PHARMACOLOGY REVISION 1

----- Active space -----

General Pharmacology

00:00:10

Types of drugs :

Types of drugs	Description
Orphan drug	Used in the treatment of rare diseases.
Essential drugs	Satisfying the health care need of majority of the population. Features : a. Single molecule (Not FDC). b. Safe. c. Easily available. d. Affordable.
Prescription drugs	Belonging to schedule H class. Given only after producing prescription.
Spurious drugs	Not producing adequate response due to inadequacy in the drug.
Misbranded drugs	Wrongly labelled drug.
Adulterated drugs	Drugs with additional unwanted component.

Rational drug use :

- The use of the right drug for the right disease & patient, at the right dose, duration & route, with the right dispensation and monitoring.
- Right price is not a part of rational drug use.

Pharmacokinetics and Pharmacodynamics :

Pharmacokinetics	Pharmacodynamics
1. Drug Absorption 2. Drug Distribution 3. Drug Metabolism 4. Drug excretion	Drug → Target → Effect

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Pharmacokinetics : Absorption

00:06:57

m/c mechanism : Passive diffusion.

Passive diffusion : Maximum at unionised/non-polar (Lipid soluble) state.

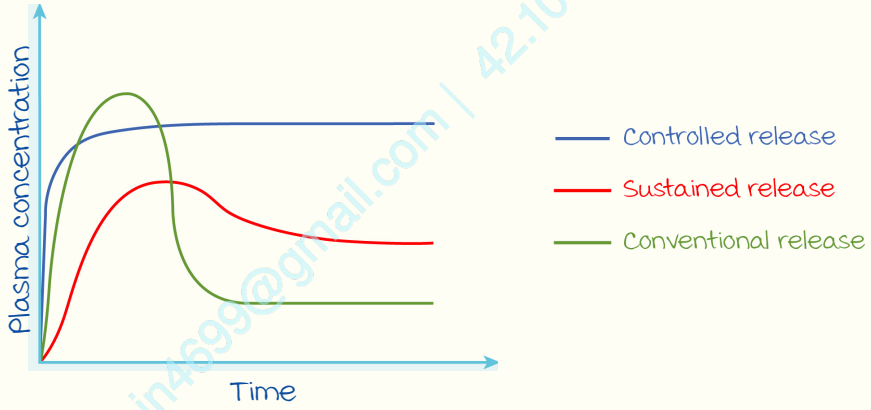
- Acidic drugs → Acidic medium (Stomach : HCl).
- Basic drugs → Alkaline medium (Duodenum : bile).

Maximum absorption of drugs : Small intestine (Duodenum) d/t large surface area.

Poor oral absorption : Proteins/large-size molecules :

- Peptides (Ends with tide).
- Enzymes (Ends with ase).
- Monoclonal antibodies (Ends with mab).

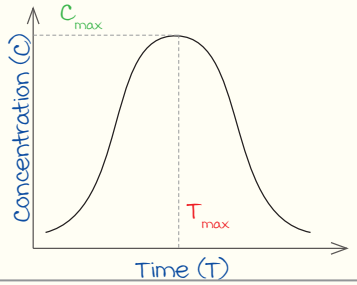
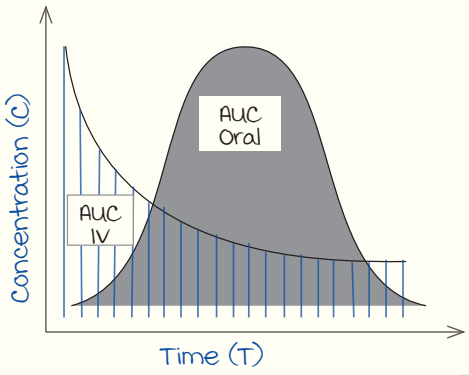
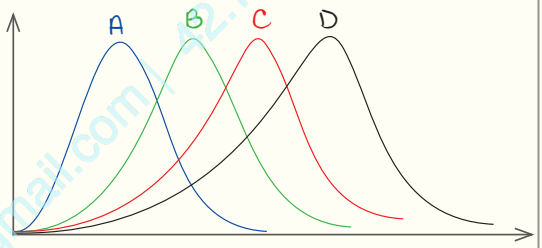
Types of tablets/capsules :



Sustained release & Controlled release	Enteric coated
↑ duration of action of drugs. Used in drugs with short $t_{1/2}$ (< 4h).	Used for : 1. Acid labile drugs. Eg. : PPI. 2. Prevention of gastric irritation. Eg. : Aspirin.

Active space

Extent and rate of absorption :

Bioavailability (BA)/ Extent of absorption	Rate of absorption
Fraction of unchanged drug reaching the systemic circulation. Ranges from 0–1 (0 = 0% ; 1 = 100%). Only route with 100% : IV.	
Depends on : • First pass metabolism. • Absorption.  (AUC : Area Under Curve). $BA = \frac{AUC\ oral}{AUC\ IV} \times 100$ AUC denotes : Bioavailability.	C_{max} : Maximum concentration of drug that can be achieved. T_{max} : • Time taken for C_{max}. • Marker for rate of absorption.  Rate of absorption : A > B > C > D.

P-Glycoprotein (Pgp)/MDR-1 (Multi Drug resistance-1) pump :

Membrane protein on intestinal epithelial cells.

Pgp → Drug efflux → ↓ Absorption → ↓ BA.

- Pgp inducer → Drug failure.
- Pgp inhibitor → Drug toxicity.

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Pgp substrates	Pgp inducers	Pgp inhibitors ("VACINE")
Digoxin Protease inhibitors. Loperamide Bile acid	Enzyme inducers. Eg. : Rifampicin.	V : Verapamil A : Amiodarone C : Cyclosporine I : Itraconazole N : Nifedipine E : Erthyromycin/Clarithromycin Quinidine

Pharmacokinetics : Distribution

00:26:10

Volume of Distribution (VD) :

Apparent VD (aVD) :

Factors affecting :

1. Lipid solubility/pK_a (pH at which the drug is 50% ionized).
2. Adipose tissue (more in obese people).
3. Plasma protein binding :
    a. Albumin binds to acidic drugs.
    b. α-1-acid glycoprotein binds to basic drugs.

Formulae :

$$aVD = \frac{D}{C_0}$$

D : Dose of the drug.

C_0 : Initial plasma concentration.

Loading dose = aVD × C_t.

C_t : Target plasma concentration

Loading dose depends on apparent volume of distribution.

Dialysis :

Ineffective against drugs with high VD : "BAD-DOC".

Drug	Antidote
Benzodiazepines	Flumazenil
Beta blockers	Glucagon
Amphetamine	Ammonium chloride
Digoxin	Digibind
-	-
Opioids	Naloxone
Organophosphates	Atropine
Calcium channel blockers	Calcium gluconate

Pharmacokinetics : Metabolism

00:35:18

Active space

Phase I reactions	Phase II reaction
Drug inactivation. Exception : Prodrugs → Activation.	Make the drug water soluble.
m/C reaction : Oxidation.	m/C reaction : Glucuronidation
Enzymes : • CYP450 enzymes (Cytochrome pigment). • m/C : CYP3A4. 3 → Family. A → Subfamily. 4 → Gene locus.	m/C enzyme : Glucuronyl transferase. Deficiency ↓ Criggler Najjar syndrome ↓ ↑ Toxicity of : • Atazanavir. • Irinotecan.

	Enzyme Inducers	Enzyme Inhibitors
Effect	Drug failure	Drug toxicity
Examples	Rifampicin → OCP failure	Erythromycin → Theophylline toxicity. Clarithromycin → Statin toxicity.
Drugs	"GRAB Priyanka Chopra"	"QUICK VEG Dish"
	G : Griseofulvin	Q : Quinidine
	R : Rifampicin	I : Isoniazid. Inhibitors of protease.
	A : Alcohol	C : Cimetidine, Chloramphenicol, Ciprofloxacin
	B : Benzopyrene	
	P : Phenytoin. Primidone. Phenobarbital.	K : Ketoconazole. Itraconazole. Fluconazole.
	C : Carbamazepine. Cigarette smoking.	V : Valproate
		E : Erythromycin/clarithromycin
		G : Grape juice
		D : DEC. Delavirdine. Disulfiram.

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Drugs metabolised by plasma esterase :

"Plasma Esterase Can Readily metabolise Short Acting drugs".

Procaine, Cocaine

Esmolol

Clevidipine

Remifentanil, Remimazolam

Mivacurium

Succinylcholine

Acetylcholine

Pharmacokinetics : Excretion

00:41:34

m/c organ for excretion : Kidney.

For excretion :

- Best state of drug : Water soluble/Ionised/Polar.
- pH of medium (urine) and drug must be different.

Drug toxicity	Antidote
Aspirin	Bicarbonate
Amphetamine	Ammonium chloride

Mechanism of excretion :

Filtration	Tubular secretion
20% of excretion	80% of excretion
Excretes only free drugs (Not plasma protein bound)	Excretes both free and plasma protein bound drugs.

Formulae :

Rate of drug elimination (mg/h) = PC × C_L.

Infusion/Dosing rate (To acheive steady state) = PC × C_L.

Maintenance dose = PC × C_L × t.

$t_{1/2} = 0.693 \times VD/C_L$

$t_{1/2} = 0.693/K_e$.

PC : Plasma concentration.

C_L : Clearance.

t : Time.

VD : Volume of Distribution.

K_e (Elimination constant) = VD/C_L.

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Zero order Vs. First order Kinetics :

		Zero order Kinetics	First order Kinetics
mechanism		Constant amount of drug is eliminated per unit time.	Constant proportion of drug is eliminated per unit time.
		Zero order Kinetics	First order Kinetics
↑ Dose	Clearance	↓	Constant
	Half life	↑	Constant
	Plasma concentration	↑ Disproportionately	↑ Proportionately
Examples		Alcohol Theophylline Tolbutamide Phenytoin Heparin Methanol Warfarin	Most of the drugs follow first order kinetics.

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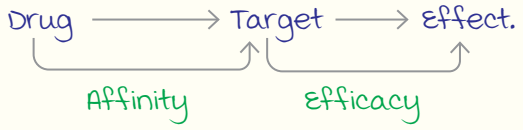
PHARMACOLOGY REVISION 2

Pharmacodynamics

00:00:09



Terms	Definition
Affinity	• Tendency of a drug to bind to a target. • Dose required to bind to target.
Efficacy	• Maximum clinical effect produced by a drug. • Effect produced (most important clinically).
Potency	• Relative dose of a drug required to produce a particular effect. • Potency α 1/Dose.

Dose Response Curve (DRC)

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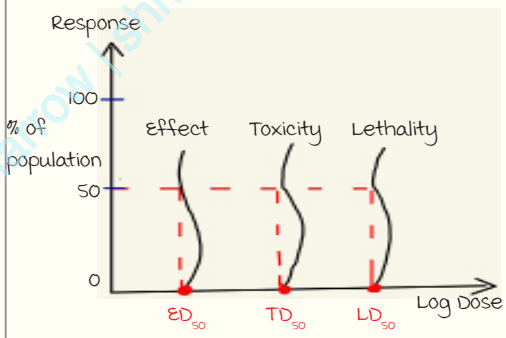
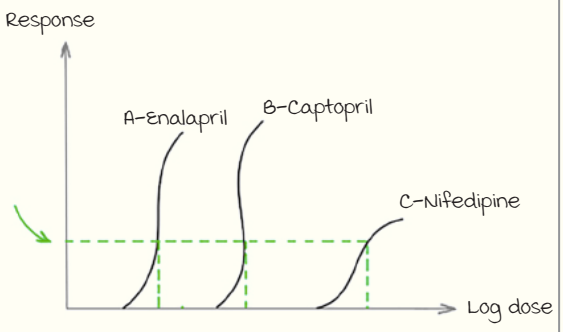
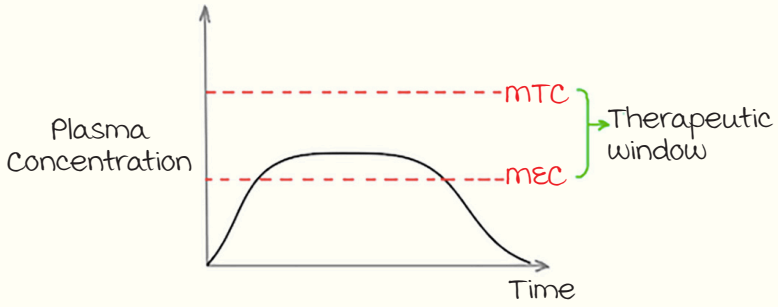
Quantal DRC	Graded DRC
Response : Binary (Yes/ No). Eg. : Sedation, Pregnancy.	Response : Graded.
DRC in a population.	DRC in an individual.
	
