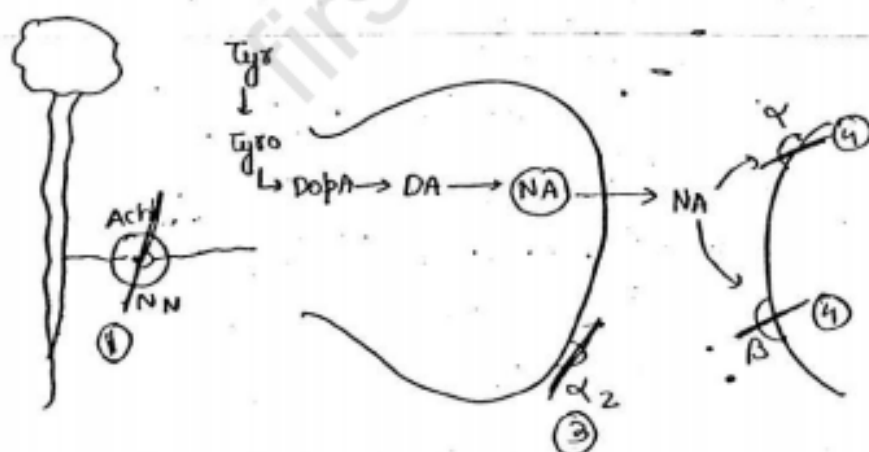
L Type
(Heart + Blood vessels)

T Type
(Brain)

- Verapamil
- Diltiazem

DHPs —
Nifedipine
Amlodipine
Clevidipine
Nicardipine

3) → Sympathetic blocker →





① Ganglion blockers $\rightarrow$ they block N_N (N_N antagonist)

- Trimethaphan
- Hexamethonium

S/E $\rightarrow$ anticholinergic ~~sub~~ S/E

• So No use in HTN

• these are use for NICOTINE poisoning

② Neuron Blocker $\rightarrow$

- Metyrosine
- Reserpine
- Guanethidine

} they can cause Postural Hypotⁿ

③ α_2 agonist $\rightarrow$ • Clonidine

• methyl dopa $\rightarrow$ Prodrug

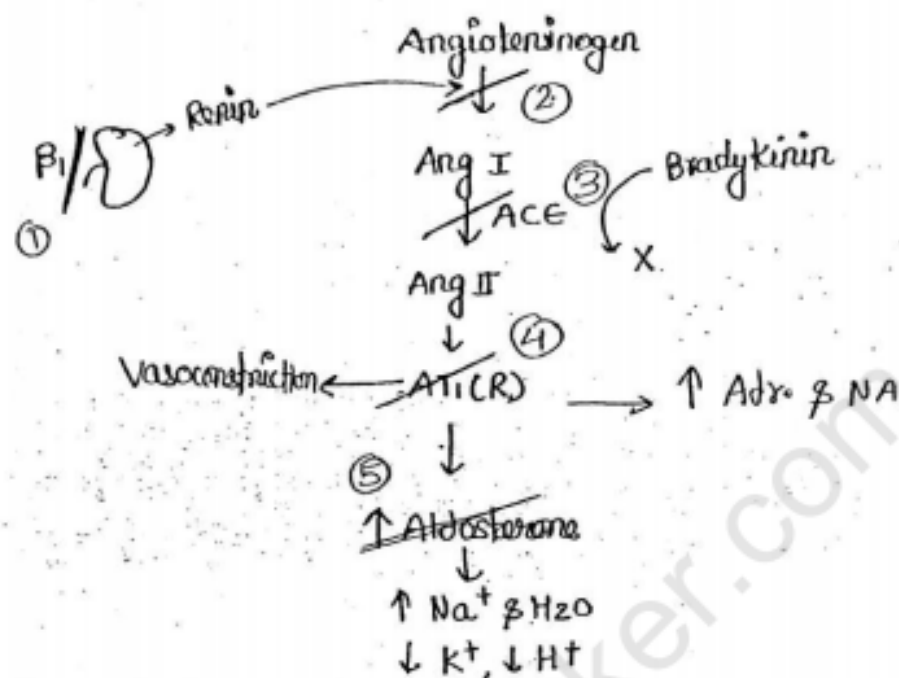
} • orally given
• S/E - Sedation
Dry mouth
• Safe in Pregnancy

$\rightarrow$ clonidine can cause Rebound Hypertⁿ

$\rightarrow$ methyl dopa can cause Hemolytic anemia

④ Receptor # $\begin{cases} \alpha \# \\ \beta \# \end{cases}$

D) RAAS block →



Renin Inhibitor → ALISKIREN
REMIKIREN
ENALKIREN } they given orally

β-Blocker Inhibit
Secretion of Renin.

ACE Inhibitor → • ACE is involved in metabolism of Bradykinin
• ACE is also K/a kinase

S/E → • Dry cough

• Angioedema.

ARBs → it not cause Dry cough & Angioedema.

ACE Inhibitors →

- Captopril → shortest acting
- Lisinopril
- Ramipril
- Perindopril → longest acting
- Moexipril
- Spirapril
- Trandolapril

C → Cough

A → Angioedema

P → Prodrug except Captopril & Lisinopril

T → Taste alteration K_{fa} → Dysgeusia

O → Orthostatic Hypotension (max Captopril)

P → Pregnancy

R → B/L Renal artery stenosis

I → Hyperkalemia

L → Lower the Diabetic Nephropathy → so it is very good for Diabetic pt

} C/I of ACE

ARBs →

• No cough & Angioedema

• Not a prodrug & not are same.

• Losartan → it produce active metabolites

• Valsartan → it can ↓ uric acid

Antipletlet Action

• Telmisartan → longest acting, & can stimulate PPAR-γ

• Eprosartan → Shortest acting

• Candesartan

• Olmesartan

Aldosterone antagonist $\rightarrow$ Spironolactone.

$\leftarrow$ T/T of Hypertⁿ $\rightarrow$

† JNC-8 Committee guideline (Joint National committee)

BP $\geq$ 140/90 mm Hg

Goal BP $\rightarrow$ $<$ 140/90

• Except $\rightarrow$ $>$ 60yr (without DM/CKD) = $<$ 150/90 mmHg

JNC-7

A

B

C

D

JNC-8

A $\rightarrow$ ACEI/ARB

C - CCB

D - Diuretic

} Ist line
Hypertⁿ drug

JNC-7

DOC $\rightarrow$ HTN $\rightarrow$ Thiazide

HTN in preg $\rightarrow$ methyldopa

HTN Emergency $\rightarrow$ Na-Nitroprusside

Emerg HTN in preg $\rightarrow$ Hydralazine

Harrison ✓

Thiazides

Labetalol

Nicardipine

Labetalol

← Pulmonary Hypertension →

- i.v Vasodilator testing → +ve in very few people
• if +ve then give CCB

- Endothelin antagonist → Drugs are →

Bosentan
Ambrisentan
macicentan

• Doc for Pul. HTN
• m/c drug use
• Best drug

Pt who does not respond to endothelin antagonist

↓
then PDE inhibitor given → Sildenafil
Tadalafil

↓
if PDE inhibitor Not work then

Prostacyclin given PGI_2 → • Epoprostenol
↓ • Treprostenil
Best Drug • Iloprost

→ use
last
b/c rare
is i.v
7 S/E

SELEXIPAG (New Drug)

- given orally
- Prostacyclin agonist

⑤ → Guanylate cyclase Agonist → Riociguat → given orally

Angina

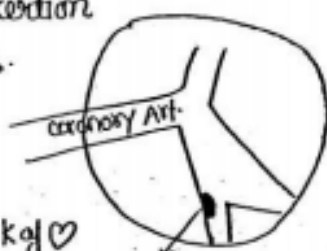
Classical angina

- atheromatous plaque. Involvement fair over only on exertion. Involve small vessels.

for T/T

blood

↓ work of heart



atheromatous plaque

Vasospasmodic or Vasospastic or Prinzmetal

- mostly occurs in big vessels
- spasm of main artery
- Chest pain at rest

for T/T → dilation of coronary Art.

Drugs

- 1) Nitrate
- 2) CCB
- 3) β -Blocker
- 4) Na^+ channel opener

- 1) Nitrates → • NO → $\uparrow$ cGMP → VD (vein $\gg$ Art)
- in classical angina → $\downarrow$ preload ($\downarrow$ work of heart)
- in vasospasmodic angina → dilation of

- Glycerol Trinitrate } given sublingual route & Doc for acute attack of angina
- Iso Sorbide Dinitrate }
- Iso Sorbide Mononitrate } minimum first pass metabolism
- Pentaerythritol tetranitrate → Longest acting
- Amyl Nitrate → Shortest acting

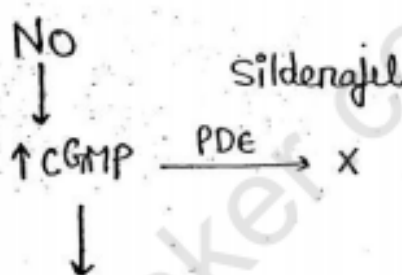


φ if we use Nitrate long term then develop Tolerance.

← Tolerance →

- 4-6 hr → • Nitrate free period. (4-6 hr body Nitrate free होना चाहिए, वही तो Tolerance हो जायेगा)
- TDS
 - Say to pt Night में नहीं लेगे to prevent the Tolerance.

→



φ Nitrate + Sildenafil → Never given b/c cause Severe Hypotension.

φ Amyl Nitrite → it is antidote for cyanide poisoning given by Inhalational route.

Cyanide + cytochrome oxidase

(Main)

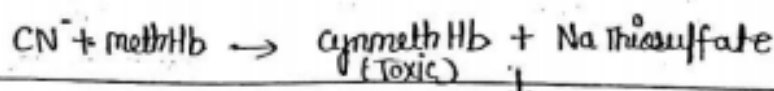
Amyl Nitrite + Na Thiosulfate

use for CN poisoning

product

(due to this ATP Not formed)

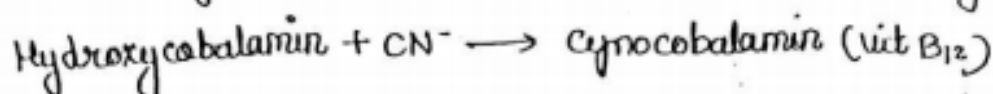
- When meth hemoglobin given → CN bind to this & cyt-oxidase release
- Amyl Nitrite → convert Hb to meth Hb.



Na-Thiocyanate → water soluble excreted by kidney

* * *

→ Hydroxycobalamin (B_{12}) → this is also antidote of choice for CN poisoning
↳ given i.v route



2) CCB Blocker →

	BP	HR
Verapamil VD	↓	Direct ↓↓↓
Diltiazem VD	↓	Indirect ↑ = ↓↓
DHPs VD	↓	↑ = ↓
		↑ = ↑

↳ it cause Tachycardia.

- Clevidipine
 - Nimodipine
- shortacting they Not given in Angina
- Amlodipine → longacting → they can give in Angina

§ Nimodipine → it is Cerebroselective CCB

- work only in blood vessels of brain
- use → SUB Arachnoid Hemorrhage.

③ β Blocker $\rightarrow$ • MOA $\rightarrow$ $\downarrow$ HR

• β Blocker is c/I in variant angina
b/c it cause vasoconstriction.

④ K^+ opener $\rightarrow$ Nicorandil

$\downarrow$
MOA $\rightarrow$ K^+ opener + NO releaser

$\rightarrow$ New Drug in Angina $\rightarrow$

① Metabolic modulators $\rightarrow$

Fatty acid + $^{100}O_2 \rightarrow ^{100}ATP$ (fatty acid is bad
(Heart) fuel, req. more O_2
than Glucose)

Glucose + $^{50}O_2 \rightarrow ^{100}ATP$
(all organ except $\heartsuit$)

$\rightarrow$ Fatty acid oxidase Inhibitors $\rightarrow$ • Ranolazine

• Trimetazidine } $\rightarrow$ they
Do Not
effect
on BP

② funny current blocker (If #)

$\downarrow$
IVABRADINE $\rightarrow$ MOA $\rightarrow$ $\downarrow$ HR (Bradycard)

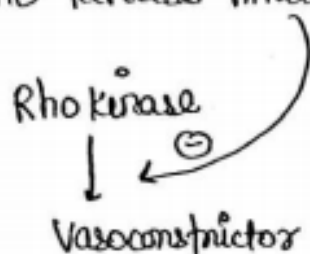
$\downarrow$ $\hookrightarrow$ K/a Bradycardiac agent

S/E it effect visual field defect

$\rightarrow$ it block funny current

$\rightarrow$ it also approved in chronic CHF

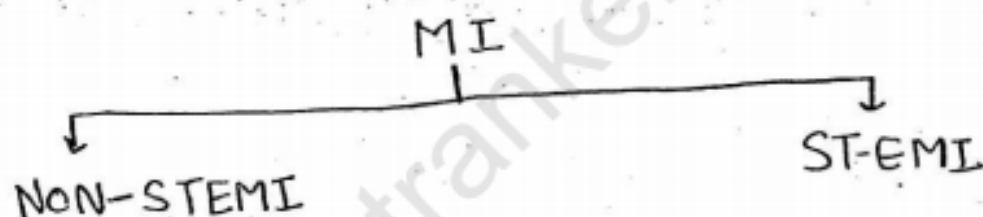
③ Rho Kinase Inhibitor → cause Vasodilation



Ex → fasudil



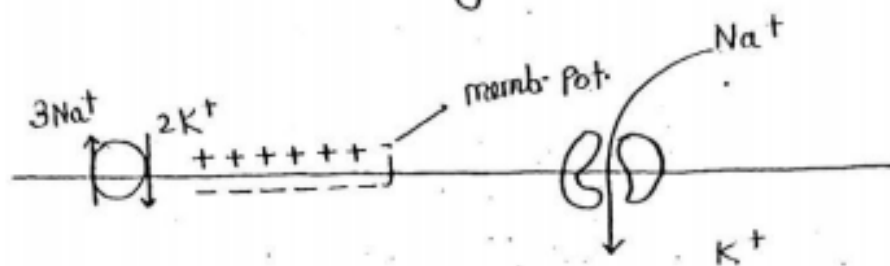
Cardiac Enzyme → use in Δ of MI



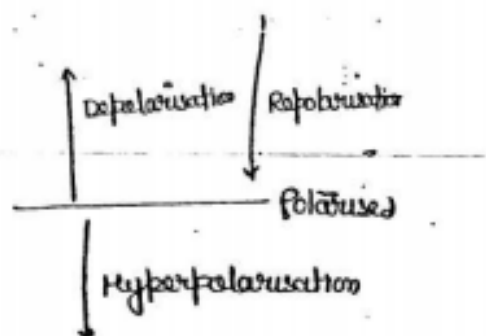
↓
M → Morphine
O → O₂
N → Nitrates
A → Aspirin

S → streptokinase ***
O - O₂
N - Nitrate
A → aspirin
M → Morphine

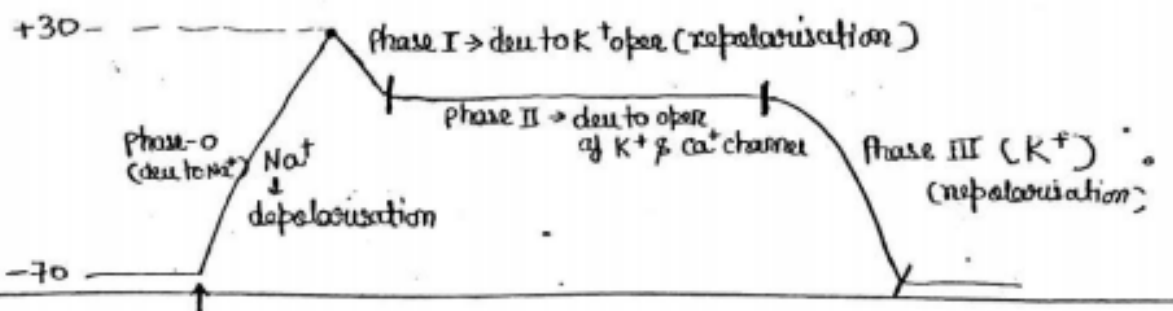
← Arrhythmia →



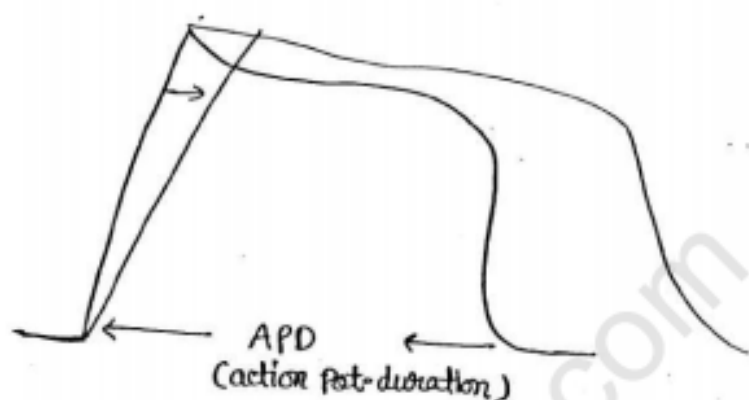
- Resting memb. pot. $\rightarrow -70\text{ mV}$
- Depolarisation is done by opening of Na^+ channel.
- Hyperpolarisation is done by opening of K^+ channel.
- Repolarisation is done by K^+ channel.



Action pot. of Heart



Effect of drug on this Action Potential →

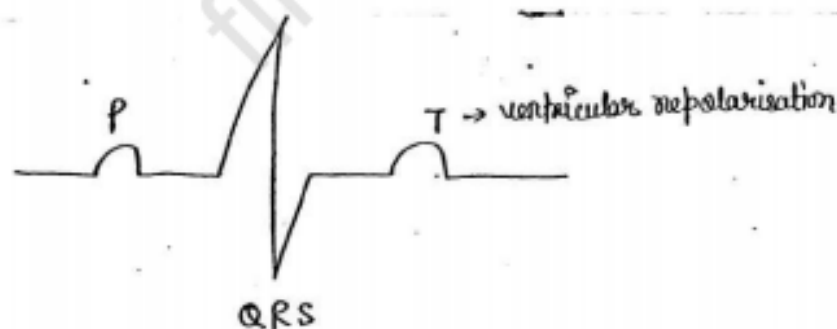


Na^+ channel blocker →

- ↓ slope of phase 0
- ↓ $\frac{dV}{dt}$ of phase 0

K^+ channel blocker → APD increased

K^+ channel opener → APD decreased



K^+ channel blocker → ↑ QT Interval → occurs Arrhythmia
K/a ↓
Torsade's de Pointes (TDP)



Antirhythmic Drug, $\rightarrow$

Vaughan Williams classification $\rightarrow$ on the basis of major mech. of Action.

Class

I Na^+ blocker

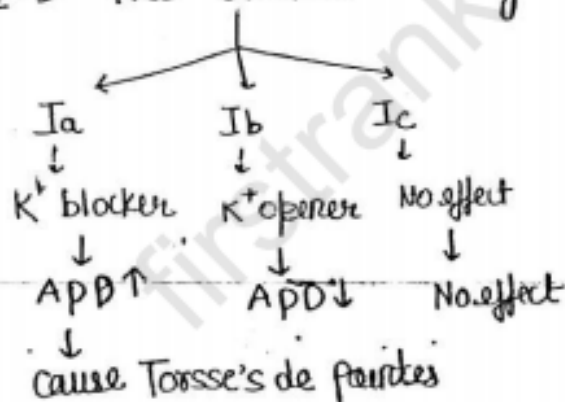
II β Blocker

III K^+ blocker

IV Ca^{+2} blocker

V others.

Class I $\rightarrow$ Na^+ blocker $\rightarrow$ they $\downarrow$ the slope of phase 0



Ia $\rightarrow$ ^{slow} Quinidine
^{fast} Procainamide
Ib $\rightarrow$ ^{slow} Lignocaine
^{fast} Phenytoin
Ic $\rightarrow$ ^{slow} Tocainide

Encinide
flecainide
Propafenone

Tocainide $\rightarrow$ can cause Thrombocytopenia.

Procainamide $\rightarrow$ • Can cause SLE
• metabolised by Acetylation.

• Ib $\rightarrow$ use only in Ventricular arrhythmia.

• Class II

β Blocker $\rightarrow$ • HR $\downarrow$ $\rightarrow$ so it use in both atrial & ventricular
Tachycardia.
 $\hookrightarrow$ DOC for vent. fibr.

• Class III $\rightarrow$ K^+ channel blocker $\rightarrow$ cause Torsades de pointes



~~Class IV~~ $\rightarrow$

B - Bretylium $\rightarrow$ use in ventricular fibrillation
K/a pharmacological Defibrillator $\hookrightarrow$ Toc $\rightarrow$ cardioversion

I $\rightarrow$ Ibutilide

n

D $\rightarrow$ Dofetilide

A $\rightarrow$ Amiodarone

S $\rightarrow$ Sotalol

$\rightarrow$ use in atrial fibrillation DOC

50

φ m/c Drug use in Atrial fibrillation → Warfarin
(anticoagulant)

* * * * * ← Amiodarone →

○ longest acting antiarrhythmic drug → $t_{1/2} > 3 \text{ week}$

○ Amiodarone given as loading dose.

○ it have all the 4 mechanism

→ $\text{Na}^+ \#$
→ $\beta \#$
→ $\text{K}^+ \#$
→ $\text{Ca}^{++} \#$

○ it give any arrhythmia except Torsades de pointes
& Digitalis induced arrhythmia.

○ A/E of Amiodarone →

The → Thyroid $\begin{cases} \uparrow \\ \downarrow \end{cases}$
Periopathy of → peripheral neuropathy
my → myocardial depression
lung & → lung fibrosis
cornea is → corneal deposit
photosensitive → photosensitive.

Amiodarone → 200 mg
↓
75 mg I_2
*** (40% I_2)
contain in amiodarone

Class IV Ca^{+2} channel blocker $\rightarrow$

Verapamil } work as β Blocker
Diltiazem } So β Blocker + verp β Diltiazem not given साथ में

DHPs $\rightarrow$ Not use in arrhythmia.

Class V $\rightarrow$ Other

- Digitalis $\rightarrow$ use in when $\rightarrow$ CHF + Atrial fibrillation
- Atropine $\rightarrow$ DOC for Bradycardia & AV Bloc
- Adenosine $\rightarrow$ shortest acting anti arrhythmic drug
- Magnesium $\rightarrow$ $t_{1/2} < 10$ PSVT
 $\downarrow$
 DOC for Torsades de pointes
 Route $\rightarrow$ Jugular vein
 • Rapid intravenous push
- DOC for prevention of PSVT $\rightarrow$ Verapamil

$\beta \rightarrow$ in Heart glucagon receptor $\oplus$

- $\downarrow$
- Glucagon is used in β -Blocker poisoning b/c it stimulate cAMP
- DOC for β Blocker poisoning $\rightarrow$ Glucagon.

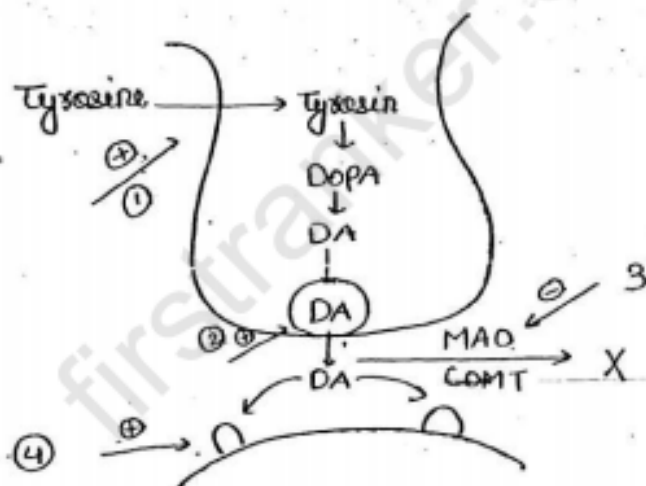
CNS

← Parkinsonism →

- deficiency of Dopamine in brain
- In (N) person → $Ach \rightleftharpoons DA \rightarrow \text{Balance}$
(100) (100)
- Bt Parkinson → $Ach \rightleftharpoons DA \rightarrow \text{Balance altered}$
(100) (50)

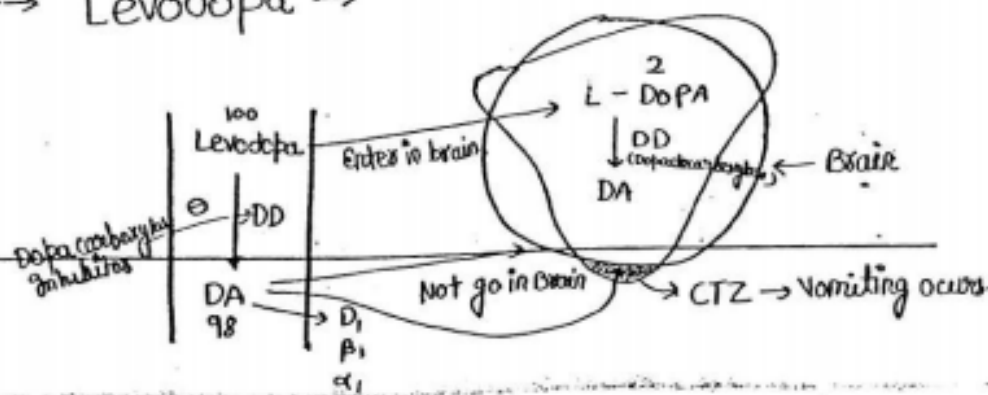
Drugs →

↓ Drug use → $\begin{cases} DA \uparrow \\ Ach \downarrow \end{cases}$



→ Dopamine can not cross BBB

→ Levodopa →



↳ Peripheral Dopadecarboxylase Inhibitors →

- ① Carbidopa
- ② Benserazide

in brain ↑↑ Dopamine → cause Psychosis

↓
Levoda Induced psychosis symptom - change in behaviour
• Dyskinesia

φ Carbidopa can not Reduce the central S/E → Psychosis

→ On off Phenomenon →

- Seen in parkinsonism
- in late parkinsonism → on → ↑ action cause psychosis
off → Not work at all parkinson symptom

• if on & off Phenomenon start then Levodopa dena bandh kar do

① Drug Releasing Dopamine →

Amantadine → use for Influenza A virus

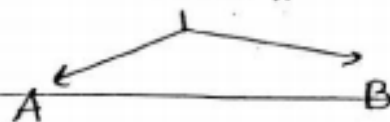
↓
it is antiviral
drug use in parkinson

- S/E → • ankle edema
• Livedo reticularis
↳ skin pigmentation

③ Inhibit MAO & COMT

MAO #

COMT #





MAO Inhibitor

A

- all place
- metabolised all substance

↓
Ady
NA
5HT
Tyramine
Pethidine

B

- in Brain
- mainly metabolised

↓
Dopamine

↓
So in Parkinsonism
MAO B Inhibitor are
use

↓
EX - SELEGILINE
RASAGILINE

COMT Inhibitor

↓

- ENTACAPONE → use

- TOLCAPONE → Not use
b/c
Hepatotoxic

④ Dopamine Agonist

Ergot derivative (Ergot alkaloids)
Derivatives

- Bromocriptine
- Pergolide → banned b/c
cause cardiac
fibrosis
- ↓
- they cause Vasoconstriction
 - Ischemia
 - Gangrene

- Long Term use of Drugs
Leads → fibrosis

↓
pulmonary, Renal
cardiac
Retroperitoneal

NON Ergot derivative

- Pramipexole }
• Ropinirole } → DOC for
Parkinsonism

- ↓
- major S/E Excessive day time
Sleep

- These Drug associated 2 Impulse
control → ① Pathological gambling
② compulsive shopping

- There are DOC for → Restless leg
syndrome
- most effective drug in Parkinsonism
↓
Levodopa

§ Drug which cause parkinsonism → antipsychotic drug.

§ Drug Induce parkinsonism → DOC → anticholinergic drug.

① • Benhexol
• Benztropine
• Biperiden } DOC for Drug Induce parkinson

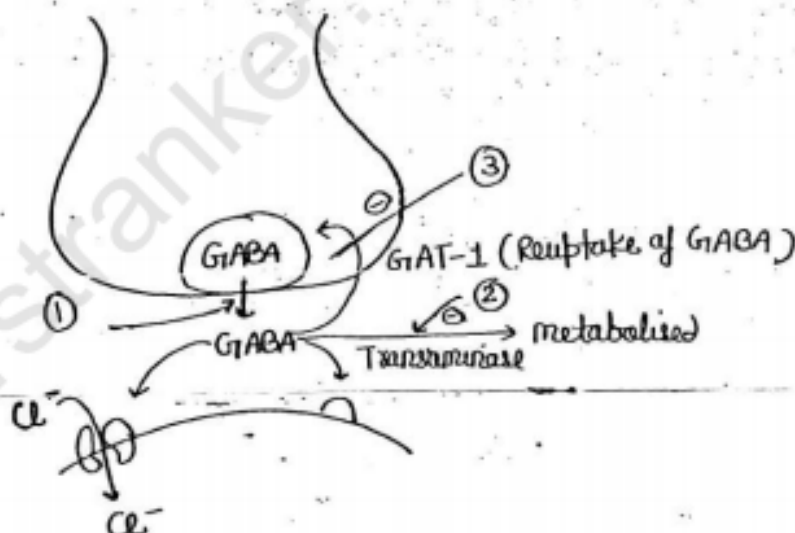
② 1st Generation antihistamine drug
• Promethazine

← Epilepsy →

- (A) ↑ GABA
- (B) ↓ Glutamate
- (C) Na⁺ channel blocker
- (D) K⁺ channel opener

method to treat epilepsy

(A) ↑ GABA



(A) Release GABA →

- Gabapentin
 - Pregabalin
- main mech. Ca⁺⁺ blocker.

These are DOC for Neuropathic pain → Diabetic & post Herpes Neuralgia
 Pregabalin > Gabapentin

2) Gaba Transaminase Inhibitor →

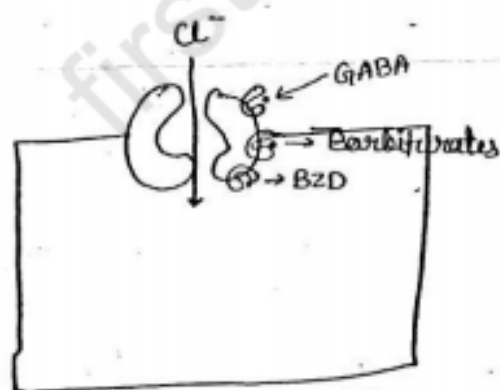
VIGABATRIN

↓
S/E → Visual field defect *** AIIMS
use also → in Infantile spasm
↓
DOC → ACTH

3) GAT₁ Inhibitor (Reuptake Inhibitor)

↓
TI GABINE

4) Drugs acting on channels →



Barbiturates → GABA mimetic

BZD → only GABA facilitatory.



