GENERAL PHARMACOLOGY

Formula and graphs

Volume of distribution

$$V_d\ (L) = \frac{\text{Amount of drug in the body}\ (mg)}{\text{Plasma drug concentration}\ (mg/L)}$$

Half-life

$$t_{1/2}\ (min) = \frac{0.7 \times V_d\ (L)}{CL\ (L/min)}$$

Drug clearance

$$CL = \frac{\text{Rate of elimination of drug}}{\text{Plasma drug concentration}} = V_d \times K_e \text{ (elimination constant)}$$

$CL = \frac{U_x \times V\ (ml/min)}{P_x}$

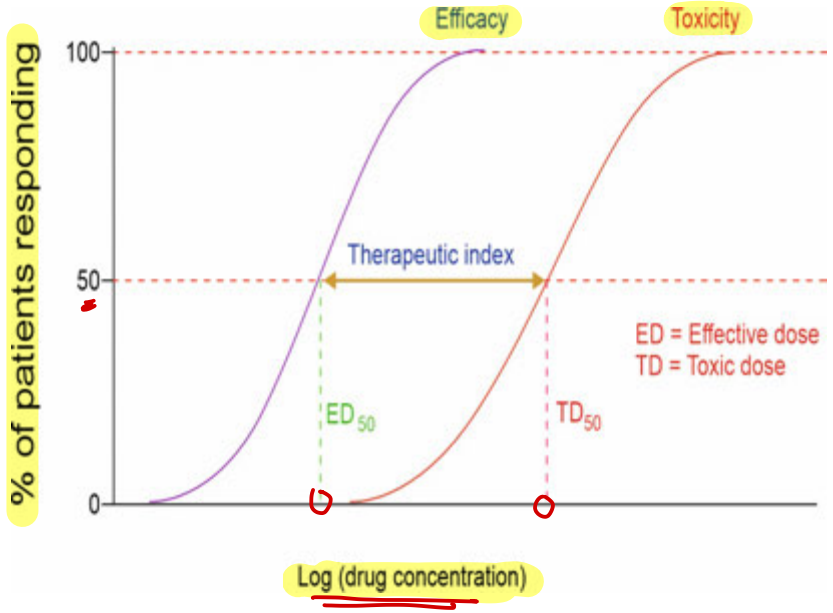
Volume of distribution
Plasma protein binding: $\propto 1/V_d$
Lipid solubility: $\propto V_d$