ED_{50} : Dose required to produce effect in 50% population. Marker of potency. TD_{50} : Dose required to produce toxicity in 50% population. marker of toxicity. LD_{50} : only in animals. Dose required to kill 50% animals. marker of toxicity.	Efficacy : B > A > C. Taller graph → Higher Efficacy. Potency : A > B > C. Lesser dose → more potent. Affinity : A > B (Affinity can be compared only if the drugs act on same target → Only if DRCs are parallel).

Active space

Therapeutic index (T.I) :

- Humans = $\frac{TD_{50}}{ED_{50}}$, Animals = $\frac{LD_{50}}{ED_{50}}$
- Measure of drug safety range.

Therapeutic window/range :

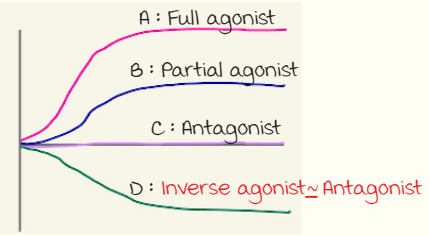


- MEC (Minimum effective concentration) : Effect seen only beyond MEC.
- MTC (Minimum toxic concentration) : Toxicity begins beyond MTC.
- Therapeutic range = between MEC & MTC.

Drug receptor interaction

00:16:24

- Full agonist : Maximal effect (+1).
- Partial agonist : Submaximal effect (+1 to 0).
- Antagonist (m/c) : No effect (0).
- Inverse agonist : Opposite effect (0 to -1).



Types of antagonism :

Types	Examples
1. Physical/pharmacokinetic	Alcohol : Charcoal.
2. Chemical	Heparin : Protamine sulphate. Iron : Desferrioxamine.
3. Physiological	Histamine (H1) → Bronchoconstriction. Adrenaline (β2) → Bronchodilation.

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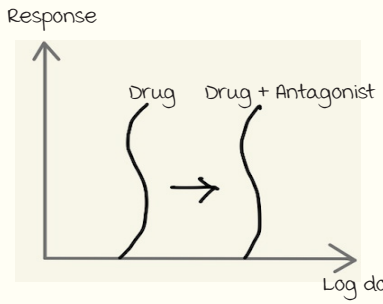
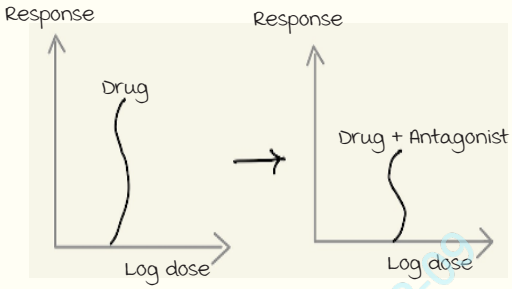
4. Competitive (Pharmacological)	5. Non-competitive
	
Right shift of DRC.	Decrease in height of DRC.
Efficacy → Same, Vmax → Same.	Efficacy ↓, Vmax ↓.
Potency ↓, K_m ↑.	Potency → Same, K_m → Same.

Vmax α Efficacy, K_m α 1/Potency.

Receptors :

1. Ligand gated ion channel

- $GABA_A$.
- Glutamate.
- Nicotinic.
- $5HT_3$.

2. Nuclear

Located in cytoplasm :

- Vitamin D receptors.
- Androgen receptors.
- Mineralocorticoid receptors.
- Glucocorticoid receptors.

Located in nucleus :

- Thyroid receptors.
- Estrogen receptors.
- Progesterone receptors.

3. Enzymatic

Tyrosine Kinase receptors :

- EGFR (Epithelial growth factor receptor).
- VEGFR(Vasculo Endothelial growth factor receptor).
- Her-2.
- Insulin, IGF-1.
- Toll like receptors.

Janus Kinase Receptors(JAK) :

- Leptin.
- Growth hormone receptor.
- Prolactin receptor.

Guanylate cyclase receptors :

- Atrial natriuretic peptide (ANP).
- Brain natriuretic peptide (BNP).

4. G-Protein Coupled Receptors (GPCRs) :

Gs :

- Gs → Stimulates Adenylate cyclase → ↑ cAMP → Smooth muscle relaxation (bronchodilation), cardiac & skeletal muscle contraction.
- E.g : β1 receptors → Dobutamine used in Congestive Heart failure (CHF).
  β2 receptors → Salbutamol.
- cAMP is metabolised by
  a. PDE 3/4 in bronchi ⟵(⊖)— Theophylline (used in asthma).
  b. PDE 3 in heart ⟵(⊖)— Milrinone (used in CHF).

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Gq :

- Gq → Stimulates Phospholipase C → ↑PIP2 → ↑IP_3 → ↑ Ca^{2+} → Smooth muscle Contraction.
- Eg. : α_1 receptor, Angiotensin Receptor, Oxytocin, M1, M3 receptors.

Gi/o :

- Gi/o → ↓ cAMP & ↓ Ca^{2+} → Relaxation.
- Eg. : M2 receptors in heart.

G12/13 :

- G12/13 → Stimulates Rho Kinase.
- Rho Kinase blockers :
  a. Fasudil → Vasodilator in stable angina.
  b. Netarsudil → Glaucoma.
  c. Belumosudil → Graft v/s host reaction.

Trials

00:33:39

Preclinical Trials : Animals.

Clinical Trials : Human → Drug under trial is called as investigational new drug.

Phases	Features (mnemonic : TEL)
I	Human Pharmacology and Toxicity Study Pharmacokinetics. Toxicity. Pharmacodynamics. Safety. Maximum tolerable dose. } 20-100 normal healthy volunteers. 1-2 years. Open label trial. Exception for normal healthy volunteers in Phase I : Trial for anti-cancer & anti- HIV drugs.
II	Therapeutic Exploratory Trial. Dose range. Safety. Determine Efficacy. } 100-500 patients, Unicentric. 2-3 years. Randomized Controlled Trial (RCT).
III	Therapeutic Confirmatory Trial. Safety. Confirm Efficacy. } 500-3000 patients, Multicentric. 3-5 years. RCT/RUCT. Drug is approved by CDSCO/FDA & marketed.
IV	Post Marketing Surveillance. Rare Adverse Drug Reaction (ADR). Long term ADR. } Many thousands. No specific duration. Open label trial.
Others	Phase 0 : Microdosing. Phase V : Pharmacoepidemiology.

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Adverse Drug Reactions (ADR) 00:38:14

ADR types	Examples
A (Augmented) Dose Dependent	Antihypertensive causing hypotension.
B (Bizarre) Dose independent	Drugs causing hypersensitivity.
C (Chronic) Dose and Duration dependent	Steroids causing HPA suppression.
D (Delayed)	Drugs causing teratogenicity.
E (End of use : Withdrawal)	Opioid withdrawal. Clonidine withdrawal hypertension.
F (Failure of drug)	Enzyme inducers causing OCP failure.

Pharmacovigilance :

ADR reporting software : Vigiflow.

National coordinating centre : IPC ghaziabad (Forms conclusive report).

CDSCO Delhi : Bans the drug based on the report.

International pharmacovigilance center : Uppsala, Sweden.

Therapeutic drug monitoring 00:41:42

Principle : The plasma concentration of a drug should have a good correlation with effects or side effects.

Indications :

- Clinical effect of a drug cant be easily quantified. E.g., antiepileptics
  If can be quantified, TDM not done. Eg. : β blockers, antidiabetics, Warfarin.
- Low therapeutic index, E.g.
  A : Aminoglycosides.
  Low : Lithium.
  Therapeutic : Theophylline.
  Drug : Digoxin.
  Causes : Cyclosporine.
  Toxicity : Tacrolimus, Tricyclic antidepressant.
- Drugs with variable metabolism. Eg. : Drugs metabolized by acetylation.
- To check compliance. Eg. : Antipsychotic.

Active space

Important drugs :

Digoxin :

- Therapeutic range : 0.5–0.9 ng/ml.
- Toxicity : >2 ng/ml.

Lithium :

- Therapeutic range :
  Mania prophylaxis : 0.6–1.0 mEq/L.
  Mania treatment : 1.0–1.5 mEq/L.
- Toxicity : >1.5 mEq/L.
- Dialysis : >4 mEq/L.

Theophylline :

- Therapeutic range : 5–15 mg/L.
- Toxicity : > 15 mg/L.

Pharmacogenetic conditions

00:44:04

A : Acetyl transferase polymorphism (NAT-1 gene – Fast acetylators; NAT-2 gene – Slow acetylators).
Malignant : Malignant hyperthermia with lignocaine, halothane, Succinylcholine.
Gene : G6PD deficiency associated hemolysis,
Glucunoryl Transferase polymorphism causing irinotecan toxicity.
Causes : CYP 450 enzyme polymorphisms.
Very : VKORC1 gene polymorphism causing variable metabolism of warfarin
Severe : Succinyl choline associated prolonged apnea.
Toxicity : Thiopurine methyl transferase polymorphism causing azathioprine, 6-mercaptopurine, 6-Thioguanine toxicity.

Drugs causing hemolysis in G6PD deficiency
Dr → Dapsone.
m → methylene blue.
A → Antimalarial (Primaquine).
N → Nalidixic acid, Nitrofurantoin.
I → Isoniazid.
S → Sulfonamides.

Drugs metabolized by acetylation	
H → Hydralazine.	S/E : SLE.
I → Isoniazid.	
P → Procainamide.	
S → Sulfonamides.	
Dance → Dapsone.	

CYP450 polymorphism :

- CYP2C19 → ↓ Effect of clopidogrel.
- CYP2C9 → Variable effect of warfarin.
- CYP2D6 → ↑ Toxicity of antidepressants/antipsychotics.

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Pregnancy drug categories

00:47:02

Classified into 5 categories based on safety in pregnancy :

1. Cat A.
2. Cat B.
3. Cat C.

} Safe in pregnancy.

4. Cat D : Can be used in pregnancy because of benefits greater than risk might be acceptable.
   Eg. : Valproate in juvenile myoclonic epilepsy.
5. Cat X : Absolutely contraindicated in pregnancy because of risk greater than benefits.
   Eg. : Thalidomide.

} Unsafe in pregnancy.

PHARMACOLOGY REVISION 3

----- Active space -----

Autonomic Nervous System

00:02:47

ANS is divided into sympathetic and parasympathetic systems.

Type of NS	Receptors	Neurotrans-mitters	Rate Limiting Step	Drugs
Para sympathetic	Muscarinic (G-protein coupled) & Nicotinic (ionic)	Acetylcholine (ACh)	Choline reuptake.	• Aminoglycosides : Block pre-synaptic voltage gated Ca^{2+} channels → ↓ release of ACh. • Botulinum toxin : Blocks the release of ACh.
Sympathetic	α_1, α_2, β_1, β_2 & β_3 β_3 : +nt on adiopocytes	Nor epinephrine. Exceptions : • Renal blood vessels : Dopamine (diuresis). • Adrenals & sweat glands : ACh.	Tyrosine to dopa (using tyrosine hydroxylase).	• Metyrosine : Blocks tyrosine hydroxylase (Rx of pheochro-mocytoma). • Blocker of VMAT 2 (vesicle monoamine transmitter) : Tetrabenazine : Huntington's chorea (DOC), Tourette syndrome (DOC for ticks). Deutetrabenazine & Valbenazine : DOC for tardive dyskinesia.