(5)

Barbiturates

- ① GABA-mimetics
- ② ↑ duration
- ③ DRC - Steep
- ④ Highly addictive +++++
- ⑤ Powerful enzyme inducer
- ⑥ Severe Amnesia
(anterograde amnesia)
↓
Automatism
- ⑦ we have No antidote for Barbiturates

→ Barbiturates

- Thiopentone → use in anesthesia
- phenobarbitone → used in epilepsy
↳ S/E in children → Hyperkinesia

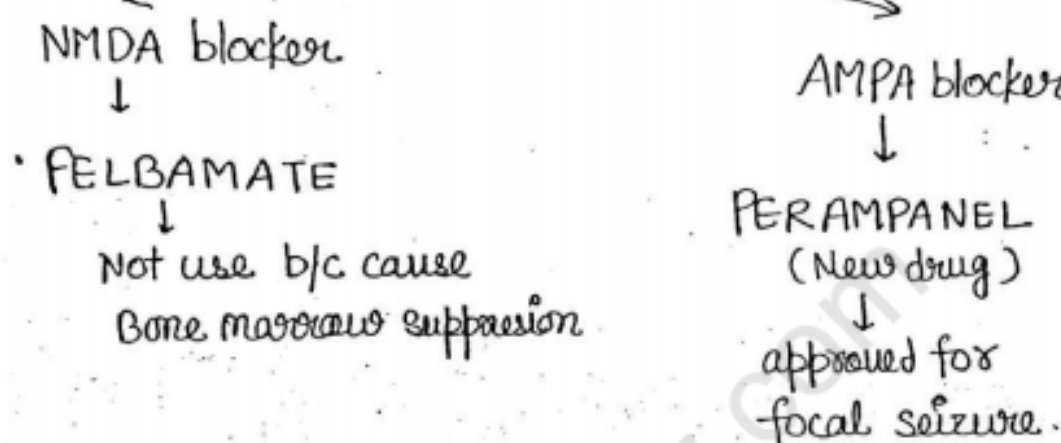
- BZD →
- Diazepam → Doc for febrile seizure
 - Lorazepam → Doc for status epilepticus
 - Clozapepam → can be use in Absence seizure
↳ Doc-Valproate
 - Clobazam → use for Lennox-Gastaut synd.
↓
Doc-Valproate

BZD

- ① fasciculatory
- ② ↑ frequency
- ③ DRC - flat
- ④ less addictive.
- ⑤ X
- ⑥ less amnesia.
- ⑦ Flumazenil is antidote for BZD



2) ↓ Glutamate



3) Na^+ channel blockers →

- Phenytoin
 - Carbamazepine
- } they commonly use GTCs & focal seizure
C/S in absence seizure & myoclonic seizure
- ** Topiramate
- Zonisamide
 - Lacosamide
 - Rufinamide
- } they can cause renal stone.
- } New Drug for focal seizure.
- ↓
it is also used for Lenox-Gastaut syndrome

- Topiramate — use for prophylaxis of migraine
- ↓ craving of alcohol.
 - ↓ weight → so use in obesity
- use in Bipolar disorder

- Carbamazepine →
- it is Enzyme Inducer
 - It induce own metabolism so k/a Auto Induction
 - Doc → focal seizure / any particular Brain lobe seizure
 - Doc → carbamazepine > Lamotrigine
 - Doc → Trigeminal Neuralgia
 - Can be used → Bipolar Disorder

Doc - Lithium

• Diabetes Insipidus

Doc → Desmopressin

- Phenytoin →
- Powerful Enzyme Inducer
 - it follows zero order kinetic
 - Not Bioequivalence
 - it is antiarrhythmic drug (class Ib)
 - used for → GTCS
 - focal seizure
 - C/I in → absence & myoclonic seizures

• Adverse Effect of Phenytoin →

H → Hirsutism, Hypertrophy of Gums

O → Osteomalacia (↓ vit D)

T → Teratogen (fetal Hydrantir syndrome)

M → megaloblastic anemia (↓ folic acid)

A → arrhythmia (only when use in over dose) → so it is Acute S/E

L → Lymphadenopathy (Pseudolymphoma)

I → ↓ Insulin → so avoid in DM

K → vit K ↓

PCM → cyclosporin
↓
phenytoin
→ minoxidil
→ Paresthesia

Metformin
↓
also cause
megaloblastic
anemia (vit B₁₂)

A → Ataxia, Nystagmus, vertigo (cerebellum dysf) → seen only in over dose
acute S/E

1) Ca^{++} channel blocker $\rightarrow$ T type Ca^{++} #

- Ethosuximide $\rightarrow$ can be use in absence seizure only
- effective only in absence seizure.

2) K^+ channel opener $\rightarrow$

Retigabine k/a - Ezogabine $\rightarrow$ used for focal seizure
• they are New Drugs

comp $\rightarrow$

- ① $\uparrow$ GABA
- ② $\downarrow$ Glutamate
- ③ Na^+ #
- ④ T type Ca^{++} #



Valproate

Lamotrigine



S/E - Steven Johnson Syndrome

• C/F - sloughing of skin

• skin bn $\rightarrow$ $< 30\%$

wide spectrum
Drug for
epileptic drug

↓ Valproate $\rightarrow$

GTCs
Absence seizure
myoclonic
Atonic seizure
Lenox Gastaut synd.



DOC for Valproate



(56)

⌕ Adverse effect of Valproate →

V → Vomiting

A → Alopecia

(L) → Liver children → m/c in children ***

(P) → PCOD, Pancreatitis ***

R → Rash

O → obesity

A → Aggranulocytosis

T → Tremor (in over dose)

E - Epigastric pain

← New Epileptic Drugs →

- ① Levetiracetam
② Brivaracetam
- } these bind to SV_2A protein.

→ ϕ PTZ Induce seizure
(Pentylenetetrazole)
↓
it is chemic can induce seizure

ϕ MES Induce seizures
(max. electroshock)

ϕ for absent seizure

ϕ for GTCS

→ Ethosuximide effective

→ Not effective

→ Valproate effective

→ effective

DOC for Epilepsy →

DOC

GTCS (Grand mal epilepsy) → Valproate

Absence (Petit mal epilepsy) → Valproate

focal → CBZ

myoclonic → Valproate

Atonic → V

febrile → Diazepam

Status epilepticus → Lorazepam

Lennox Gastaut synd. → Valproate

Infantile spasm. → ACTH

Eclampsia seizure → $MgSO_4$

Epilepsy in pregnancy → Don't change the Drug when coho
Take before pregnancy

• bt folic acid should be started
(dose 400 μ g) / 0.4 mg

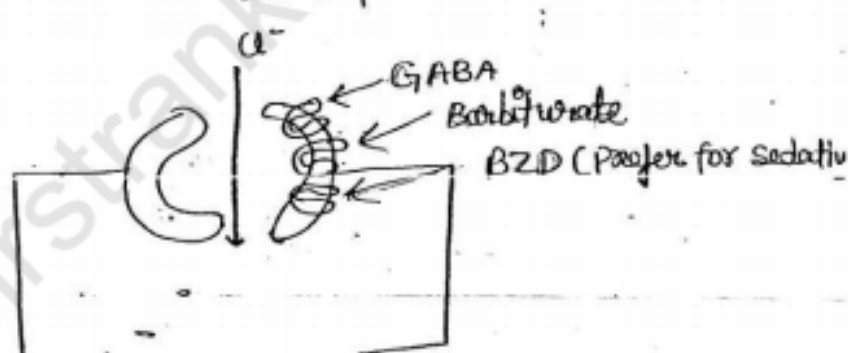
↓
if High risk / any previous teratogenic
in past → 10 time dose of folic acid

- in USG, if see Neural Tube defect → abortion done.
- after delivery vit K can be given must
- if female have NO H/O seizure & at pregnancy He suffer to seizure → Lamotrigine Drug given

first time seizure in pregnancy
Lamotrigine & Levetiracetam given

← Sedative Hypnotics Drug →

CNS Depression



• Benzodiazepines →

- ① Diazepam
- ② flurazepam
- ③ Nitrazepam
- ④ flunitrazepam

they have active metabolites so
it have long duration of action
↓
• So long term action → it cause
• so it avoid in Elderly Hangover.
• it C/I in Liver failure.

BZD those Not produce Active metabolites $\rightarrow$

S $\rightarrow$ short acting BZD

T $\rightarrow$ Temazepam

O $\rightarrow$ oxazepam

L $\rightarrow$ Lorazepam

E $\rightarrow$ Estazolam

- ① short acting
- ② Not produce active metab
- ③ least Hangover
- ④ safe in elderly pt
- ⑤ safe in liver ds

Sleep

REM phase

• Dream remember

NON REM

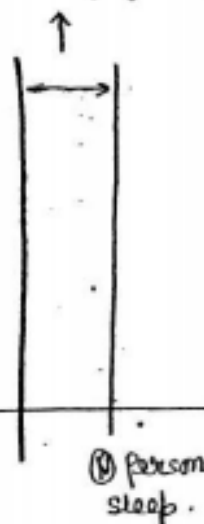
• Dream not remember

• most effective phase - 2

Barbiturate & BZD $\rightarrow$ cause Distortion of sleep architecture

latency of sleep onset $\uparrow$

means duration of sleep $\uparrow$
But quality of sleep $\downarrow$



Z Drugs

- ① zolpidem
- ② zaleplon
- ③ zopiclone

- they $\uparrow$ latency of sleep onset
- they do not effect on quality of sleep & duration
- They act on ω_1 receptor

φ flumazenil → DOC for BZD & Z Drugs.

φ Advantage of Z Drugs

- Do not cause disruption of sleep
- Not cause Hangover
- Not addictive
- DOC → for Insomnia

φ Melatonin → Sense the Day Night cycle
↓
Secreted by pineal gland.

→ Shift worker Jet lag } in these pt. Melatonin Receptor agonist is use for change the cycle.

EX → RAMELTEON

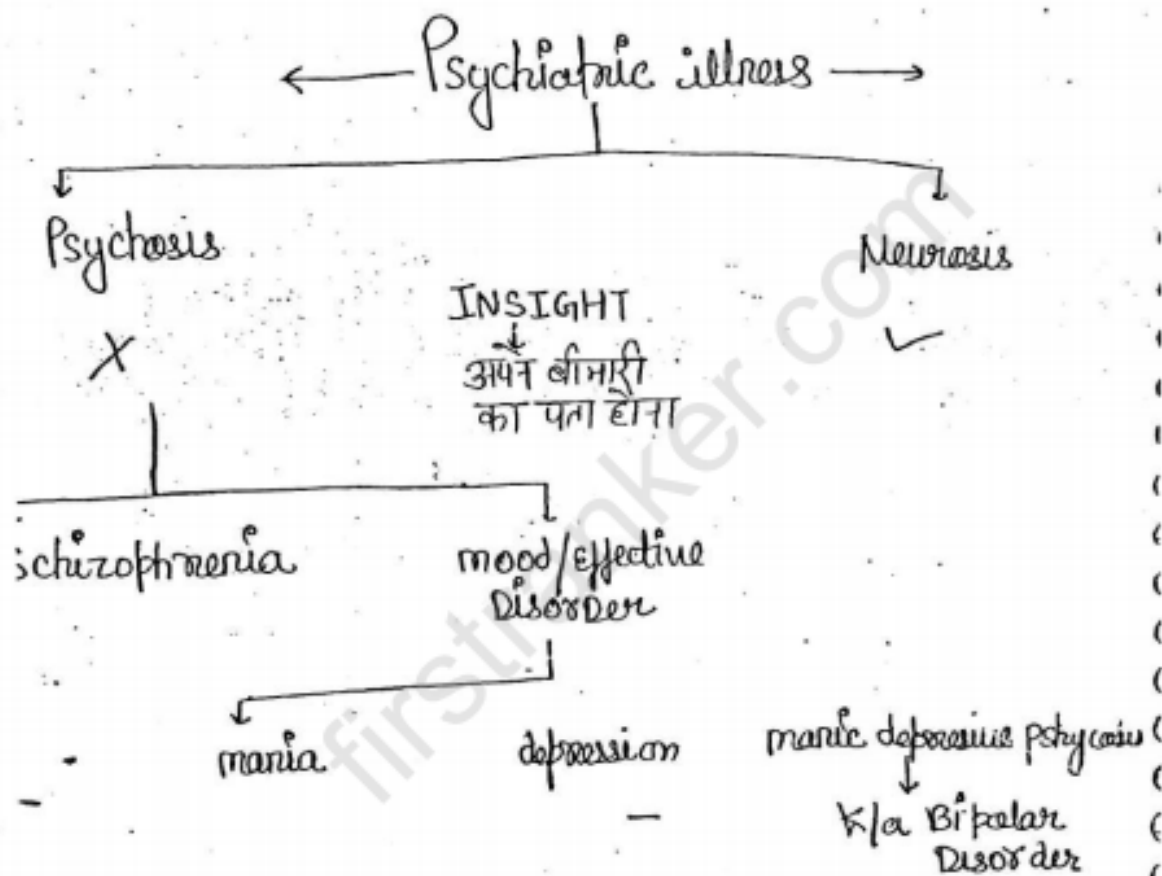
- very poor Bioavailability
- given oral
- Not addictive
- microsomal enzyme inducer

• TASIMETON } New Drug
• RAMELTEON }



→ New Drug for Insomnia →

OREXIN Receptor antagonist → suvorexant



← Nervous →

- ① Generalised anxiety disorder
- ② obsessive compulsive disorder → repetitive work
- ③ phobia → fear → Claustrophobia → fear of close face
- ④ Bulimia → eating disorder $\begin{matrix} \text{ब्यादा खाना} \\ < \text{ना खाना} \end{matrix}$
- ⑤ Post traumatic stress disorder
- ⑥ Impulse control → kleptomania → चोरी करना

→ Schizophrenia →

$\frac{D_2 \#}{5HT_2 \#}$ ratio → ≥ 1 → Typical Antipsychotics → only use for Schizophrenia
 ≤ 1 - atypical

Typical (Highly Non selective)

(Block D_2 Receptor of Dopamine)

$\phi \frac{D_2 \#}{5HT_2 \#} = \geq 1$

ϕ Haloperidol
 Droperidol
 fluphenazine

Higher risk for Hyperproliferation
 max chance cause of EPS

Strong $D_2 \#$

Highest risk of causing seizure/convulsion.

ϕ chlorpromazine
 thioridazine

Weak $D_2 \#$

ϕ thiothixene
 chlorprothixene

Intermediate $D_2 \#$

Atypical

($5HT_2$ Receptor blocks)

$\frac{D_2 \#}{5HT_2 \#} = \leq 1$

> Extra pyramidal symptoms → due to Excess D₂ Receptor block

Involuntary movement

5 type of Extra pyramidal symp Disorder →

- ① Dystonia → ^{Altered Tonicity of muscles} m/c Torticollis → SCM on side Toned
one side relaxed } Earliest EPS to come (in few hr after taken drugs)
- ② Akathisia → Rolling back of Tongue
oculogyric crisis
- ③ Parkinsonism → come same month
- ④ Tardive dyskinesia → ^{10-12 yr} very late appear, when antipsychotic stop
overstimulation of D₂ receptor b/c of receptor upregulation
- ⑤ malignant Neuroleptic synd →

Akathisia → m/c EPS, comes in few day

- Constant
 - Purposeless
 - Involuntary movement from one place to another place
 - without anxiety
- } K/a

> malignant Neuroleptic syndrome →

- cause by Neuroleptic / antipsychotic
- person having High grade fever & muscle spasm, severe pain
- most dangerous EPS

⊥ T/T of EPS → anticholinergic drugs (Benzhexol)
but it is c/I in Tardive dyskinesia

Benzhexol → DOC → • Dystonia
• Parkinsonism (drug induced)

860

φ Propanolol (β -H) → • Doc for Akathisia

• Benhexol also used

φ Dantrolene → • Doc for malignant Neuroleptic synd.

• Benhexol can be use

→ Tardive dyskinesia

• No specific T/T

• Benhexol is C/I

} BZD can be use, for T/T

φ

→ Hypothalamus

↓
Prolactin Releasing Inhibiting Hormone = Dopamine

↓
So typical antipsychosis Drug cause

Hyperprolactinemia

↓
lead Galactorrhea

↓
Infertility

⇒ Typical antipsychotic Drug have also properties →

① α receptor blocker → lead ↓ BP

② Ach H (anticholinergic) →

③ H₁ H → Sedation cause

④ seizure

→ these S/E is more in weak Drugs

Typical Drug → • can control only +ve symptoms
• Not control -ve symptoms

Atypical Drug → • can control both +ve & -ve symptoms.
• less cause EPS & akathisia

Atypical Antipsychotic

- Clozapine → first antipsychotic drug.
- olanzapine → Highest risk of S/E → Lipodystrophy synd.
- Quetiapine → cause cataract.
- Zotepine
- Aripiprazole → route: Sublingual
- Risperidone
- Paliperidone
- Iloperidone
- Ziprasidone → cause QT prolongation → Torsades de pointes
- Lurasidone
- Aripiprazole
- Brexipiprazole
- Pimavanserin } New Drug
- Pimavanserin → approved for Parkinson's psychotic effect



S/E → atypical Drug cause Lipodystrophy Syndrome

- Hyperglycemia
 - Hyperlipidemia
 - wt gain
 - Insulin Resistance
- } 1st like metabolic ds.

Clozapine → • Seizures (Dose dependent) | Seizure S/E
 • Agranulocytosis Dose independent | Typical → chlorpromazine
 • Myocarditis | Atypical (Clozapine)
 • m/c → sedation | (chlorpromazine) cheap
 • Lipodystrophy

φ • Haloperidol
 • Fluphenazine
 • Risperidone
 • Paliperidone

} the drug available Long acting Injection (i)
 use for highly Non compliant pt.

T/I of schizophrenia →

1st episode → minimum T/I for 1 yr (when symptom are disappear the 1 yr तक और देगे)

2nd episode → life long T/I

Anti
↓
antiemetic

Pshy
↓
Psychosis

cho
↓
chorea
(Huntington's chorea)
के T/I में देते हैं।

Tics →
Gilles de la Tourette
Syndrome

(Newmg) → Tetra benzazine is drug also
 given in chorea (Huntington's chorea)
 DOC

Φ Gille de La Tourette syndrome →

- characterised by Vocal Tick (feel like pt gali दे रेट)
- T/t → Doc → Haloperidol.

Φ Mania →

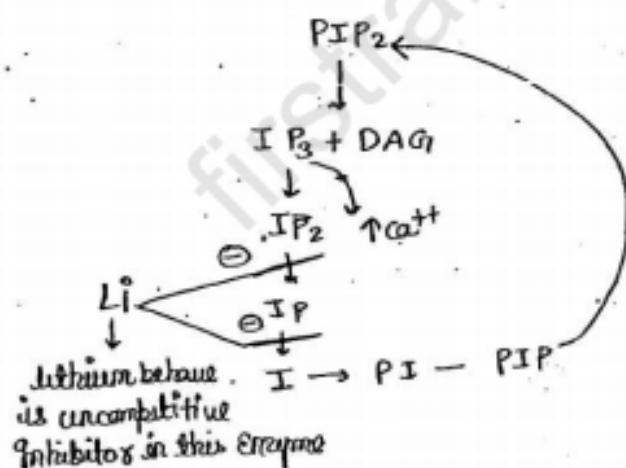
It is aggressive, Hyperactive

Doc → BZD → Sedative

BZD / Antipsychotics

t/t of choice → Sedative + Lithium ^{atypical used} > BZD > Li

Doc for Prophylactic → Lithium ^{not given alone b/c it slow acting}



(62)

In depression deficiency of $\rightarrow$ BDNF $\rightarrow$ (Brain derived Neurotrophic factors)

$\downarrow$
neural plasticity

BDNF $\xrightarrow[\text{Lithium}]{\text{GSK-3}}$ X

ϕ Lithium can be use for depression

ϕ Imp of Lithium $\rightarrow$ S/E

L $\rightarrow$ Leucocytes }
I $\rightarrow$ $\uparrow$ } Leucocytosis

T $\rightarrow$ Tremor (m/c)

H $\rightarrow$ Hypothyroidism

I $\rightarrow$ $\uparrow$ }
U $\rightarrow$ urine } Polyuria (m/c Renal side effect)

M $\rightarrow$ Mother $\rightarrow$ Ebsteins anomaly

$\downarrow$
• defect Heart
• congenital malformation.

leucocytosis occurs $\rightarrow$ Li
Steroid
Growth factor

Dose $\rightarrow$ Acute mania $\rightarrow$ 0.8 - 1.2 mg/L

Prophylaxis $\rightarrow$ 0.5 - 0.8 mg/L

Toxic $\rightarrow$ > 2 mg/L

$\leftarrow$ Manic depressive psychosis $\rightarrow$
(Bipolar disorder)

ϕ T/T of Bipolar disorder $\rightarrow$ we want to prevent mania & depression
(prophylaxis)

$\rightarrow$ Doc for Bipolar Disorder $\rightarrow$ Li

Prophylaxis of mania

Prophylaxis of Depression

$\downarrow$
 $\rightarrow$ Lithium

$\rightarrow$ antipsychotics $\rightarrow$ Doc in Bipolar disorder in pregnancy

$\rightarrow$ CBZ

$\rightarrow$ Valproate

$\rightarrow$ Topiramate

$\rightarrow$ clonidine

$\rightarrow$ Doc Rapid cycler

$\downarrow$
Lamotrigine

$\downarrow$
Doc for BPD for depression

← Antidepressants →

5HT, NA

↓
↑ BDNF

↓
Neural plasticity

↓ 5HT, NA

↓
↓ BDNF

↓
↓ Neural plasticity
↓
Depression

antidepressant

Typical
(↑ 5HT)

atypical
(other)



MAO Inhibitor

reuptake Inhibitor

MAO Inhibitor →

MAO

A

B

↓ MAO A+B Inhibitor → • Tranylcypromine
Phenelzine → structure very similar
to INH
ISOCARBOXAZIDE

↓ MAO B Inhibitor → Selegiline

↓ MAO A Inhibitor → Moclobemide → reversible (only MAO
inhibitor is reversible)
k/a RIMA
Note: only this is used



Reuptake Inhibitor →

Non selective
(5HT + NA)

↓
• In cardiac pt Non selective
is Not given

• use for severe depression

↓
Non selective

Tricyclic antidepressant

- Imipramine
- clomipramine
- Desipramine
- Amitriptyline
- Nortriptyline

↓
these all drug have
property of →

- α #
- Ach #
- H_1 #
- seizure

→ TCA → cause ① metabolic acidosis
② arrhythmia

③ these are very dangerous → They kill the pt.

Selective
(SSRI)

§ TCA Poisoning →

- Dry mouth
- Tachycardia
- metabolic Acidosis
- Seizure

7/T → • NaHCO_3

- Doc for arrhythmia in TCA poisoning → No Doc
- physostigmine use for anticholinergic symptom.

← SNRI →

• SNRI → Doc for severe depression

- ↓
- Ex - Venlafaxine
Desvenlafaxine
Duloxetine
milnacipran
levonacipran

← SSRI → very safe drugs

Safe for cardiac pt.

Doc for mild to moderate depression.

minimum risk of Discontinuation syndrome

→ • fluoxetine

→ Longest acting

- Paroxetine
- Sertraline

φ this is Doc for all Neurotic disorder.
φ Doc. for depression.

• citalopram

• Escitalopram

• fluvoxamine

→ Shortest acting

(64)

S/E of SSRI →

• m/c → Nausea vomiting > anxiety > Diarrhea.

• Sexual S/E → Can cause → delayed ejaculation

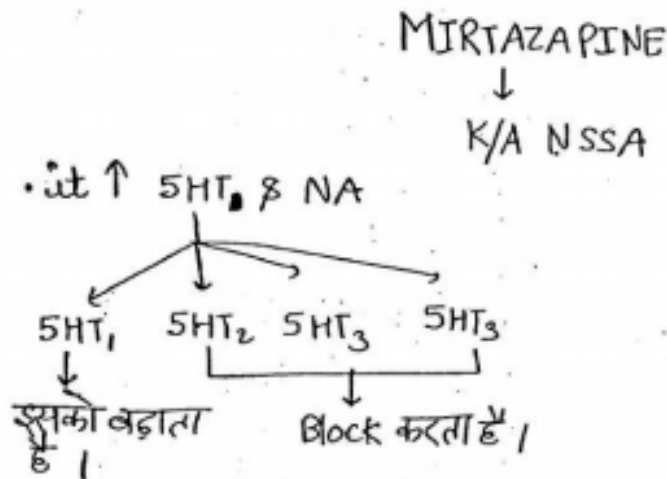
↓
So it SSRI use in Premature ejaculation

✓ All the antidepressant drugs are slow acting.
When ever any antidepressant drugs are stop then developed
Discontinuation syndrome.

↓
• So that's why antidepressant drugs are stop very slowly slow

← Atypical →

- Vortioxetine } → these drug are New Drugs for depression.
- Vilazodone } • They SSR₁ + agonist 5HT₁, 5HT₃ #
- Desvenlafaxine } → have 5HT_{2A/2C} #
- Trazodone } → anti smoking drug. But BUSPIRONE → anti anxiety
- Bupropion } → ↑ reuptake of serotonin (5-HT)
- Tianeptine } • K/A → SSR-Enhancer.
- Amineptine } • K/A → NSA
- Mirtazapine } → Drug have D₂ receptor blocker.
- Amoxapine } → use in ADHD
- Atomoxetine } → use in ADHD



so it t/t the depression without causing sexual problem:

it is α_2 antagonist



Opioids $\rightarrow$ any drug $\approx$ fⁿ like morphine

$\downarrow$
derived from opium $\rightarrow$ k/a $\rightarrow$ opiate

$\downarrow$
Poppy (Papaver Somniferum)

Morphine $\rightarrow$ • Relieved pain

3 receptors

	μ	κ	δ
• work on	analgesic	• analgesic	analgesic
S	Sedation	• Dysphoria	
A	analgesia	$\downarrow$	
C	constipation	(manifest Hallucination)	
R	Resp $\downarrow$ (Resp depression)		
U	Euphoria $\rightarrow$ मजा आना-ना		
M	miosis		

• In bilious colic pain opium/morphine is C/I b/c it cause in spasm of sphincter oddi

• Morphine is addictive drugs.

$\rightarrow$ Tolerance $\rightarrow$ • Do not occur in constipation & miosis (contraction of pupil)

• Cross Tolerance $\rightarrow$ is partial

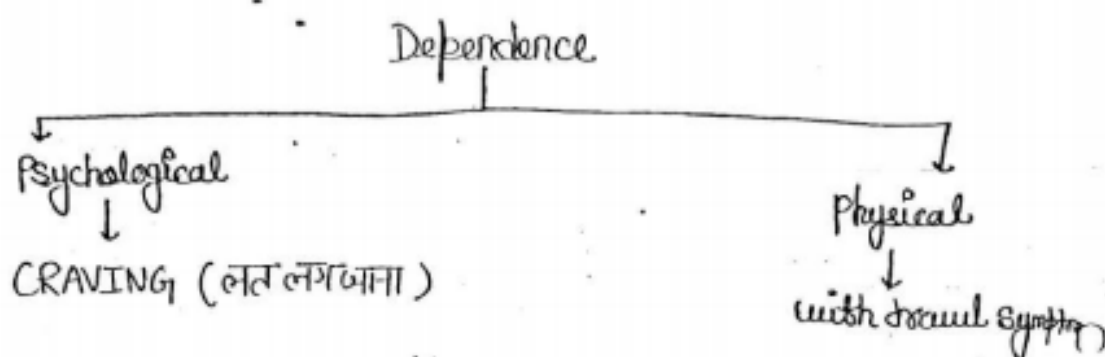
opioid 1

10
 $\downarrow$
20
 $\downarrow$
30
 $\downarrow$
40
 $\downarrow$
50
 $\downarrow$
60

opioid 2

10
 $\downarrow$
20
 $\downarrow$
30
 $\downarrow$
40
 $\downarrow$
50
 $\downarrow$
60

k/a Cross opioid Tolerance Test



! Morphine → Not cause miosis in eye when give in eye
Drop way
↓
b/c miosis due to brain Not eye.

Drugs

Agonist → stimulate all μ , κ , δ

Partial agonist → μ stimulate → Buprenorphine

Agonist-Antagonist → κ agonist & μ antagonist

Antagonist → block μ , κ , δ .

! Partial agonist → it stimulate μ receptor

• Ex → Buprenorphine

- it is equal to low dose of morphine
- ceiling effect of Resp depression

! Agonist-Antagonist

P	Pentazocine	} → cause Hallucination
N	Nalbuphine	
B	Butorphanol	



Agonist → ① Heroin

② Methadone → long acting
• use for deaddiction

③ Pethidine (meperidine) → Not use long period.



metabolised by MAO Enzyme 99%.

1% make → Nor pethidine (very long)



Stimulate brain

↓
Seizure occurs

Pethidine is C/I in MAO Inhibitor

④ Codeine

Pholcodeine

Dextromethorphan

Noscapine



Anti fissive

use for Dry cough.

⑤ Loperamide

Diphenoxylate



use for Diarrhoea

Not given in Infectious diarrhoea.
(C/I)

These drug Not available in alone always
atropine added. b/c decrease abuse (addiction)

⑥ Tramadol

Tapentadol



• μ , κ , δ → stimulate

• ↑ Serotonin in spinal cord.

• Two mech. of action so its effect
Not stop completely when we given
any antagonist

⑦ Fentanyl →

Alfentanil → use in Day care surgery

Sufentanil → most potent

Remifentanyl → shortest

Anesthetic

φ Opioid antagonist → μ, κ, δ #

- NALOXONE → short acting, i.v route
- NALTREXONE → long acting, oral.

→ Naloxone is Doc for acute opioid poisoning

→ Doc for maintenance → NALTREXONE

↓
it also ↓ alcohol craving
also use for prevent long term
addictive pt.

φ Alcohol craving ↓ by →

Nore → Naltrexone

of → Ondansetron

the → Topiramate

above → Acamprosate

← Opioid de-addiction →

Short term addiction pt

↓
stop opioid

↓
withdrawal symptom

↑ Sympathetic system

Tachypnea
seizure
mydriasis

} i.e opposite to Drug action

↑ T/T by Beta blocker

φ T/T - Symptomatically

T/T by BZD

give Naltrexone

longer term

substitute given
Not stop to given

long acting
delayed acting

methadone given

K/a methadone
substitution/
maintenance
Therapy given

Slowly - slowly
Dose ↓
Dose stop & then

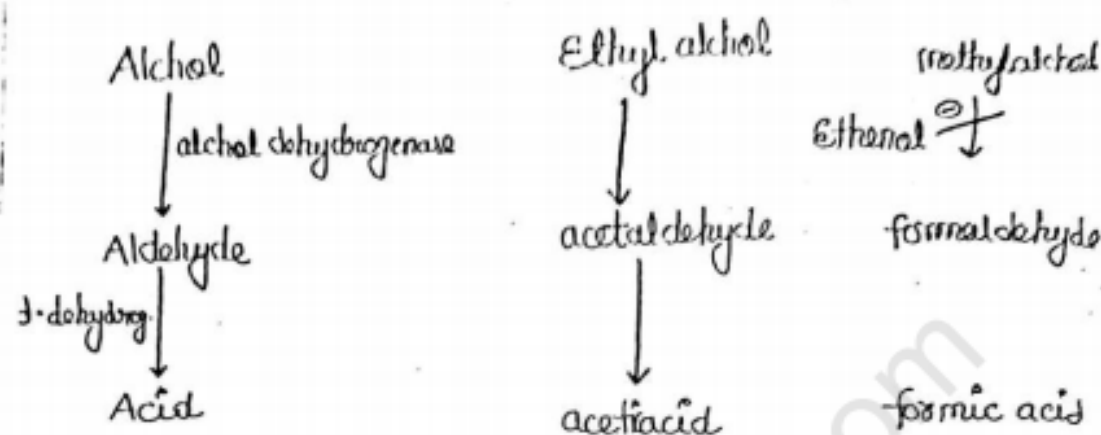


Qus → T/T of withdrawal sympt - ①
prevent of " " → ②
prevent relapse → ③
Acute poisoning → ④

- ① B # or clonidine or BZD
- ② methadone
- ③ Naltrexone
- ④ Naloxone



← Alcohol poisoning



Disulfiram → Inhibit Aldehyde dehydrogenase

Disulfiram like rxn →

cyclic → chlorpropamide
 → cefoperazone
 → cefotetan

G → Griesofluir →

M → metronidazole

P → Procarbazine

these drug c/I in alcoholic pt

formaldehyde & formic acid → both cause blindness

& glycolic acid → they are poisonous



← Antimicrobial drug →

Classification on the basis of Mech. of Action →

- ① cell wall
- ② membrane
- ③ metabolism
- ④ DNA
- ⑤ protein synthesis

→ Drug Inhibiting cell wall synthesis →

firmly → fosfomycin → use in UTI

BIND → Betalactams

To → Bacitracin → it used only locally

Bacterial

cell → cycloserine → S/E Neuropsychiatric side effect (like INH)

wall → vancomycin → they are static

use for TB

all drug in this category are bactericidal except cycloserine

these drug having ring $\leftarrow \beta\text{-lactum} \rightarrow$

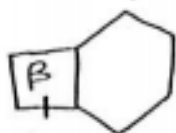
X $\rightarrow$

1) penicillins

2) cephalosporins

3) carbapenems

4) monobactams $\rightarrow$ it have only one ring i.e. β



β -lactamase works at this place.