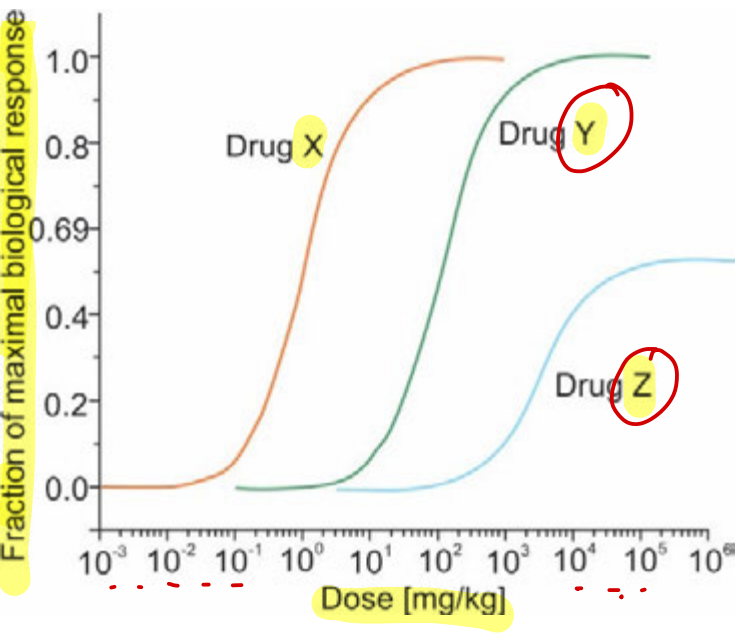
↑↑ – (x) dialyse Max V_d – Chloroquine

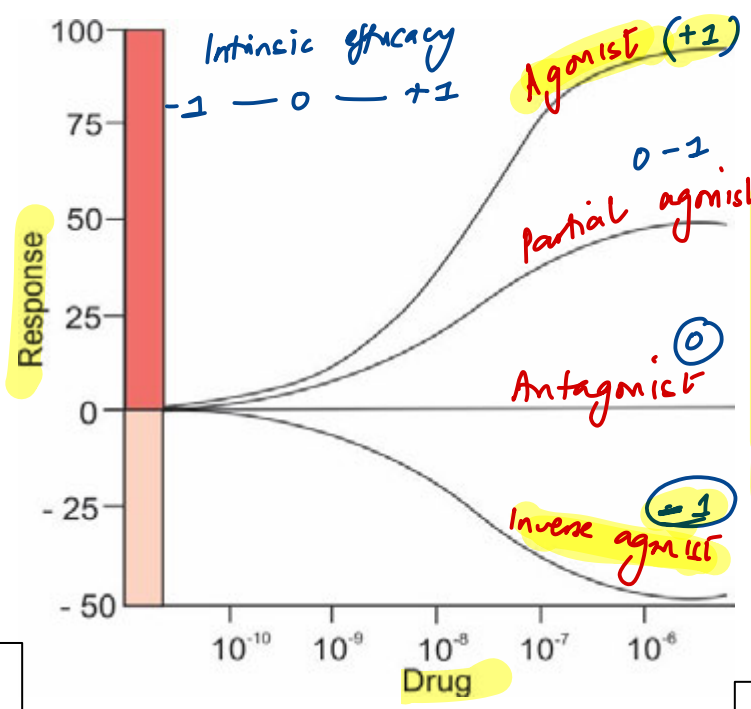
Loading dose: Target conc x **Vd**

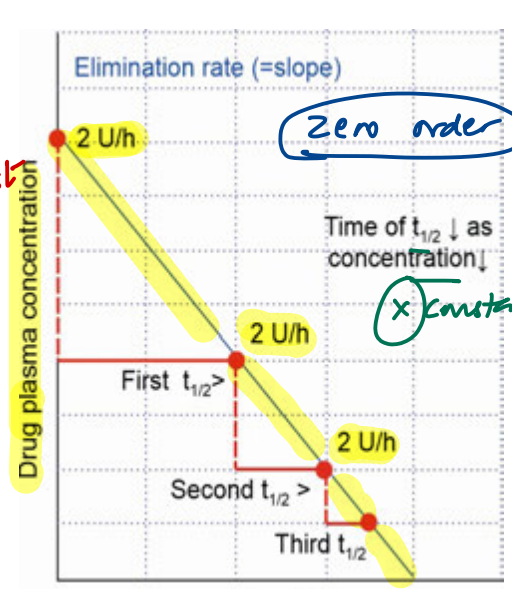
Maintanence dose: Target conc x **CL**

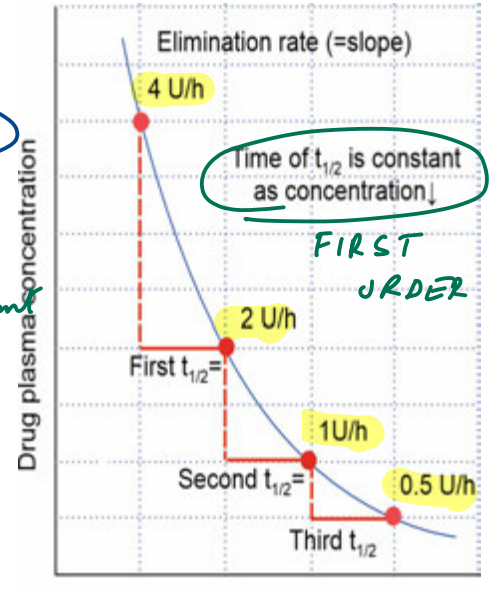
TI= Median toxic dose /median effective dose
TD_{50}/ED_{50}











- same amount in $t_{1/2}$

- same fraction in $t_{1/2}$

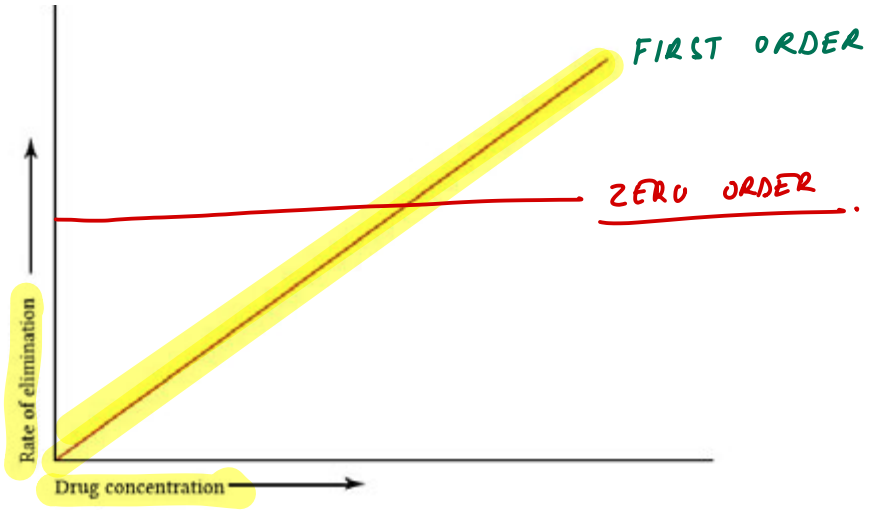
zero order

Potency VS Efficacy 'HELP'

Competitive antagonist: ↓potency (y)

Non-competitive: ↓efficacy

Phenytoin/Warfarin
Ethanol aa
Aspirin ↑↑ dose



a. Aspirin+ PCM (2+2=4) Additive action
b. Clopidogrel + Aspirin (2+2>4) Synergistic
c. Carbidopa-Levodopa (2+0>2) Potentiator
Permissive Cortisol BP + cortisol NE/E

General Pharmacology tables

Enzyme inducers	Enzyme inhibitors
Griseofulvin	Valproate
Barbiturate/Phenytoin	Ketoconazole
Carbamazepine	Ciprofloxacin
Rifampicin	Erythromycin
Nevirapine	INH
Smoking, Ethanol (Chronic)	Cimetidine
St.John's wort	Omeprazole
	Protease inhibitors

Schedules:
Under medical supervision: G
With prescription only: H
Cannot be treated: J
Addictive potential: X
Veterinary drugs
Category:
X:

CYP2C19:
CLOPIDOGREL -> active

CYP2C9: both zero order
WARFARIN
PHENYTOIN

CYP 3A4
CAT
Cisapride
Astemizole
Terfenadine
OCP(ESTROGEN)
Cyclosporine/ Tacrolimus
Statins / Amiodarone