Sys-tem	Parasym-pathomimetic	Parasympatholytic	Sympathomimetic	Sympatholytic
CNS	↑ Cognition Donepezil (DOC for Alzheimer's disease).	↓ Cognition Scopolamine (truth se-rum in narcoanalysis). Thiopental sodium : DOC- narcoanalysis	-	S/E of Beta blockers (lipid soluble, crosses BBB) : Depres-sion, Insomnia, Nightmares
Pupil	Active Miosis (M3 receptor stimulation). Drugs : • Pilocarpine • Physostog-mine	Passive Mydriasis (M3 receptor block) + Cycloplegia (block M3). Drugs : • Tropicamide • Atropine • Homatropine • Cyclopentolate	Active Mydriasis (α_{1a} stimulation) Drugs : • Phenylephrine • Ephedrine	Passive Miosis (α_{1a} block) Drugs : • Phenoxyben-zamine • Prazosin

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System	Parasympathomimetic	Parasympatholytic	Sympathomimetic	Sympatholytic
	Uses : Closed angle glaucoma : Pilocarpine (DOC).	Uses : • Ocular fundus exam • Prevention of synechiae formation in uveitis.		–
		• Adjuvant in fungal corneal ulcer • ↓ pain in iridocyclitis. • Refractive error test	–	
Oropharynx	↑ Secretions. Used in Xerostomia (Pilocarpine, Cevimeline).	↓ Secretions. Preanesthetic drug Glycopyrrolate (quaternary amine, no BBB crossing) > Atropine.	–	–
Brochi	Constriction	Dilation	Dilation	Constriction
	C/I in asthma & COPD.	Inhalational – PMDI : • LAMA (OD) : Tiotropium (DOC in COPD), Umeclidinum , Revefenacin. • IAMA (BD) : Aclidinium • SAMA (QID) : Ipratropium. m/c S/e : Dry mouth	• SABA : Salbutamol, Terbutaline, Pirbuterol (COPD & BA). • LABA : Formoterol, Salmeterol • VLABA : Olodaterol, Vilanterol, Carmoterol	Beta blockers C/I in asthma & COPD. (Cardioselective beta blockers can be used with caution).
Heart	↓ HR & AV conduction. Edrophonium. used in PSVT / SVT.	↑ HR & AV conduction. Atropine. used in : • Bradycardia (DOC, at dose > 0.5mg). • AV block (digoxin toxicity)	↑ HR, AV conduction & ↑ Contractions. Epinephrine. Used in : • Bradycardia (Children) • Cardiac arrest	↓ HR & AV conduction. ↓ Contractions DOC for : 1. A. fibrillation/ flutter : Rate control 2. HOCM 3. Aortic dissection

LAMA : Long acting muscarinic agent ; IAMA : Intermediate acting muscarinic agent,
SAMA : short acting muscarinic agent.
OD : once daily, BD : twice daily, QID : Four times a day.
PMDI : Pressurized metered dose inhaler
SABA : short acting Beta Agonists, LABA : Long acting Beta Agonists,
VLABA : Very Long acting Beta-Agonists.
PSVT : Paroxysmal supraventricular tachycardia.
HOCM : Hypertrophic obstructive cardiomyopathy.

Note :

- Salbutamol, Terbutaline, Pirbuterol, Formoterol : Long acting → Can be used as reliever in intermittent asthma (<2 attacks/ week).
- Formoterol/salbutamol + ICS (inhaled corticosteroids) : Used in persistent

asthma.

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- Olodaterol, Vilanterol, Carmoterol : Not used in asthma, only used in COPD.
- S/E of β_a agonist : Palpitations & tremor d/t hyperglycemia & hypokalemia.

System	Sympathomimetic	Sympatholytic

Blood vessels	Vasoconstriction
	Uses :
	• Spinal anesthesia induced hypotension:
	  • Normal/ ↑ HR : Phenylephrine
	  • ↓ HR : Ephedrine
	• Postural hypotension : Midodrine (DOC)
	• Cardiogenic, septic, neurogenic shock : IV Norepinephrine (DOC).
	• Anaphylactic shock : Epinephrine (DOC)
	• decreases NE release (exception) : Clonidine (α_a agonist).
		Vasodilation
		Uses :
		• Preoperative HTN in pheo : Phenoxybenzamine (DOC)
		• Cheese reaction, Clonidine withdrawal HTN , Intraoperative HTN in pheo : Phentolamine (DOC)
		• Scorpion bite induced HTN or pulmonary edema : Prazosin (DOC)
		• HTN + BPH : Terazosin , Doxazosin
		• HTN (young age) : Beta blockers

Note :

- Epinephrine acts on beta 2 receptor (0.5 mg IM at 1: 1000 dilution).
- S/E of clonidine : withdrawal HTN d/t α2 down regulation (Rx : Phentolamine).
- Rx of pheochromocytoma : Alpha blockade → Beta blockade.

GIT	Parasympathomimetic	Parasympatholytic
HCl & contractions	↑	↓
Uses	Gastroparesis & Postop ileus : Bethanechol, Neostigmine	• Antispasmodics : Glycopyrrolate, Dicyclomine, Scopolamine. • Peptic ulcer disease (rarely used) : Pirenzepine, Telenzepine.

Note :

- DOC for motion sickness : Scopolamine (transdermal patch at least before 4 to 5 hours of travel, to achieve steady state concentration).

Bladder :

	Parasympathomimetic	Parasympatholytic	Sympathomimetic
MOA	Detrussor contraction (M3 agonism)	Detrussor Relaxation (M3 blockade)	Detrussor Relaxation (M3 blockade)
Uses	Bladder atony/ Overflow incontinence. Post operative urine retention.	Overactive bladder/Urge incontinence	Overactive bladder/Urge incontinence : mirabegron,Vibagron (β_3 agonists).

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	Parasympathomimetic	Parasympatholytic	Sympathomimetic
	eg : Bethanechol Neostigmine	eg : Friend DOST : Fesoterodine, Darifenacin, Oxybutynin, Solifenacin, Tolterodine, Trospium	Stress incontinence : Duloxetine (SNRI) by ↑ NE stimulating α_1 (Bladder sphincter).

Note :

- "-fenacin" drugs : Selective M3 blockers.
- Trospium : Quaternary amine, no BBB crossing.

Skeletal muscles	Parasympathomimetic	Parasympatholytic	Sympathomimetic	Sympatholytic
MOA	Contraction	Relaxation	Contraction	Relaxation
Uses	• Myasthenia Gravis (MG): Pyridostigmine (DOC). • Differentiating between myasthenic crisis from cholinergic crisis & diagnosis of MG (Tensilon test) : Edrophonium. • Cobra bite reversal & NDMR reversal : Neostigmine.	Non-depolarizing muscle relaxants (NDMR) during anesthesia.	β_2 agonist : (Clenbuterol) Performance enhancer by athletes (banned in Olympics) Side effects : Tremors.	$\beta -$: ↓ exercise tolerance (not prescribed in athletes).

Note : Always add Atropine while using Neostigmine & Edrophonium.

Side effects of ANS drugs

00:40:50

	Cholinergic poisoning (ie, OP poisoning)	Anticholinergic (Atropine/Datura/Belladona) poisoning	Beta blockers	Alpha blockers
C/F	• Miosis. • Salivation, Sweating • Involuntary urination & defecation • Bradycardia	• Mydriasis • Dry mouth • Urine retention • Constipation • Tachycardia • Hyperthermia, Dry skin	• Bronchospasm. • Bradycardia/Conduction block. • Insomnia, Nightmares, Depression. • Block symptoms of hypoglycemia (exception of sweating). • Exercise intolerance .	• Postural hypotension • Ejaculation abnormality • Floppy iris
Rx	Atropine (DOC) → ↑ Pupil size + ↓ respiratory secretions.	Physostigmine (DOC)	Glucagon (DOC)	

Most specific drug for OP poisoning : Pralidoximes (Acetyl Esterase reactivator).
Most specific sign of Atropinisation : Decreased respiratory secretions.

Active space

Beta blockers :

Cardioselective beta blockers (Mr. BEAN Cardiologist) :

- Mr. – Metoprolol
- B – Bisoprolol, betaxolol
- E – Esmolol
- A – Atenolol, Acebutolol
- N – Nebivolol (most cardioselective BB)
- Cardiologist – Celiprolol

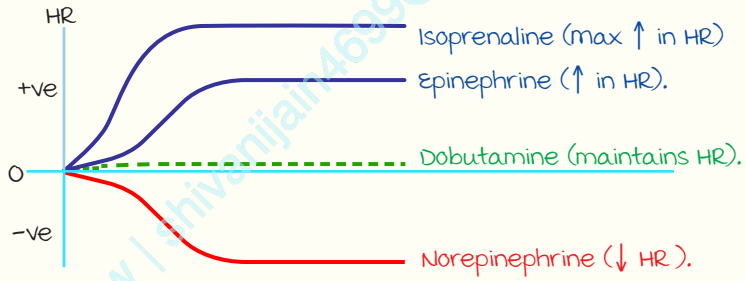
3rd generation beta blockers : Betaxolol, nebivolol & celiprolol.

Beta blockers with :

- Alpha blocking functions : Carvedilol, Labetalol.
- NO release : Nebivolol.
- Antioxidant functions : Carvedilol, Nebivolol.

Effect of catecholamines on HR :

All ↑ contraction of heart.



- Norepinephrine ↑ HR in a transplanted heart / pt on atropine (exception).
- Ivabradine : Normal contraction of heart + ↓ HR.

Dopamine :

Continuous IV infusion.
Dose dependent action (mcg/kg/min) :

- 0-2 : D_1 → Renal vasodilation → Diuresis.
- 2 to 10 : β_1 → increases cardiac contraction.
- >10 : α_1 → vasoconstriction.

Uses : similar to Epinephrine

----- Active space -----

Epinephrine dilution :

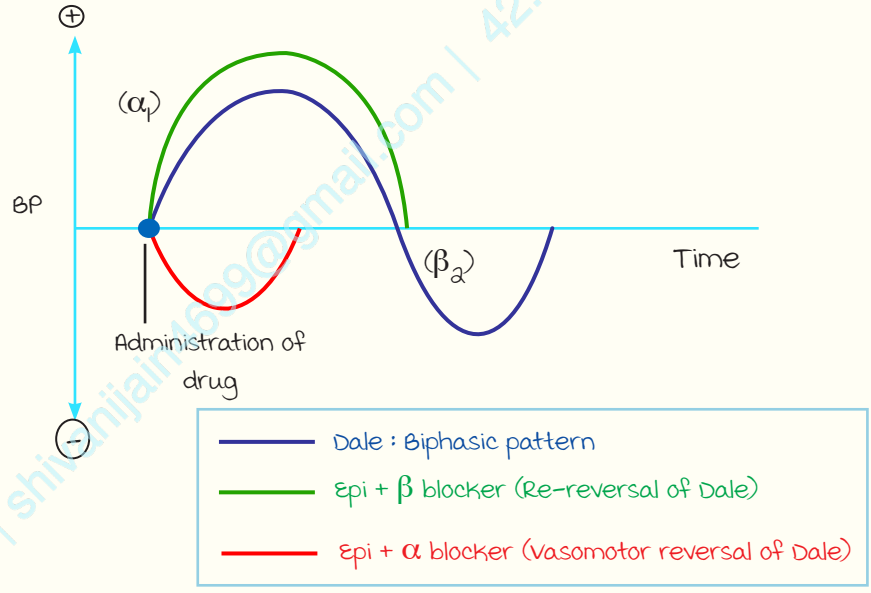
- S/c, I/m, endotracheal – 1:1000.
- IV, intraosseous , Intracardiac – 1:10,000.
- For local vasoconstriction – 1:100,000.
- Epinephrine along with local anaesthetic (Lignocaine) – 1:100,000 or 1:200,000.

Dale's phenomenon :

BP changes when epinephrine is administered.

Biphasic pattern changes in BP d/t :

1. Initial high epinephrine concentration (as it is administered from outside) → activates α_1 → ↑ BP
2. Epinephrine reaches a lower concentration → β_2 stimulated → ↓ BP.