Penicillin $\rightarrow$

- Penicillin G $\rightarrow$ • oldest penicillin
- only one it is Natural penicillin

1) Drawback

it is short acting $\rightarrow$ b/c it have tubular secretion $\rightarrow$ so Probenecid added to $\uparrow \pm 1/2$

It is narrow spectrum

Not effective orally $\rightarrow$ given i.v $\rightarrow$ drawback

Resistance

Allergy cause

- $\Rightarrow$ ① Short acting $\rightarrow$ • b/c of higher tubular secretion.
- $\pm 1/2 \uparrow$ by $\rightarrow$ combination $\Rightarrow$ Probenecid

Depot preparation $\rightarrow$ $\left[\begin{array}{l} \text{Benzathine penicillin G} \\ \text{Procaine penicillin G} \end{array} \right]$ • it $\uparrow \pm 1/2$ by

$\downarrow$ given i.m. • longest acting • Deposition in muscles

• i.m route

② Not effective orally →

• b/c it is acid labile

So → Acid Resistant penicillin
or^{or} oral penicillin

V → Penicillin-V

O → Oxacillin

D → Dicloxacillin

K → Cloxacillin

A → Ampicillin

Amoxicillin

③ Narrow spectrum →

1/2 effect only for gram +ve

↓
So make New penicillin k/a

Extended spectrum penicillin / wide spectrum penicillin → against gram -ve

A → Ampicillin

Amoxycillin

Cl → carbenicillin

Ty → Ticarcillin

M → mezlocillin

A → Azlocillin

P → Piperacillin

all kill pseudomonas.

Vancomycin is Not effective for pseudomonas

④ Resistance →



Penicillin-G

β-lactamase / Penicillinase

→ So we make β-lactamase inhibitor

β -lactamase Inhibitor $\rightarrow$

C $\rightarrow$ clavulanic acid + Amoxy

S $\rightarrow$ sulbactam + Ampicillin

T $\rightarrow$ Tazobactam + piperacillin

> Penicillinase resistant penicillin

C $\rightarrow$ cloxacillin

O $\rightarrow$ oxacillin

N $\rightarrow$ Nafcillin

D $\rightarrow$ Dicloxacillin

O

M $\rightarrow$ methicillin $\rightarrow$ strongest

1 MRSA $\rightarrow$ No β -lactam is not effective.

1 Allergy $\rightarrow$

Penicillin can cause anaphylactic shock

so check penicillin by intradermal before given the pt.

if any penicillin se allergy $\hat{=}$ then don't give any penicillin

b/c cause cross allergy penicillin

$\downarrow$
except - Monobactam.



(7E)

φ uses of penicillin →

L → listeria	} → DOC penicillin
A → Actinomyces	
S → syphilis	
T → Tetanus	
M → meningococcus	
AN → Anthrax	

G } Gonococcus → DOC → ceftriaxone.
O }

φ Ampicillin } → they secreted in bile
Nafcillin } . So it is safe in renal failure

φ which antibiotic secreted in bile →

R → Rifampicin	} → they safe in renal failure
E → Erythromycin	
N → Nafcillin	
A → Ampicillin	
L → Linezolid	
Disease → Doxycycline	

← Cephalosporin →

divide in 5 generation based on spectrum of action

1 st gen	2 nd gen	3 rd gen	4 th gen	5 th gen
Effective against Gram +ve	↓ effective against anaerobes	↓ wide spectrum +ve -ve	↓ effective against gram -ve	effective against MRSA

1st generation → Cefazolin
Cefalexin
Cefadroxil
Cefaclor
Cefprozil
Cefprozil
Cefprozil

2nd gen → Cefuroxime
Cefaclor
Cefprozil
Cefprozil
Cefprozil
Cefprozil

3rd gen → Ceftriaxone
Cefotaxime
Cefixime
Cefprozil
Cefprozil
Cefprozil
Cefprozil
Cefprozil
Cefprozil

Me
ONE
TEN

(71)

4th generation → cefepime

5th generation → cefpirime

cefbioprole

ceftriaxone

→ • ceftriaxone
• cefoperazone } • Secreted in Bile
• Safest in Renal ds.

→ • cefoperazone } most effective against cephalosporin
• cefazidime } they effective against pseudomonas
• cefepime
• cefpirime

→ • cefoperazone
Moxalactam
cefomandole
cefotetan } • cause disulfiram like rxn.
• they cause Hypoprothrombemia
avoid in bleeding
Tendency pt.

3rd generation →

Bacteriocin → secreted by commensal
Bacteria
they kill pathogenic Bacteria

Infection due to antibiotic → k/a. Superinfection

↓
m/c by *Clostridium difficile*

Pseudomembranous colitis
↓
(it is superinfection
form by WBC.)

‡ Pseudomembranous colitis → (PMC)

* m/c antimicrobial implicated in causing pseudomembranous colitis → 3rd gen cephalosporin > Clindamycin

** → max risk → clindamycin
of causing PMC

m/c Bacteria causing PMC → *Clostridium difficile*

T/T mild → metronidazole → Doc
Vancomycin
fidaxomicin

Severe → Vancomycin only → Doc
↳ orally given

Bezlotoxumab → monoclonal antibody
against *C. difficile*
Toxins.

3) Carbapenems.

Ex → Imipenem → effective against

- Gram +ve
- Gram -ve
- Anaerobes

So → Imipenem + Cilastatin → But it is broken by Dehydropeptidase
they inhibit. all bacteria including Pseudomonas

(12)

- MEROPENEM
- ERTAPENEM
- DORIPENEM
- FAROPENEM → oral

i.v

Fluoroquinolone
carbapenems

↓
these are 2 antibiotic
cause seizure

→ Carbapenem cause → Seizures

↓
so c/i in Epilepsy

φ Extended Spectrum β -lactamase → (ESBL)

- ESBL can break almost all antibiotic except Carbapenem
- so Carbapenem is DOC → for ESBL prodⁿ bacteria
- ESBL producing bacteria → Klebsilla

④ Monobactam → only one ring
do not show cross allergy

ex- AZTREONAM

↳ it for gram-ve only.

← Vancomycin →

- chemical structure is glycopeptide.
- Vancomycin is not effective orally → given i.v.
↓
b/c No absorption
- when it give i.v → release Histamine → Vasodilation
↓
cause Red man syndrome
- effective only for Gram +ve.
- S/E → Nephrotoxic
ototoxic

→ uses of Vancomycin →

- DOC → for MRSA
- DOC → for severe pseudomembranous colitis
↓
given orally***

Other glycopeptides →

- Teicoplanin
 - Oritavancin
 - Dalbavancin
 - Telavancin
- they are New glycopeptides drugs
- long acting
 - Jst like vancomycin
 - Not cause Red man Syndrome

§ Drug acting on cell membrane →

- Daptomycin → • DOC → VRSA (Vancomycin Resistant Staph Aureus)
• S/E → myopathy
- Polymyxin B
- Polymyxin-E (Eteplatin)
↳ Colistin
- ↳ Used for pseudomonas.

§ Drug acting on Metabolism

Pteridine + PABA + GLUT

Sulfonamides ⊗ f.A synthetase

FH₂ → use in diet (folic acid)

methopterin ⊗ DHFase

methamine ⊗ FH₄ (active)

↓
DNA

→ Drug Synergism ($2+2=10$) eg → Sulfonamide + Trimethoprim

Drug antagonism ($2+2=<4$) → Sick drug + static drug (mostly
except TB Drug

Drug Addition → ($2+2=4$)

Drug potentiation → ($2+0=5$) eg → β lactam + LST
(inactive drug) (Levodopa + carbidopa)

← Sulfonamides →

m/c cause of Steven Johnson syndrome

- Sulfadoxine → longest acting
- Sulfacycline → shortest acting
- Sulfasoxazole → most soluble → min risk of crystalluria
- Sulfamethoxazole
- Sulfasalazine → Prodrug, use → ulcerative colitis, Rheumatic arthritis
- Sulfadiazine → use for Burn dressing
- Sulfacetamide
- Dapsone → DOC → Dermatitis Herpetiformis

→ S/E of Sulfonamide →

A - aplastic anemia

B - Bilirubin displacement → so c/I in New born baby → cause (Kernicterus)

C → Crystalluria → so strict the pt Plenty of fluid should be taken.

R → Rash (m/c - Steven Johnson syndrome)

A → metabolised by Acetylation

S → cause SLE

H → cause Hemolysis

↓ Indiet we eat folic acid $\rightarrow$ FH₂ (dihydrofolate^{pn})

→ Trimethoprim & pyrimethamine $\rightarrow$ cause megaloblastic anemia
 $\downarrow$
 b/c it inhibit Dihydrofolate Reductase

φ **CO-TRIMOXAZOLE**

Trimethoprim
+
Sulfamethoxazole

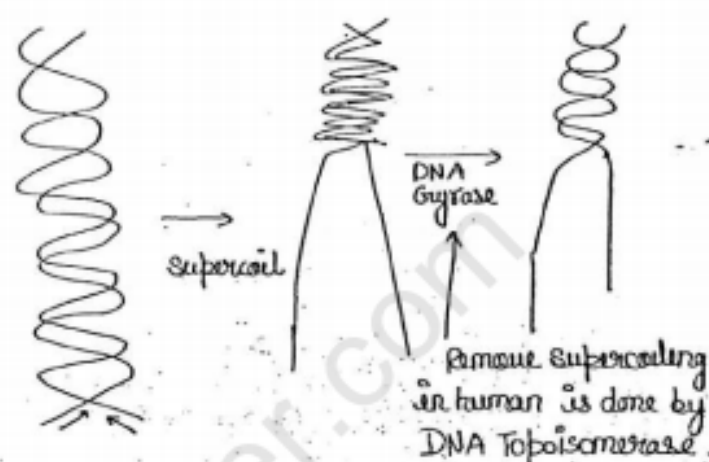
} Doc for $\rightarrow$ • Pneumocystis
 • Nocardia
 it has high absorption & low distribution

→ Trimethoprim + Sulfamethoxazole
 n tab 1 : 20 $\rightarrow$ best bactericidal Action
 2 pt. 1 : 5 is given $\rightarrow$ it goes to blood in the form $\rightarrow$ 1:20

→ Pyrimethamine + Sulfadoxine $\rightarrow$ use for malarial parasite & Toxoplasma

Drug acting on DNA / Nucleic acid →

Drug Inhibit DNA Gyrase enzyme → K/a QUINOLONES



QUINOLONES

Nalidixic acid

- Not contain fluoroide
- Commonly use in UTI

Fluoroquinolones

- End Z floxacin
- they are cidal & effective orally
- they have very wide spec^o (Gram +ve & -ve)

Fluoroquinolones →

Norfloxacin → minimum bioavailability

Ciprofloxacin →

Ofloxacin

Levofloxacin → max bioavailability

Moxifloxacin → safe in Renal failure

Gatifloxacin → Banned b/c cause ^{1st sup} Dysthymia

Pefloxacin → safe in Renal failure

Sparfloxacin → max phototoxic

Irovafloracin → safe in Renal failure

• C/I in epilepsy b/c cause seizure

• C/I in pregnancy & seizure

b/c these drug effect on cartilage & tendon

φ → so 18 yr old & 17 yr old

φ can cause → Phototoxic

φ C/I → Renal failure

EXCEPT P.M.T.

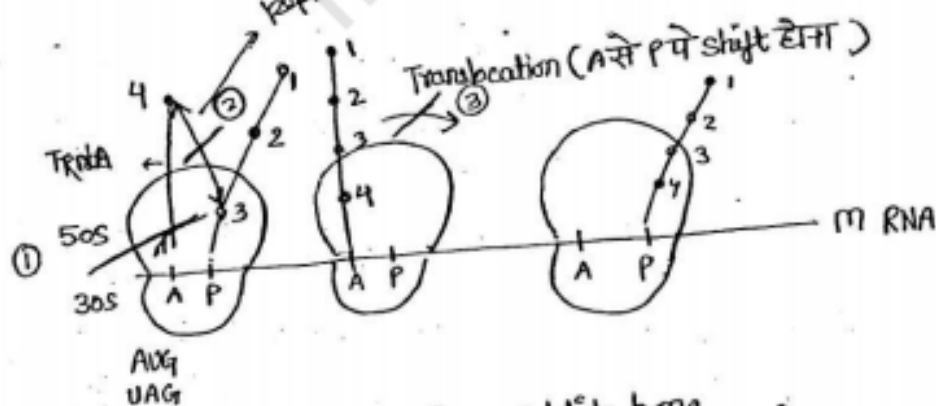
§ Respiratory fluoroquinolones → they kill all bacteria
those effect in Respiratory
Tract Infection → Gram +ve
Gram -ve
atypical bact
Mycoplasma
TB

O → ofloxacin
M → moxifloxacin
G → gatifloxacin
L → levofloxacin → it is longer action than ofloxacin
other all both are similar

→ Moxifloxacin →
• Safer in Renal ds.
• K/a Resp. fluoroq.
• longest acting sparfloxacin > moxifloxacin
• effective against anaerobic bacteria.

§ aminoglycosides are Not effective for anaerobic bacteria.

5) Drug Inhibiting Protein →



→ peptidyl transferase enzyme form peptide bond

1) Tetracycline → stop tRNA to bind A site

2) chloramphenicol → inhibit the peptide bond formation



(75)

23 Drug Inhibit Translocations $\rightarrow$

M $\rightarrow$ Macrolides

C $\rightarrow$ Clindamycin -

Q $\rightarrow$ Quinupristin + Dalfopristin

(i) misreading of mRNA code $\rightarrow$ Aminoglycosides

$\downarrow$
it is fatal

ϕ all protein inhibitors drugs are bacteriostatic but aminoglycosides are bactericidal.

ϕ • A T $\xrightarrow{\text{tetracycline}}$ Bind to 30S unit
 $\downarrow$
aminoglycosides

• all other bind to 50S unit.





← Tetracyclins →

- Tetracycline
- oxytetracycline
- Chlorotetracycline
- minocycline
- Demeclocycline
- Doxycycline

Tetracycline is C/I in →

- K → kidney failure (except Doxycycline)
- A → anti-anabolic
- P → phototoxic → most Demeclocycline
- I → Insipidus Diabetes → max Demeclocycline
- L → Liver failure
- D → Dentition & Bone formation → C/I in pregnancy & children
- E → expiry date के बाद ही देते • 8Yr के बाद देते हैं ।
 ↳ B/c cause S/E → Fanconi Syndrome
 ↓
 Renal Tubular Acidosis
- V → vestibular dysfⁿ → max minocycline
- antibiotic safe in pregnancy →
 - P → penicillin
 - C → cephalosporin
 - M → macrolides



76

uses of Tetracycline →

S → SIADH → use Demeclocyclin

R → Rickettsial Infection → DOC

I → Inguinal granuloma → STD (DOC)

L → Lymphogranuloma venereum → DOC

A → Atypical pneumonia → cause by Mycoplasma
↳ DOC → Macrolides

N

K → Cholera → DOC

A → Amebiasis → Bt DOC → Metronidazole

φ Tetracycline resistance is due to → efflux pump

φ Tigecycline → New Drug
• Jst like Tetracycline
• Resist Resistance to efflux pump

← Chloramphenicol →

- Bind to 50S Ribosome.
- Inhibit peptide bond formⁿ
- Static Drug.
- Now day rarely use → b/c
 - Toxic → Bone marrow suppression
 - Grey baby syndrome
 - less effective
 - C/I in New born
 - b/c of resistance b/c it is inactivated by enzyme.

← Clindamycin →

- Drug have max risk of pseudomembranous colitis.
- effective against anaerobic bacteria.

← Macrolides → drug end 2 Thromycin

- Erythromycin
- Roxithromycin
- Clarithromycin
- Azithromycin

- it is alternative to penicillin
- mainly effect gram +ve

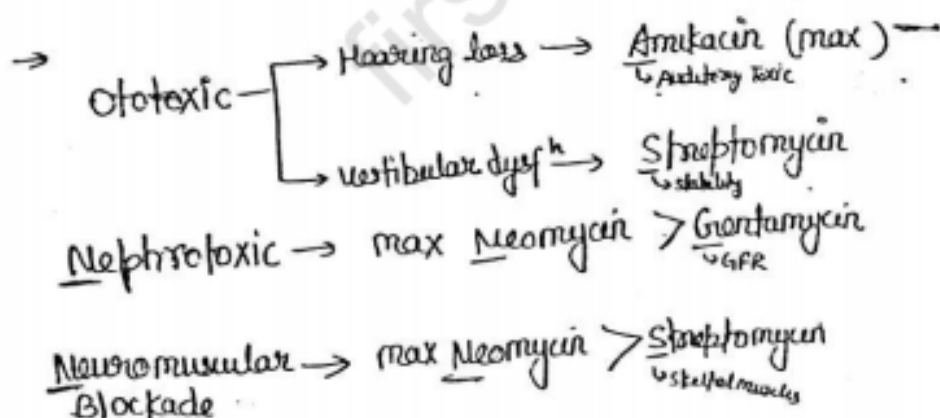
DOC → C → Chancroid
 L → Legionella
 A → Atyp. pneumonia
 P → Pertussis

S/E of Macrolides →

- M → ↑ motilin Receptor stimulate → ⊕ in GIT
 - ↑ GI motility
 - Cause diarrhoea
 - Use in Diabetes Gastroparesis
- A → Allergy
- C → Cholestatic jaundice → by Erythromycin - Estolate
 - ↓
 - C/I in pregnancy only eryth. estolate
- R → Reversible ototoxicity
- O →

Aminoglycosides

- Streptomycin → given in TB
→ Doc → plague
- Gentamycin
- Tobramycin
- Netilmycin
- Neomycin → use for Hepatic coma.
- Capreomycin** → 2nd line anti TB drug.
→ str. f^{ns} are same as aminoglycosides but not Aminogly.
- Kanamycin
- Amikacin → if resistance develop for this then all Aminogly. are resistant
- Spectinomycin → PPNG (Penicillinase producing *Neisseria gonorrhoea*)
→ single dose IV dr^g & Spectinomycin &
Doc → ceftriaxone
- S/E → • Nephrotoxic
• Ototoxic
• Neuromuscular blockade





φ Empirical therapy → (STRT therapy)

→ ^(gram +ve) Penicillin + ^(gram -ve) Aminoglycosides.
Ampi - Gent.

→ if anaerobic suspected → Add antibiotic to work against Anaerobic Bact.

φ when blood report come then give → Definitive Therapy

φ Note → Resistant develop due to enzymes →

A → Aminoglycosides

B → β -lactam

C - chloramphenicol.

Hepatic coma → seen in urease producing Bacteria & liver dysfunction

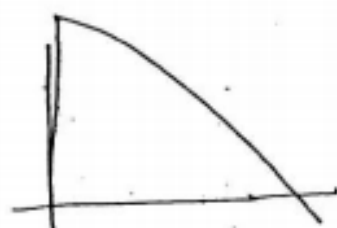
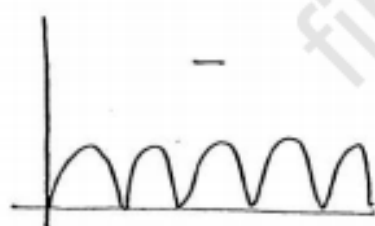
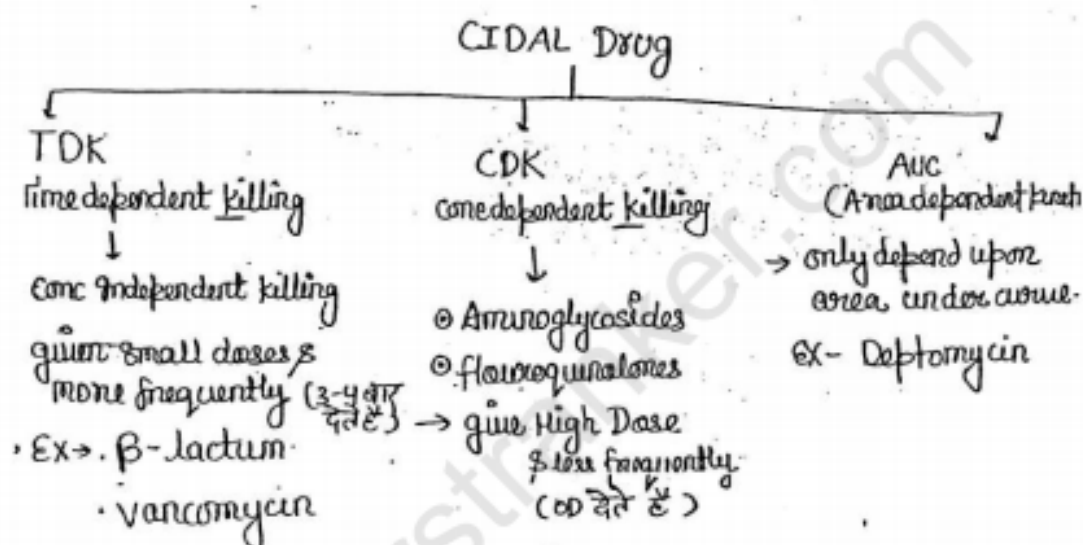
• T/R - Neomycin

↳ cause → gut sterilization

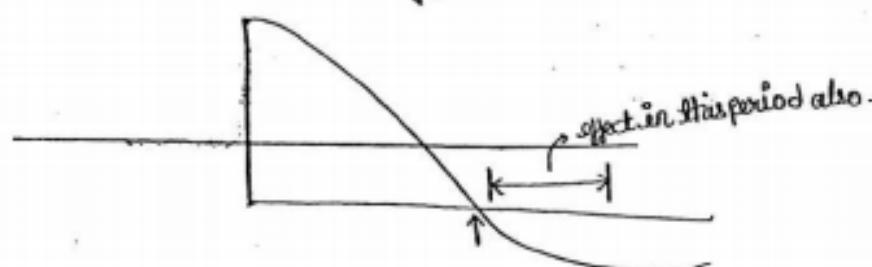
• route - oral.

Rajeev GUSM -

→ Cidal Drug → β -lactams
Vancomycin
Aminoglycosides
Fluoroquinolone.



Post antibiotic effect → (PAE)





(79)

φ

Long PAE > 1.5 hr

- Gram +ve antibiotic (all)
- Gram -ve antibiotic
 - Prot. synthesis ⊖
 - DNA ⊖
 - carbapenems.

Qus which drug long PAE & follow CDK → Fluoroq & AG.

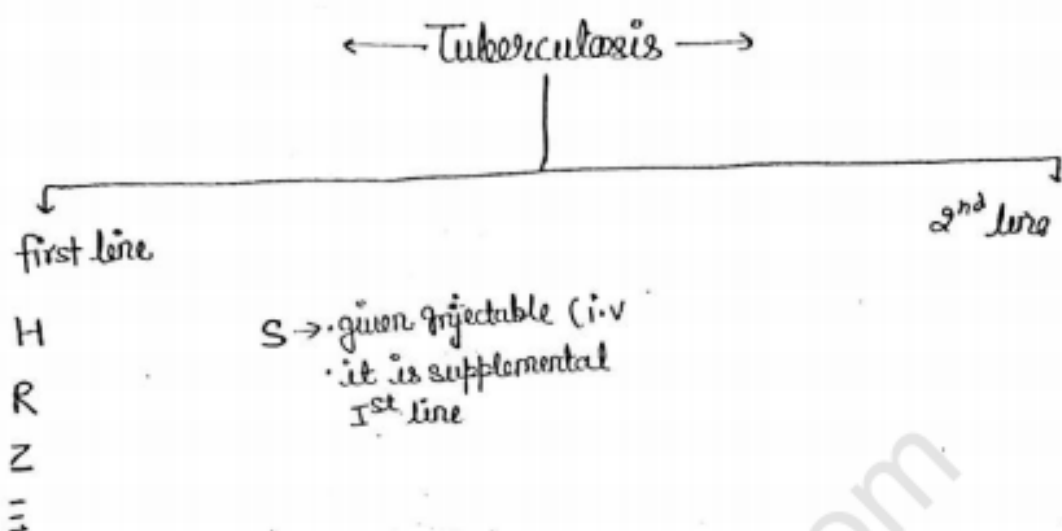
which drug follow IDK + Long PAE → ~~β~~ β-lactam

Ⓐ Vanco

Ⓑ clindamycin → not
b/c static

Ⓒ FQ





New classification of anti TB Drug for MDR (2016)

Group

- A → fluoroquinolones [O, M, G, L]
- B → injectables [Strepto, capromycin, Kanamycin, Amikacin]
- C → other core drugs →
 - C → Cycloserine (Terizidone)
 - Y → Clofazimine
 - C → Linezolid
 - E → ethionamide (Prothionamide)
- D → Divide in 3 part
 - gpD K/a add on Drug
 - D₁ → Z, E, INH (High dose)
 - Ethambutol
 - D₂ → latest drug of TB →
 - Bedaquiline
 - Delamanid
 - D₃ →
 - PAS
 - Amoxy-caliumic
 - Imipenem + cilast
 - Meropenem
 - Thioacetazone



(6)

→ first line Drugs → HRZES

H	R	Z	E	S
↓	↓	↓	↓	
CIDAL	CIDAL	CIDAL	Sien Stati c	• CIDAL
Both Extra & Intra	Both Extra & Intra	kills both Intracellular & Extracellular Bacilli	Both Extra & Intra	• kills only <u>Extracellular</u>
		• Not given in Pregnancy (<u>Avoid</u>)		C/I in <u>pregnancy</u>

• Safest Drug
in Renal ds• most efficacious
TB Drug

Hepatotoxic

Hepatotoxic

more hepatotoxic

No
HepatotoxicNo Hepato
Toxic

φ fast growing bacteria → seen in wall of cavity — H

φ Intermediate (spore formers) → caseous Necrosis — R

φ slow → intracellular — Z

INH →

- ① Metabolise by acetylation
- ② cause SLE
- ③ ↓ vit B₆ (Pyridoxine) → cause peripheral Neuropathy
- ④ Neuropsychiatric S/E

Rifampicin → • MOA → RNA Polymerase - β (rpo β)

• given empty stomach

• powerful enzyme inducer

↓
by mutation
Resistance to
Rifampicin

R + warfarin → warfarin R₁ β के साथ
Heparin भी add करेंगे (Immediately)

R + OCP → long term के लिए ↑ dose of warfarin

R + anti HIV → use other method of contraception

R + anti HIV → change the Rifampicin &
give Rifabutin

Rifampicin

- Enzyme Inducer +++
- more effective for TB
- less effective for MAC
- short duration of action
- Hepatotoxic

- +
- less effective
- More effective MAC
- Long duration of action
↓
bt Pseudojaundice cause
- No Hepatotoxic
- they cause → uveitis
Pseudojaundice

(8)

• Rifampicin other uses →

- DOC → Prophylaxis of meningococcal meningitis
- " " H. Influenza meningitis
- effective for MRSA
- Effective for pseudomonas
- Most efficacious drug in Leprosy
- T/T of Brucella [Doxy + Rifampicin]

φ Pyrazinamide → • ↑ uric acid
 • more Hepatotoxic

φ Ethambutol → • Eye → • Optic Neuritis
 • colour blindness (Red Green)
 initially reversible but continue
 Drug $\rightarrow$ then it, irreversible
 • So C/I in <6 yrs child.

φ Streptomycin → • Hypokalaemia (Z > E)
 given injectable.

- Cycloserine → cause Neuropsychiatric effect
- Clofazimine →
 - cause → Ichthyosis (Dryness of skin)
 - use in leprosy

Linezolid → mainly for MRSA

Ethionamide →

- Hepatotoxic
- S/E → Hypothyroidism
- MOA → ⊖ ATP synthase

⇒ Bedaquiline
Delamanid } → cause QT prolongation
 → ⊖ mycolic acid

⇒ Thioacetazone → C/I in HIV



(8)

RNTCP- ~~2010~~ Old → 3 a week.

Drug Sensitive

IP

CP

Cat-1 New (New + <1 month
therapy less than 1 month)

4 HR

Cat-2 - Old (Opt + >1 month
therapy)
↓
1 HRZE

4 HRE

New RNTCP- 2016 → Daily

IP

CP

Cat 1

2 HRZE

4 HRE

Cat-2

2 HRZE
+
1 HRZE

4 HRE

→ In adult → only 1st direct, daily therapy started.

• In children → daily therapy ही देगे

⇒ if sputum smear at end of IP → No Need to extend the
Even if smear +ve
according to New guidelines

Drug resistance →

Monodrug → HRZE for any of the resist except R

Poly drug → ≥ 2 Drug Resistant except (H+R)

MDR → for H+R Resistance

Rifampicin-Resistant → for R Resist. → T/T like MDR

XDR → MDR + Resistance to 1 Fluoroquinolone + 1 injectable Drugs

MONO DRUG	IP 3 [1st line drug + levoflox + kanamycin (inj.)]	CP 6 [FLD + levoflox]
Blydrug	3 [FLD + levoflox + kanamycin + Ethionamide] inj	6 [FLD + Levoflox + ethionamide]
MDR ↓ resists to HR	6 [ZE + levoflox + kanamycin (inj.) + Ethionamide + cycloserine]	18 [E + levoflox + ethionamide + cycloserine]
Rifampicin Resistant	6 [HZE + levoflox + kanamycin (inj.) + ethionamide + cycloserine]	18 [HE + levoflox + ethionamide + cycloserine]
XDR	6 INH fluoroquinolone clarazimine PAS clarazimine PAS	18 CIPA-Q clarazimine PAS



(8)

Bedaquiline → use in MDR & XDR

Indication →

MDR { resistance to all fluoroquinolones
resistance to all inj. Drug } or failure of MDR

XDR → 6 months { 2 week 400 mg OD
200 mg thrice a week }

Shorter MDR- Regimen → 2016

① it is only for pulmonary TB

② it is CI in pregnancy

③ when pt is not exposed / resist. to 2nd line drug then given

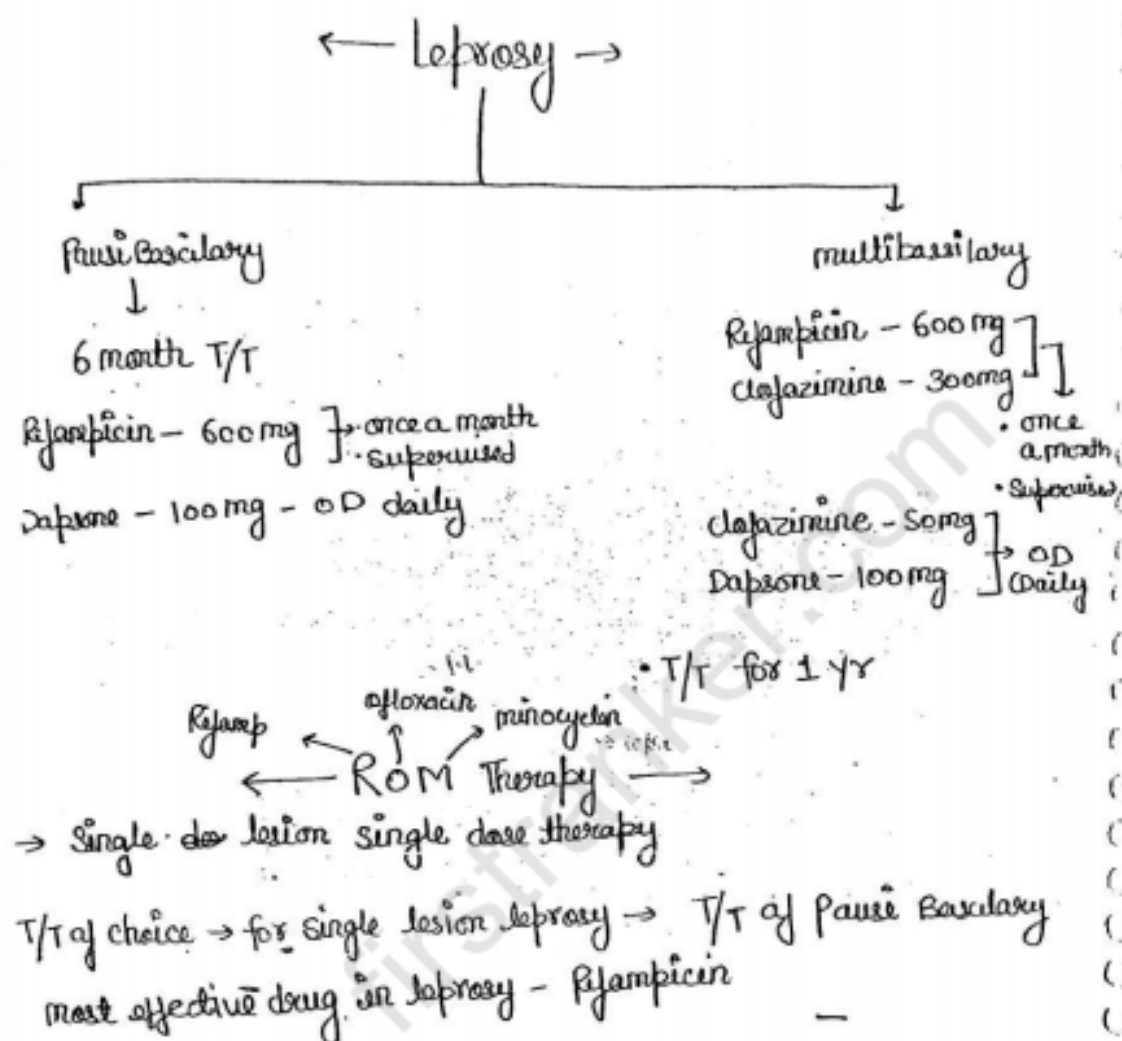
IP

4 [ZE H + fluoroq. + Kanamycin
Highdose moxiflox
clofazimine + prothionamide]

CP

5 [ZE Moxi Clofazimine]

TB + HIV pt → then 1st treat TB (earlier in 8 week) then HIV
V/T



(84)

← leprosy →

Type-I }
Type-2 } Doc → Steroid.