CYP2D6
TAMOXIFEN -> active
Bblocker/ SSRI

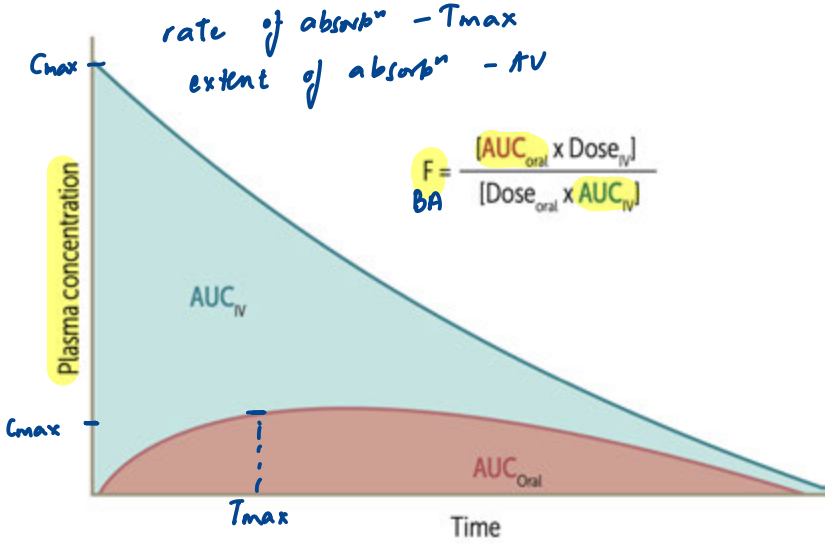
CYP2E1: PCM

Gynecomastia

D I S C
Digoxin INH Spironolactone
Cimetidine
Ketoconazole

Aminophylline:
PDE-4 inhibition
PDE-3 inhibition
Adenosine antagonism
Histone deacetylase activation

Essential drugs :
Cost effective
Prevalent diseases
Available easily
No combination
Orphan drugs:
<1/5 lakh
Beer criteria:



Bioequivalence: 80-125%

Pharmacokinetics - ADME study

absorb" distrib" metab excr"

Phase 1 reaction: Oxidation/ reduction/ deH/ Deamination/ cyclization

- exposing a functional grp
- NADPH
- ↓ elderly
- MICROSOMES = SER (LIVER)

Phase 2 reaction: adding a grp

glucuronid" / acetyln / glycine

↓

microsome

Trandermal patch

Nicotine patch - smokers
Hyoscine - antichol
Diphenhydramine - antiH } motion sickness
Nitrates
Clonidine HyTN
Seligiline/Ritogitine - PD
Rivastigmine - Alz D
HRT / Contraceptive

High first pass metabolism: x oral / ↑↑ dose

Lignocaine
Fentanyl
Natural steroids-GC, MC, E, PR
Propranolol (↑↑ dose)
Morphine
Nitrates
Verapamil
Salbutamol
Imipramine

parenteral / buccal / SL / rectal / td

Anti-obesity Approved drugs:

Phentermine + topiramate — sympathomimetic
Bupropion + zonisamide — NDRI; Na⊖
Liraglutide, Semaglutide → GLP-1
Tirzepatide GLP 1 + GIP ⊕ - max wt loss
Orlistat, Cetilistat - Lipase ⊖

PRODRUGS:

Carbimazole
Clopidogrel
Prednisone
Prasugrel
Levodopa
ACE- except: Captopril / Lisinopril
Sulfasalazine → 5 ASA
Mycophenolate
Acyclovir/ Gancyclovir

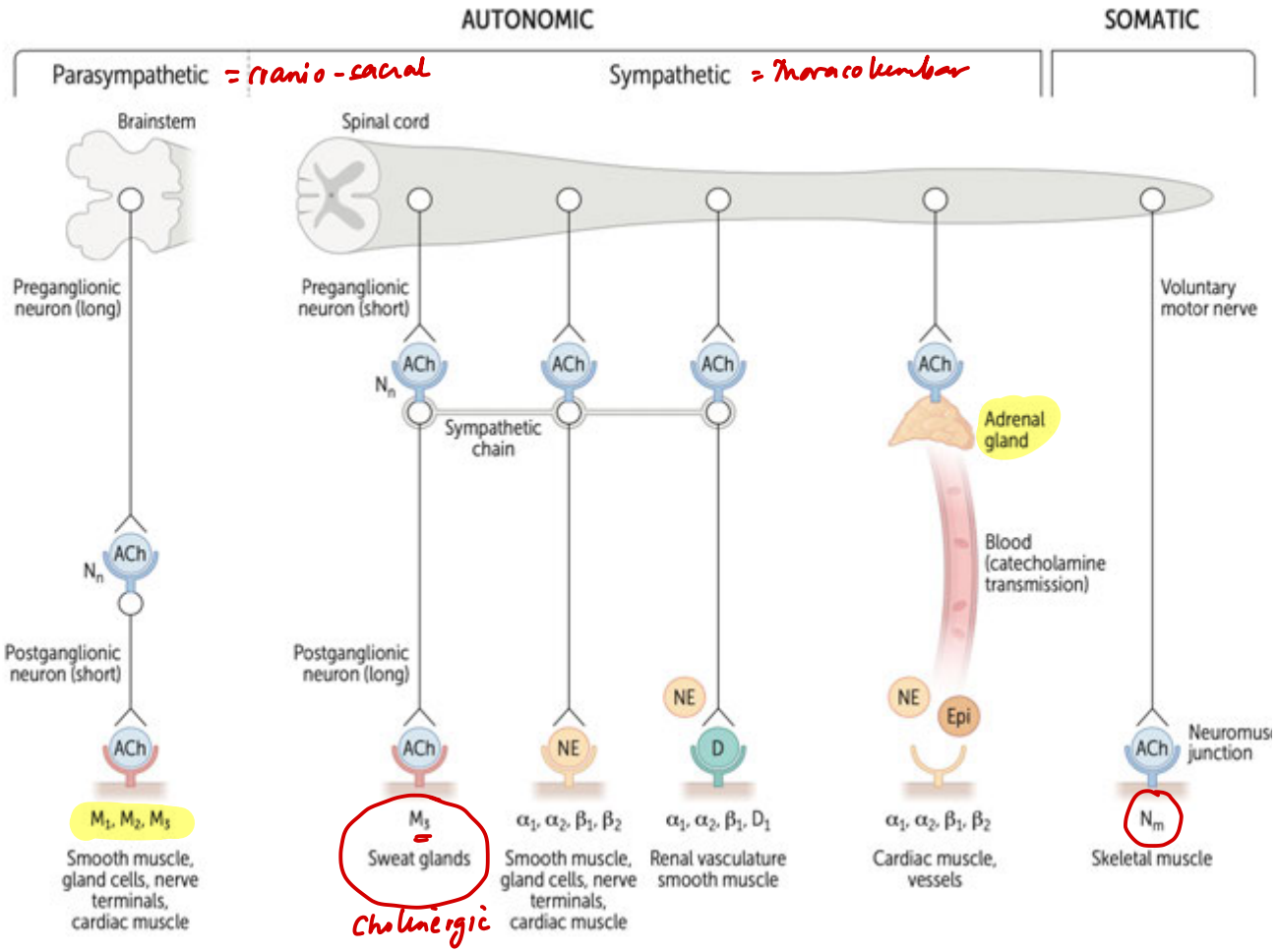
Suicide inhibitors:

PPI
MAO inhibitors
OP
Aspirin
Guanethedine/ reserpine — INE synapse

500mg PCM containing only 200mg PCM/ Missing info on packet/ Misleading claims: Misbranded drug
500mg PCM containing only no PCM/ Falsified component/Substitutes other drug: Spurious drug
500mg PCM containing harmful substances: Adulterated drug

Types of ADR	Name	Example
A	Augmented dose	• Hypoglycemia to insulin
B	Bizarre (genetically) Idiosyncratic reactions	• Allergic reactions
C	Continuous use of drug	• Peptic ulcer to aspirin
D	Delayed onset	• Teratogenic
E	End of treatment	• Withdrawal reactions
F	Failure of effects	• Antimicrobial resistance

ANS



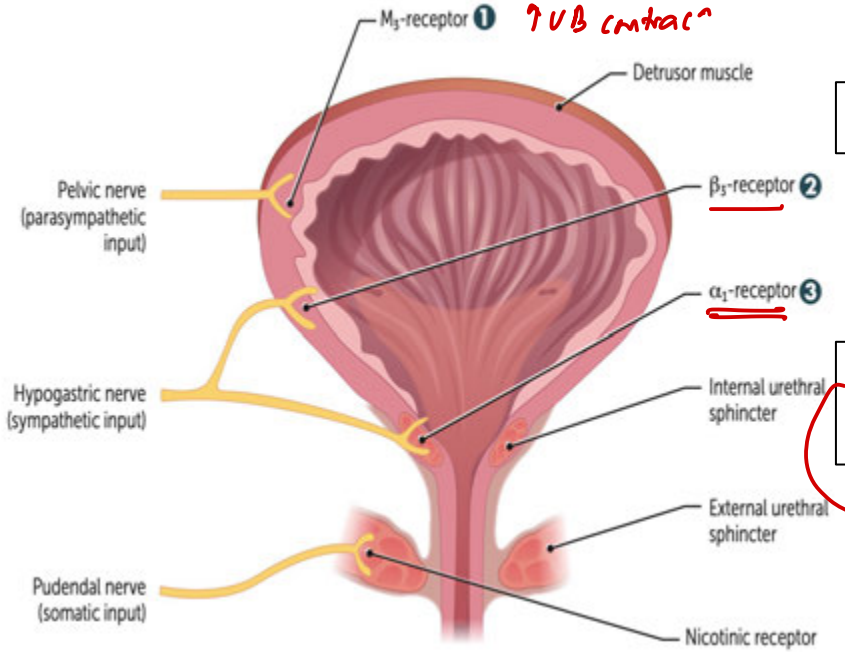
M1	stomach =
M2	♡
M3	- other organ

Cholinergic
- miosis
- HR ↓
- secr ↑

M3

Agonist: BETHANECHOL → Rx: Flaccid UB

Antagonist: Solifenacin, Oxybutynin, Flavoxate, Tolterodine, Darfenacine (- spasmolytic ++)
Rx - OAB / urge incontin
X BBB: TROSPIUM (M2 D + incontinence)



β3 ⊕
MIRABEGRON
Rx - OAB

α_1 ⊖ - BPH
Prazosin α ⊖
Tamsulosin α_{1A} ⊖
↓ **
s/e: Hypotension

CHOLINERGIC / ANTICHOLINERGIC

CHOLINERGIC

Direct
- Bethanechol - UB ++ — Rx - Flaccid UB
- Carbachol - most potent N_{Ach}
- Methacholine - asthma - FEV_1 ↓ >20%