Antiglaucoma Drugs

00:55:57

Active space

Class	Drugs	MOA	Use	Side-effects
Prostaglandin analogs	Latanoprost, Bimatoprost	↑ uveoscleral outflow	DOC in open angle glaucoma (latanoprost). No response → add beta blockers	• Iris pigmentation • Trichomegaly • Dry/ Sandy eyes • Cystoid macular edema • C/I : Uveitis/ Herpetic Keratitis (prostaglandins ↑ inflammation)
Beta blockers	Timolol, metipranolol, Levobunolol, Carteolol, Betaxolol	↓ aqueous production (sympathetic nervous system)	2nd line in open angle glaucoma.	• Timolol : NLD obstruction d/t stenosis • Metipranolol : Granulomatous anterior uveitis • C/I : Systemic beta blockers
	Epinephrine, Dipivefrine		Open angle glaucoma (3rd line)	• Ocular allergy • Black pigmentation of conjunctiva (Epinephrine → melanin)
Alpha-2 agonists	Apraclonidine Brimonidine			• Apraclonidine (also on α_1 Gq → ↑calcium) → Lid retraction, mydriasis, conjunctival blanching. • Brimonidine (can cross BBB → central sympatholytic) : Apnea in neonates, drowsiness/somnolence, hypotension.
miotic agents	Pilocarpine, Physostigmine, Echothiophate, Carbachol	↑ trabecular outflow	Pilocarpine is DOC in closed angle glaucoma (3rd line in open angle glaucoma)	• Pi-Lo at BAR (brow ache, accommodation spasm, retinal detachment, corneal edema. • Echothiophate : Iris cysts • Echothiophate/Physostigmine : Cataract
Carbonic anhydrase inhibitors	Oral/IV : Acetazolamide Topical : Brinzolamide Dorzolamide	↓ aqueous production	Acetazolamide : Acute congestive glaucoma (DOC : mannitol) Brinzolamide/ Dorzolamide : Open angle glaucoma (3rd line)	-
Rho-kinase inhibitor	Netarsudil	↑ trabecular outflow	Open angle glaucoma (3rd line)	• Conjunctival hyperemia • Corneal verticillata

No two beta blockers should be given together (even if it is topically administered) as AV conduction is decreased.

----- Active space -----

PHARMACOLOGY REVISION 4

Anti arrhythmic drugs

00:00:15

Arrhythmias arising from atria :

1. Supra ventricular tachycardia (SVT)
2. Paroxysmal ventricular tachycardia (PSVT)
3. Atrial fibrillation.
4. Atrial flutter.

1. Rx of SVT/PSVT :

AV node blockers (Rate control) : ABCD drugs.

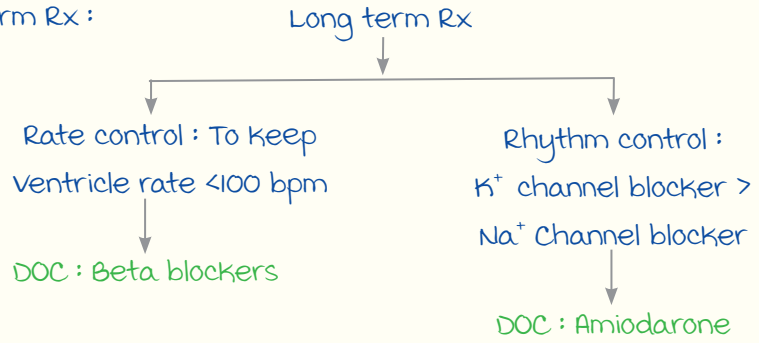
Drug	Route	Uses	C/I
Adenosine	I.V	DOC for an acute attack SVT (Rapid I.V push).	C/I in COPD, asthma & atrial fibrillation (Induces AF).
Beta blockers	I.V & oral		C/I in COPD & bronchial asthma.
Calcium channel blockers (CCB) : • Verapamil • Diltiazem	I.V & oral	DOC for SVT in COPD /asthma Pt.	
Digoxin	Oral		

In acute attack : use I.V drugs (Adenosine > Beta blockers > CCB).

In long term Rx : use oral drugs (Beta blockers > CCB > Digoxin).

2. Rx atrial fibrillation/atrial flutter :

- Acute attack (TOC) : Cardioversion ± Ibutilide
- Long term Rx :



Active space

Arrhythmias arising from ventricles :

1. Ventricular tachycardia (VT).
2. Ventricular fibrillations (VFib).

Management :

Inhibiting myocardial cells with K^+/Na^+ channel blockers.

Amiodarone	Lidocaine
K+ channel blocker	Na+ channel blocker
DOC : VT/VFib	DOC : VT/VFib d/t MI, angina & digoxin toxicity.

Management of long QT syndrome :

- Acute attack (Aka torsades de pointes)
  - Congenital/Acquired
  - DOC : $MgSO_4$
- Long term Rx
  - Congenital
    - DOC : Beta blockers
    - TOC : Cardiac pacemaker
  - Acquired
    - Avoid drugs that prolong QT interval

Management of WPW syndrome :

- DOC : Oral Flecainide
- TOC : Radiofrequency ablation
- DOC in AF d/t WPW syndrome : IV Procainamide

Heart failure drugs:

00:16:05

Acute heart failure	Chronic heart failure
DOC to ↑se contraction : Dobutamine → no response → PDE-3 inhibitor : Milrinone (Inodilator).	Drugs for symptomatic Rx : • Furosemide (Preferred). • Digoxin Drugs to ↓ cardiac remodelling : 1. Sacubitril : • Blocks neprilysin & ↑ BNP. • S/E : Angioedema (C/I with ACE inhibitors). • Can be given with valsartan (ARB).

----- Active space -----

Acute heart failure	Chronic heart failure
DOC for pulmonary edema : Furosemide ↓ no response IV Nitroglycerine (Reduces preload) ↓ no response BNP analogue (IV Nesiritide) Nesiritide is metabolized by neutral endopeptidase (Neprilysin).	2. Omapatrilat : Neprilysin inhibitor + ACE inhibitor. Other drugs : SHIVA Beta 3. Spironolactone. 4. SGLT 2 inhibitors. 5. Hydralazine + Isosorbide dinitrate. 6. Ivabradine. 7. Vericiguat. 8. ACE inhibitors/ARB. 9. Beta-blockers.

Regimen for CHF :

1. Furosemide
2. ACE Inhibitor/ARB or Sacubitril + Valsartan
3. Beta blocker

Anti hypertensive drugs

00:24:42

Management of mild – moderate HTN :

1st line drugs :

- ACE inhibitors/ARB
- CCB
- Thiazides

2nd line drugs : All other drugs.

Approach :

Age of the patient (No comorbidities)

Young age (↑ Renin)	Old age (↓ Renin)
DOC : ACEI/ARB	DOC : CCB
2nd line : Beta blockers	2nd line : Thiazides

Resistant hypertension :

Patient does not respond to atleast 3 drugs of which one must be a diuretic.

Rx : Add spironolactone (Aldosterone levels are ↑ in resistant HTN).

Active space

Rx of hypertension with comorbidities :

Hypertension with :	DOC
Diabetes mellitus CKD Nephrotic syndrome Scleroderma	ACE inhibitors/ARB
Migraine Hyperthyroidism Stable angina Anxiety disorder Essential tremor	Beta blockers
Osteoporosis Edema	Thiazides
Raynaud's disease Cyclosporine induced hypertension	CCB
BPH	Alpha blockers
Hypertensive urgency (BP ≥ 200/125 mmHg with no end organ damage)	Oral Clonidine Other : Captopril & Nifedipine
Hypertensive emergency (↑BP + end organ damage)	IV Nicardipine
Hypertensive emergency in pregnancy	IV Labetalol

Anti Anginal drugs

00:31:30

Anti anginal drugs	MOA (In stable angina)
CCB	• Stable angina : ↓ Preload • Variant angina : Coronary vasodilation
Nitrates (Sublingual nitroglycerine) : DOC for an acute attack of angina	
Beta blockers	Decrease myocardial O2 demand
Ranolazine (↓ Risk of AF & ↓ HbA1c)	• Block late inward Na channels (1° MOA) • PFOX inhibition/Beta blockade (2° MOA)

----- Active space -----

Antianginal drugs	MOA (In stable angina)
Ivabradine ↑ risk of AF & luminous phenomena (seeing colorful halos).	Funny channel inhibition
Nicorandil	K+ channel opener
Fasudil	Rho kinase inhibitor
Trimetazidine	PFOX inhibitor
Statins, Aspirin, ACE inhibitors	↓ mortality in stable angina.

Side effects of CVS drugs

00:34:41

Amiodarone:

Mnemonic : Potassium channel blocker makes liver, nerve and skin toxic

- Pulmonary fibrosis
- Cornea verticillata (Whorl like deposits in cornea)
- Blue colored skin (Ceruloderma, on sun exposed areas)
- Myocarditis
- Liver toxicity
- Neurotoxicity
- Alpha receptor block : Causes hypotension
- Photosensitivity (Brown skin : on sun exposed areas)
- Thyroid (Hypothyroidism > Hyperthyroidism)

Anti arrhythmics causing QT prolongation :

Class Ia	Class III
Quinidine Procainamide Disopyramide	Sotalol Amiodarone Dronedarone Dofetilide Ibutilide Vernakalant

Active space

Digoxin :

Side effects	Contraindications
m/c & Earliest : Nausea & vomiting. Xanthopsia (Yellow vision). Gynecomastia. Hyperkalemia. Arrhythmias : • m/c : Ventricular bigeminy. • Most characteristic : Atrial tachy-cardia with AV block.	1. Conditions that increase risk of digoxin toxicity : KMC in Manipal Rocks • K : Hypokalemia • M : Hypomagnesemia • C in : Hyercalcemia • Manipal : MI • Rocks : Renal failure 2. WPW syndrome 3. HOCM
Rx of digoxin toxicity : Digibind	

RAAS inhibitors

1. ACE inhibitors :

All are pro drugs except :

- Captopril
- Lisinopril

S/E :

- Dry cough (m/c).
- Angioedema.

2. ARB :

Losartan :

- PPAR γ agonist : ↓ Insulin resistance.
- ↑ Uric acid excretion (Can be used in HTN + gout).
- Blocks thromboxane A_2 (Anti aggre-grant).

Telmisartan : max PPAR γ agonist.

3. Direct renin inhibitors : Aliskiren.

C/I of RAAS inhibitors :

- Pregnancy
- B/L Renal artery stenosis
- Renal failure

S/E of CCB :

- Headache
- Constipation (Only verapamil)
- Ankle edema (Prevented by ACEi/ARB)
- AV block (Only verapamil & diltiazem)

Verapamil & diltiazem should not be given with beta blockers.