← Mycobacterium Avium complex (MAC) →

① Seen in immunocompromised pt.

② Prophylaxis → Azithromycin → once weekly

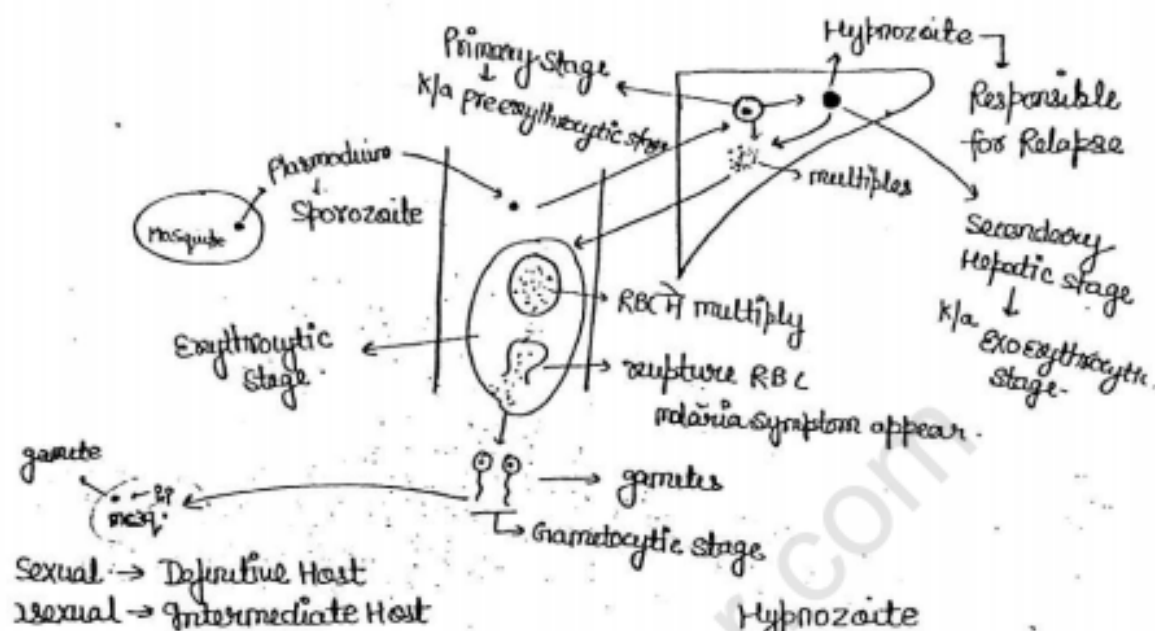
or
Clarithromycin → OD Daily

③ T/T → R (Rifabutin)

+
E → Ethambutol

+
C → Clarithromycin

← antimalarial drugs →



Relapse → due to Hypnozoite

Recrudescence → RBC वाले ही पूरे नहीं मरे

Stages →

• Pre-Erythrocytic stage → cause of malaria • T/T - causal prophylaxis

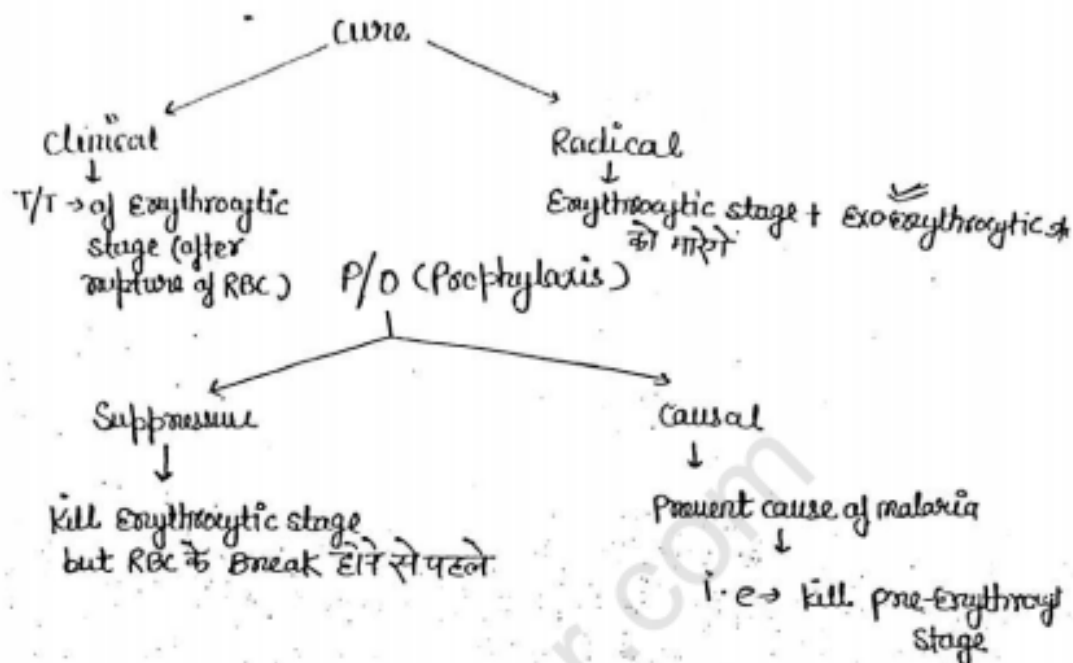
• exo-Erythrocytic stage → for Relapse • Radical

• Gametocytic stage → for Transmission of malaria • ☹ Transmission

Erythrocytic stage → for symptom of malaria < Suppression Prophylaxis, clinical cure

Primaquine → use for ①, ② & ③ stage.

① stage → Primaquine not work 2 week 1/1 one dose req.



Erythrocytic stage

Fast acting anti malarial drug

SLOW

- | | |
|---|--|
| <p>M → Mefloquine → s/e Neuropsychiatric effect</p> <p>A → Atovaquone</p> <p>C → Chloroquine gp →</p> <p>H → Halofantrine gp</p> <p>A → Artemisinin gp</p> <p>R → Res-Q (Quinine)</p> | <p>• Sulfadoxine</p> <p>• Pyrimethamine</p> <p>• Proguanil</p> <p>• Doxycycline</p> <p>• Clindamycin</p> |
|---|--|
- Not preferred in cerebral malaria
- Not preferred in prophylaxis

- Chloroquine gp
- C - chloroquine
- A - Amodiaquine
- P - piperaquine

⊕ Halofantrine gp
→ Halofantrine
→ Lunifantrine

⊕ Artemisinin gp →

Artesunate
Artemether
Artemether
Dihydroartemisinin

- } • fastest acting malarial drug
• use for MDR
• Very short acting
• S/E - Recrudescence

↓ oral
→ SO ACT Therapy given

• Artesunate + sulfadoxine / pyrimethamine

but in North east state → long acting

• Not use ACT

• Artemether + Lunifantrine use

⊕ Chloroquine → • High Vd > 1300L

• Can cause → Bull's Eye maculopathy
↳ occurs when we use for long term



8

Other use of Chloroquine →

R → Rheumatoid arthritis

E → Extraintestinal amebiasis

D → DLE

L → Leprosy

I → Infectious mononucleosis

(ampicillin not give in Inf. mononucleosis
b/c it cause rash)

P → Photogenic rxn में T/T के लिए देते हैं

Mahatma → malaria

Gandhi → Giardiasis

← T/T of Malaria →

• NVBDCP → National Vector Borne Disease control prog.

→ P. vivax / malar → Doc → chloroquine + Primaquine (2week)
↳ C/I → Pregnancy < 1 yr age

→ P. falciparum / malar → Doc → ACT + Primaq. (single dose) G6PD deficiency
• P. falc → chloroq. neustant Hota है।

φ ← T/T of malaria in Pregnancy →

→ Primaquine → C/I in Preg.

→ No Drug is given for cure Radical T/T

→ ACT is C/I in 1st Trimester

→ P. vivax → Doc → chloroquine

→ P. falciparum → Ist trimest → Quinine

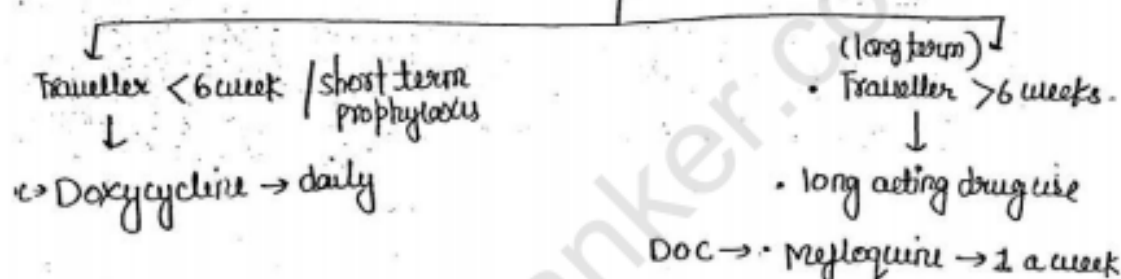
↳ IInd & IIIrd Trimest → ACT

T/T of cerebral malaria
or
complicated/severe malaria

φ T/T of choice → Artesunate (48 hr)
↓
i.v route

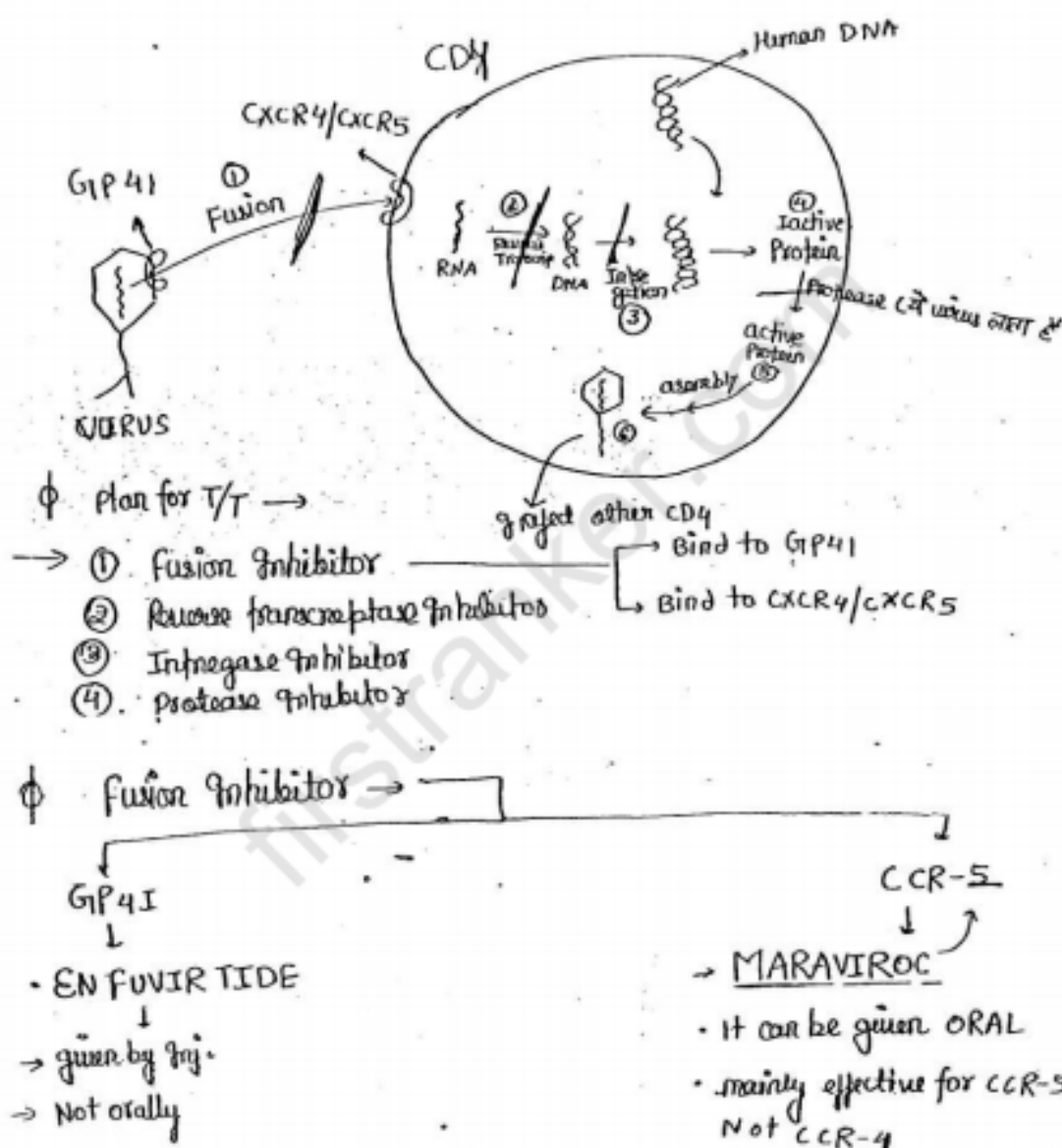
! In pregnancy में भी 1st trimester में भी Artesunate देगे

← Prophylaxis of malaria →

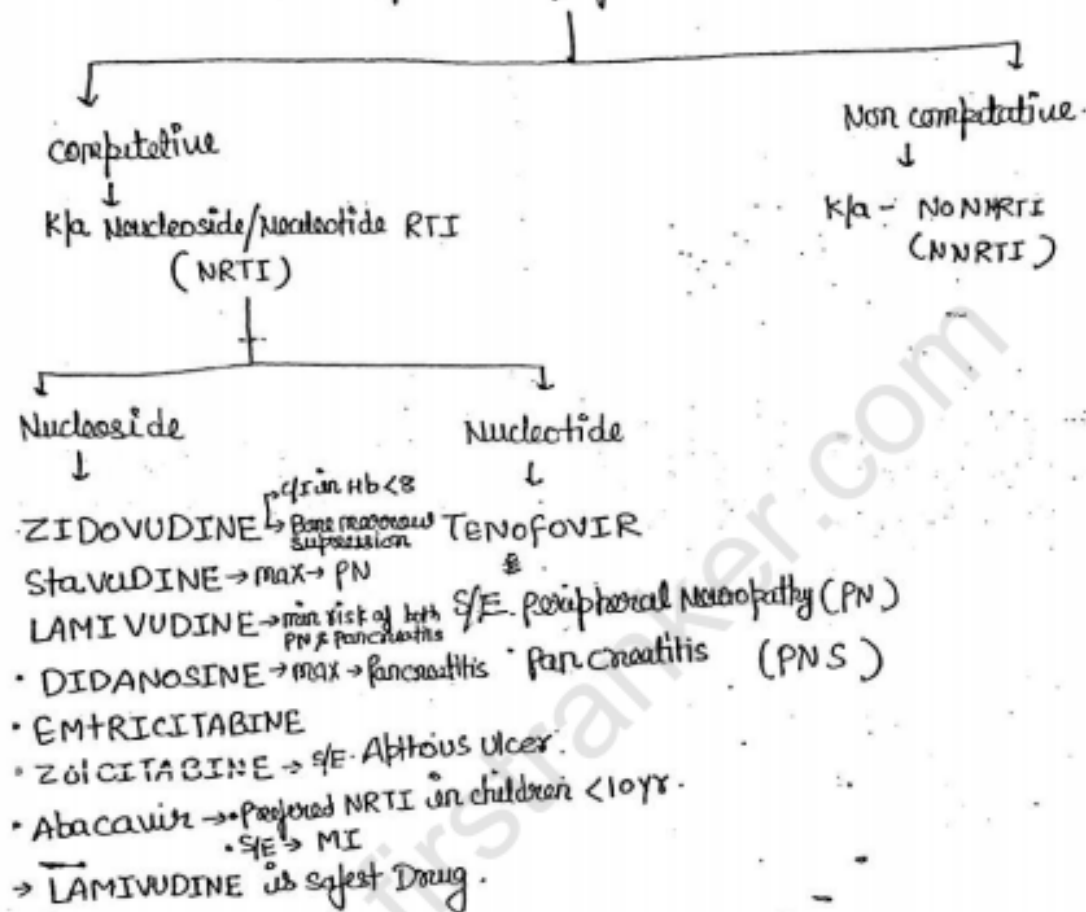


(87)

← HIV → Retro virus



Reverse Transcriptase Inhibitor (RTI) RNA Depend. DNA polymerase Inhibitors



Grancyclavir → DOC → cytomegalovirus
s/e BM Suppression

ZIDOVUDINE → cause - BM LL
c/I in Hb < 8
Not give ZIDOVUDINE + Grancyclavir combination
b/c it also cause BM LL



Q6

Q which NRTI T/T Hep B

L → Lamivudine

E → Emtricitabine

T → Tenofovir → 1st line drug for Hep B.

NON-NRTI

First generation → E - EFVIRENIZ → Neuropsychiatric S/E

N - NEVIRAPINE → Hepatotoxic S/E

D - DELAVIRIDINE → Not @ India

Second generation →

• Etravirine

• RILPIVIRINE

Q Note → • NON-NRTI only against for HIV Type I

• all NON-NRTI substrate for microsomal enzyme so
it can't given 2 Rifampicin

← Integrase Enzyme Inhibitors →

- RALTEGRAVIR
- ELVITEGRAVIR
- DOLUTEGRAVIR

→ Protease Inhibitors →

↓
Drug End C NA VIR

- RITONAVIR → Strongest enzymatic (CYP3A4) Inhibitor
- LOPINAVIR → very low dose देते हैं।
- SAQUINAVIR
- ATAZANAVIR → S/E Hyperbilirubinemia
- Nelfinavir → least risk of lipodystrophic synd.
- Nelfinavir → metabolised by Non metabolised Drug
- AMPRENNAVIR
- FOSAMPRENNAVIR
- DARUNAVIR
- TIPRANAVIR
- INDINAVIR → cause Renal stone.

S/E of Protease # → Lipodystrophic syndrome.

- ① Protease # is metabolised by microsomal enzyme - CYP3A4
- ② So they are prone to Drug Interaction so Rifampicin के साथ नहीं दे।
- ③ Protease # is also inhibited → CYP3A4
- RITONAVIR Boosting the effect of other Prot. # except Nelfinavir

(8)

T/T of HIV

↓
K/a → (HAART)

→ when to start → all pt of HIV should be treated, No matter CD4 count

- minimum 3 Drugs
- minimum 2 groups

FIRST line →

2 NRTI + 1 NNRTI
or
2 NRTI + 1 I I

m/c Regimen →

T + L + E → efavirenz
↓ or
tenofovir ↓ Dolutegravir
lamivudine

• < 10 yr →

A + L + E
↓
abacavir

• given → life long.

← Infant prophylaxis →

→ Z + N

- for 6 week
- child after birth

← Post exposure prophylaxis →

Done in 72 hour → as early possible

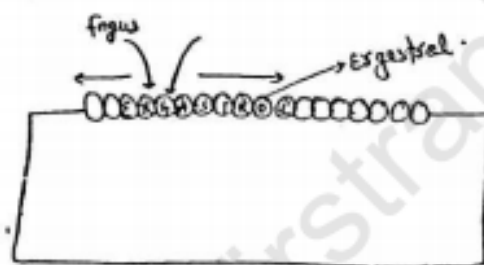
it therapy for 4 week

• Drugs → adult → T + L + Prot. Inhibitor

• < 10yr → Z + L + Prot. Inhibitor

← Antifungal Drugs →

① Amphotericin B → bind at ergosterol.



- can not given orally
- route - i.v
- m/c S/E → Infusion related rxn
- other S/E → Renal Tubular acidosis & Hypokalemia

m/c ~~sp~~ dose dependent S/E

Doc → all serious fⁿ infection

Doc → Kala azar / leishmaniasis → single dose (i.v)

for ↓ S/E make lipid preparation →

- Liposomal Amphotericin B
 - Amphotericin B lipid complex
 - Amphotericin B colloidal dispersion
- } they DO NOT
cause
↓
• Nephrotoxic
- They are very costly.

② Azoles → static

- Ketoconazole → cause gynecomastia & Enzyme Inhibitor
- fluconazole → max oral absorption, & max conc go in CNS
 - Doc → Cryptococcus, Candida Inf.
- Itraconazole
 - ↳ Doc → Sporothrix, Blastomycosis, Histoplasma.
- Voriconazole → Doc → Invasive aspergillosis
- Posaconazole → only azole effective against Mucormycosis
 - ↳ Bt Doc → Amphotericin B

③ Terbinafine

- Butenafine
- Naftifine

- these all three are Bactericidal
- given ORAL
- affinity max in Keratin
 - ↳ skin
 - ↳ Hair
 - ↳ nail

so given in Dermatophytosis → Doc → Terbinafine



1) Griseofulvin → • oral

- high affinity to keratin
- Bacteriostatic
- So max. Relapse occur 2 Griseofulvin
- SE → Disulfiram Like rxn
- No preferred Nausea

2) Echinocandins → act on fungal cell wall

↓
ex → Caspofungin

use for → • Candida
• Aspergillosis



(9)

← Antiviral Drugs →

① Herpes

Herpes simplex virus → Doc → Acyclovir

Acyclovir → Acy. Monophos → Acy. Di Phos

Inhibit DNA
Polymerase

↓
Acy Tri Phos

• So Resistance of Acyclovir → due to mutation in viral thymidine kinase

• HSV }
VZV } Doc → Acyclovir

• CMV → Doc → Ganciclovir

↓
S/I → BM ↓↓

• Hepatitis virus → A, D, E No T/T req.

• Hep B → acute → No T/T

↓ chronic → Entecavir / Tenofovir

• Hep C → Acute
↓ chronic

IFN + Ribavirin

↓
Inj.

↓
Inhalation



oral drug for Hep. C →

- 1) protease Inhibitors
- 2) NS5A Inhibitors
- 3) NS5B Inhibitors

} all are given orally

→ Protease # → end Z protease

- Telaprevir
- Boceprevir
- Simeprevir
- Grazoprevir
- Paritaprevir

→ NS5A # → end Z Asvir

- Elbasvir
- Ledipasvir
- Ombitasvir
- Daclatasvir
- Velpatasvir

NS5B # → end Z buvir

- Sofosbuvir
- Dasabuvir

92

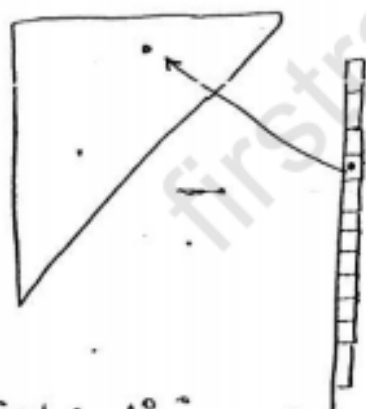
φ Influenza virus →

→ Amantadine
→ Rimantadine } for Influenza A.

→ Neuroaminidase Inhibitor →

Oseltamivir
Zanamivir
Peramivir } DOC → Bird flu
Swine flu.

← Antiamoebic Drug →



• mild Amebiasis → DOC → Diloxanid furoate
other → Tetraacycline
• Paramomycin
• Quinidochlor

• Intestinal amebiasis / Amebiasis → Metronidazole
Hepatic amebiasis

- Metronidazole → S/E Disulfiram like rxn
- Metronidazole
- Tinidazole
- Secnidazole
- Oxidazole
- Sapropteridazole → Not cause disulfiram like rxn.
- Metronidazole m/c use →
 - G → Giardiasis → DOC
 - U → Ulcer peptic (Triple Drug)
 - P → Pseudomembranous colitis
 - T → Trichomonas
 - A → anaerobic bacteria

← KALA AZAR →

- DOC → Liposomal Amphotericin B (i.v)
- m/c use → stibogluconate
- Oral drug for kala azar → Miltefosin
 - ↓
 - Doc - Post kala azar
 - Dermeto leishmaniasis

9

← Trypanosoma →

African Tryp.
(Sleeping sickness)

- Early stage → Doc Suramin
- Late stage → Doc → Melarsoprol

South-American
↓
(Chagga's disease)

Doc → Benznidazole

← Anthelmintic drugs →

Platyhelminths

- Tape worm
- fluke

- Doc → Praziquantel (farall)
- but except → Dog Tapeworm (Echinococcus)
↓
Doc → Albendazole
- Liver fluke (fasciola) → Doc → Triclabendazole

Nematodes

- Round worm
- Hook worm
- Pin worm

Doc → Albendazole

• except → filarial worm

Doc → Diethyl carb

Strongylidae
Onchocerca
↓
Doc

Ivermectin

• Scabies

Doc → Permethrin
(locally applied)

also
• Oral

← Anticancer Drugs →

↓ Rapidly dividing cells →

① BM → ↓

② Hair - Alopecia

③ GIT → Diarrhea
• Vomiting

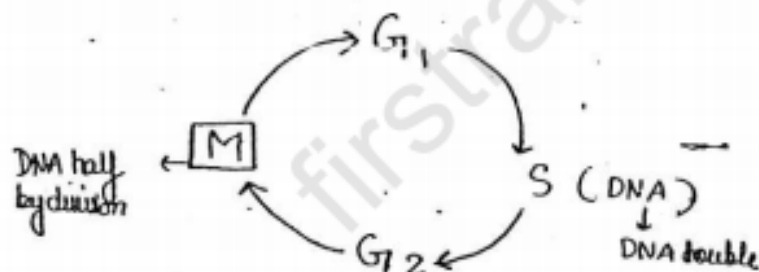
anticancer drug leads

- Hyporecemia
- gout

S/E of anticancer drugs →

- Bone marrow suppression
- Alopecia
- Diarrhea
- Vomiting
- Hyporecemia
- gout

Cell cycle →



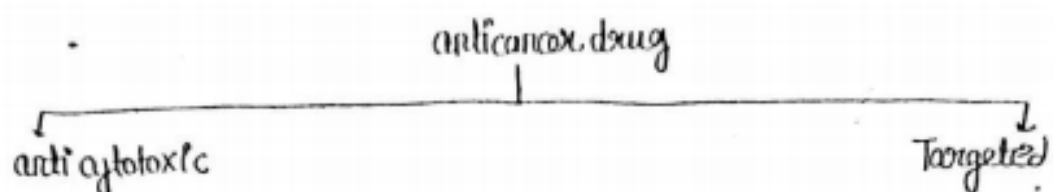
→ Drug S phase specific → K/a → Antimetabolites

→ Drug M phase specific → Ex → VINCISTINE
VINBLASTIN
PACITAXEL
DOCETAXEL

→ Drug G₁ " " → ETOPOSIDE

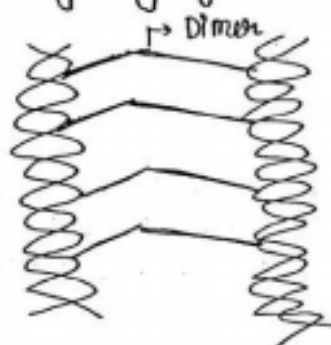
→ Drug G₂ " " → ETOPOSIDE
IRINOTECAN
BLEOMYCIN

(94)



⌀ anticytotoxic drugs →

① alkylating agents → Cause - Dimer formation



→ m/c site of alkylation is N7 of Guanine

→ S/E of alkylating agent → 2° leukaemia + 4 (BM ↓, Gout, Hyperuricaemia, Infectility, Vomiting, Diarrhoea)

Ex → Mechlorethamine → use T/T of Hodgkin lymphoma (Not Now)

• Melphalan → for multiple myeloma (if asked single drug is effective in m-myl)

• Cyclophosphamide } → cause Hemorrhagic cystitis

• Ifosfamide

• Chlorambucil → use for CLL, Doc → fludarabine

• Busulfan → S/E pulmonary fibrosis

• Mitomycin-C → use for

• Procarbazine → cause disulfiram rxn

• Dacarbazine

• Nitrosourea ÷ Carmustine (BCNU)

↓
• Can cross BBB Lomustine (CCNU)

• 1st line drug for Brain TM Samustine (methyl CCNU)

T/T of Hodgkin Lymphoma

M → mechloroethamin
O → oncovin (vincristin)
P → Prednisolone
P → procarbazine

} New day Not used

A → Adriamycin
V → vinblastine
B → Bleomycin
D → Dacarbazine

} New day used

T/T of NON Hodgkin Lymphoma →

T/T of choice → CHOP ± R

C → Cyclophosphamide

H → Hydroxydaunorubicin (Doxorubicin)

O → Oncovin (vincristine)

P → prednisolone

+

R → Rituximab



← T/T of colo-rectal carcinoma →

FOLFOX / FOLFIRI

Folinic acid

+

5 Fluorouracil

Oxaliplatin⁺ / Irinotecan

φ Cyclophosphamid / Ifosamide

↓
metaboles

↓
Acrolein

(S/E) Hemorrhagic cystitis ⇒ Ifosamide > Cyclophospha

T/T → Mesna → mercapto ethane sulfonic acid

↓
& /
prevention

DOC

→ Hemorrhagic cystitis

route - oral / i.v

← Mitomycin-Cl →

it is given Intravesical Injection route

use for. Superficial bladder cancer → also used BCG

use for → Laryngeal tracheal stenosis

↓
Re stenosis को prevent करने के लिए देते हैं

> use for Hypoxic Tumour cell → b/c it is prodrug & active in anaerobic condⁿ

↓
Best drug. Mitomycin-C

Nitrosourea →

they can cross BBB

1st line drug for Brain TM

- ② Platinum comp →
- These attache to platinum gb
 - at N₇ of Guanine
 - A/E → 2nd leukemia
 - Infertility
 - Cisplatin
 - Carboplatin
 - Oxaliplatin → use for ano-rectal carcinoma

Cis platin → S/E →

- max risk of vomiting
- Nephrotoxic →
- Ototoxic

• Ondansetron → Doc for chemotherapy induce vomiting
↓
5HT₃ #

• Doc for delayed vomiting → Aprepitant

↓
it is substance P antagonist

φ Cis platin → given by slowly i.v b/c Nephrotoxic से बचने के लिए

• Nephrotoxicity prevent by saline loading (2lit)

• T₁ of Nephrotoxicity → Amifostine

use → Cisplatin induce Nephrotoxic

• Radiotherapy induce xerostomia (dry mouth)

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③ Antimetabolites → • They inhibit formation of DNA
• they are S-phase specific

④ Folic acid metabolism

⑤ Purine metabolism

⑥ Pyrimidine metabolism

① Folic acid metabolism

Pteridine + PABA + glutamate

↓ FA synthetase

Diet → FH₂

⊙ ↓ DHFRase

Methotrexate

↓
DHFRase
inhibitor

FH₄ (folic acid)

↳ r/a - Leucovorin / Citrovorum

↓
use for T/T of Methotrexate
S/E →

DNA

→ for severe toxicity (Methotrexate)

Glucoylidase → • Methotrexate blocking enzyme

↳ given only severe methotrexate poisoning

Other S/E

→ • megaloblastic anemia
• Hepatotoxic

use of methotrexate →

C - choriocarcinoma → DOC

A - Abortion

N - NHL

⌒ - Crohn's disease

≡ - Ectopic preg.