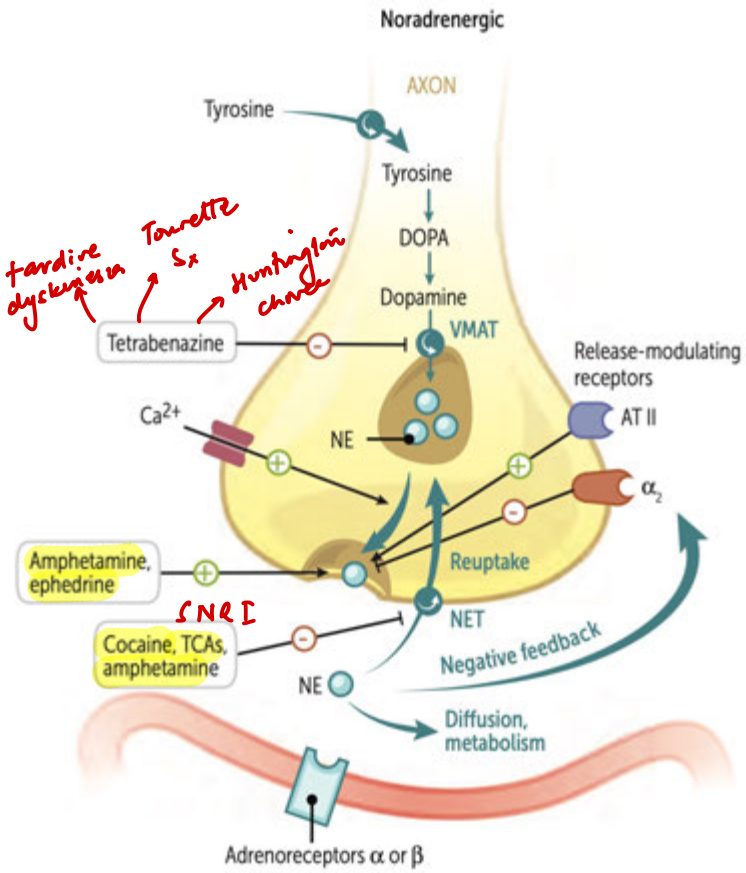
InD
- Pilocarpine - miosis / secrns ↑ Rx - Arg / Sjogren's
- Donepezil, Rivastigmine, Galantamine AchE⊖ - AlzD
- Neostigmine - x BBB - 4° amine — postop ileus, reversal NDMR, snake bite → + atropine
- Pyridostigmine Myasthenia gravis
- Physostigmine ✓ BBB — 3° amine — Datura Toxicity
- Varenicline α4β2 partial agnist N_N → smoking cessation

ANTI- CHOLINERGIC

- Atropine, Homatropine, Tropicamide → mydriasis + cycloplegic (longest - children; shortest - adults)
- Benztropine, Trihexyphenidyl → EPS Rx
- Glycopyrrolate ↓secrns preop.
- Hyoscyamine, Dicyclomine motion sickness
- Ipratropium, Tiotropium COPD > asthma
- Solifenacin, Oxybutynin, Flavoxate, Tolterodine, Darfenacine OAB Rx
- Scopolamine motion sickness
- Pirenzepine ↓acid
- BT ↓ release ↑ Ach - relaxes Achalasia / dystonia

Adrenergic agonists/ antagonists

	Receptors
a1	BV: VC PUPIL: mydriasis UB/Viscera: relax Agonist-Phenylephrine, Midodrine Antagonist-Phenoxybenzamine (irreversible) - Pheo (preop) MAOI ⊖ Phentolamine (reversible) - intra op Pheo / clonidine withdrawal / Cheese rxn Selective alpha-1: Prazosin, Terazosin, Doxazosin - Hytn + BPH Tamsulosin α_{1A} ⊖ → BPH
a2	Presynaptic break Agonist- Clonidine, Methyldopa (pregnancy), Tizanidine (↓spasticity) Rx - Hytn Antagonist-Yohimibe, Mirtazapine
b1	HR: ↑ Renin + Agonist-Dobutamine
b2	BV: vd Bowel-bladder-uterus: relax Bronchus: Bronchodil" Tremor: ↑ Sugar: ↑ - gluconeogenesis / glycogenolysis Agonist-Salbutamol, terbutaline Antagonist-Butoxamine (s/e · p. edema)
b3	UB relax / Lipolysis Agonist-Merabegron



Indirect agonists
- Amphetamine
- Cocaine
- Ephedrine

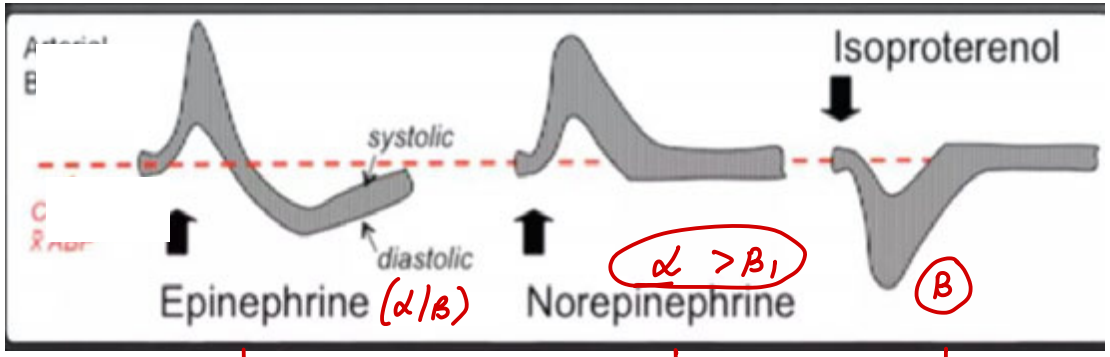
x B-blockers

ANS graphs

α_1 - vc (↑ potent)
B2 - vd (↑ sm)

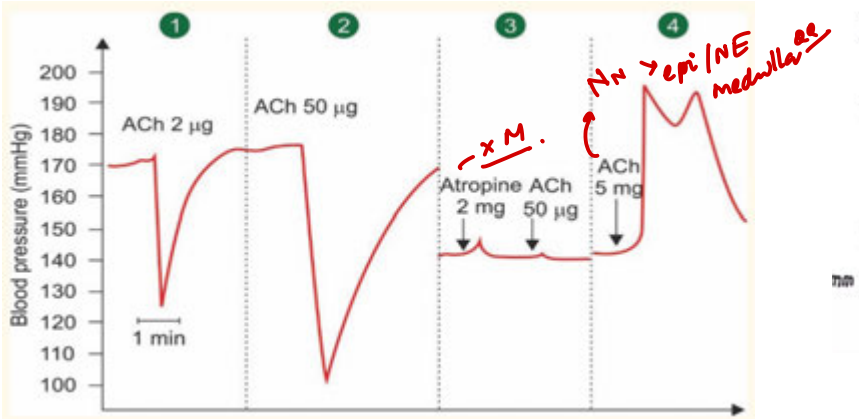
	DOC
Septic shock, Neurogenic shock Cardiogenic shock-refractory	Norepi N
Cardiogenic shock	Dobutamene (β_1)
Cardiogenic shock + oliguria	Dopamine
Postural hypotension	Midodrine
Spinal induced hypotension aa	Phenylephrine