----- Active space -----

Hypolipidemic drugs

00:41:28

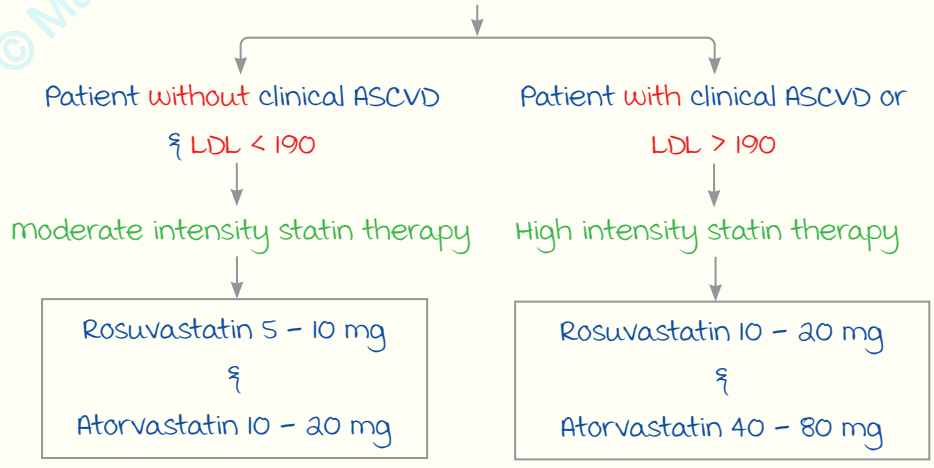
Decrease LDL	Decrease triglycerides	Increase HDL
1. Statins. 2. Bempedoic acid. 3. Ezetimibe. 4. Inclisiran. 5. PCSK-9 inhibitors. 6. Bile acid binding resins. 7. Lomitapide.	1. Fibrates. 2. Icosapent. 3. Omega-3 fatty acids.	Niacin

Hypolipidemic drugs	MOA	Uses	S/E
Statins : Most potent : Pitavastatin > Rosuvastatin (maximum LDL ↓ among statins). Longest acting : Rosuvastatin > Atorvastatin All metabolized by CYP450 except Pravastatin.	• Hypolipidemic effect : Inhibit HMG CoA reductase → ↓ LDL, VLDL & triglycerides • ↑ HDL. Pleiotropic effects : • Anti aggregrant • Anti coagulant • Anti inflammatory • Anti oxidant • Increases NO • Plaque stabilization	DOC : Type II hypercholesterolemia. DOC : Familial hyperlipoproteinemia. 1°/2° prophylaxis of MI & stroke. Night time dosing : Not mandatory with rosuvastatin & atorvastatin. Pravastatin : DOC in Protease inhibitor induced dyslipidemia.	Myopathy Hepatotoxicity Insulin resistance C/I : Pregnancy Children <10 years Pravastatin : C/I in children <8 years
Bempedoic acid	Inhibits ATP citrate lyase, decreases LDL	Add on to statins	
Bile acid binding resins : Cholestyramine Colestipol Colesevelam	Inhibit enterohepatic circulation of bile acid, ↓ LDL.	Add on to statins Preferred in pregnancy & children.	Hypertriglyceridemia Hyperchloremic alkalosis GI upset & ↓ Absorption of other drugs (minimum with colesevelam)

Active space

Hypolipidemic drugs	MOA	Uses	S/E
PCSK 9 inhibitors : Evolocumab Alirocumab	Prevent degradatiion of LDL receptors → max ↓ in LDL.	Add on to statins	
Inclisiran	Si RNA → Breaks mRNA of PCSK 9 → ↓ LDL.	Add on to statins	
Evinacumab	Blocks angiopoie-tin like protein 3 →Blocks LPL→ ↓ LDL & triglycerides	Familial hypercholes-terolemia Add on to statins	
Lomitapide	Blocks MTP	Familial hypercholes-terolemia Add on to statins	
Fibrates : Clofibrate Fenofibrate Bezafibrate Gemfibrozil	Stimulate PPAR α & ↑ LPL synthesis ↓ triglycerides, chy-lomicrons & VLDL.	DOC : Hypertriglycer-idemia DOC : Chylomi-cronemia syndrome	Cholethiasis Myopathy
Icosapent	↓ Triglyceride rich VLDL synthesis/se-cretion by liver. Inhibits platelet ag-gregation	Hypertriglyceridemia Add on to statins (↓ CVS mortality).	
Niacin : Max ↑ in HDL.	↓ Hormone sensi-tive lipase syn-thesis.	Dyslipidemia with ↓ HDL	Hepatotoxicity Insulin resistance Flushing

High LDL with or without ASCVD (MI, Angina, Stroke) :



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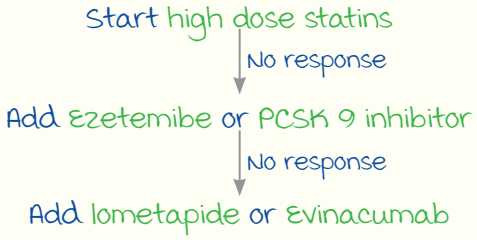
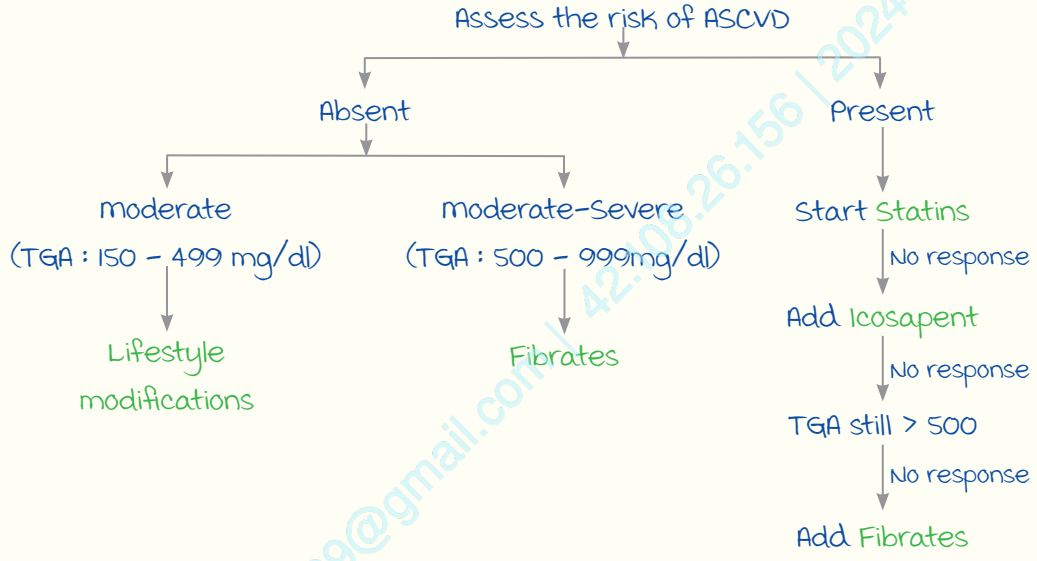
Rx of Familial hypercholesterolemia :



Rx of Hypertriglyceridemia :



PHARMACOLOGY REVISION 5

----- Active space -----

Renal pharmacology

00:00:15

I. Diuretics

Drug class	MOA	Uses
Carbonic anhydrase inhibitors	Block carbonic anhydrase in PCT.	• Acetazolamide : DOC in acute mountain sickness. • Acetazolamide/Dichlorphenamide: Familial hypokalemic periodic paralysis.
Loop diuretics	• Blocks Na/K/2Cl pump in thick ascending limb. • Indirect vasodilators : ↑ Prostaglandins. NSAIDs → ↓ effect.	DOC in (renal/cardiac) edema. • Furosemide : DOC in cardiogenic pulmonary edema. • Torsemide : Longest acting. • Bumetanide : Most potent. • Ethacrynic acid : Most ototoxic. Most effective if GFR< 40.
Thiazides	• Blocks Na/Cl cotransporter in DCT. • Direct vasodilators : • Open K channels, so they are effective in HTN.	Uses : First-line in mild/moderate HTN, add-on drug in edema mx. • Chlorthalidone : Longest acting, preferred in HTN mx. • Chlorothiazide : Shortest acting. • Indapamide : Predominantly hepatic excretion. All others → Renal excretion. Metolazone : Effective in GFR <40.
K sparing diuretics Spironolactone, Eplerenone	Aldosterone antagonist.	DOC in cirrhotic edema, resistant HTN.
Amiloride	Blocks ENaC channels in collecting duct.	DOC in Li-induced DI, Liddle syndrome, cystic fibrosis.

----- Active space -----

Osmotic diuretics (mannitol)	Promotes solute free water loss	A : Acute congestive glaucoma (DOC). B : Braking of diuretics (resistance) C : Cerebral edema (DOC). D : Dialysis disequilibrium. E : Expected renal failure [but C/I in established renal failure].

Side effects of diuretics : 00:08:41

Carbonic anhydrase inhibitors	Loop diuretics	Thiazides	K sparing diuretics	Osmotic diuretics
Hypokalemia	Hypokalemia	Hypokalemia	Hyperkalemia	Hypo/hyper-kalemia
Metabolic acidosis	Metabolic alkalosis	Metabolic alkalosis	Metabolic acidosis	Hypo/hyper-natremia
Renal stones	↓ Mg ↑ Glucose ↑ Uric acid	↓ Mg ↑ Glucose ↑ Uric acid	Gynaecomastia (d/t spironolac-tone)	Pulmonary edema (even though it is used as DOC for cer-ebral edema)
Hyperam-monemia (C/I in liver cirrhosis)	↓ Ca^{2+}	↑ Ca^{2+}		
Hypersensi-tivity; bone marrow sup-pression	Cause oto-toxicity : C/I with amino-glycosides	Worsens DM, gout		

a. Other renal drugs : 00:17:15

Drugs	Uses	Side effects
Vasopressin antagonists (Vaptans) :		
Conivaptan (IV) Tolvaptan (PO) Mozavaptan (PO)	SIADH (IV for emergency, oral for longterm mx)	Tolvaptan : Hypokalemia, hepatotoxicity (max use dura-tion : 1 month)

Active space

Vasopressin analogues :		
Terlipressin	DOC acute variceal bleeding	
Desmopressin	• DOC central diabetes insipidus, nocturnal enuresis. • Used in Von Willebrand disease type I, hemophilia A.	Water intoxication, headache.
Vasopressin	Used in : • Central diabetes insipidus for replacement. • Acute variceal bleeding. • NE resistant shock.	Facial pallor, nausea, vomiting.

CNS pharmacology

00:19:30

1. Drugs for epilepsy

Seizure disorders	DOC
GTCS Myoclonic seizure (JME), Dravet syndrome	Valproate
Absence seizure	Typical : Ethosuximide. Atypical (change in muscle tone) : Valproate.
Partial seizure, Rolandic epilepsy	Carbamazepine
Lennox Gastaut syndrome	Valproate (DOC). Topiramate, lamotrigine, rufinamide.
Seizures in neonates	Phenobarbital
Alcohol withdrawal seizures	Diazepam. Lorazepam (safe in liver dysfunction).
Status epilecticus	Lorazepam
Infantile spasm with Tuberous Sclerosis (TS)	Vigabatrin
Infantile spasm without TS/West syndrome/ Salaam spasm	ACTH

----- Active space -----

Epilepsy mx in pregnancy :

Pregnant + JME + on Valproate → Continue valproate while performing TDM.

+

Folic acid supplementation is a must.

+

Usual dose : 400 mcg (If h/o neural tube defects : 4000 mcg).

DOC for epilepsy in pregnancy : Levetiracetam > Lamotrigine.

Least teratogenic drugs :	Most teratogenic drugs :
• Epilepsy : Levetiracetam. • Bipolar disorder : Lamotrigine.	• Epilepsy. • Bipolar disorder. } Valproate

2. Drugs for mood disorders

00:25:55

Mood disorders	DOC
Acute mania, mania in pregnancy	Atypical antipsychotics (aripiprazole) > typical antipsychotics
Mania prophylaxis, bipolar disorder	Lithium
Rapid cycling bipolar disorder	Valproate
Depression	SSRI (DOC) > SNRI
Depression with insomnia	Mirtazapine
Depression with Erectile Dysfunction (ED)	Mirtazapine > bupropion (since they don't cause ED)
Suicidal tendency	Lithium. Clozapine. ECT. [Mnemonic : Life Can End]

Drugs causing ED (d/t ↑ serotonin) : MAO inhibitors, TCAs, SSRIs, SNRIs.

Novel antidepressants :
• Vilazodone : SSRI + 5HT1A agonist. • Vortioxetine (MSAA drug : Multiple Serotonin Agonist Antagonist). Reserved for treatment of resistant or major depression.

3. Drugs for parkinsonism

00:31:00

----- Active space -----

New case of Parkinson's disease

↓

Effect on lifestyle

↓

Negligible

1. No drug treatment ideally.
2. If needed,
   - DOC : MAO-B inhibitors (Selegiline, Rasagiline).
   - Amantadine.
     S/E :
     -Ankle edema
     -Livedo reticularis

Significant complaints

↓

Age<65

DOC : D2 agonist (pramipexole, ropinirole)

S/E :
-Fatigue
-Compulsive gambling/ sexual activity

Age≥65

DOC : Levodopa + Carbidopa

Side effects of levodopa Rx	Considerations
Psychosis d/t D2 stimulation	• DOC : Pimavanserin. • Psychosis is a C/I for levodopa rx.
Dyskinesia	DOC : Amantadine
mydriasis	Can worsen glaucoma
On-off phenomenon	DOC : COMT inhibitors (entacapone).