⌞ → Rheumatoid arthritis (NMARD) → DOC

⌞ Pemetrexed → use for mesothelioma

⌞ Pralatrexate → use for Peripheral T-cell lymphoma

φ Purine

- Adenine
- Guanine

Pyrimidines

- Cytosine
- Thymine

φ Purines metabolism Inhibitors →

metabolised by → Xanthine oxidase

- ① 6-mercaptopurine
 - ① 6-Thioguanine
- } Hepatotoxic

① Glabridine → DOC → Heavy cell lymphoma

① Fludarabine → DOC for CLL

Xanthine
↓ xanthine oxidase
Uric acid

φ allopurinol is always given for anticancer drug for prevent Hyperuricemia

φ bt allopurinol & 6-mercaptopurine given the 6-mercaptopurine dose are decreased

φ Pyrimidines metabolism Inhibitors →

① 5-FU → S/E • Hand foot syndrome.
bt m/c S/E → Diarrhea

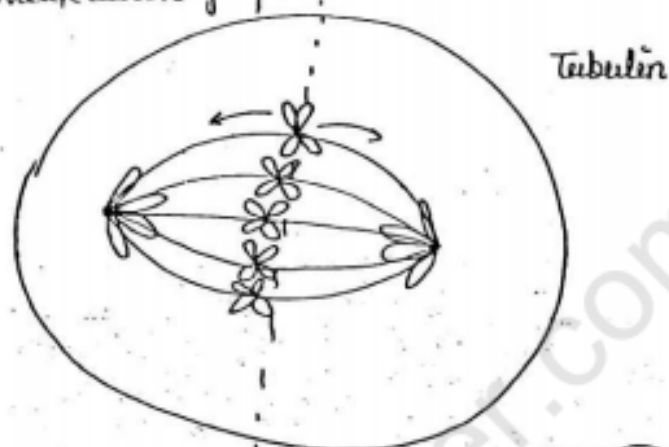
• Capecitabine → Prodrug & metabolised form 5-FU
• so it also cause → Hand foot syndrome
• bt it can be given oral route

• Gemcitabine → DOC for pancreatic carcinoma

• Cytarabine → S/E → cerebellar S/E → ataxia, nystagmus, vertigo

④ Drug acting on mitotic spindle →

2 type → formation of spindle
Break down of spindle



Drug Inhibiting formation of spindle → **VINCRIStine**
Vinblastin } S/E
• peripheral Neuropathy
• STADH

Drug Inhibiting form Break down of spindle →

Paclitaxel → S/E
allergy

Vincristine do not cause BM suppression

New Drug → acting on mitotic spindle → M phase

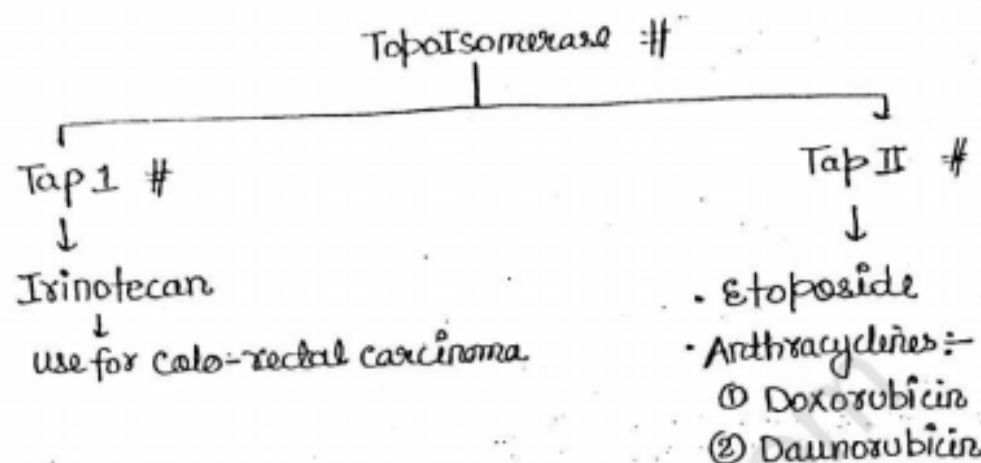
ERBULIN → use for Breast ca

Estramustine → use for prostate cancer

Ixabepilone → use for Breast cancer

(97)

⑤ Topoisomerase Inhibitor →



• Etoposide → it is Topoisomerase II Inhibitor

• S/E Alopecia

• Uses → T → Testicular carcinoma
O → oat cell carcinoma of lung
P → prostate carcinoma

• S/E → 2° leukemia

• * occur 1-2 yr

• No myelodysplasia

Alkylating agent

S/E 2° Leukemia

• * occur in 4-5 yr

• myelodysplasia occur

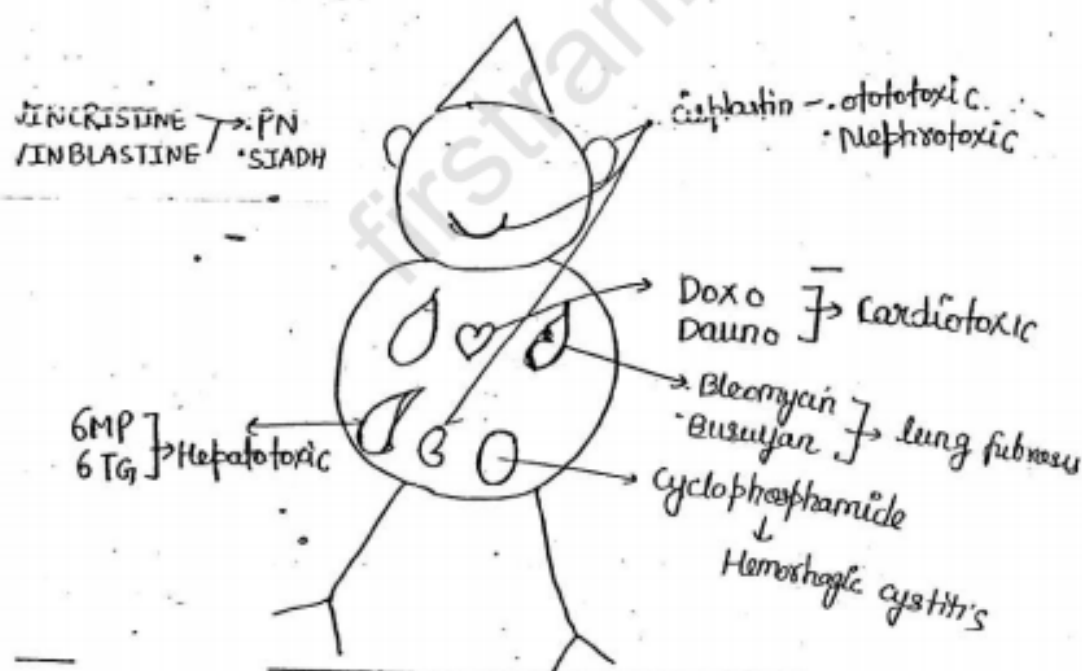
→ Anthracyclines →

- Doxorubicin
- Daunorubicin

} they are cardiotoxic (dilated cardiac myopathy)
↓
b/c of free Radical produce

Dexrazoxane → is ↓ the risk of free Radical prodⁿ

- ⑥ Bleomycin → • Not cause BM ↓
• S/E → Pulmonary fibrosis → Type I pneumocyte kills by Bleomycin
↓
So Hyperplasia of Type II pneumocyte.
↓
Pul. fibrosis
- L - Asparaginase → Not cause BM ↓
↓
• Use for ALL
• S/E - Severe Hypersensitivity rxn
• Acute severe pancreatitis
- ⊆ Anti-cancer Drug Not cause BM ↓
V → Vincristine
B → Bleomycin
L → L-Asparaginase



Targeted anticancer Drugs

Small molecules Inhibitors

Monoclonal Ab
Route i.v / injectable.

→ Small molecules Inhibitors →

① Proteasome Inhibitors → end 2 Zomib

Protease

| ⊖

IκB

| ⊖

NF-κB

↓

Growth

BORTEZOMIB

CARFILZOMIB

IXAZOMIB

} → use in multiple myeloma

② PARP Inhibitors → (Poly ADP Ribose Polymerase)

↓
OLAPARIB → for ovarian carcinoma

RUCA PARIB → ovarian carcinoma

3) CDK 4 & CDK 6 Inhibitor →

- PALBOCICLIB → use for Breast cancer
• given orally

1) Histone deacetylase Inhibitor (HDAC #.]

- Vorinostat
 - Romidepsin
- } use for cutaneous T-cell lymphoma

New Drug → Belinostat → use for Peripheral T-cell lymphoma.

Panobinostat → use for multiple myeloma

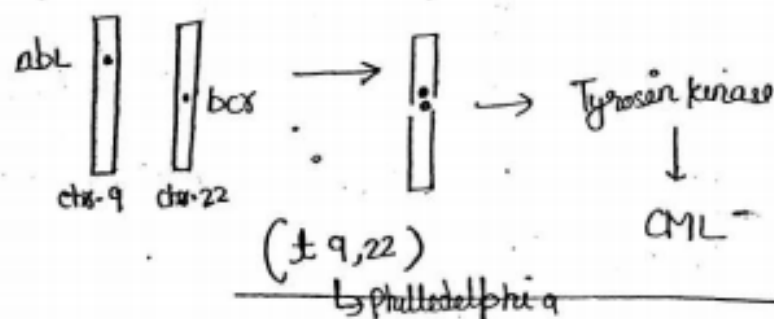
2) BCL-2 Inhibitor →

- VENETOCLAX → use for CLL

3) Hedgehog Pathway Inhibitor →

- Sonidegib
 - Vismodegib
- } use in Basal cell carcinoma

4) Tyrosine Kinase Inhibitor →





(10)

- ◊ Tyrosin kinase are given orally
- ◊ all are metabolised by microsomal enzyme CYP3A4
- ◊ they S/E skin rash
- ◊ Name end with NIB

→ Kinase ⊖ use in CML →

- B Bosutinib
- I Imatinib → Doc for CML
- N Nilotinib
- D → Dasatinib
- Proteins → Ponatinib

→ Kinase ⊖ use for Non-small cell Lung cancer →

- perate → osimertinib
- after → Afatinib
- E → Erlotinib
- C → Cestirib
- G → Gefitinib

→ Key Ty. Kinase ⊖ for Renal cell carcinoma →

- P - Pazopanib
- A → Axitinib
- S → Sorafenib
- S → Sunitinib



Ty. Kinase Inhibitor for Hepatocellular carcinoma

SORRY - SO RAFENIB

Ty. Kinase Inhibitor for GIST

S - Sorafenib

I → Imatinib → DOG

R → Regorafenib

φ Ty. Kinase Inhibitor for Breast carcinoma

Lapatinib

φ Ty. Kinase Inhibitor for malignant melanoma

D → Dabrafenib

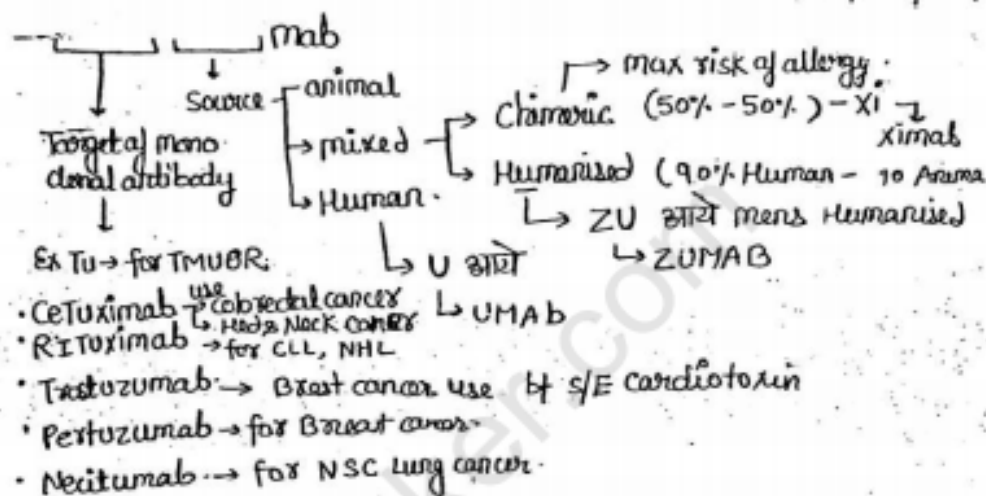
V → Vemurafenib

T → Trametinib

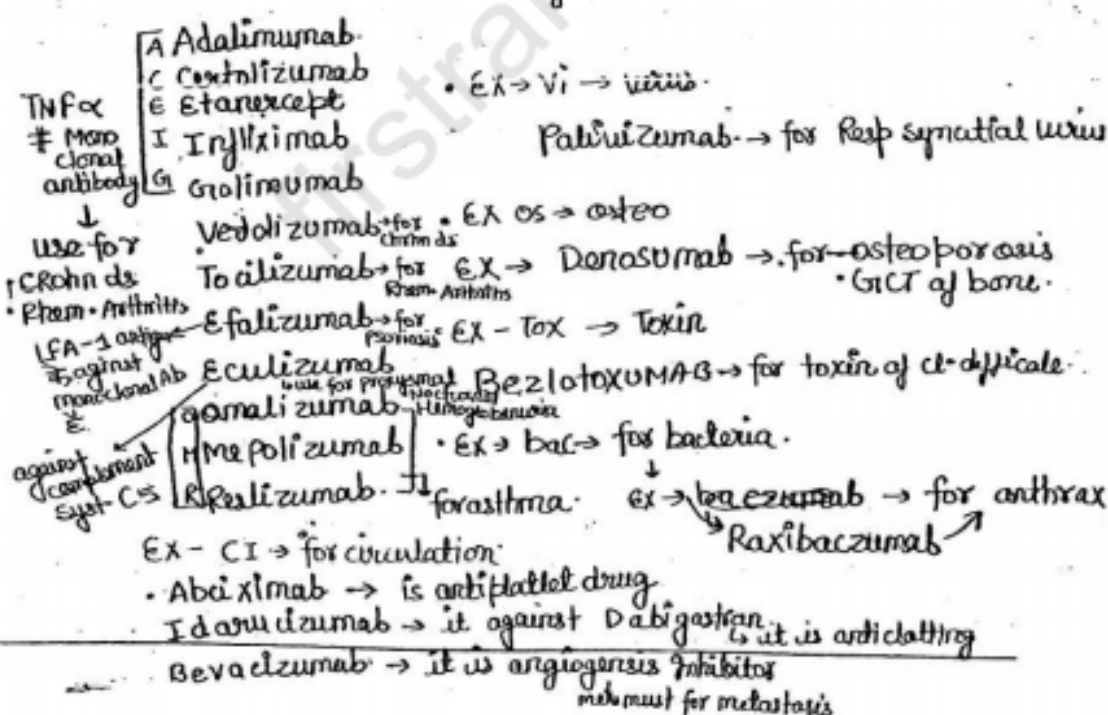
φ Vandetanib → use for medullary carcinoma of thyroid
कंदे मातृग

← Monoclonal antibody →

→ Name end to Mab except → mureo monab. → first monoclonal antibody made
 • Use for Transplant



Ex LI → for Lower Immunity



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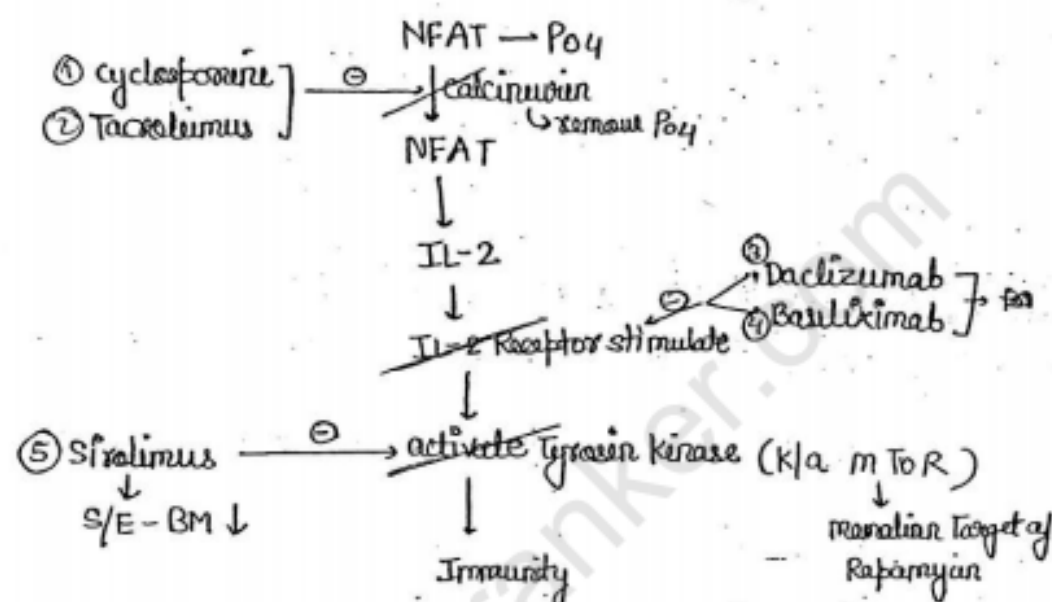
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← Immunosuppressant Drugs →

① Glucocorticoids

② Calcineurin Inhibitor's pathway



These all (5) use in Transplantation

• Calcineurin Inhibitors →

cyclosporine } it cause Hirsutism
tacrolimus } they S/E - Nephrotoxic
 } Hepatotoxic
 } Neurotoxic
 } it does not cause Hirsutism

↑ BP
↑ SUGAR
↑ LIPIDS
↑ K

) monoclonal antibody

) antimetabolites → Azathioprine

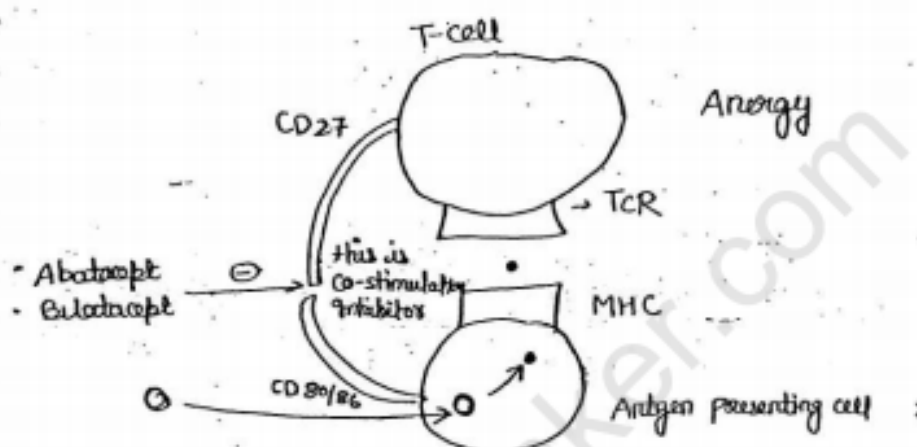
• 6-MP

• methotrexate

• mycophenolate

⑤ Co-stimulation Inhibitor →

Ex → • Abatacept → use for Rheumatoid arthritis
• B-latacept



⑥ IL-1 antagonist → Anakinra → use for Rheum. Arth

⑦ TNF- α # →

A → Adalimumab

C → certolizumab

E → etanercept

Inhib → infliximab

Goli → Golimumab

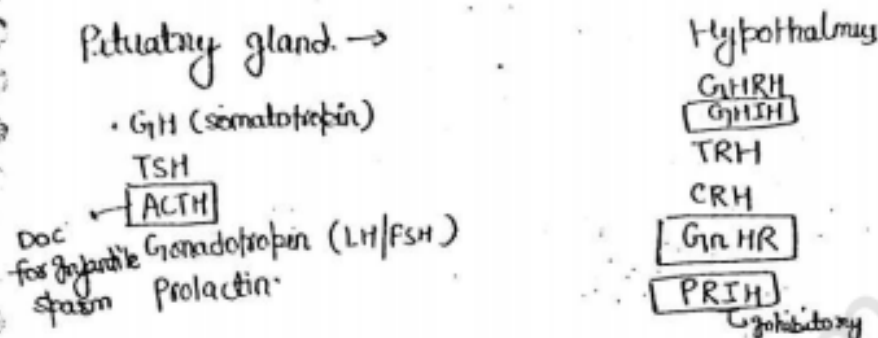
⑧ IL-6 antagonist → • Tocilizumab → for Rheum. Arthritis

⑨ IL-5 antagonist →
M - mepolizumab
R - Reslizumab } use for Bronchial asthma

;) IgE-antagonist → omalizumab

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← Endocrine →



← **GH/HR** → k/a somatostatin
Growth Hormone Inhibitory Hormone

- ⊙ ↓ GH → ±/± → Acromegaly
- ⊙ Somatostatin also secreted by pancreas
 ↓
 it inhibit both $\begin{cases} \text{Glucagon} \\ \text{Insulin} \end{cases}$
- ⊙ Somatostatin also ⊕ in gastric → they help in secretion
 ↓
 L use T/T secretory diarrhea
- ⊙ also use Name in → Esophageal varices
 Use → S → secretory diarrhea
 O → esophageal varices
 M →
 A → Acromegaly

⊙ clinically not useful somatostatin b/c very short acting

⊙ analogues of somatostatin → Octreotide
 L long t_{1/2}



GnRH (Gonadotrophic releasing hormone)

- ↑ Gonadotrophic [LH/FSH]

secreted in pulsatile manner.

so it given in pulsatile manner → ↑ Gn [LH/FSH]

if given continuous → ↓ Gn → (↓ LH/FSH)
↓
↓ E/P/T

~~use~~ use → pulsatile manner → ↑ Gn [LH/FSH]

↓
E/P/T ↑

① → Anovulatory infertility

② - Hypogonadism.
↳ Klinefelter → Hypogonadotropic

③ Delayed puberty.

if continuous given → ↓ Gn (↓ LH/FSH)

↓
↓ E/P/T

use → ① Precocious puberty

② Cancer (breast, prostate)

③ Endometriosis

Drog → GnRH agonist → End $\bar{c}$ RELIN

- ① Leuprolide
- ② Goserelin
- ③ Buserelin
- ④ Histarelin
- ⑤ Nafarelin

φ if we given pulsatile manner → Gn ↑ → ↑ T/FSH
φ if we given continuous manner → Gn ↓ → ↓ T/FSH

→ Flare up seen → it is due to ↑ in symptom due to GnRH continuous manner → GnRH for first few day

φ Drog → GnRH antagonist → End $\bar{c}$ RELIX

- Cetrorelix
Ganirelix
Abarelix
Degarelix

• it only for ↓ Gn (LH/FSH)
• it does not cause flare up seen.

φ PRIH → Prolactin Releasing Inhibiting Hormone = Dop. Agonist

Dopamine agonist

↓ also use (New use) → T₂ DM ***

• Bromocriptine
• Cabergoline } they ↓ prolactin & they can also ↓ GH

use → • Hyperprolactinemia → • Galactorrhea

• Parkinsonism

• Infertility

• Acromegaly → Cabergoline → Doc

↳ only Drog in Acromegaly given orally.

PEGVISOMANT also use in Drog Acromegaly.

↳ GH Receptor antagonist, very long acting

↳ S/E VISUAL FIELD DEFECT

Polyarthralgia - myalgia is use for long action & it inhibits metabolism & excretion

← Thyroid glands →

Hormone Release from thyroid → T_3
 T_4
Calcitonin

T_3 ① Human में T_3 कम होता है

- more active
- short active
- it is Liothyronine
- it given in emergency

↓
myxedema coma

- T_3 given for T/T
- Not a DOC
- DOC → T_4

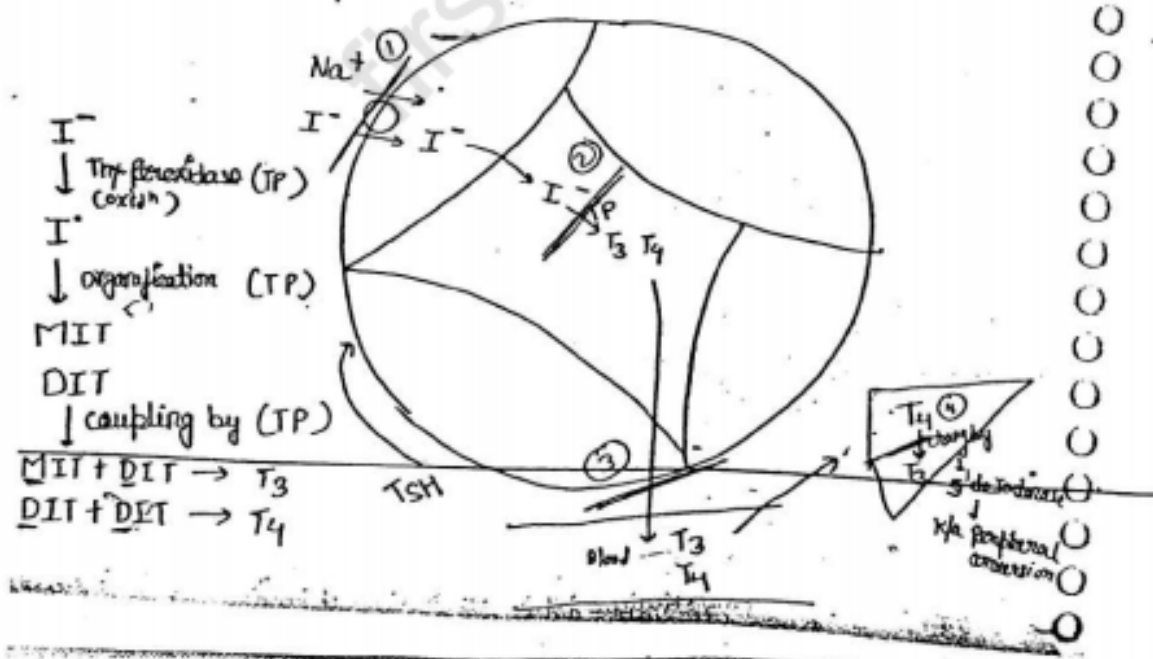
> Hyperthyroidism →

Na^+/I^- symport transport ① in thy thyroid

T_4 → ② Human में T_4 ज्यादा होता है

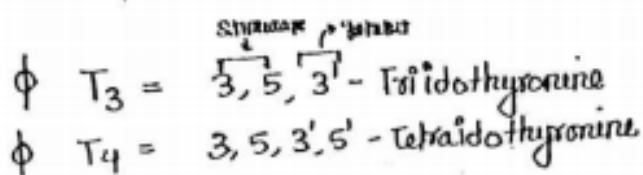
- less active
- long active
- T_4 is DOC for pt. Hypothyroidism
- it is → L-thyroxine

↓
DOC → Hypothyroidism





(10)



→ Reverse T_3 is totally inactive
 ↓
 it is form 2 the help of 5 deiodinase

- ① NIS Inhibitor Drugs → $\text{Na}^+ \text{I}^-$ symport transport
- ② TP Inhibitor Drugs (Thyroid peroxidase)
- ③ Secretion Inhibitor Drug
- ④ PC Inhibitor drug
- ⑤ Thyroid destroying Hormone Drug
- ⑥ symptomatic

- ① NIS Inhibitor Drugs

Perchlorate
 Pertechnate
 Thiocyanate

} → No use clinically
 } → only experiment

- ② TP Inhibitor drug

Thioamides gp → carbimazole → prodrug

methimazole

propyl thiouracil

→ Hepatotoxic

→ SE - Aggranulocytes

Carbimazole
Methimazole

- ↑ Potency
- ↑ Plasma $t_{1/2}$
- ↑ Placenta cross

NO

DOC for Hypothyroidism

Except → 1st trimester pregnancy

Propylthiouracil

- ↓ Potency
- ↓ Plasma $t_{1/2}$
- ↓ Placenta cross
- DOC in 1st trimester pregnancy
- ↓ Peripheral conversion
- $E/E \rightarrow$ Hepatotoxic

Hypothyroidism → Symptom → ↑ Sympathetic system.

in (N) person → There is T_3 & T_4 store in colloid & is sufficient for 2 week

but in Hypothyroidism → Store for 3-4 month

So Dose is ↑ in this pt after 4 week

Hypothyroidism due to drug of Hyperthyroidism.

3) Secretion inhibitor drug → fastest acting antithyroid drug
• Not use for long time.

NaI

KI

Lugol's Iodine

Lithium Inhibit secretion of Thyroid hormone.

Thyroid escape →

↓
if use for long term

↓
so use for short term only

④ PC Inhibitor →

- ① Propylthiouracil
- ② Propazolate
- ③ Prednisolone → S/E Hypothyroidism

⑤ Thyroid destroying drugs → ① $I_2 \rightarrow I^{127}$

Iodine → I^{131} → Radioactive I_2

• Radioactive I_2 given oral

• Radioactive I_2 emits radiation → by β particle
↓
low radiation

↓
So radioactive $I_2 \rightarrow$ C/I in pregnancy

• Half life of radioactive $I_2 \rightarrow$ 8 DAY

↓
it's k/a → Physical Half life

• if give excess/overdose radioactive $I_2 \rightarrow$ ~~to~~ then

Irreversible
Hypothyroidism

So → Radioactive I_2 C/I < 35 yrag
adult में use कर सकते हैं।

⑥ Symptomatic → Symptom → like activate Sympathetic Syst.

- Beta Blocker
↓
• Propranolol

• Thyroid storm pt



Doc → Propranolol is life saving Drug

- anti-thyroid Doc



Propylthiouracyl

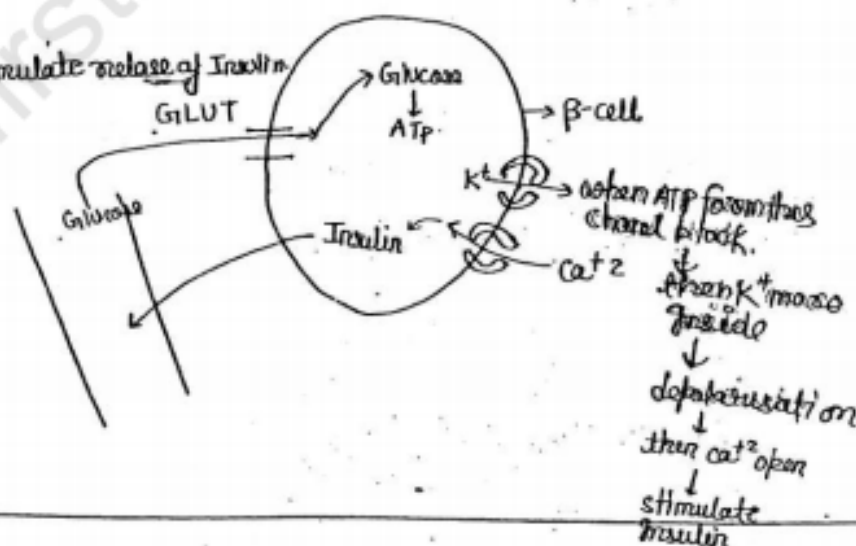
← Pancreas →

- $\alpha \rightarrow$ Glucagon
 - $\hookrightarrow$ Glucose by Glycogenolysis
- $\beta \rightarrow$ Insulin & Amylin
 - $\hookrightarrow$ Glucose
 - $\hookrightarrow$ it also $\downarrow$ Glucose
- $\delta \rightarrow$ Somatostatin

- ϕ Glucagon $\rightarrow$
- use in t/t of Hypoglycemia
 - Not useful in starving Hypoglycemia
 - Not useful in alcoholic Hypoglycemia
 - Glucagon is DOC $\rightarrow$ β Blocker poisoning

ϕ Insulin $\rightarrow$

Hypoglycemia $\rightarrow$ stimulate release of Insulin



Indication of Insulin →

- 1) Insulin Dependent Diabetes mellitus (DM-1) → all pt
- 2) Non Insulin Dependent Diabetes mellitus (DM-2) → 1st try to oral drug
↓
then Insulin therapy
use Insulin for uncontrolled pt
- 3) DKA → i.v regular Insulin → DOC
- 4) Pregnancy → DOC for Diabetes in pregnancy → Insuline
- 5) Acute Hyperkalemia.