	DOPAMINE
<2 ug/kg/min	D_1 → renal vasodil" (Fenoldopam)
2-10	B_1 → ionotropy ↑
>10	A_1 → vc ↑



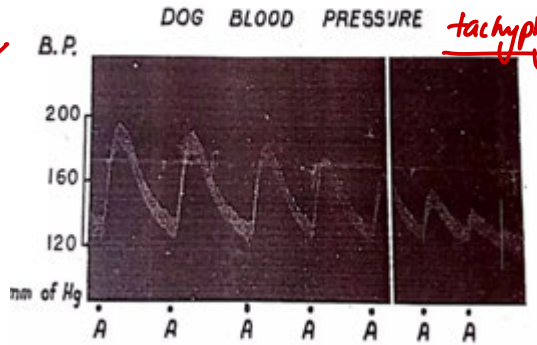
α-blocker

vasomotor reversal of Dale

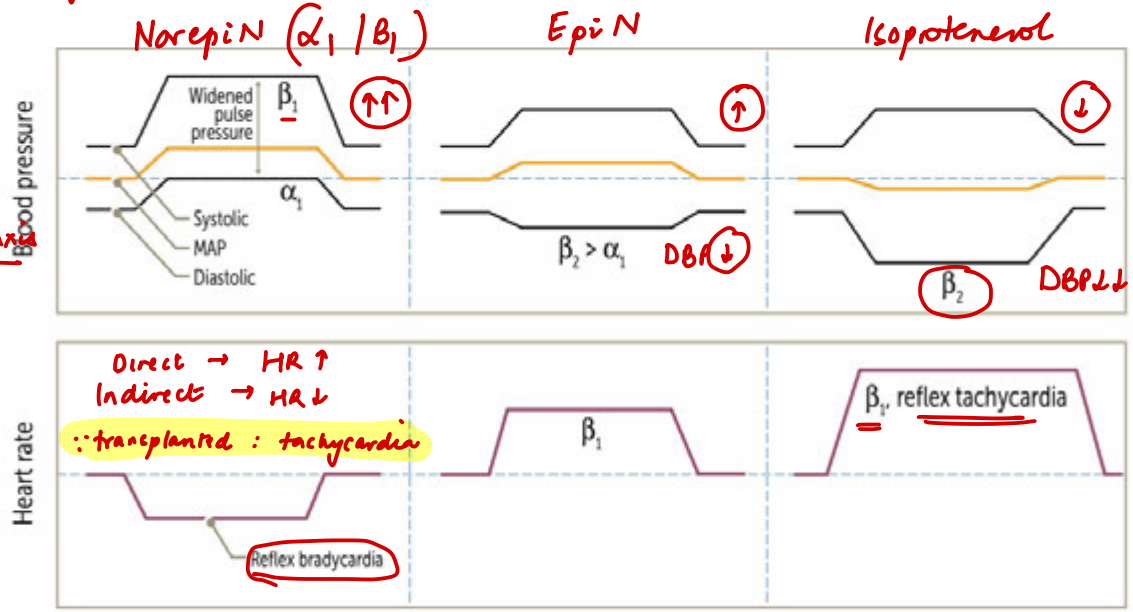


-xM.