3. Drugs for other neurodegenerative disorders

00:36:50

Disorders	DOC
ALS	1. DOC : Riluzole. 2. If not responsive, Edaravone. 3. Newer agents : • Sodium phenylbutyrate taurursodiol. • Tofersen.
Alzheimer's disease	1. DOC : Cholinergics (Donepezil/rivastigmine/ galantamine). 2. Add memantine (NMDA receptor blocker) in mod-to-severe cases. 3. Newer agents : β amyloid blockers (aducaNumab, lecaNemab) in mild cases.

----- Active space -----

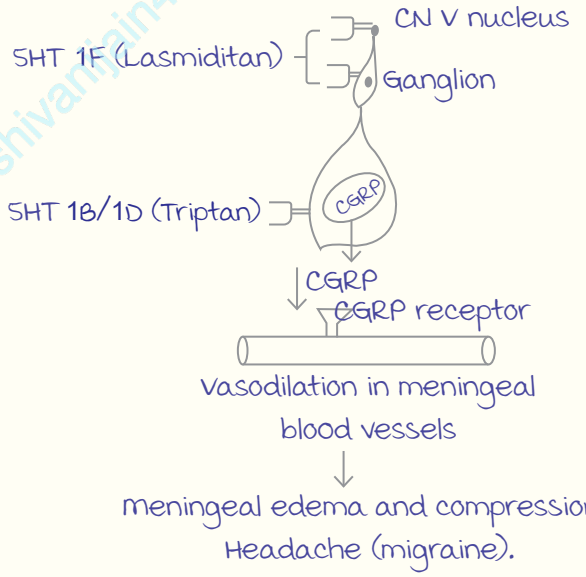
4. Drugs for some other disorders

00:40:18

Disorders	DOC	Other considerations
Trigeminal neuralgia	Carbamazepine	
Restless leg syndrome, Postherpetic neuralgia	Gabapentin/pregabalin	MOA : Binding to $\alpha_2\delta_1$ subunit of presynaptic Ca channels.
Psychosis	Atypical antipsychotics	
Resistant psychosis	Clozapine	
ADHD	Methylphenidate	Drawbacks : Worsen ticks, abuse potential
ADHD with Tourette syndrome	Clonidine	
ADHD with family history of drug abuse	Atomoxetine/Viloxazine	MOA : Selective NE reuptake inhibitors (not SNRI).
Tics associated with Tourette syndrome	Tetrabenazine	

5. Drugs for migraine

00:43:54



Active space

Goal	Treatment
Migraine treatment	DOC : Triptans (5HT 1B/1D agonist). Oral (fast acting) : • Rizatriptan • Sumatriptan } Acute attacks • Eletriptan Oral (slow acting) : • Frovatriptan } Protracted attacks • Naratriptan
Migraine prophylaxis	Propranolol (DOC). Topiramate.

Rizatriptan : Fastest oral triptan.

Sumatriptan : Overall fastest (s/c administration).

Triptans are C/I in angina, other ischemic conditions, due to their vasoconstrictive action.

Ergotamine : Can cause gangrene of organs with end artery supply.

New drugs for migraine :

5HT-1F agonist : Lasmiditan (oral Rx).

CGRP ligand blockers :

- Eptinezumab
- Fremanezumab } S/C, prophylaxis
- Galcanezumab

CGRP receptor blockers :

- Erenumab : S/C, prophylaxis.
- Olcegepant
- Rimegepant } Oral, treatment & prophylaxis
- Ubrogepant

6. Narcolepsy & insomnia

00:51:30

Disorders	DOC
Narcolepsy	Modafinil
Insomnia :	
Sleep induction, jet lag	1. DOC : Ramelteon (lesser dependence, less effective). 2. Zolpidem (if non-responsive).
Sleep maintenance	1. DOC : DORA (dual orexin receptor antagonist) : Suvorexant, daridorexant. 2. Zolpidem (if non-responsive).

----- Active space -----

7. Opioid agents

00:53:40

Disorders	DOC
Opioid toxicity	DOC : Naloxone
Opioid dependence :	• To ↓ withdrawal symptoms : Methadone, Buprenorphine • To prevent relapse : Naltrexone.
Labour analgesia	Morphine > Pethidine
Opioid induced constipation	Methylnaltrexone
Postoperative ileus	Alvimopan
Postanaesthetic chills	Pethidine/Tramadol (MOA: α2 agonist)

Characteristics	Opioid drug
Partial agonist at mu and antagonist at Kappa	Buprenorphine.
Partial agonist at mu and full agonist at Kappa.	Pentazocine.
5HT and NE reuptake inhibition.	Tramadol.
MAO inhibitory effect.	Pethidine.
C/I in MI	Pentazocine d/t ↑ HR

Note : Tolerance to constipation, convulsions, and miosis is not seen with opioids.

New agents :

- Rett syndrome : Trofinetide.
- Fredrich's ataxia : Omaveloxolone.

8. Drugs for alcohol and smoking dependence

00:57:45

Alcohol dependence drugs	Considerations
FDA approved :	
Disulfiram : Aversive agent	Blocks aldehyde dehydrogenase → ↑ acetaldehyde → palpitations, tremors, sweating, chest pain, anxiety, feeling of doom. Requires 12 hours of abstinence before administration.

Active space

Naltrexone	Anti-craving agents	Hepatotoxicity. Depression, suicidal tendency.
Acamprosate		Depression, suicidal tendency.
Non-FDA Approved anti-craving agents : Benzodiazepines, clonidine, topiramate, baclofen, ondansetron.		

Smoking Dependence Drugs	Considerations
First line :	
Bupropion	Anti-depressant
Varenicline	P. A. at $\alpha_4\beta_2$ nicotinic receptor. most effective anti-smoking drug.
Nicotine replacement	1. Nasal Spray : Most effective replacement route 2. Patch. 3. Gums 4. Lozenge Need to avoid liquids 15 mins before and after
Second line :	TCA, clonidine, cytisine.

9. Side effects of anti-epileptics

01:01:25

Valproate		Phenytoin		Carbamazepine	
Mnemonic: T. VALPROIC Acid		Mnemonic : HYDANTOIN		Mnemonic : HEADS	
Tab.	Tremor, Teratogenic (max)	H	Hirsutism, Hyperplasia of gums	H	Hyponatremia [Delayed side-effect, M.C in elderly]
V	Vomiting, nausea	Y	LYmphadenopathy	E	Eosinophilia
A	Ammonia increased	D	Diplopia*, Decreased vit D (Hypocalcemia)	A	Ataxia*, Aplastic anemia
L	Liver toxicity	A	Ataxia*, Agranulocytosis	D	Diplopia*
P	Pancreatitis	N	Nystagmus	S	Stevens-Johnson syndrome : HLA-B1502 gene
R	Rash	T	Teratogenic – Facial clefts	Oxcarbazepine, Eslicarbazepine : less toxicity, but more hyponatremia	
O	Obesity	O	Osteomalacia		

----- Active space -----

I	Infertility in females (PCOS)	IN	Increased bleeding in Newborns : Vit K should be administered	
C	Carnitine used as antidote for liver toxicity	* Ataxia and diplopia : Managed with therapeutic drug monitoring and dose adjustment		
Acid	Alopecia			

Lamotrigine : Causes SJS, start at low doses as a precaution.

Topiramate : Renal stones, acute closure glaucoma, metabolic acidosis, weight loss (off-label use in obesity).

10. Side effects of anti-depressants

01:04:20

Anti-depressant		Side effects	Considerations
SSRIs (↑ 5HT)	5HT2 : Brain	Anxiety/insomnia/vivid dreams.	• Benzodiazepines given for 1 month for a pt on SSRI. • SSRIs can used in premature ejaculation (dapoxetine). • ED : m/c delayed side effect • Nausea : m/c side effect.
	5HT2 : Spinal cord.	Erectile dysfunction (ED)/ anorgasmia/ delayed ejaculation.	
	5HT3	Nausea, vomiting.	
	5HT4	Loose stools.	
SNRI		Similar to SSRI	
TCA	m (–)	Constipation, dry mouth, mydriasis, urine retention.	• Avoid in glaucoma, BPH. • TCA toxicity : High risk of mortality d/t arrythmias, DOC : Bicarbonate.
	5HT (–)	Obesity.	
	H1 (–)	Sedation.	
	α1 (–)	Postural hypotension.	
Mirtazapine		Sedation, Obesity	Noradrenergic and specific serotonine agonist, 5HT2 and α_2 blocker
Trazodone		Priapism	
Bupropion		Seizure, max anxiety	
MAO inhibitors		Cheese reaction, serotonin syndrome	Not used frequently anymore

II. Side effects of anti-psychotics

01:08:11

----- Active space -----

D2 receptor blockade	Other receptor blockade
EPS Hyperprolactinemia Max = Risperidone Min = Clozapine Zero = Pimavanserin (Pure 5HT2 H1 (-))	M : Constipation, dry mouth, mydriasis, urine retention (avoid in glaucoma, BPH). H1 : Sedation. H1 & 5HT : Obesity. α1 : Postural hypotension. Metabolic side-effects : Dyslipidemia, hyperglycemia. Max = Clozapine > Olanzapine. Min = Risperidone. Zero (weight neutral) = Aripiprazole/cariprazole (Partial agonist at D2 and 5HT1A), Ziprasidone.

EPS	Treatment
Akathisia (M/C) : Restlessness.	1. DOC : Beta blockers. 2. Add on : Benzodiazepines.
Acute dystonia (earliest) : Abnormal posturing, facial grimacing. Parkinsonism : Tremor, bradykinesia. (Also seen with metoclopramide). Cause : D2 block	1. DOC : Anticholinergics : Benzhexol (trihexyphenidyl). 2. Antihistamine : Promethazine
Neuroleptic malignant syndrome (most lethal) : Muscle rigidity, hyperthermia, autonomic instability (sweating, tachycardia, tachypnea, labile BP) Cause : D2 block	• DOC : Dantrolene* • Bromocriptine (most specific drug) *Also, DOC for malignant hyperthermia
Tardive dyskinesia (most delayed). Facial dyskinesia (tongue protrusion, lip smacking), Limb dyskinesia (piano finger movements, foot tapping). Cause : D2 upregulation	VMAT-2 inhibitors : Valbenazine, deutetrabenazine

----- Active space -----

12. Lithium

01:16:05

Side effects : Mnemonic → HOTHEAD

H : Hypothyroidism.

O : Obesity.

T : Tremor (at normal conc → Fine, at toxic conc → Coarse).

H : Hypercalcemia.

E : Ebstein's anomaly (C/I in 1st trimester of pregnancy).

A : Acne.

D : Diabetes insipidus – Thirst (DOC : Amiloride).

Food and drug interactions :

Li and Na are similar in structure.

Na deficiency/loss d/t diuretics (thiazides > K sparing > loop), diarrhea/vomiting & fasting, can lead to Li retention & toxicity.

TDM : Blood sample taken 12 hours after last dose.

- 0.6 – 1.0 mEq/L : Therapeutic range for prophylaxis of mania.
- 1.0 – 1.5 mEq/L : Therapeutic range for acute mania.
- > 1.5 : Indicative of toxicity.
- > 4 : Indication for dialysis.

11. Side effects and withdrawal symptoms of opioids

01:19:48

Side effects (d/t mu receptors)		Withdrawal symptoms
M	Miosis	Symptoms d/t withdrawal are opposite those d/t mu receptor stimulation
U	Urine retention	
S	Sedation	
C	Constipation, Convulsion	
A	Analgesia	
R	Respiratory depression	
I	Increased muscle rigidity	
N	No bile flow – Contraction of sphincter of Oddi	
E	Euphoria	

Note : Opioids are no longer C/I for pain management in biliary colic.