Classification of Insulin →

- 1) Short acting → • Regular Insulin (give i.v)
• Semilente
- 2) Intermediate acting → • NPH (Neutral Protamine Hagedron)
• Lente
- 3) Long acting → ultralente
[lente more Insulin proprore & zinc]



Rapid (ultrashort) • Lispro

s गले ultrashort

- Aspart
- Glulisina

- ultra long → Glargine → available in acidic $\text{pH} = 4$
↓
Determir
Degludec.
they have lesser incidence of hypoglycemia
• also K/A → Peakless

φ all insulin given → S.C route except regular insulin

φ Sites of Insulin route →

- Subcutaneous → m/c
- abdomen (except 2 inch near umbilicus)
 - Thigh
 - Buttock
 - Dorsal arm.

φ Site should be rotate/alternate b/c it can cause lipodystrophy

φ Inhalational Insulin → Exubera → banned Now

A freeza → New
• Not use alone

Adverse effect of Insulin →

- m/c → S/E → Hypoglycemia
- most dangerous S/E → Hypoglycemia
- Reversible S/E → Hypoglycemia

← ORAL antidiabetic Drug →

action by drug releasing Insulin

- this drug req 30% β cells.
- S/E - Hypoglycemia

other

- No req. β cell
- No Hypoglycemia

§ Drug releasing Insulin → MoA → K^+ channel blocker in β -cell.

① Sulfonylurease → 1st gen → Chlorpropamide
• Tolbutamide → zero order kinetic
• SHORTEST Acting
2nd gen → drug start name $\bar{C}$ GLI
• GLIPIZIDE

Gliclazide
Glibenclamide K/a → Gliburide
Glimepiride

② meglitinides → end $\bar{C}$ linide
Nateglinide → Indication → Post Prandial Hyperglycemia
Repaglinide → very short acting (1 hr तक काम करता है)

Φ in antidiabetic Drug → जो ide में खत्म होगा → वो Hypoglycemia करेगा

φ Sulfonylurease →

- Cause weight gain → so Not given in obese
- 1st generation → Potency ↓
- 2nd generation → Potency ↑

○ Tolbutamide — zero order kinetics
Shortest acting

○ Chlorpropamide — cause cholestatic jaundice
— Disulfiram rxn (like rxn)
— ↑ ADH
→ Dilutional Hyponatremia

- it is use both DM & DI (Diabetes Insipidus)
- chlorpropamide is longest acting.

φ 2nd gen →

- GLIPIZIDE → Safe Drug in elderly pt
- GLICLAZIDE → having anti platelet property
- GLYBURIDE → • $\pm \frac{1}{2}$ → 1-2 hr
- it sequestered in β -cell.

② other mechanism →

① Biguanides → Metformin
phenformin | → they do NOT cause Hypoglycemia

S/E → • megaloblastic anemia → metformin > phenformin

• Lactic acidosis → phenformin > metformin
↓
SO NOT use.

Φ Risk factor where Metformin cause Lactic acidosis →

- Elderly
- renal disease
- Liver ds
- Lung ds (Hypoxia)

→ Metformin → • DOC → T₂ DM
↓
• max effective → HbA_{1c}
↓
• HbA_{1c} ↓

also used in Polycystic ovarian ds (PCOD)

↗ ↑ risk of Bladder carcinoma

③ GLITAZONES →

work on
PPAR-γ

(Peroxisome proliferator
Receptor activator γ)

PPAR-γ
↓
γ → गल करत है।

PIoglitazone → preferred

Rosiglitazone → RISK of MI ↑ (so NOT preferred)

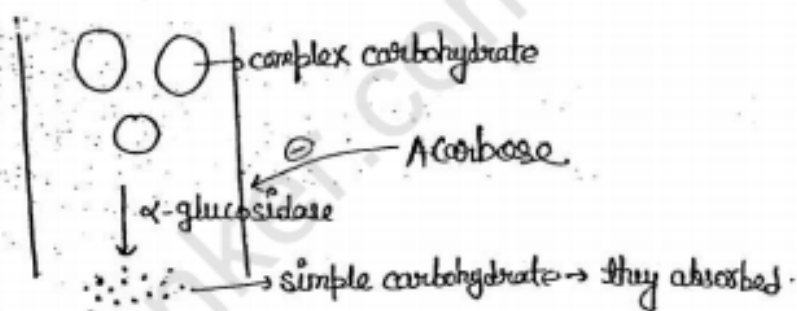
Troglitazone → banned b/c Hepatotoxic

• use → Insulin Resistance को Reverse करती है

• all these drug cause Na⁺ water Retention
↓
so avoid in CHF/cardiac pt.

③ PPAR- γ $\oplus$ PPAR- α
 $\hookrightarrow$ Thiazolidine work on PPAR- γ
 $\downarrow$
 K/a $\rightarrow$ Saraglitazar
 $\downarrow$
 it control DM & dyslipidemia

④ $\rightarrow$ α -glucosidase Inhibitor $\rightarrow$ Acarbose.



ϕ m/c side effect is $\rightarrow$ Flatulence

ϕ C/I in $\rightarrow$ Inflammatory Bowels $\begin{cases} \text{chron's} \\ \text{ulcerative colitis} \end{cases}$

ϕ they don't cause Hypoglycemia.

ϕ Acarbose + Glipizide $\rightarrow$ Hypoglycemia

ϕ if Hypoglycemia $\bar{c}$ Acarbose the t/t is $\rightarrow$ Glucose.

← NEW Antidiabetic Drugs →

① Incretins → • • in body

① GLP-1 (Glucagon Like peptide)

~ GLP-1 is metabolised by DPP-4

- ↓
- ↑ Insulin
 - ↓ appetite
 - ↓ apoptosis of β -cells

→ GLP-1 agonist →

- Exenatide
- Liraglutide
- Albiglutide
- Dulaglutide
- Lixisenatide

approved for Tx of obesity

- short acting BD दोटे
- given by subcutaneous
- Not preferred
- they cause hypoglycemia
- These can cause wt loss
- long acting
- week मे 1 बार देते है

• m/c side effect → Nausea

• Vomiting

• they cause - acute pancreatitis

• ↑ risk of medullary carcinoma of thyroid.

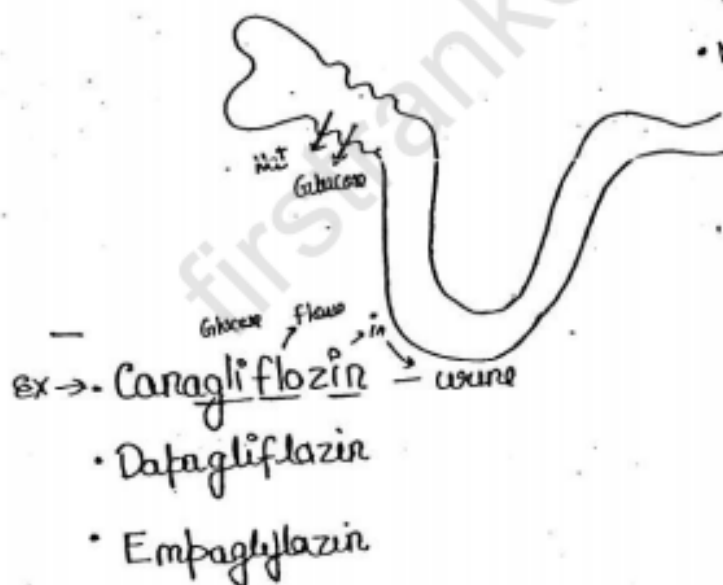
• they also cause Hypoglycemia.

(11)

- ⑥ DPP-4 Inhibitor → (oral given)
- do not cause Hypoglycemia
 - Sitagliptin
 - Vildagliptin → req. dose adjustment for both liver & kidney failure
 - Alogliptin
 - Saxagliptin
 - Linagliptin → safe in renal failure

m/c side effect → Nasopharyngitis

- ⑦ SGLT-2 Inhibitor → act by causing glucosuria
- m/c side effect → UTI
 - No cause Hypoglycemia





3) [Amylin]
agonist → they ↓ Glucagon.

Ex → . PRAMLINTIDE



- it cause Hypoglycemia

- Not given orally

- given subcutaneous

***. it is only Drug use for Both T₁DM & T₂DM

1) Bromocriptine

2) Bile acid binding agent.



← ADRENAL GLAND →

Cortex

Medulla

→ Adrenal cortex → 2 hormone

① Glucocorticoids → Cortisol

② mineralocorticoids → Aldosterone → for BP maintenance
Electrolyte maintenance

↓
↑ Na^+ , H_2O
↓ K^+ & ↓ H^+

• Conn's syndrome
• Cushing syndrome

• Addison disease → due to ↓ Aldosterone → ↓ Na^+ & H_2O
↑ K^+ & ↑ H^+

φ Glucocorticoids → it is catabolic

• CHO → Glucose

it break Glucose, Prot, fat, Ca^{+2}

• Protein → Break → myopathy

• fats → Break only peripheral → cause centripetal obesity

• Ca^{+2} → break → osteoporosis

↓
Cushing syndrome

φ Glucocorticoids are powerful anti-inflammatory action.

φ they inhibit Chemotaxis (m/i → anti inflammatory action)

disadvantage of Anti Inflammatory property $\rightarrow$ Delay healing

Glucocorticoids $\rightarrow$ are powerful immunosuppression

Advantage $\rightarrow$ use in transplant

disadvantage $\rightarrow$ cause 2^o infection

Glucocorticoids have anticancer property

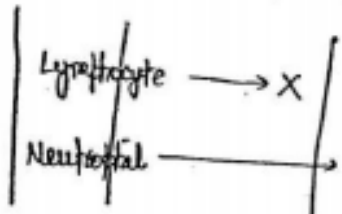
but not in Kaposi cancer.

$\hookrightarrow$ occurs in HIV pt.

Glucocorticoids cause in Blood $\rightarrow$ Neutrophilia
 $\rightarrow$ Lymphopenia.

Bone marrow

Blood



adrenal cortex is more imp than medulla

***** Glucocorticoids Drug

Short acting $\rightarrow$ ① Cortisone

② Hydrocortisone (Cortisol)

$\hookrightarrow$ max mineralocorticoid active in all glucocorticoids

Intermediate

$\rightarrow$ Prednisolone

Triamcinolone

Methylprednisolone

$\rightarrow$ zero mineralocorticoid activity
 $\rightarrow$ Selective glucocorticoid

Long acting

$\rightarrow$ Betamethasone

Dexamethasone

Paramethasone

$\rightarrow$ most potent glucocorticoids

$\rightarrow$ max glucocorticoid activities/efficacy

(11)

← MINERALOCORTICOIDS →

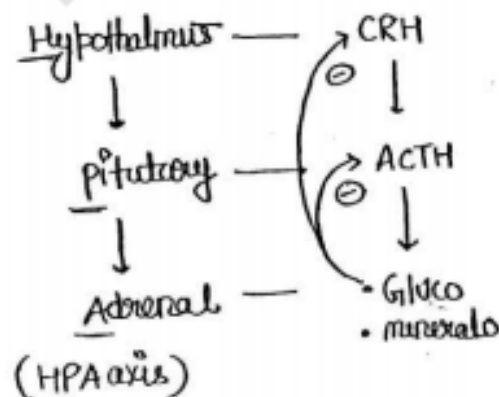
- ① Aldosterone → max mineralocorticoid activity
- ② Fludrocortisone → max potency mineralocorticoid
- ③ DOCA (Deoxycorticosterone) → max glucocorticoid action in mineralocorticoids
↓
zero cortisone like activity

Uses of Glucocorticoids →

- ① Replacement use → Adrenal Insufficiency
- acute → Addisonian crisis (oral) i.v
 - chronic → Addison's disease (oral)

- ② antenatal use → Premature labor में देते हैं baby के lung को develop करने के लिए
- Dexamethasone - 6 mg 12 hrly x 4 dose i.m
 - Betamethasone - 12 mg 24 hrly x 2 dose i.m
 - Total 2 day में 24 mg देते हैं।

- ③ other →



→ HPA-axis suppression → m/c S/E of steroids

Prevent HPA-axis suppression →

- Avoid to give Glucocorticoids
- give for < 2 week
- No long term use b'coz if necessary to give the give Drug alternate day.
↳ except long term Glucocorticoids
- if give daily then don't stop the immediately, stop slowly slowly

Use →

- ① anti-inflammatory (itis)
- ② Immunosuppression → Transplant
↳ Autoimmune.

Deflazacort → for Duchenne's muscular dystrophy (DMD)

Eteplerson → New Drug for DMD

↓
they remove EXON-51 from the m-RNA
(from Dystrophin gene)
(antisense oligonucleotides)

③ anticancer → HL
NHL
LL
Except Kaposi sarcoma.



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φ S/E → G. Glaucoma → open angle glaucoma by eye drop

L • limb muscle atrophy

U • can cause peptic ulcer

C • Cataract → by oral when intake

• post subcapsular cataract

O • osteoporosis

C • Cushing syndrome

O • osteonecrosis → Avascular Necrosis in Bone

R • C/I in Renal failure

T • C/I in Ileocaecal T.B.

I • Impaired Healing

C • C/I → CHF & Edema.

bt in CHF use → zero mineralocorticoid properties.
can be given in CHF

I • Infection

D • C/I in DM → b/c cause Hyperglycemia

S • suppression of HPA axis → most dangerous S/E

	Serum Ca^{+2}	Serum PO_4^{-3}
• Vit D	↑	↑
• PTH	↑	↓
• Calcitonin	↓	↓

Vit D ↑ Blood Serum Ca^{+2} → $\begin{cases} \uparrow \text{absorption} \\ \downarrow \text{excretion} \end{cases}$

PTH → ↑ bone resorption → ↑ Ca^{+2} → So Not use in osteoporosis

Calcitonin → Blood → Bone → So use in osteoporosis

← Osteoporosis →

• Caused by PTH

• T/r by $\begin{cases} \uparrow \text{Vit D} \\ \downarrow \text{Calcitonin} \end{cases}$

Drug for osteoporosis →

→ Ca^{+2}

→ Vit D

→ Calcitonin

→ Thiazides → Retain Ca^{+2}

→ Bisphosphonates → Alendronate

Risedronate

Zoledronate

↓
it inhibit osteoclast

DOC for Osteoporosis

→ DOC for Hypercalcaemia of malignancy (it is due to metastasis to bone)

→ DOC for Paget's ds of bone

φ Hypercalcaemia of malignancy →

- DOC → BISPHOSPHONATES
- First done → i.v fluid.
- fastest Ca^{2+} lowering agent → Calcitonin

φ S/E of Bisphosphonates →

① major S/E → Toxic to esophagus

- So it given at empty stomach [before (>30 min)]
- Not lying down for (>30 min)
- large amount of water intake

② → osteonecrosis of mandible → ~~Zoledronate~~

③ Zoledronate → Can cause renal failure

- approved for i.v use.
- give once in a yr.

← Post menopausal osteoporosis →

• due to estrogen deficiency

① effect of estrogen → Bone → ↑ bone formⁿ

Blood → ↑ HDL

Breast → ↑ risk of Breast cancer

Endometrium → ↑ endometrium cancer

Liver → ↑ clotting → cause Thromboembolic episode

For this reason
in post menopausal
osteoporosis estrogen
Not given

use Drug → Selective Estrogen Receptor modulator → [SERM]

Bone ⊕ agonist
Blood ⊕ agonist
Breast ⊖ antagonist
Endometrium ⊖ antagonist
Liver ⊖ antagonist

Raloxifene →
max good property
S/E Thromboembolism

• Doc for post menopausal osteoporosis → BISPHOSPHONATE

SERM →

1) Raloxifene → given when post menopausal osteoporosis is associated to one more any dz.

2) Tamoxifen

3) Doloxifen

4) Toremifene

• S/E ⊖ Thromboembolism

⊖ ↑ risk of ca endometrium

• use → T/T of Breast ca.

⑤ Clomiphene → it is SERM

↳ it is estrogen antagonist at puberty.

• use for → Anovulatory Infertility

• S/E → multiple pregnancy. C/m/c

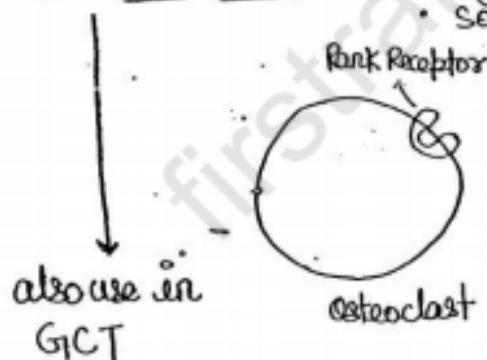
(1)

← SOME NEW DRUGS for osteoporosis →

- ① Teriparatide → it is PTH 1 to 34
 ↓
 PTH 84 amino acid
- Parathyroid Hormone
- it stimulate osteoblast.

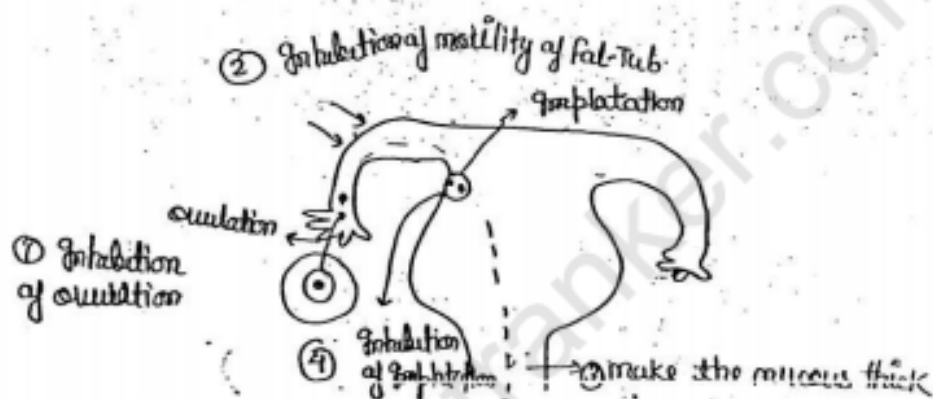
- ② Strontium ranelate → it have dual action
- ↓
- osteoblast stimulate
 osteoclast inhibit
- More toxic so not use.
 - M/C → S/E → Thrombocytopenia

- ③ Denosumab →
- Against RANK Ligand
 - so inhibit osteoclast



← OCP →

- 1) Combined OCP → E + P → major mech. → Inhibit ovulation
- 2) Progesterone only pills → only progesterone, major mech. → make the mucus thick
- 3) Emergency pills → major mech. → Inhibition of Implantation



Combined OCP

- 21 day + 7 day
- (E + P) → withdrawal bleeding
- if bleeding @ these day k/a break through bleeding → due to ↑ progesterone
- So use ↓ progesterone
- By Phasic pills



(119)

→ Monophasic pills → on strip 2 colour ⊕

→ Biphasic pills → on strip 3 colour ⊕

→ Triphasic pills → on strip 4 colour ⊕

⊕ if one Tab miss to take any lady → then जैसे चाद चाये खानो

⊕ ≥ 2 Tab miss → take another contraceptive method.

• Discard missing pills & continue as such.

← Progesterone only pills → (less efficacy) less efficacy

⊕ LNG → Levonorgestrel.

• preferred in lactation.

• Risk of Thromboembolism

← Emergency / Post-coital control / morning after pills

• Take < 72 hr.

① use combined ocp → 2 Tab

② LNG → 1 Tab.

③ CuT

④ Selective progesterone Receptor modulators (SPRM) → Mifepristone
↳ also use for MTP

• Uli pristal → can be given up to 5 day.
↓
it contain combined ocp



Adverse effect of ocp

mild

- ↓ Nausea
- Oedema
- Recurrent headache
- ↓ mastalgia
- abnormal bleeding
- loss of withdrawal bleeding

moderate

mostly due to progestins

- Acne
- wt gain
- Chloasma

Severe



- C → Thromboembolism (CVS) ()
- MI, DVT, PE, embolism ()
- C (CVS) → Depression ()
- C → cholestasis jaundice ()
- C → Cancer { ↑ risk of breast ca ()
- ↑ risk of cervical cancer ()
- but it ()
- ↓ risk of Endometrial ()
- ↓ risk of ovarian ca ()

↓
Stop the pills

Other use of ocp

Other → ↓ risk of ovarian cyst → PCOD → DOC → ocp

B → ↓ risk of Benign Breast ds.

E → ↓ risk of Endometrial ds.

N → ↓ Neoplasm - { ovarian

E → ↓ ectopic preg.

F → ↓ fibroids.

I → ↓ Iron deficiency anemia

T → ↓ Pre menstrual Tension Syndrome

S → ↓ skeletal → osteoporosis

S

(120)

← Uterine Stimulate →

- Oxytocin →
- it stimulate the uterus
 - can be use for Breast Enlargement
 - k/a milk Ejecting Hormone.
 - use in PPH → DOC → Oxytocin, but misoprostol can also used.
 - use for Induction of labour.

DOC → oxytocin

- dose → 300 µg
- route - S/L

misoprostol can also use for
Prophylaxis for PPH →

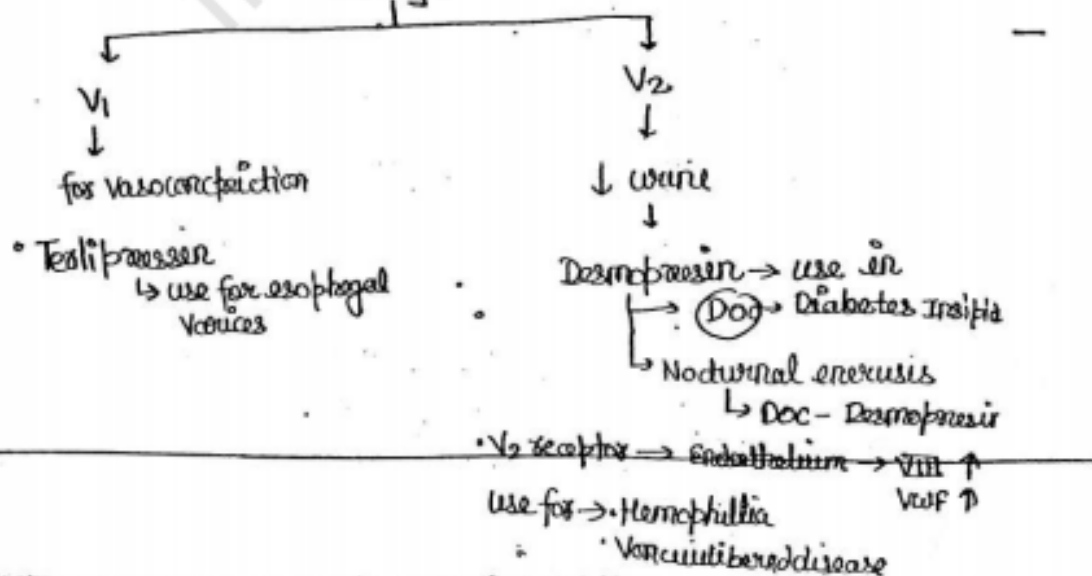
Dose - 600 µg
Route → ORAL

φ Methergin (methylergometrine)

- it is given at the delivery of ant. shoulder
- But preferred oxytocin.

Vasopressin / ADH

2 Receptors





Vasopressin antagonist →

φ Conivaptan } → injectable
Tolvaptan } → it is Vasopressin antagonist

SIADH



- give doctex restriction
- give Hypertonic saline (3% NaCl)



if No control then given Drugs

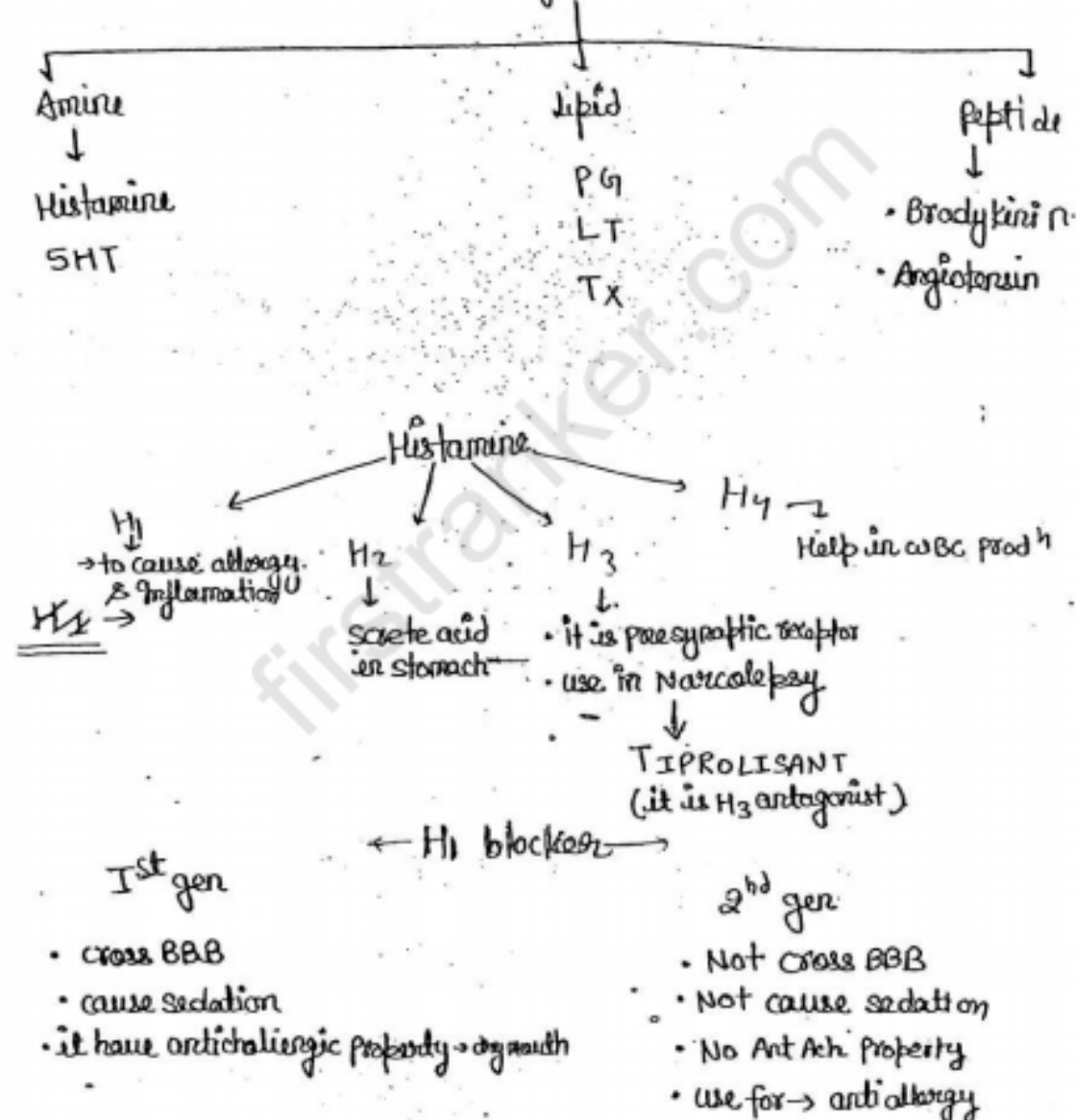


Doc → Conivaptan > Demeclo

← Autacoids →

- Autacoids are those substance it work where it produce.
- it's Non selective. origin

→ on the basis of chemical structure Autacoids are



← 1st Generation →

- ① Promethazine → market name → Phenargan
 use for prophylaxis of motion sickness
 max anticholinergic property
 preferred in t/r of drug induce Parkinson
 use in muscular dystonia
- ② Diphenhydramine
- ③ Dimenhydrinate
- ④ Pheniramine
- ⑤ Chlor-pheniramine → it is AVIL (market name)
- ⑥ Cinnarizine
- ⑦ Erolizine
- ⑧ Cyclizine

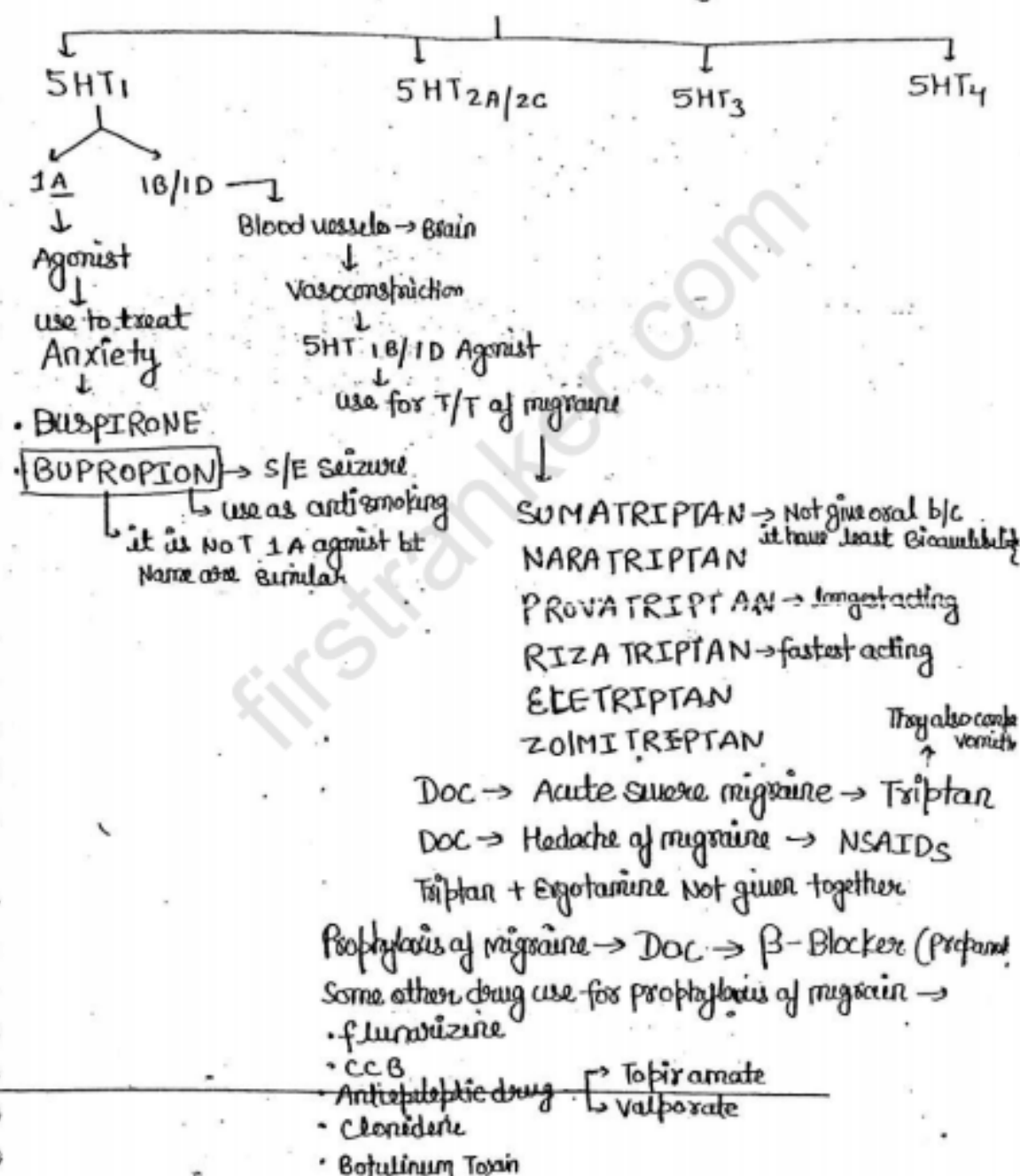
← 2nd gen →

- Terfenadine } CAT Drug cause QT Prolongation & cause Torsades de point
- Astemizole } metabolized by CYP3A4
- Loratadine
- Cetirizine → can cross BBB → so it cause sedation
 + bit little bit
- Olopatadine } max Topical activity
- Azelastine }
- Fexo Fenadine } is active metabolite of Terfenadine & it Not cause
- Des-loxatidine } QT Prolongation
- Levo-cetirizine } ये cetirizine से भी कम BBB cross करता है

Some book say it is 3rd gen of Histamine

Serotonin (5-HT)

- 7 receptors of serotonin
- but we know about only 4



5HT_{2A/2C}

atypical anti psychotic drug are 5HT_{2A/2C} Receptor Blocker.