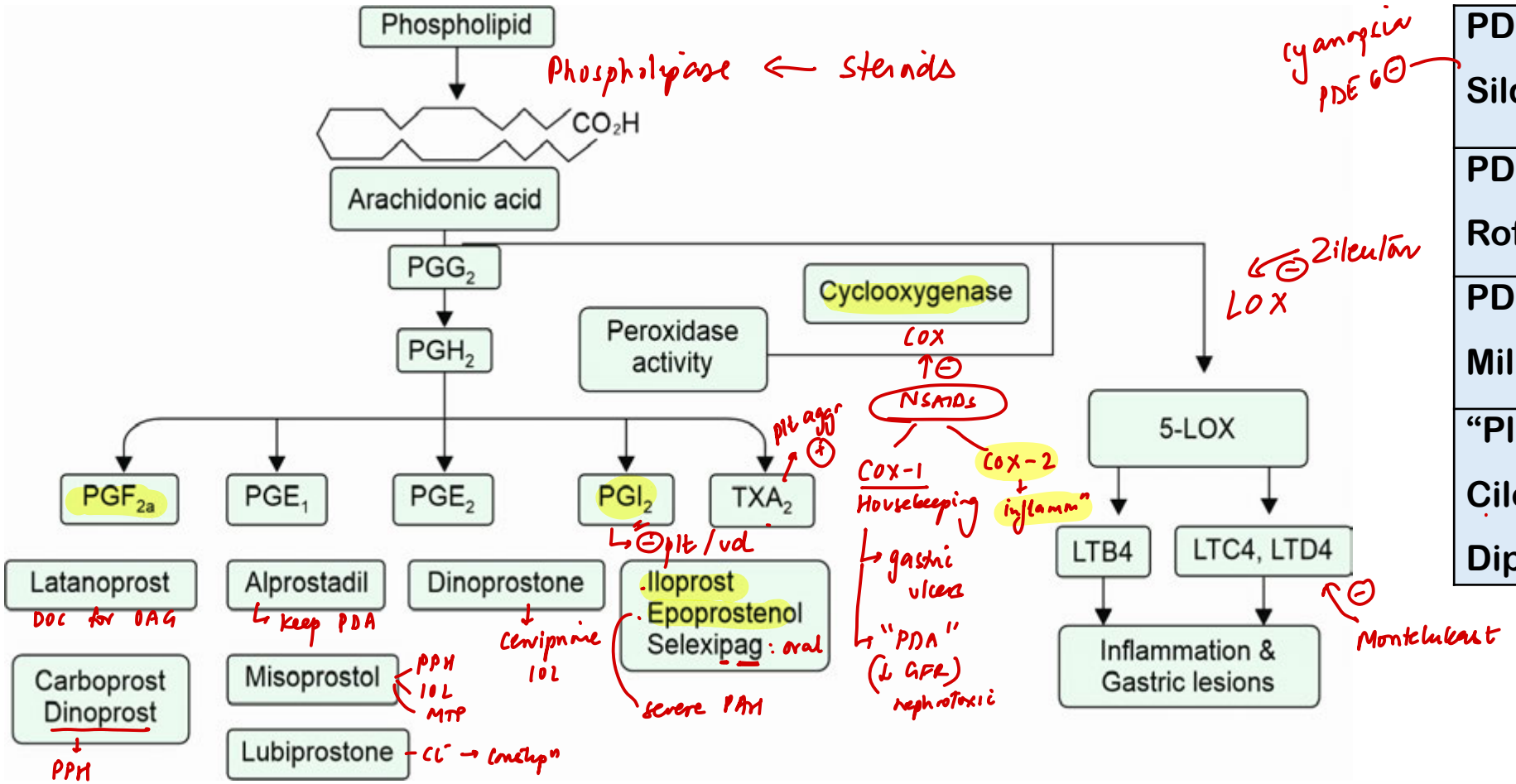
NN > epiNE medullae



tachyphylaxis



PG analogues



PDE-5 inhibitors → vd - ED / PAH Sildenafil , vardenafil , tadalafil
PDE-4 inhibitor → COPD Roflumilast
PDE-3 inhibitor → "ino dilatas" CHF Milrinone
"Platelet inhibitors" Raynaud / TAO Cilostazol (+PDE3-) → vd Dipyridamole (+adenosine) — coronary vd

- Celecoxib – COX-2 selective inhibitor (↑ r/o thrombosis)
- Aspirin – Irreversible COX inhibitor (<325mg: Antiplatelet; <2g-Analgesic; 2-5g-Anti-inflammatory)
- Other NSAIDs (Reversible COX inhibitors):
- Diclofenac/ Ibuprofen/ Indomethacin/ Ketorolac (IV)/ Naproxen/ Piroxicam → longest acting
- Lecofelone: Dual COX + LOX