PHARMACOLOGY REVISION 6

----- Active space -----

Antimicrobial drugs : Classification

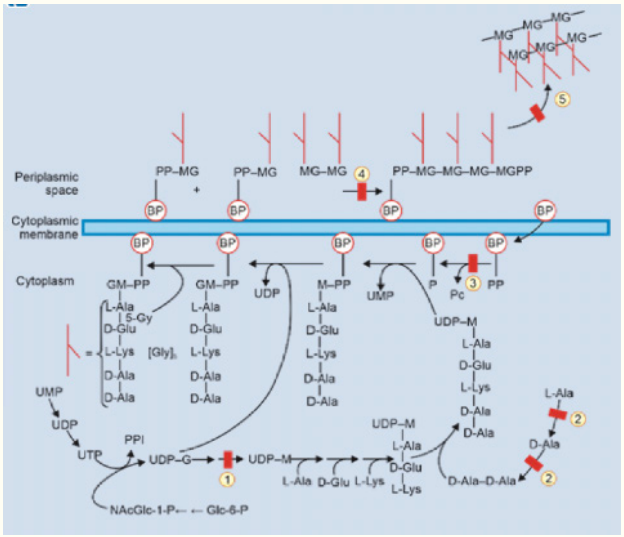
00:00:18

Class of drug	Drugs	
Cell wall synthesis inhibitors (Cidal)	1. Beta lactams • Penicillins. • Cephalosporins. • Carbapenems. • Monobactams.	2. Vancomycin (Glycopeptide). 3. Bacitracin. 4. Cycloserine. 5. Fosfomycin.
Protein synthesis inhibitors (Static)	1. Tetracyclines. • MOA : Block A site on mRNA. • Mechanism of resistance : Drug efflux. 2. Aminoglycosides (Cidal). • MOA : Misreading of mRNA. • Mechanism of resistance : Enzymatic inactivation (Except amikacin). • Not effective against anaerobes & typhoid.	3. Macrolides. 4. Linezolid. 5. Streptogramins. 6. Clindamycin.
Drugs acting on cell membrane (Cidal)	1. Daptomycin (Lipopeptide) : MOA → Depolarization of bacterial cell membrane leading to K+ efflux. 2. Polymyxins : Colistin.	
Antifolate drugs	1. Sulfonamides (Static). 2. Cotrimoxazole (Cidal).	
Fluoroquinolones (Cidal)	MOA : Inhibits DNA gyrase. 1. Ciprofloxacin. 2. Ofloxacin. 3. Respiratory quinolones (Rx of pneumonia). • Gemifloxacin. • Levofloxacin : Maximum oral bioavailability. • Moxifloxacin : Maximum $t_{1/2}$, QT prolongation, seizure potential, hepatic excretion (So never used in UTI).	

----- Active space -----

Cell Wall Synthesis Inhibitors : Site of action

00:06:30



1. Fosfomycin.
2. Cycloserine.
3. Bacitracin.
4. Vancomycin (inhibit transglycosylation).
5. β lactams.

Antibiotics : Uses

00:08:25

Antibiotic	DOC in
Azithromycin	• Atypical pneumonia : Chlamydia, mycoplasma, legionella. • Campylobacter. • Cholera in children. • Cholera and chlamydia in pregnancy.
Ampicillin	• Listeria meningitis. • Enterococcus faecalis endocarditis (Along with gentamicin).
Ceftriaxone (IV)	• Gonorrhea. • Typhoid (Note : Oral DOC in typhoid → Cefixime). • Haemophilus influenzae meningitis. • Empirical treatment of meningitis. • Infections of E. coli, Klebsiella & Providencia.
Ceftazidime	Pseudomonas (Gentamicin is added in severe infections).
Carbapenems	• Extended spectrum β lactamase producing organisms. • Serratia. • Acinetobacter. • Enterobacter. Note : Imipenem is metabolized by renal dehydropeptidase and is combined with cilastatin, a renal dehydropeptidase inhibitor.

----- Active space -----

Cefazolin	Surgical prophylaxis.
Clindamycin	• Toxic shock syndrome. • Supradiaphragmatic anaerobic infections. Note : metronidazole is preferred in infradiaphragmatic anaerobic infections.
Ciprofloxacin	• Contacts of meningococcal meningitis. • Pyelonephritis. • Typhoid carriers. • Shigella. • Travelers diarrhea.
Cotrimoxazole (Combination of trimethoprim & sulfamethoxazole in the ratio 1:5)	• Burkholderia cepacia. • Cyclospora. • Pneumocystis pneumonia. • Isospora. • Nocardia. • Sarcocyst. • Stenotrophomonas (Along with piperacillin).
Daptomycin S/E : Myopathy. C/I : Pneumonia.	VRSA (Vancomycin Resistant Staphylococcus Aureus).
Doxycycline	• Mycoplasma pneumonia. • Plague prophylaxis. • Rickettsia. • Borrelia. • Brucella. • Cholera. • Chlamydia.
Erythromycin	• Pertussis. • Diphtheria. Note : Erythromycin can be used in gastroparesis as a prokinetic drug due to motilin receptor stimulation.
Gentamicin	• Plague. • Tularemia.
Mupirocin (Topical)	Staphylococcal nasal carrier Note : Bacitracin is also used.

----- Active space -----

Benzathine penicillin G (IM)	• Syphilis. • Streptococcus. • Leptospira. • Yaws. • Gas gangrene. • Rat bite fever. • Actinomycosis. • Meningococcus. Note : DOC in neurosyphilis → IV aqueous penicillin G.
Silver sulfadiazine	Burns patients.
Vancomycin	IV : • Methicillin resistant S. aureus. • Enterococcus faecium endocarditis (Along with gentamicin). Oral : Pseudomembranous enterocolitis. Note : The latest drug used as DOC in pseudomembranous enterocolitis is oral fidaxomicin.
Linezolid	Vancomycin resistant enterococcus.

Antibiotics : Side Effects

00:24:12

Antibiotic	Side effects
Tetracyclines	• Photosensitivity. • Acute renal failure (Except doxycycline). • Blocks bone growth due to calcium binding. • Diabetes insipidus. • Esophagitis. • Yellowing of teeth. • Vestibular toxicity : Minocycline. C/I : • Pregnancy. • Children. • Along with antacids.

Active space

Aminoglycosides	• Nephrotoxicity. • Ototoxicity (Irreversible). Auditory : Amikacin. Vestibular : Streptomycin. • Neuromuscular toxicity. C/I : Pregnancy.
Erythromycin	• Motilin receptor stimulation : Hypertrophic pyloric stenosis. Diarrhea. • Skeletal muscle weakness. • QT prolongation. • Cholestatic jaundice.
Fluoroquinolones	• Photosensitivity. • QT prolongation. • Rash. • Seizure. • Tendinitis, tendon rupture (Increased risk is seen in elderly, renal failure and steroid use).
Linezolid	• Bone marrow suppression. • MAO inhibition. • Mitochondrial toxicity : Optic neuritis. Lactic acidosis.
Beta lactams	• Pseudomembranous enterocolitis (3rd generation cephalosporins > amoxicillin). • Hypersensitivity.
Cefoperazone, moxalactam, cefamandole, cefotetan	• Disulfiram like reaction. • Hypoprothrombinemia.
Imipenem	• Seizures.
Sulphonamides	• Kernicterus after birth. • Acute intermittent porphyria. • Methemoglobinemia. • Rash. • Bone marrow suppression. • Crystalluria.

----- Active space -----

Antiviral drugs

00:28:48

Anti herpes drugs	DOC in	S/E
Oral valacyclovir > oral acyclovir/topical acyclovir	HSV/VZV	Crystalluria.
IV Acyclovir	HSV encephalitis.	
Oral valganciclovir > oral ganciclovir	CMV.	Bone marrow suppression.
IV ganciclovir	CMV with high risk of blindness.	
Foscarnet	Resistant herpes.	Electrolyte abnormalities.
Cidofovir	• Recurrent laryngeal papillomatosis. • BK virus. • Adenovirus.	

Anti influenza drugs		Used in
Neuraminidase inhibitors (Block viral release)	Oral oseltamivir.	Influenza A & B, bird flu.
	Inhalational zanamavir.	Oseltamivir resistant cases.
RNA polymerase inhibitors : Baloxavir.		

Anti hepatitis B drugs	Anti hepatitis C drugs
Specific : • Entecavir. • Adefovir. Non specific (Anti HIV drugs used for hep B) : • Tenofovir. • Lamivudine. • Emtricitabine : Derivative of lamivudine (Not to be given in combination with it). • Clevudine. • Telbivudine. Miscellaneous drugs : • Interferon α : used for short duration treatment (max for 48 w).	• Interferon α. • Oral ribavirin. • Direct-acting antivirals (DOC) : Paritaprevir (Protease blockers). Sofosbuvir (NS5B blockers). Velpatasvir (NS5A blockers).

Active space

Note : DOC in

- RSV Rx : Inhalational ribavirin.
- RSV prophylaxis : Palivizumab.

Anti retroviral drugs	
Nucleoside reverse transcriptase inhibitors :	
• Zidovudine : Anemia d/t bone marrow suppression. • Lamivudine. • Emtricitabine : Pigmentation of palms & soles. • Tenofovir : Nephrotoxic, safety unknown in age < 10 years & weight < 30 kg (Abacavir is used). • Abacavir : Steven Johnson syndrome. Lamivudine, Emtricitabine and Tenofovir : Least toxic and preferred drugs.	
Non nucleoside reverse transcriptase inhibitors :	
Nevirapine	DOC to prevent perinatal HIV transmission (Syrup zidovudine is also used). S/E : Hepatotoxicity.

Entry inhibitors			
CD4 inhibitor	GP 120 inhibitor	CCR5 inhibitor	GP 41 inhibitor
Ibalizumab (IV). Active against HIV-1.	Fostemsavir. Active against HIV-1.	Maraviroc. Active against HIV-1 & 2.	Enfuvirtide (S/c). Fusion inhibitor.
Note : All antiretroviral drugs are given by oral route except ibalizumab and enfuvirtide.			

Protease inhibitors
Metabolized by CYP3A4 (Except Nelfinavir → metabolized by CYP2C19). Enzyme inhibitors of CYP3A4. Common S/E : • Dyslipidemia. • Hyperglycemia. • Lipodystrophy.
• Lopinavir (LPV). • Ritonavir : Most potent enzyme inhibitor. Used as a booster drug (E.g : LPV/r). • Atazanavir : Does not cause dyslipidemia. • Indinavir : S/E → Renal stones.

----- Active space -----

Note : Cobicistat is a CYP3A4 inhibitor given in combination with : • Atazanavir. • Darunavir. • Elvitegravir.
Integrase inhibitors
• Raltegravir. • Dolutegravir.
Post-exposure prophylaxis
2 NRTIs + 1 miscellaneous drug used in combination. Preferred regimen in India : Tenofovir + Lamivudine + Dolutegravir (TLD).

Antifungal drugs

00:50:00

Antifungal drugs	DOC in
Amphotericin B : • MOA : Sequesters ergosterol in the cell membrane. • Given via IV route with 5% dextrose as the carrier. • S/E : a. Hypokalemia : Prevented by administering KCl. b. Nephrotoxicity : Prevented by Preloading with NaCl. Combining with liposomes (Liposomal Amphotericin B).	• Kala azar. • Mucormycosis. • Cryptococcal meningitis.
Azoles : MOA : Inhibit ergosterol synthesis by blocking 14-α sterol demethylase.	
Fluconazole	• Candida albicans. • Mucocutaneous candidiasis.
Clotrimazole (Lozenge)	Oral candidiasis.
Itraconazole	• Endemic mycoses. • Sporotrichosis. • Allergic bronchopulmonary asperigillosis (Steroids also DOC).

Active space

Ketoconazole : S/E : Gynecomastia, impotence.	Cushing disease
Voriconazole	Invasive aspergillosis.
Posaconazole	• Mucormycosis. • Used in graft vs host disease.
Isavuconazole	• Mucormycosis. • Invasive aspergillosis.
Griseofulvin : Taken along with fatty food to increase absorption.	Tinea capitis.
Natamycin	Fungal corneal ulcer.

Antihelminthic drugs

00:57:36

Nematodes	DOC
Roundworm. Whipworm. Hookworm. Enterobius vermicularis. Trichinella spiralis.	Albendazole.
Strongyloides. Onchocerca volvulus.	Ivermectin : MOA : Produces tonic paralysis by stimulating glutamate sensitive chloride channels.
Loa loa. Filariasis.	Diethylcarbamazine (DEC). Note : Ivermectin + DEC + Albendazole regimen is used to treat filariasis.
Drancunculiasis.	Metronidazole.