S/E - metabolic syndrome of 5HT_{2A/2C}

Lorazepam Lorazepam → it is serotonin C receptor agonist

↓
5HT_{2C} agonist

↓
approved for obesity

Oxaliplatin → also use for obesity
↓
guarantee → it is not 5HT_{2A} agonist
↓
guarantee

5HT₃ → ④ on CTZ → Vomiting

↓
drug block 5HT₃ is → Ondansetron

ONDANSETRON

GRANisetron

TROPisetron

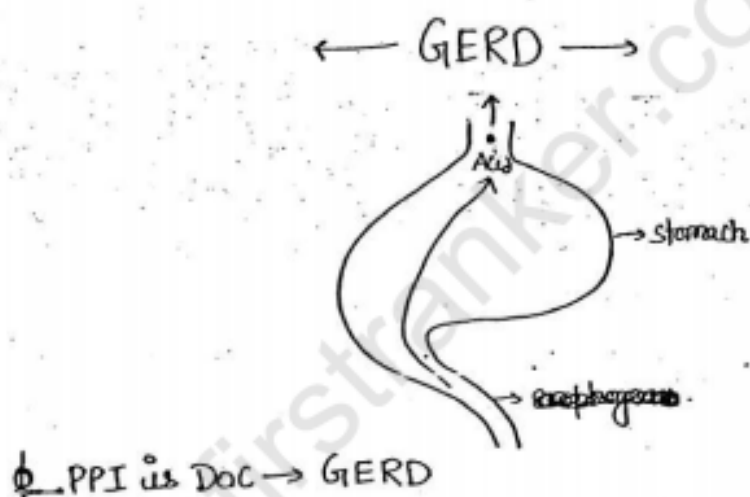
Dolasetron

Palonosetron → most potent

DOC

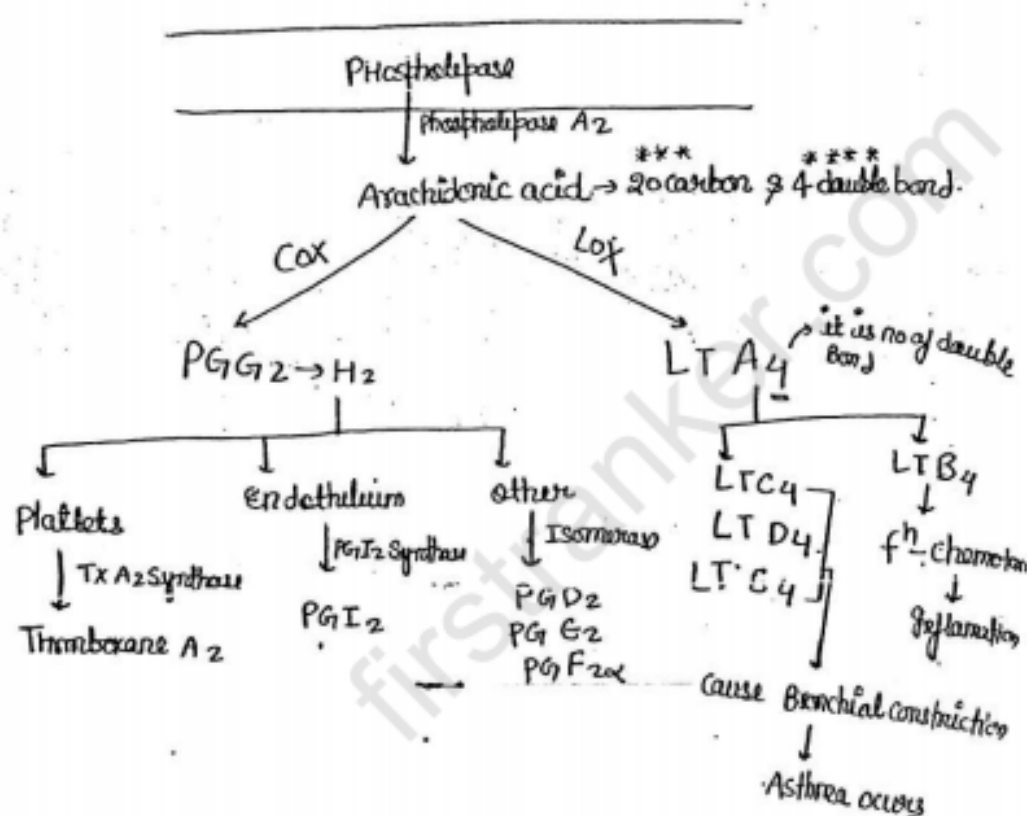
- Chemotherapy Induce Vomiting
- Radiotherapy Induce Vomiting
- Post op - Vomiting

- 5HT₄-agonist →
- 5HT₄ → ↑ GI motility
↓
K/a-prokinetics
- Cisapride → banned b/c cause QT Prolongation.
 - Tegaserod → banned b/c cause ↑ risk of MI
 - Mosapride → use in GERD



← Lipids Autocoids →

↓
Prostaglandin, Leukotrine, Thromboxane



φ Action of Prostaglandins →

① Fever
Pain
Inflammation

} COX Inhibitors use to treat
↓
• K/a NSAID
• aspirin is only irreversible COX Inhibitor

② Platelets → Thromboxane A₂ → platelets aggregation

PGI₂ → Inhibit plate aggregation

③ MOA Aspirin in antiplate action → COX ⊖

↑
TXA₂ synthesis ⊖ (best ans)
↳ Not synthesis

③ CVS → prostaglandin keep the ductus Arteriosus open → in premature

↓
Patent Ductus arteriosus open → when
(PDA) ductus arteriosus
open after birth

So → COX ⊖ use

↓
Aspirin
Indomethacin } use in PDA
↳ DOC → PDA

→ TGV (Transposition of Great vessels) → use for T/T PGE₂

Alprostadil
Misoprostol } PGE₁
↓
work like PGE₂

↓
ALPROSTADIL
↓
Help in open
Ductus arteriosus
open

3) Blood vessels → $\text{PGE}_2 \rightarrow$ Vasodilation
 $\text{PGI}_2 \rightarrow$ ↓

So use in pul. Hypertⁿ

Epoprostenol → most effective in
Treprostinil

φ Erectile Dysfunction

↳ ALPROSTADIL

DOC → SILDENAFIL

↳ it is PDE #

4) uterus → PGE_2 } contract the upper part of uterus
 $\text{PGI}_2 \propto$ }

• $\text{PGE}_2 \rightarrow$ relax the lower part of uterus.

use → ① PPH

② abortion (misoprostol) → Early pregnancy

③ use in labour locally (misoprostol) → for relaxing
lower part
↓
given intravaginally of uterus



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⑤ Stomach $\rightarrow$ Prostaglandin PGI_2 protect the stomach by inhibiting proton pump & $\uparrow$ mucous & HCO_3^-

- Doc for NSAID induce peptic ulcer $\rightarrow$ PPI
- Specific Drug use for NSAID Ind. Peptic ulcer - Misoprostol

⑥ Eye $\rightarrow$ $PGF_2 \alpha \rightarrow \uparrow$ uveoscleral out flow

Doc $\rightarrow$ Latanoprost $\rightarrow$ (POAG)
 $\downarrow$
S/E $\rightarrow$ • Iris pigmentation
• Growth of Iris



Drug that inhibit COX → NSAIDs

COX 1

- Constitutive enzyme
- ↓
- COX-2 also constitutive some place
- ↓
- Kidney
- Endothelium
- Brain

COX 2

- Inducible enzyme
- ↓
- Cause Inflammation

NSAIDs

Non selective (COX 1 & COX 2 inhibitor)

Selective COX-2 inhibitor

- Paracetamol (acetaminophen)
 - Aspirin
 - No anti-inflammatory property
 - Indomethacin → S/E - Sedation, C/I in Truck driver, PILET
 - Ibuprofen → approved for children, it is anti-inflammatory drug
 - Children
 - Ketorolac → given i.v.
 - Piroxicam → long acting (NSAIDs)
 - Nimesulide → banned in children b/c cause hepatotoxic
 - Diclofenac → Partial COX-2 # → cause minor peptic ulcer
- all of them cause peptic ulcer except PCM



◊ Paracetamol →

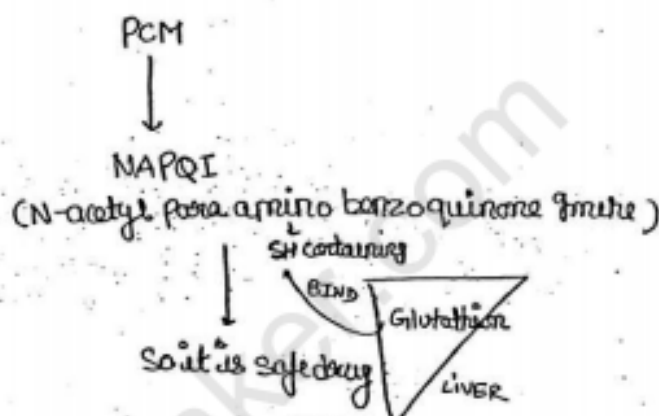
• Paracetamol become inactive in presence of H_2O_2

$H_2O_2 \uparrow$ at inflammation

• PCM is non selective & they not cause gastric ulcer etc → so PCM is not anti-inflammatory

* * * PCM is COX 3 #

PCM Toxicity →



◊ PCM overdose → m/c seen in children

• PCM bottle is child resistant cap

• m/c seen in alcoholic pt / liver dz → b/c Glutathione absent

give → N-Acetylcysteine → antidote of Paracetamol.

← Aspirin →

◊ it is irreversible COX

◊ fⁿ → antipyretic

• analgesic

• anti-inflammatory

• anti platelet

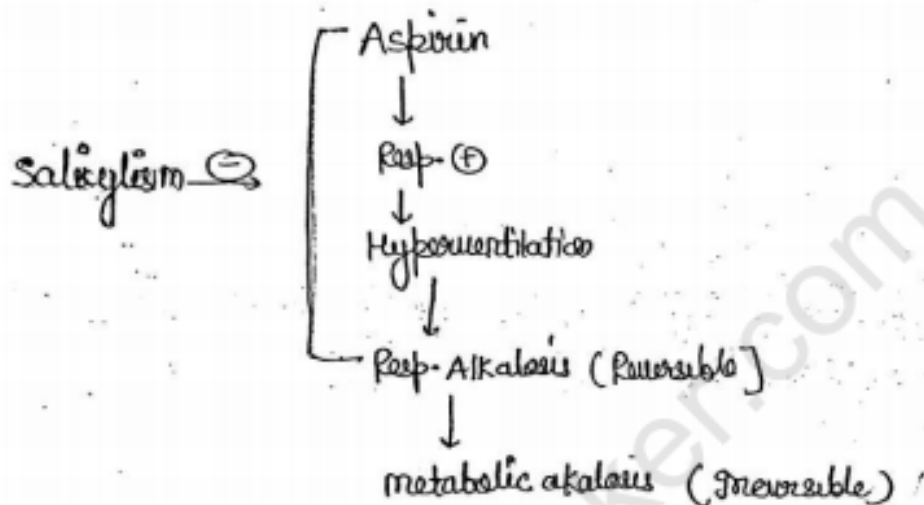
◊ aspirin cause Hyperglycemia

◊ C/I in gout b/c it cause ↑ uric acid

◊ Cause Reye Syndrome.

Rey's syndrome $\rightarrow$ in viral infection + Aspirin
 $\hookrightarrow$ so c/I in viral infection $\rightarrow$ Aspirin

Toxicity of Aspirin



ϕ NaHCO_3 is use for aspirin toxicity

ϕ No any antidote for aspirin

$\leftarrow \text{COX-2} \# \rightarrow$

- Celecoxib

• Rofecoxib

• Valdecoxib

• Etoricoxib $\rightarrow$ longest acting

• Parecoxib

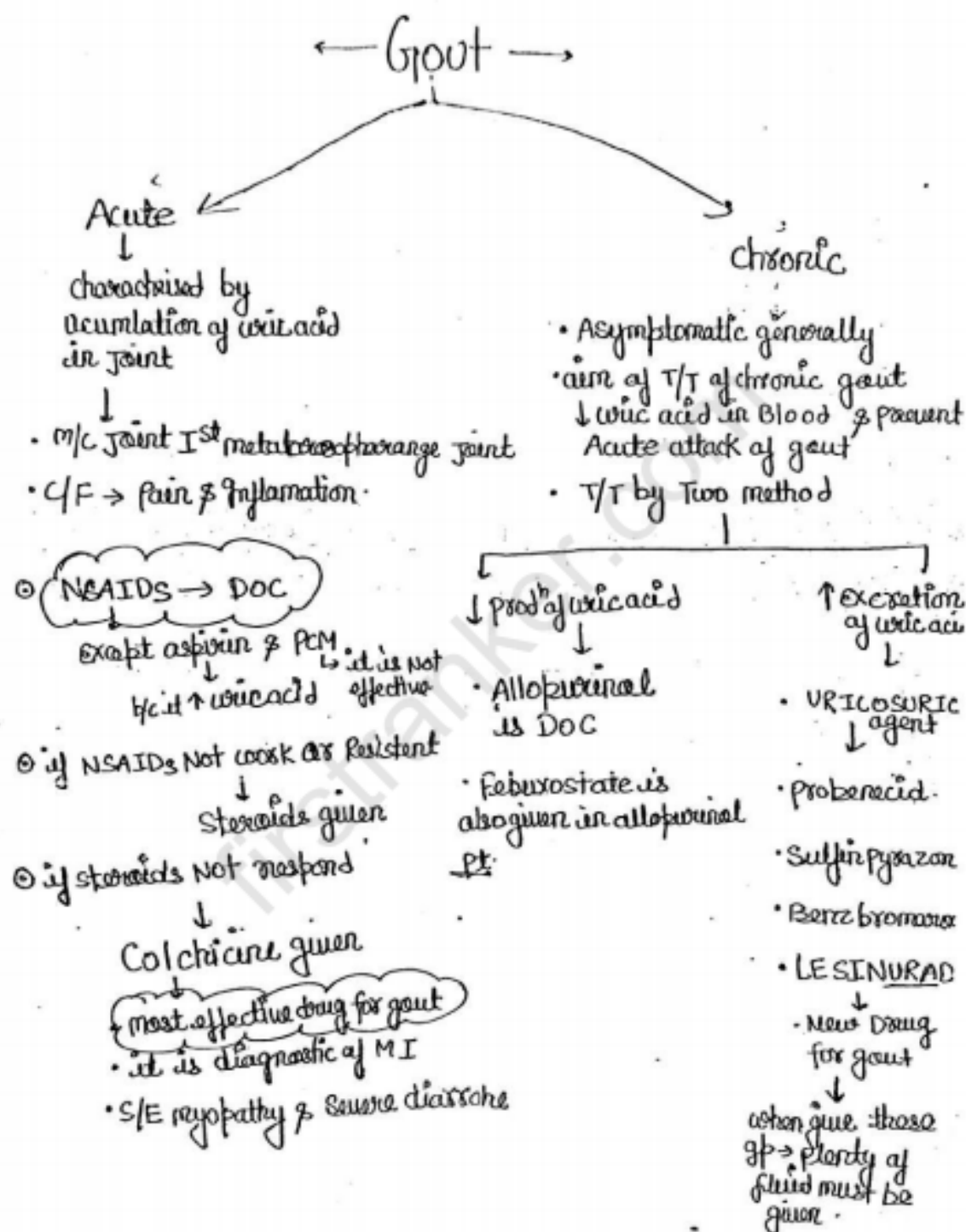
• Lumiracoxib

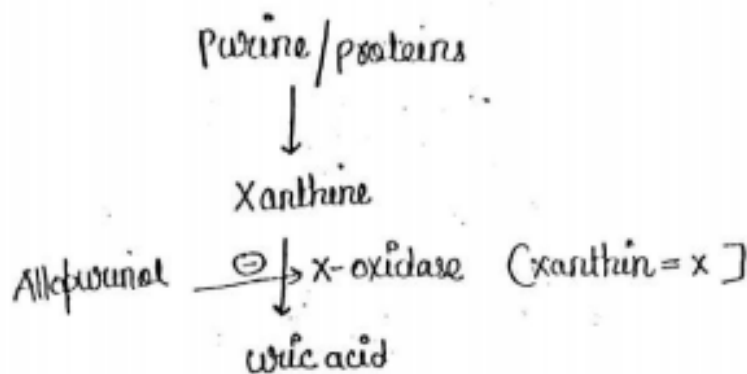
Banned b/c
max risk
of MI

• they not cause peptic ulcer

• S/E - MI

12





Diet $\rightarrow$ low protein diet intake

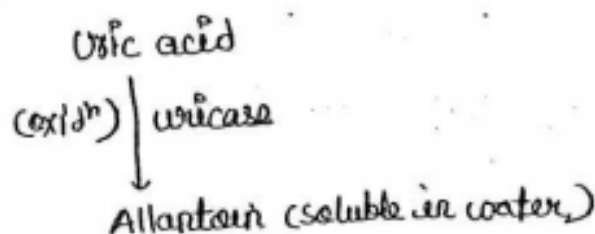
! FEBUXOSTAT is given in chronic gout pt when pt is allergic to Allopurinol

! allopurinol $\rightarrow$ also use for KALA AZAR
 $\hookrightarrow$ DOC Amphotericin B

! in acute attack of gout $\rightarrow$ any drug $\downarrow$ uric acid it is c/I in acute cont.

! allopurinol is c/I in Acute Gout.

$\rightarrow$ in BIRDS $\rightarrow$



So $\rightarrow$ RASBURICASE $\rightarrow$ made by DNA blotch
 $\uparrow$ uric acid metabolism

• PEGLOTICASE $\rightarrow$ long acting



(12)

← Rheumatoid Arthritis →

↓
Inflammation.

→ NSAIDs → it given for only symptomatic T/T

→ DMARDs → K/a - slow acting anti Rheumatoid Drug (SAARDs)

↓
Conventional

↓
Biological.

Cute → chloroquine

?

P → Penicillamine → Cu^{++} chelating agent

A → Azathioprine → use for Cu^{++} poisoning → Wilson's

G → Gold salts

L → Leflunomide → fast acting

I - Infliximab → m/c used

malika - methotrexate → Doc as DMARD

• S/E - hepatotoxic & myeloblastic anaemia

sharaxat - Sulfasalazine

→ prodrug

• used in Ulcerative colitis

← Chelating agent →

→ BAL
 ↳ Bisreuth As Pb → poisoning में देते हैं

ϕ BAL is C/I in Cadmium poisoning } Cafe
Fe (Iron) poisoning }
 $\downarrow$
मे बावरी

CaNa₂EDTA → use for →

Mn	→ I
Fe	→ I
Pb	→ L
Cd	→ K

given IV
Cramer's E-Prüfung

Desferrioxamine } → chelating agent for Iron
Deferiprone }
↓
• given oral
• for chronic Fe poisoning

↳ Penicillamine $\rightarrow$ for Cu^{++}
 $\downarrow$
 Wilson's dis.



(12)

← BIOLOGICAL D-MARD →

① IL-1 Receptor antagonist → Anakinra

• TNF- α Inhibitor → ACE In Goli

• IL-6 → Tocilizumab
antagonist

② Co-Stimulation Inhibitor → Abatacept

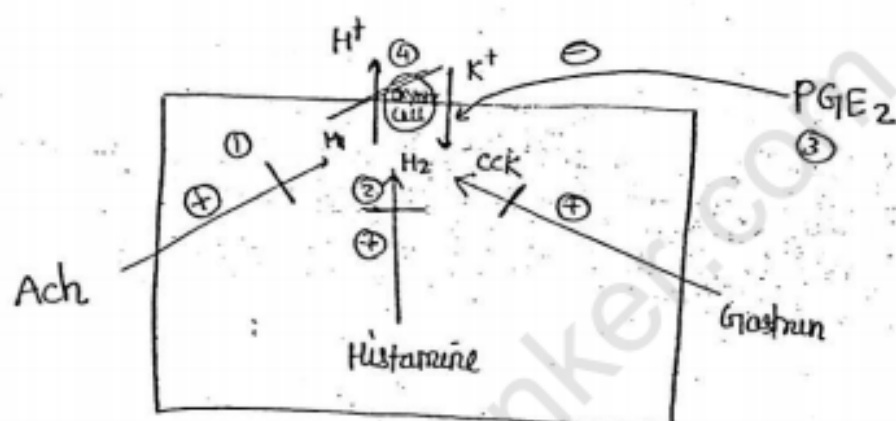
← (Smiley Face) Osteoarthritis →

→ Diacerein → it is Disease modifying anti osteoarthritis
↓
Drug
it IL-1 antagonist

← GIT →

← Peptic ulcer → b/c of ↑ acid & ↓ protective agent

$H^+ \& K^+ \rightarrow$ Proton pump



① ↓ acid by 4 mechanism →

(a) M_1 blocker → Pirenzepine
Telenzepine

(b) H_2 blocker → Drug ending Tidine → Cimetidine X Not use
Ranitidine

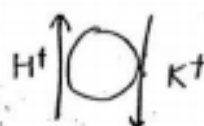
(c) Prostaglandin → misoprostol → famotidine → Most Potent
NSAID inducing Peptic ulcer → specific drug

(d) Proton pump inhibitors

→ Proton pump Inhibitors →

① K^+ competitive acid blocker (New)

- they are reversible
- fast acting



- PPI (old drug)
- irreversible
 - slow acting

→ K/a → Hit & RUN DRUG

→ PPI → irreversible, slow acting

- Omeprazole
- Lansoprazole
- Pantoprazole
- Esomeprazole
- Rabeprazole

→ all PPI are acid labile →

⊙ enteric coated

- acidic medium में ही break होता है
- basic med. में break हो जाते हैं

→ all PPI are proDrug

→ active metabolite form in acidic medium of parietal cell.

→ PPI → DOC → peptic ulcer (due to any reason)

- GERD
- Zollinger Ellison Syndrome

→ S/E → Very safe drug

• change the medium of GIT & some substance not absorb from GIT

↓
Ca ↓
vit B₁₂ ↓

- osteoporosis
- megaloblastic anemia
- long term use ↑ risk of infection

φ PPI inhibit the clopedogrel.

φ PPI inhibit the CYP2C19 → but Rabeprazole > Pantop
less affinity for
CYP2C19

> K^+ competitive acid Blocker → (New drug.)
↓
• faster acting
• Reversal inhibitors

- Vonoprazan
- Revaprazan

φ Antacid is fastest pain relief in peptic ulcer

② Antacids → $Al(OH)_3$
• $Mg(OH)_2$

③ Ulcer protective drugs → they form covering
↓ over the ulcer

- Sucralfate
- Colloidal Bismuth subcitrate (CBS)

→ Sucralfate → polymerise in acidic medium
• so do not given 2 any Acid Inhibitory drug

→ CBS → overdose → Bone → osteodystrophy
Brain → encephalopathy

Antidote - BAL

(12)

④ → H. Pylori → it cause Relapse ulcer

↓ kill by

- Amoxicillin
 - metronidazole
 - clarithromycin
 - Tetracyclines
 - CBS
- } good activity

→ T/T of H. Pylori → Triple Drug Therapy

- 2 Antibiotic + 1 PPI
- m/c preferred → CAP → PPI (Lansoprazole)
- ↓ ↓
- clarithro Amoxy



← Antiemetic drugs →

- ① Anticholinergic → Hyoscine → motion sickness
 ② H₁ # → promethazine → motion sickness

- ③ 5HT₃ # → Setron →

- ④ Sub P antagonist → Drug ending c pitant

also K_A Neurokinin

Fosaprepitant

Neupitant

Rolapitant

Aprepitant

→ Doc for
delay vomiting
due to cis platin

- ⑤ D₂ Receptor blocker → Domperidone → BBB Not cross
 (Doc) → for levodopa induce vomiting

- metoclopramide → BBB cross

- more strong

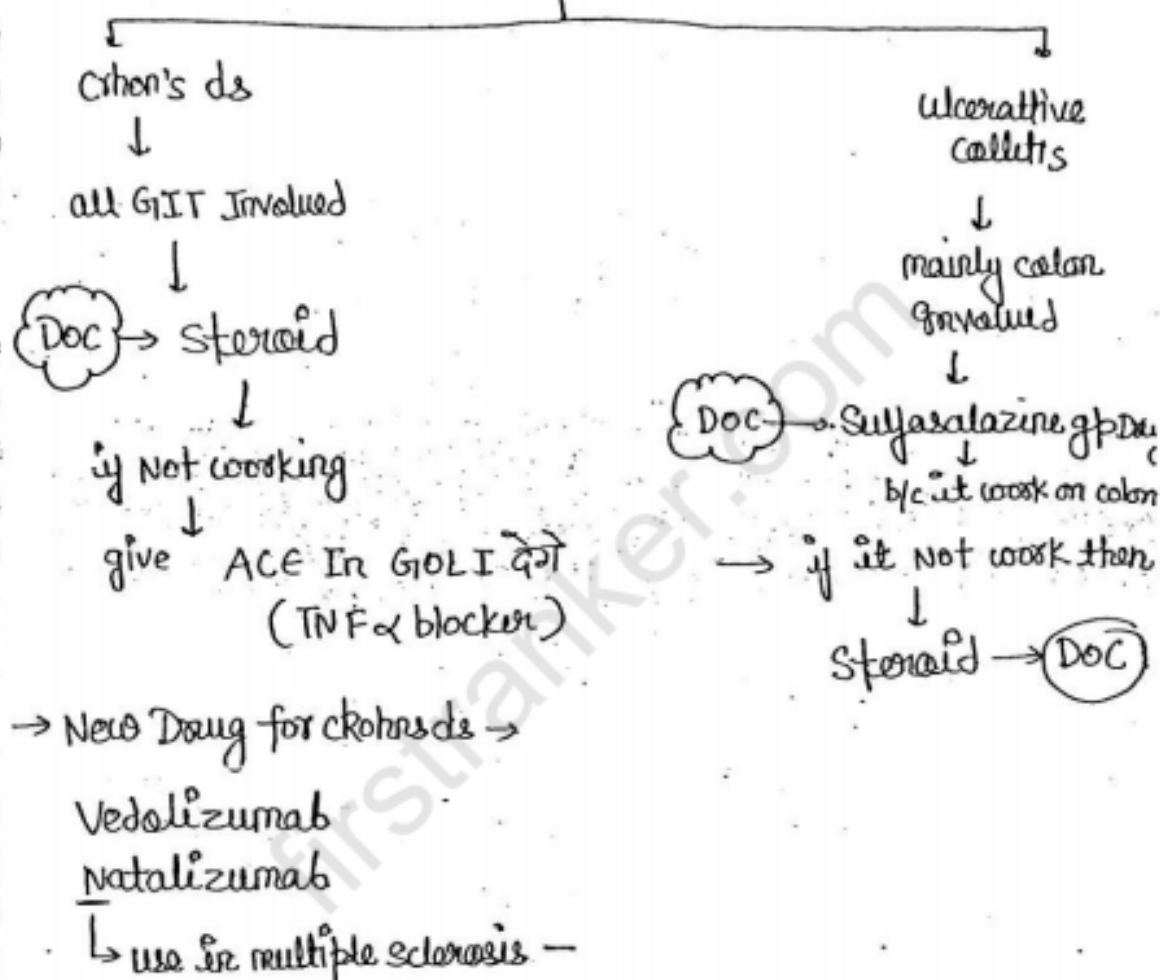
- S/E - extra pyramidal syndrome

m/c dystonia

- 5HT₃ # action
• 5HT₄ agonist

(13)

Inflammatory Bowel disease



← Diarrhea →

T/T of choice → ORS

> Bacterial diarrhea → ciprofloxacin

> Amebic diarrhea → metronidazole

↓
these both Not
Occur simultaneously

! Bacterial diarrhea → Fever EPT

! Amebic diarrhea → No fever

Loperamide } for secretory Diarrhea
Diphenoxylate } they ↓ GI motility

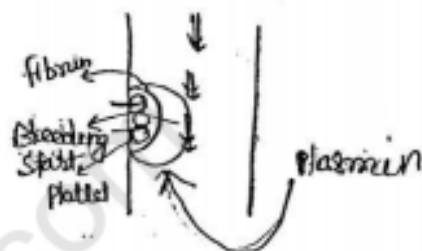
↓
add atropine to reduce Addiction

(13)

Hematology

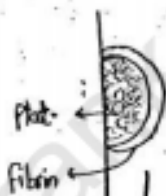
Drug affecting blood cell

Drug affecting blood flow

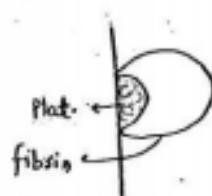


Artery

vein



in art. thrombosis
antiplatelet will
work



in vein thrombosis
anticoagulant will
work

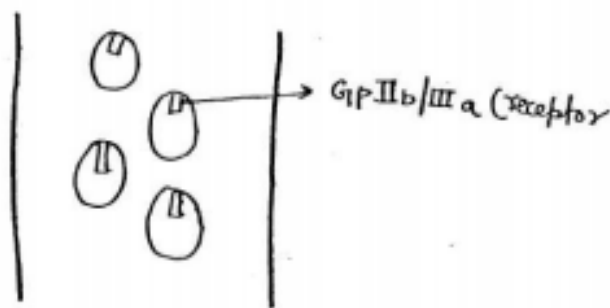
Antiplatelets

on pathway

TxA₂

ADP

→ release → expose
the receptor
• GP IIb/IIIa



① TXA_2 # $\rightarrow$ Aspirin

② ADP # $\rightarrow$ Clopidogrel $\rightarrow$ GP_{2C19}
 [P_2Y_{12}]
 Ticlopidine
 $\rightarrow$ Not use b/c cause Thrombocytopenia

③ $GP_{IIb/IIIa}$ # $\rightarrow$ Abciximab
 Tirofiban
 Eptifibatide
 Strongest antiplatelet Drug

④ Reversible ADP # $\rightarrow$ Ticagrelor
 Cangrelor

⑤ Protease Activated Receptor # $\rightarrow$ PAR #

Voraparav
 Ato Parav

(134)

← Antifibrin drugs →

K/a anticoagulant drugs.