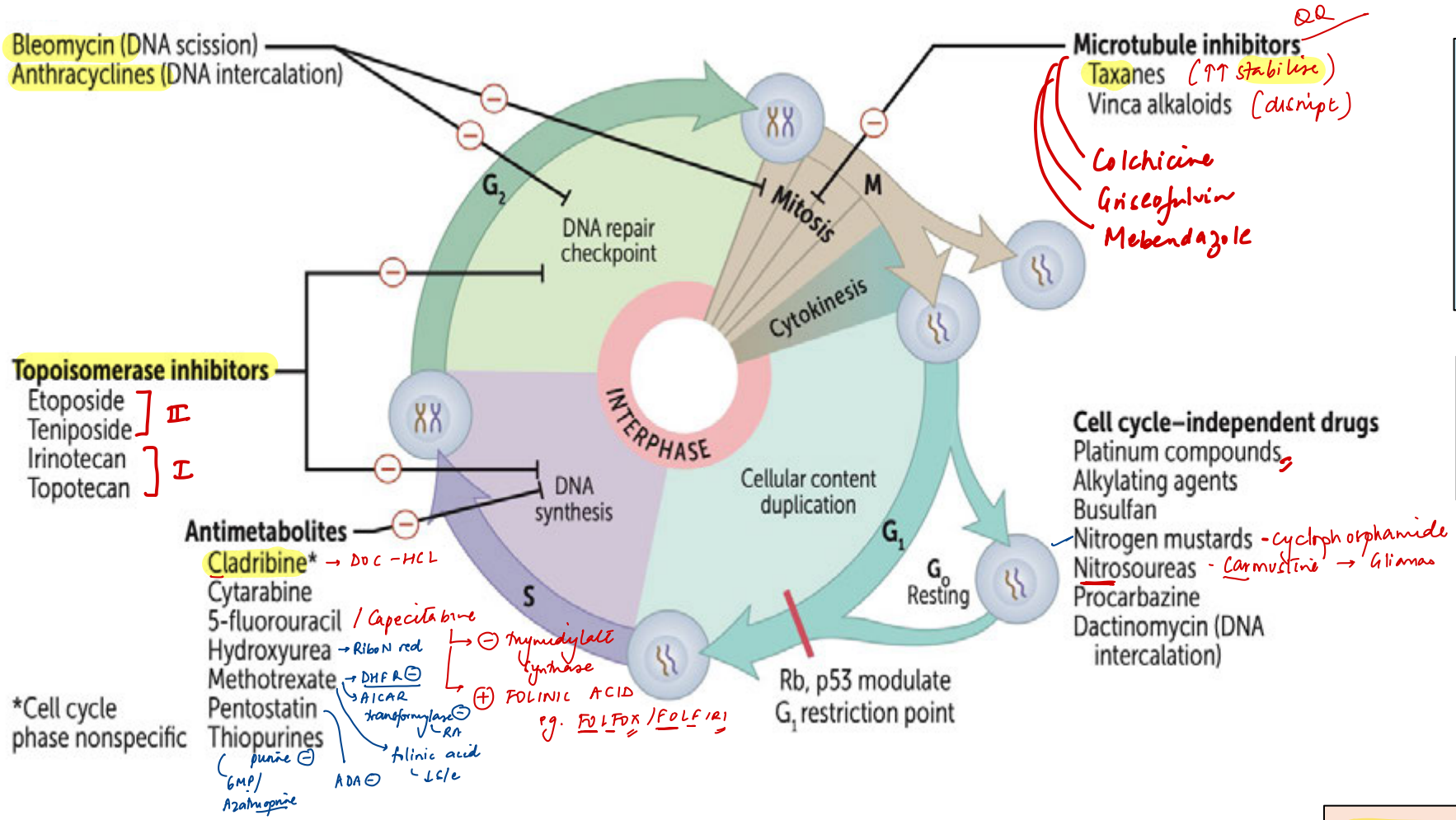
Miscellaneous

	Serotonergic drugs
5HT 1A	Agonist: Buspirone - anti-anxiety
5HT 1B/D	Agonist: Triptans - VC - acute Ap of migraine CI - PAD / ♡
5HT 1F	Agonist: Lasmiditan " "
5HT 2A/2C	Agonist: Lorcaserin (↓ apetite) Antagonist: Atypical AP ↓ s/e - metabolic s/e
5HT 3	Antagonist: Ondansetron
5HT4	Agonist: Cisapride / Tegaserod (prokinetic)
5HT2-4	Antagonist: Cyproheptadine L Ap- serotonin Sx

Biliary secretion (Safe in renal failure)
Cef in: Cefoperazone, Ceftriaxone QQ
The: Tigecycline
R: Rifampicin Q
E: Erythromycin
N: Nafcillin
A: Ampicillin
L: Lincosamide (Clindamycin)
D: Doxycycline Q

Pathology/Pattern	Causative Agent
Cholestatic pattern QQ	Contraceptive, anabolic steroids
Massive necrosis	Acetaminophen, halothane
Microvesicular steatosis	Valproate, tetracycline, aspirin (Reye syndrome), ART
Fibrosis and cirrhosis	Alcohol, methotrexate, Enalapril
Noncaseating epithelioid granulomas	Sulfonamides, amiodarone, isoniazid
Fibrin ring granulomas	Allopurinol

Anti-cancer drugs



QQ

Cyclophosphamide
Busulfan
Bleomycin
Carmustine
Methotrexate
Amiodarone

s/e : pulm fibrosis

BM spaning :

Vincristine — s/e : periph N, SIADH
Bleomycin — Pulm fibrosis, Flagellate dermatitis
L-asparaginase — s/e : pancitis

Specific Side effects:

Anthracycline (Doxorubicin, Daunorubicin) ♡ toxic - Prevent : Dexrazoxane

5FU / Capecitabine: Hand-foot Sx

Cytarabine: Cerebellar ataxia

Cyclophosphamide (N mustard): Hemorrhagic cystitis (Acrolein) — Prevent : Mesna; Rx : steroids

Cisplatin

Nephrotoxic: Prevent : Amifostine

Ototoxic

Most emetogenic

DOC early- 5HT3 ⊖

DOC delayed- Aprepitant (NK1 ⊖)

Anti-cancer small molecule inhibitors/ MAB

Agent	Target	Clinical Use
Alectinib, crizotinib	ALK (−)	Non–small cell lung cancer
Erlotinib, gefitinib, afatinib: L858R mutation Osimertinib: T790M mutation	EGFR (−)	Non–small cell lung cancer
Imatinib, dasatinib, nilotinib, Ibrutinib	TKI	CML, ALL, GIST
Bortezomib, ixazomib, carfilzomib	Proteosome (−)	Multiple myeloma, mantle cell lymphoma S/E: herpes zoster reactivation
Vemurafenib, encorafenib, dabrafenib	BRAF V600 (−)	Melanoma
Cobimetinib	MEK (−) MAPK	Melanoma
Palbociclib	CDK 4/6 (−)	Breast cancer
Olaparib	Poly ADP Ribose Polym (−)	Breast, ovarian, pancreatic, prostate cancers
Buparlisib Idelalisib	PI3K (−)	Breast Ca
Ipatasertib	AKT (−)	Breast ca
Alemtuzumab	CD52 (−)	CLL, multiple sclerosis
Cetuximab, panitumumab	EGFR / her 1 (−)	Metastatic CRC, head and neck cancer
Brentuximab	CD30 (−)	Hodgkin & ALCL
Vorinostat	histone deacytase (−)	lymphomas
Venetoclax, Obatoclax	Bcl 2 (−)	"
Belzutifan	HIF (−) → EPO ↓	VHL

NEW DRUGS

Belimumab: BLyS ⊖ → SLE

Teprotumumab: thyroid eye disease

Elacestrant, Fluvestrant: SERD → ca breast

Teplizumab: type 1 DM

Omavexolone: Friedrich ataxia

Ravulizumab, Rozanolixizumab, Zilucoplan, Efgartigimod Myasthenia gravis

Daprodustat: HIF ⊕ → EPO ↑ → anemia - CKD (CS ⊖)

Palivizumab Prophylaxis - RSV - Fpirtn

Emicizumab, Fitusiran, Concizumab, Marstacimab Hemophilia

Crinecerfont ↓ CRH ↓ ACTH → CAH

Landiolol ultrashort B-blocker

Mirdametinib MEK ⊖ → NF ↓

Iptacopan, danicopan, crovalimab → PNH

IFN-α → Hep B/C

IFN-β → MS

IFN-γ → CGD

Aldesleukin (IL-2) → RCC

Rituximab CD 20 ⊖

Fomivirsen (antisense oligo N) → CMV Retinitis

Eplontersen, Patisiren, Vutisiren, Inotersen → TTR amyloidosis

Source

- -mo mab (mouse)
- -xi mab (chimeric)
- -zu mab (humanized) 90%
- -mu mab (fully human)

ci / li / vi / tox / tu