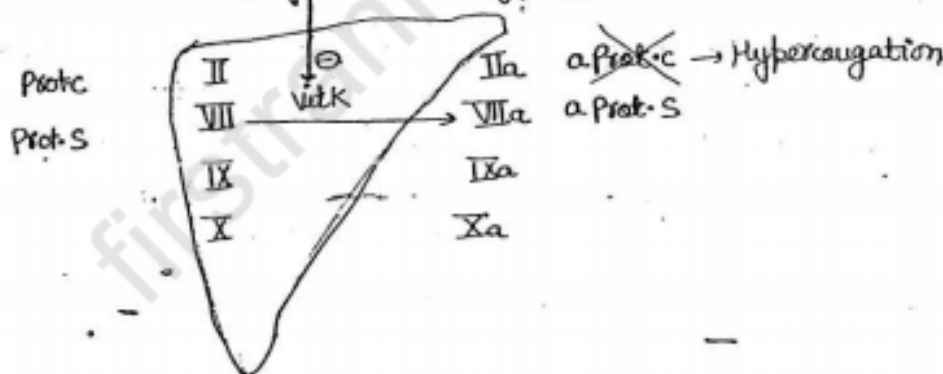
ORAL

Parenteral

warfarin → given orally

- vit K को Block करता
- action on 4-5 day
- warfarin is c/I in pregnancy b/c teratogenicity
- use as maintenance dose
- excess dose of warfarin → cause bleeding

warfarin → slow acting drug → 4-5 day

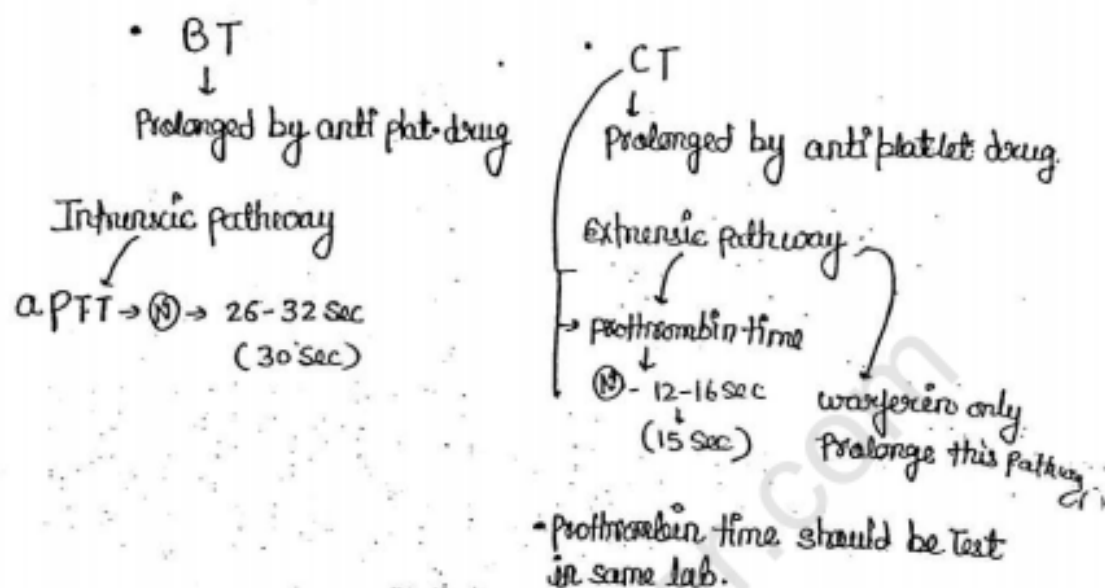


first to go protein C → Hypercoagulation

Renal Vascular Necrosis

- T/T of warfarin induced bleeding → FFP (T/T of choice)
- T/T of choice for warfarin induced bleeding tendency → Vit K

warfarin monitoring $\rightarrow$ By PT/INR



• INR $\rightarrow$ International Normalised ratio $\rightarrow$ it is the ratio $\frac{PT_t}{PT_c}$

• advantage $\rightarrow$ lab variability not occurs

$$INR = \frac{PT \text{ of test blood}}{PT \text{ of control blood}}$$

$\rightarrow$

X of warfarin induces bleeding $\rightarrow$

if INR $< 5 \Rightarrow$ Nothing do.

if INR 5-20 $\Rightarrow$ give vit K

if INR $> 20 \Rightarrow$ FFP given

Parenteral anticoagulant

→ Thrombin Inhibitor (IIa)

Two type of Thrombin #

Indirect

Heparin → S.C/i.v

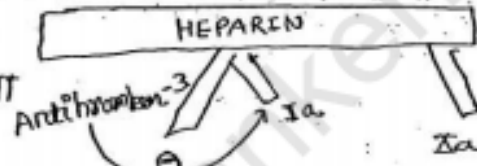
→ inhibits

Antithrombin ⊕

Immediate action
Use for acute case

→ DOC → In pregnancy

→ monitoring by aPTT



① LMWH → is inhibiting IIa.

② FONDAPARINUX

⊕ antidote for Heparin protamine

③ Heparin S/E → Heparin Induced thrombocytopenia (HIT syndrome)

DTI →

DOC - Direct Thrombin Inhibitor

HIRUDIN

LEPIRUDIN

Bivalirudin

Argatroban

Dabigatran → oral

all given parenteral

φ Idaracizumab → is antidote for Dabigatran toxicity

φ Direct Xa #

• RIVAROXABAN → New oral anticoagulant drug
• factor Xa की Reversible #

• APIXABAN

• EDUXABAN

→ Drug breaking the thrombus → K/a Thrombolytic drug

↓ or
fibrinolytic Drug

↓
these are tissue
plasminogen activator
(TPA)

TPA → use in acute thrombosis

- Streptokinase
 - Urokinase
 - Alteplase
 - Reteplase
 - Tenecteplase
- Short acting → given infusion
- long acting → given bolus
- longest acting

• MI → < 12 hr use करें हैं !

• Stroke → 3 hr तक देते हैं !

M/C → S/E → Bleeding → Cerebral Hemorrhage

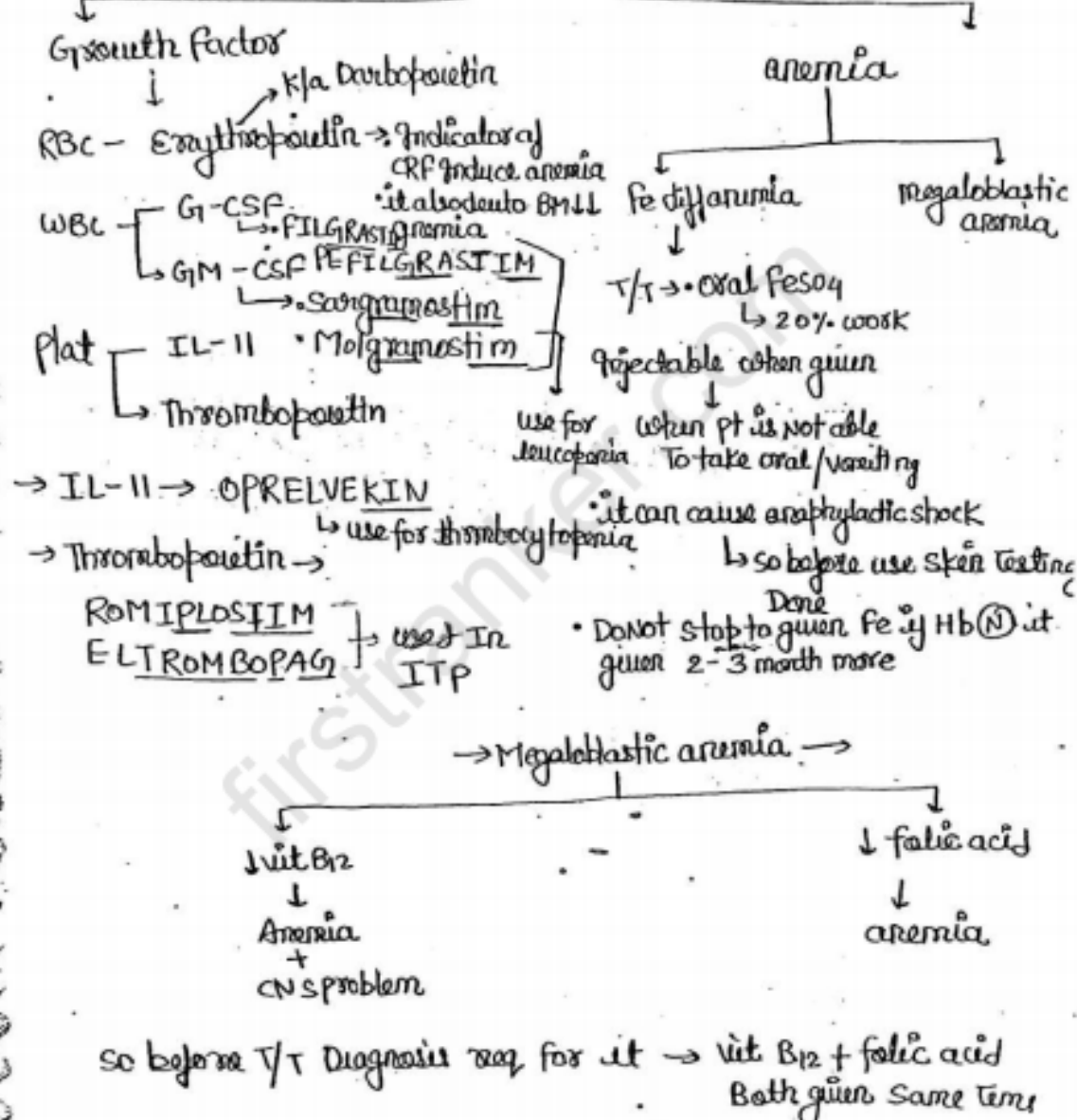
• anti Dot of fibrinolytic → anti fibrinolytics

↓
• Epsilon Amino Caproic Acid (EACA)

• Tranexamic acid.

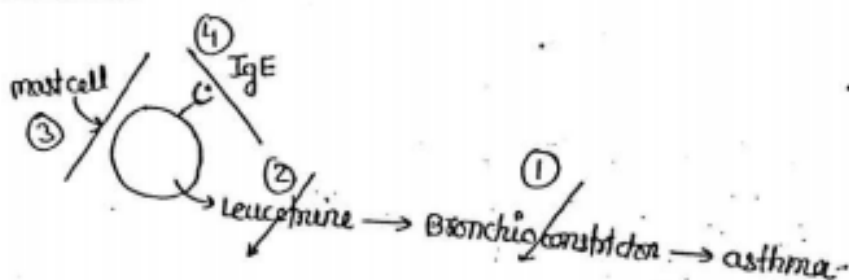
Page - 957, 822, 601

← Drug affecting cells of Blood →



← Respiratory syst →

Bronchial asthma →



D Bronchodilator →

→ Parasympatholytic → M_3 # → Ipratropium

Tiotropium

→ Sympathomimetic → β_2 agonist →

Salbutamol (albuterol) → acute attack
short acting Terbutamol → give by s.c route

Long acting Salmeterol } preferred in prophylaxis
formoterol }
↳ can use for acute attack

all of them can given by inhalation route

1) Doc for acute attack of asthma by any cause → β_2 agonist

except pt taking β # (salbutamol)

↳ Ipratropium given

2) Theophylline : given by oral/i.v

: Not given by inhalation route.

3) Leukotriene →

① PLPA₂ # → steroids

② Lox Inhibitor → ZILETON

③ Receptor antagonist → ZAFIRLUKAST
MONTELUKAST

φ these are use for prophylaxis



(137)

© Mast cell stabilizer → • Cromoglycate
• Nedocromil } only for prophylaxis

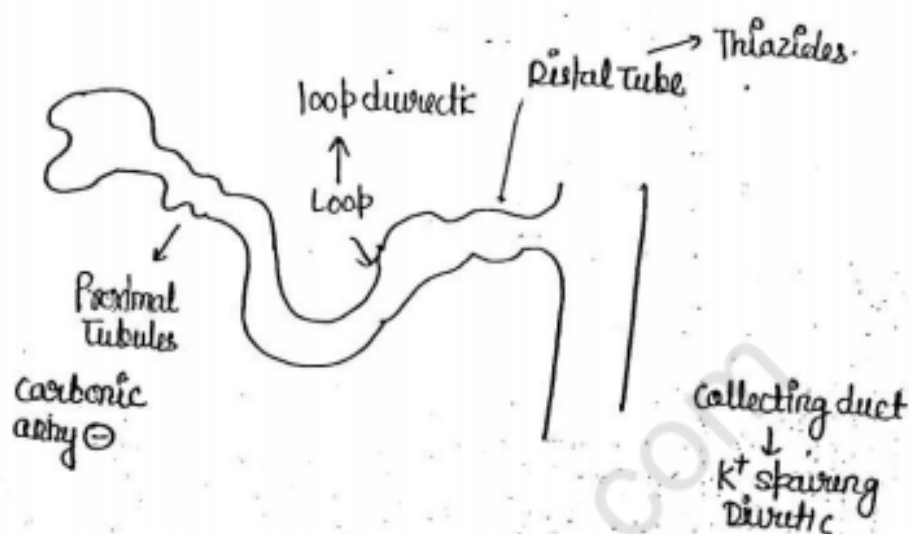
① Monoclonal antibody against IgE → OMALIZUMAB
↓
• given sc route
• use for prophylaxis

IL-5 # → MEPOLIZUMAB
RESLIZUMAB

→ DOC of acute attack of asthma → salbutamol
→ DOC of " " " " Pt take β -Blocker → Ipratropium
→ DOC for prophylaxis of B. Asthma → corticosteroid



← DIURETICS →



Osmotic Diuretics →

- work in all place of Nephron

Mannitol

- filtered
- Not reabsorbed
- Have osmotic effect

→ main use → Cerebral edema

↓
in cerebral edema, the mannitol beneficial effect is osmotic

→ mannitol C/I in active bleeding in cerebral

→ S/E → Diarrhoea

Carbonic anhydrase Inhibitor →

fⁿ →

- ① Diuretic
- ② urine alkalosis
- ③ metabolic acidosis

↑ Na⁺
↑ HCO₃⁻ → in urine

→ DRUGS → Acetazolamide → syn/oxal → in Glucoma

┌ Dorsolamide
└ Brinzolamide

eyedrop for glucoma

use → G - Glucoma

A → Alkalinisation of urine

M → maintain sickness → DOC → Acetazolamide

E → Epilepsy (not now)

⊕ Carbonic anhy Inhibitors are C/I → liver failure pt.

③ Loop Diuretics → act on thick ascending limb of loop of Henle.
↓
• it inhibit $\text{Na}^+/\text{K}^+/\text{2Cl}^-$ symport
• short acting
• Strong/High ceiling diuretic

Drug → Furosemide

• Torsemide

Bumetanide

Ethacrynic acid

↓
it is ototoxic

④ Thiazide → weak diuretic
↙ Long acting

• act on Na^+/Cl^- symport

• Drugs →

Chlorthalazide

Hydrochlorothiazide

Metolazone

Polychlorthiazide

⊕ Loop diuretics → Ca^{++} → Hypocalcemia

⊕ Thiazide like → Ca^{++} → Hypercalcaemia

Loop & Thiazide

↓ Na^+

↓ K^+

↓ Mg^{++}

↓ H^+

↑ sugar

↑ lipids

↑ U-acid

Indapamide

Xipamide

Metolazone

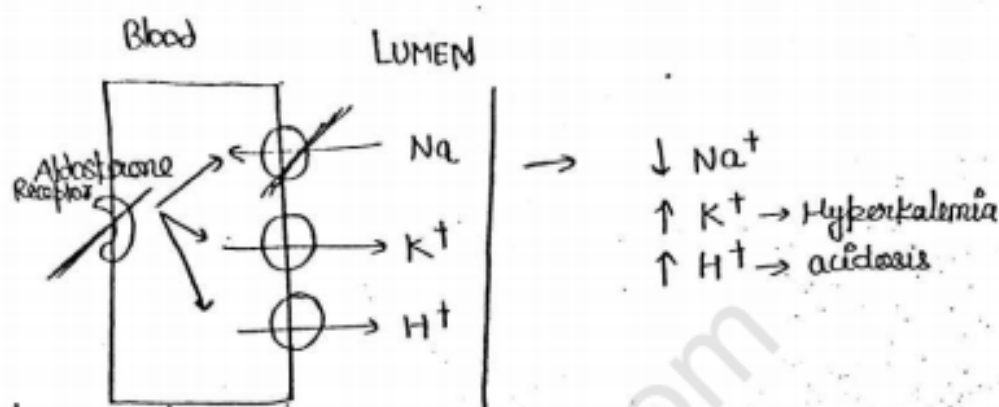
Thiazide like

Diuretics

Loop
↓
use in T/T of Hypercalcaemia

Thiazides
↓
• use for T/T of osteoporosis
• DOC → for Nephrogenic Diabetes Insipidus

Collecting duct diuresis $\rightarrow$ K^+ sparing diuretics



① aldosterone #

$\rightarrow$ SPIRANOLACTONE $\rightarrow$
 $\rightarrow$ EPLERONE $\rightarrow$ } they do not act with lumen

② Na^+ channel blocker $\rightarrow$ Amiloride
 Triamterene

$\rightarrow$ P $\rightarrow$ Pot. sparing diuretics
 A $\rightarrow$ Amiloride
 S $\rightarrow$ SPIRANOLACTONE
 T $\rightarrow$ Triamterene
 E $\rightarrow$ EPLERONE

← Free water clearance →
 ϕ +ve for dilute urine
 ϕ -ve for conc. urine



Cortex → urine dilute करता है।

Medulla → urine conc करता है।

(N) or conc. urine

→ Thiazide Inhibit free water clearance → only +ve free water clearance

→ loop Diuretic Inhibit both + & -ve free water clearance

← Diabetes Insipidus →

Iso-osmotic urine

Central D.I

→ T/T - ADH

→ DOC - Desmopressin

Nephrogenic D.I

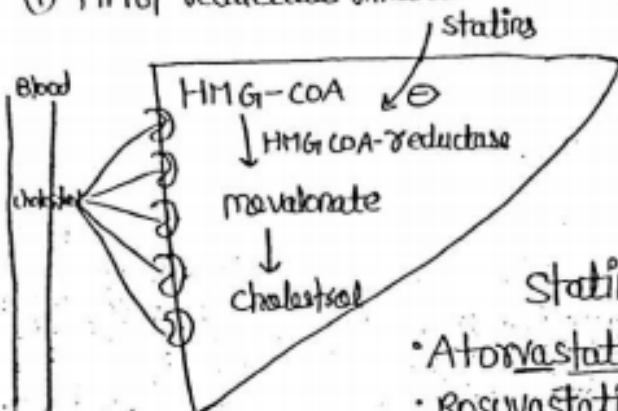
DOC → Thiazides

urine को dilutes
नहीं होने देंगे।



Hypolipidemic Drug or Antidyslipidemic Drugs.

① HMG reductase inhibitor → statins



Statins → VO & statin हे वेद stat
ent.

• Atorvastatin

• Rosuvastatin → longest acting

• Pravastatin → min risk of myopathy

• PITAVASTATIN → most potent

• SIMVASTATIN

• CERIVASTATIN

• FLUVASTATIN

no metabol
by microsomal
enzyme

f^h → • max LDL lowering capacity

• pleiotropic effect → they ↓ oxidative stress

• they ↓ endothelial dysfⁿ

• anti-inflammatory property.

} → imp

S/E → myopathy

• statin + fibrates → ↑ risk of myopathy

• 2 food ↑ absorption of statin.

Food ↑ absorption of Drug
Statin
Orlistat
Erlotinib

• Statin metabolism by CYP3A4

• risk of myopathy ≥ CYP3A4 + statin → ↑ myopathy
inhibitor

2) Intestinal cholesterol absorption Inhibitor →

→ NPLCI Inhibit

Ex → EZETIMIBE

3) fibrates → clofibrates
fenofibrate
Bezafibrate
Gemfibrozil

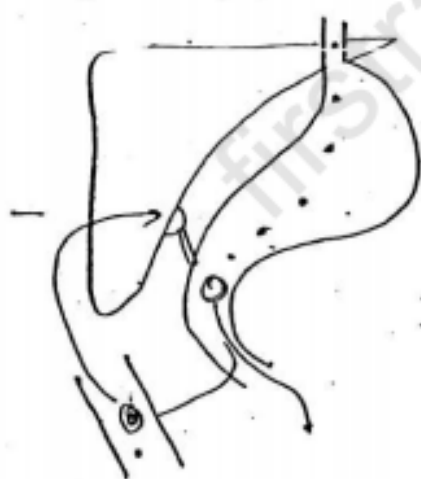
fibrate act by stimulate PPAR- α stimulation

max Triglyceride lowering agent is fibrates

Glitazone → γ PPAR α

Glitazone → $\alpha + \gamma$
PPAR
stimulat

4) Bile acid binding Agent → BABA



Drugs →

- Cholestyramine
- Colestipol
- Colesevelam

↓
Doc for dyslipidemia in pregnancy & children



(1)

⑤ Niacin $\rightarrow$ vit B₃



- ↑ HDL
- ↓ Lipoprotein(a)
- very cheap

S/E $\rightarrow$ Itching & Flushing
• Hepatotoxicity
• Hyperuricemia ***

φ b/c of compliance like limiting S/E so Pt Not take

φ PCSK-9 $\rightarrow$ Pro protein converting subtilis/kexin type 9

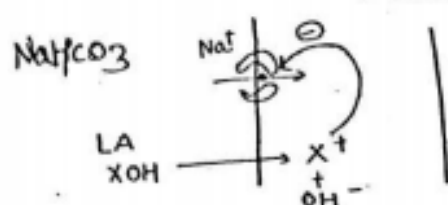
↓
f^h $\rightarrow$ broken LDL receptor

φ PCSK9 antagonist monoclonal antibody $\rightarrow$

- ALIROCUMAB
- EVOLOCUMAB

← Anesthesia →

Local anesthesia → all local anesthetics are basic in nature.
(LA)
• NaHCO_3 is added for fast action & making lipid soluble



Ester

COCAINE → vasoconstriction

PROCAINE

CHLORPROCAINE → shortest acting

TETRACAINE

BENOCAINE

Amide (1 एमिड नो एस्टर)

LIGNOCAINE → m/c use, & systemic use

BUPIVACAINE → max cardio-toxic

PRILCAINE → cause methemoglobin

ETIDOCAINE

DIBUCAININE → longest acting

• all LA cause vasodilation except COCAINE

• all LA are cardiac & neurotoxic but max → BUPIVACAINE

→ uses →

1) SURFACE → for mucous membrane anesthesia

2) skin anesthesia → $\left. \begin{array}{l} \text{Lignocaine } 2.5\% \\ + \\ \text{Prilocaine } 2.5\% \end{array} \right\} \rightarrow \text{eutectic mixture}$
anesthetizes intact skin

3) Infiltration anesthesia → • s/c route (around the lesion)
• short acting
• produce cardiac toxic & neurotoxic b/c go in blood

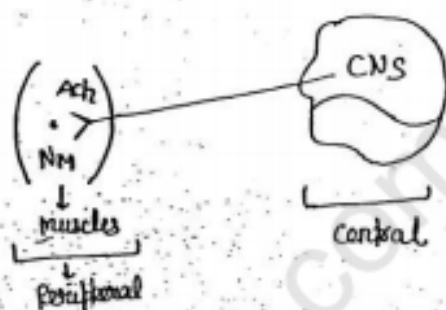
↓
so Adrenaline is added in it b/c

① make long acting

② ↓ cardiac & neurotoxic

- ③ IVRA → Intravenous Regional anesthesia → k/a BIER's Block
 → BUPIVACAINE is never use in this way b/c cardio & neurotoxic
 → w/c used → PRILOCAINE

← Skeletal muscle relaxant →



- Centrally acting muscle Relaxant →
 • GABA_A stimulator → Diazepam
 • GABA_B stimulator → Baclofen
 • α_2 stimulation → Tizanidine

→ they not effect on muscle strength only effect on spasticity

→ Peripherally acting muscle relaxant → muscle weakness करेगा

↓
Directly acting

↓
Dantrolene

↓
DOC → malignant Hypothermia

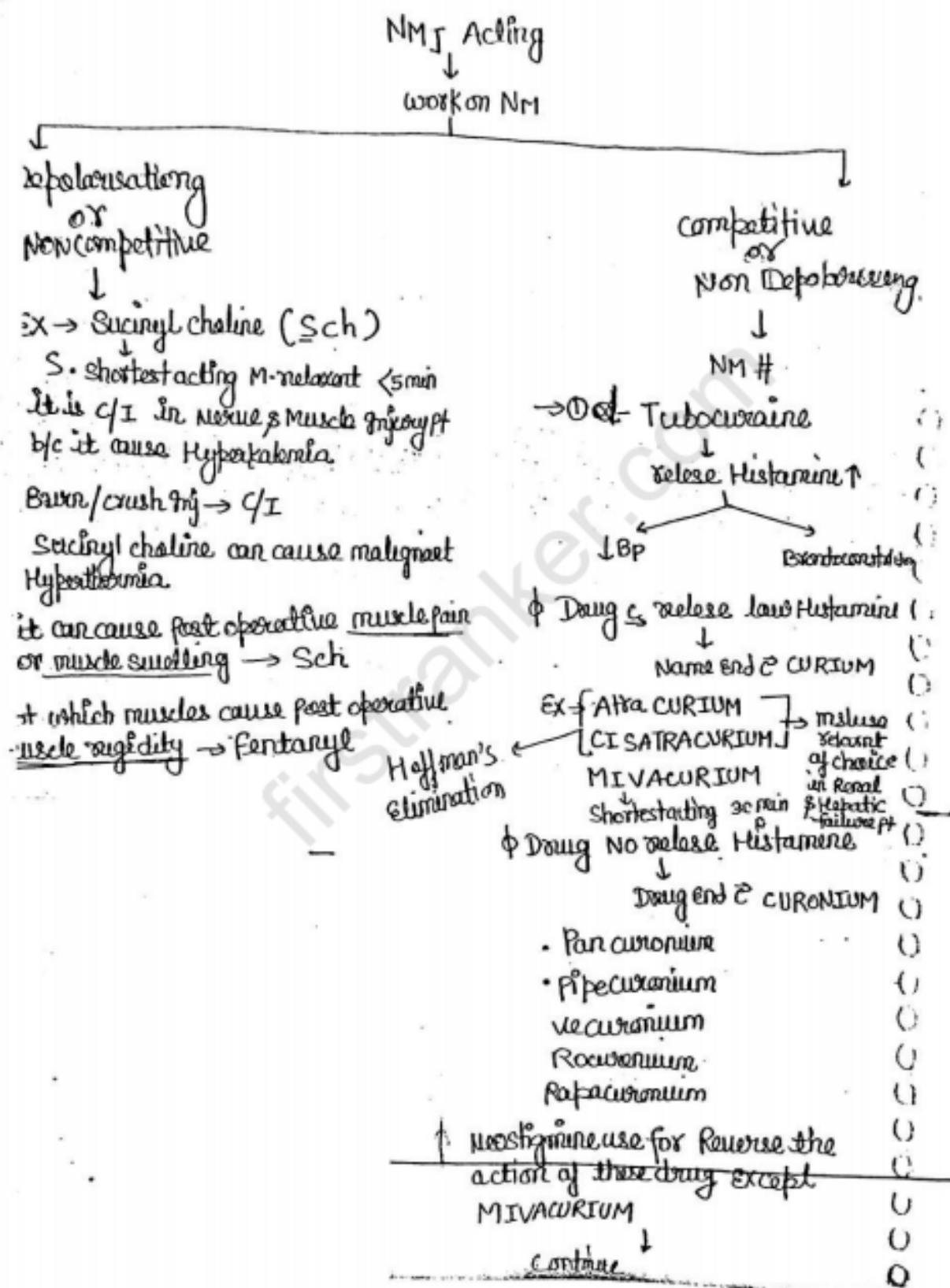
DOC → Neuroleptic malignant syn.

SE Hepatotoxic

↓
NMJⁿ acting

↓
it req. optimal stimulus

act on NMJ



φ SUGRAMADEX → New Drug
↳ K_{1a} → Selective Relaxant Binding agent (SRBA)

φ Gandacurium → shortest acting < 10 min among Non depolarising Drug

← GENERAL Anesthesia →

→ Inhalational route is route of choice for maintenance dose

G₁A

Inducing
(i.v)

Maintenance
(Inhalational)

- Thiopentone
- Propofol → i.v inj are painful
use in Day care surgery
- Etomidate → preferred in Sx of cardiovascular
cause Adrenal suppression
- Ketamine

Thiopentone → • highly soluble (lipid) barbiturate
• very fast acting (T_{1/2} in 10 sec) & short acting (T_{1/2} in 5 min)
• enter very fast in brain ***
↓
due to Redistribution

• if accidentally it go in at intra arial inj → Does Not remove the Needle

Drugs use in Day Care Surgery

Dx → Desflurane

Mamohan → midazolam

Singh → Sevoflurane

Is → Isoflurane

A → Alfentanil

Prime → Propofol → m/c use for Day care Sx

minister → rocuronium



← Ketamine → Strongest anesthetic
analgesic i.v agent

K → KIDS (i.v. ^{anesthesia} ~~choice~~ of choice in children)

E → Emergence delirium

T - Thalamo cortical Jⁿ ^{work करती है} (site of action) → Dissociative anesthesia

A → Analgesic (max strong analgesic)

M → Meals (it can given in full stomach)

I → Increase all press → BP, ICP, IOP → So anesthesia of choice in

J → NMDA # ^{Low BP pt}

→ Excellent bronchodilator → so use in asthmatic pt. ^{avoided in Hcd Inj. & Glucocoma}

Maintenance (Inhalational agent)

Chloroform
Trilene
Cyclopropane
Ether } these are inflammable.

MAC

- minimum alveolar conc
- MAC reserve potency
- $MAC \propto \frac{1}{Potency}$
- max MAC - N₂O
- lowest MAC → ~~methoxy~~ methoxy fluorine

Halothane

Enflurane

Isopflurane

Sevoflurane

Desflurane

Methoxy fluorane → also low MAC ~~also low MAC~~

XENON → ~~best~~

N₂O → max MAC & least potent

↓
10-15%

- Incomplete anesthetic agent
so never give alone

144

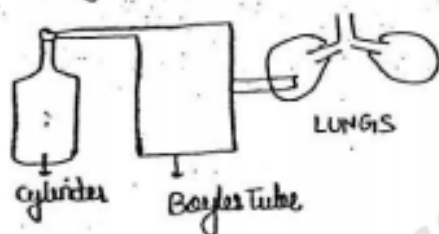
ϕ Blood gas partition coefficient $\rightarrow$ Say How much in Blood solubility

① more solubility - slower action

solubility in blood $\propto \frac{1}{\text{speed action}}$

→ max Blood gas partition coefficient → Slowest acting → methoxy
min " " " " → fastest acting → Xenon > Desflurane

→ Boyle's Tubes/machine → ↓ the pressure of O_2 cylinder



• Colour coding of cylinder

→ N_2O → Neela (Blue)

→ Cyclopropane → Santri (orange)

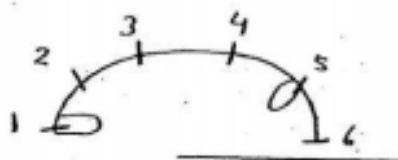
Black & white
↓
whole body except
Narrow part (shoulder)

→ Entonox

$\rightarrow$ mixt of $N_2O + O_2 \rightarrow$ Blue & white
50% 50% $\rightarrow$ shoulder white

6 PIN Index system $\rightarrow$

PIN कहाँ है & Hole कहाँ है।





PIN Index system

AIR $\rightarrow$ 1, 5

O₂ $\rightarrow$ 2, 5

N₂O $\rightarrow$ 3, 5

CO₂ > 7.5% 1, 6

CO₂ > 7.5% 2, 6

Cyclopropane 3, 6

ENTONOX $\rightarrow$ 7 (7 latter E' E'NTONOX में)

$\leftarrow$ XENON $\rightarrow$

Best anesthetic agent

b/c $\rightarrow$ anesthesia cause

- it is good muscle relaxant & analgesic both

- fast acting

- smooth induction

- safe for all organ

b/c it is not available & MAC more so not use.