Cestodes	DOC
Neurocysticercosis. Echinococcus.	Albendazole.
Intestinal Taenia solium. Taenia saginata. Hymenolepis nana. Diphyllobothrium latum.	Praziquantel MOA : Produces spastic paralysis by stimulating calcium channels.

----- Active space -----

Trematodes	DOC
Fasciola hepatica.	Triclabendazole.
All other liver flukes. Lung flukes. Schistosoma.	Praziquantel.

Anti Protozoal drugs

01:02:28

Protozoal disease		DOC
Amoebiasis		
Intestinal (Symptomatic)		Metronidazole.
Intestinal (Asymptomatic)		Luminal amebicidal drugs : • Paramomycin (DOC). • Diloxanide furoate.
Extra intestinal		Metronidazole. Note : For radical cure of amoebiasis, metronidazole is given in combination with a luminal amoebicidal drug.
Leishmaniasis		
Visceral (Kala azar)		IV Liposomal amphotericin B. Oral DOC : Miltefosine.
Cutaneous		Sodium stibogluconate.
Post Kala azar dermal leishmaniasis		Miltefosine.
Trypanosomiasis		
East African sleeping sickness	Early stage	IV Suramin.
	Late stage	IV Melarsoprol.
West African sleeping sickness	Early stage	IV Pentamidine.
	Late stage	IV Eflornithine.
Note : Fexinidazole is a recently approved oral drug for African sleeping sickness.		
American Chagas disease		Benznidazole.
Cryptosporidiosis		Nitazoxanide : S/E → Green urine.
Babesiosis		Atovaquone + Azithromycin.
Toxoplasmosis		Sulfadiazine + Pyrimethamine.

Active space

Giardiasis Amoebiasis Trichomoniasis Bacterial vaginosis	Metronidazole S/E : Disulfiram-like reaction (Avoided with alcohol).

Malaria		
Uncomplicated vivax malaria	Chloroquine (S/E : Bull's eye maculopathy, corneal deposits). (+) Radical cure with : Primaquine for 14 days (Or) Tafenoquine once.	
Uncomplicated falciparum malara and chloroquine resistant vivax malaria	• Artemisinin combination therapy (ACT). • Artesunate + Sulfadoxine + Pyrimethamine. • Artemether + Lumefantrine (Preferred in North Eastern Indian states).	
Severe falciparum malaria	IV Artesunate : most potent and fastest acting schizontocidal drug.	
Malaria prophylaxis (Based on duration of travel to endemic areas)	< 6 weeks	Doxycycline 100mg OD started 2 days before travel.
	≥ 6 weeks	Mefloquine 250mg/week started 2 weeks before travel.
Note : Malaria prophylaxis is continued for 2 weeks after return from travel.		
Malaria in pregnancy	Vivax	Chloroquine.
	Chloroquine resistant vivax malaria and falciparum malaria.	• 1st trimester : Quinine + Clindamycin. • 2nd and 3rd trimesters : ACT.

----- Active space -----

Anti Tubercular drugs

01:16:18

First line anti-tubercular drugs :

	Isoniazid	Rifampicin	Pyrazinamide	Ethambutol
MOA	Gets activated by catalase-peroxidase & blocks mycolic acid synthesis.	Blocks RNA polymerase.		
Mechanism of resistance	• Kat-G gene mutation. • InhA gene overexpression : Produces cross-resistance to ethionamide.	RPO-b gene mutation.		
Activity against mycobacterium	• Cidal. • Intracellular + extracellular. • Replicating bacteria.	• Cidal (maximum). • Intracellular + extracellular. • Non replicating bacteria aka persistors (maximum).	• Cidal. • Intracellular. • Non replicating bacteria.	• Static. • Extracellular. • Replicating bacteria.
Organ of excretion	Liver.	Liver. (Safest drug in renal failure).	Liver.	Kidney.
S/E	D/t ↓ vit B6 : 1. Pyridoxine dependent anemia. 2. Reduced GABA levels : • Neuropathy. • Psychosis. Toxicity : Seizures. Treatment : Vitamin B6.	• Red/orange urine. • Flu-like symptoms. • Thrombocytopenic purpura. • Pulmonary syndrome.	• Hepatotoxicity (maximum). • Hyperuricemia. • Gout. • Arthralgia.	• Optic neuritis. • Red-green color blindness (Green > Red).

Note :

- Purpura and pulmonary syndrome are indications to discontinue rifampicin forever.
- Order of hepatotoxicity : Pyrazinamde > Isoniazid > Rifampicin.

Active space

Second line antitubercular drugs :

Used in :

- MDR TB : TB resistant to Isoniazid + Rifampicin.
- XDR TB : TB resistant to Isoniazid + Rifampicin + Fluoroquinolones + One injectable drug like aminoglycoside.

	Bedaquiline	Delamanid	Pretomanid
MOA	Blocks ATP synthase.	Nitroimidazoles : Block mycolic acid synthesis.	
Route	Given by oral route along with food as it increases absorption.		
Pharmacoki-netics	• Seques-tered in tissues. • Long t 1/2 : 165 days.	• High plasma protein binding of 99%. • metabolized by albumin (C/I if serum albumin < 2.8 mg/dL).	
S/E	QT prolongation (C/I in arrhythmia).		
Safety in pregnancy	Safe.	Safety unknown.	

Anti Leprosy drugs

01:30:57

First-line anti-leprosy drugs :

	Rifampicin	Dapsone	Clofazimine
Activity	Cidal (maximum)	Static	Static
S/E		Hemolysis in G6PD deficiency	Ichthyosis

Second-line anti-leprosy drugs :

	Minocycline	Clarithromycin	Fluoroquinolones (Ofloxacin, moxifloxacin)
Activity	Static	Static	Cidal

----- Active space -----

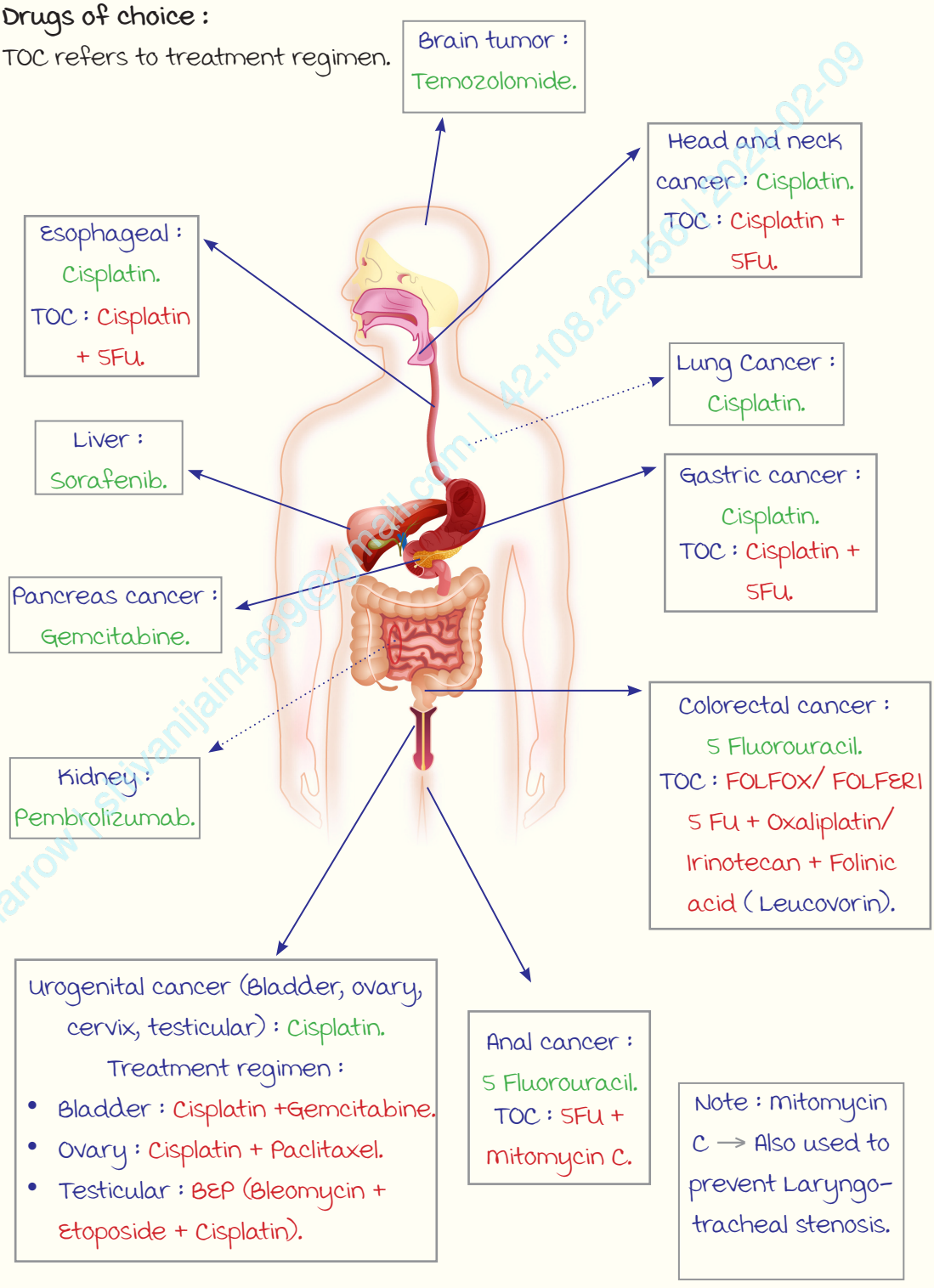
PHARMACOLOGY REVISION 7

Anti cancer drugs

00:00:42

Drugs of choice :

TOC refers to treatment regimen.



Breast Carcinoma :

00:08:24

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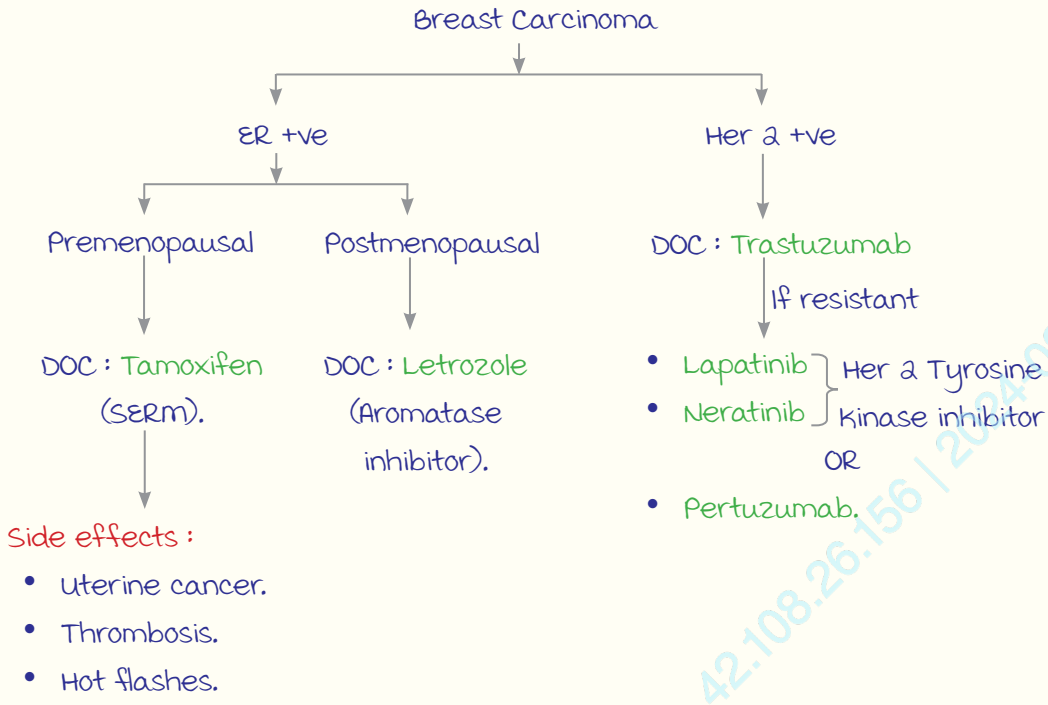
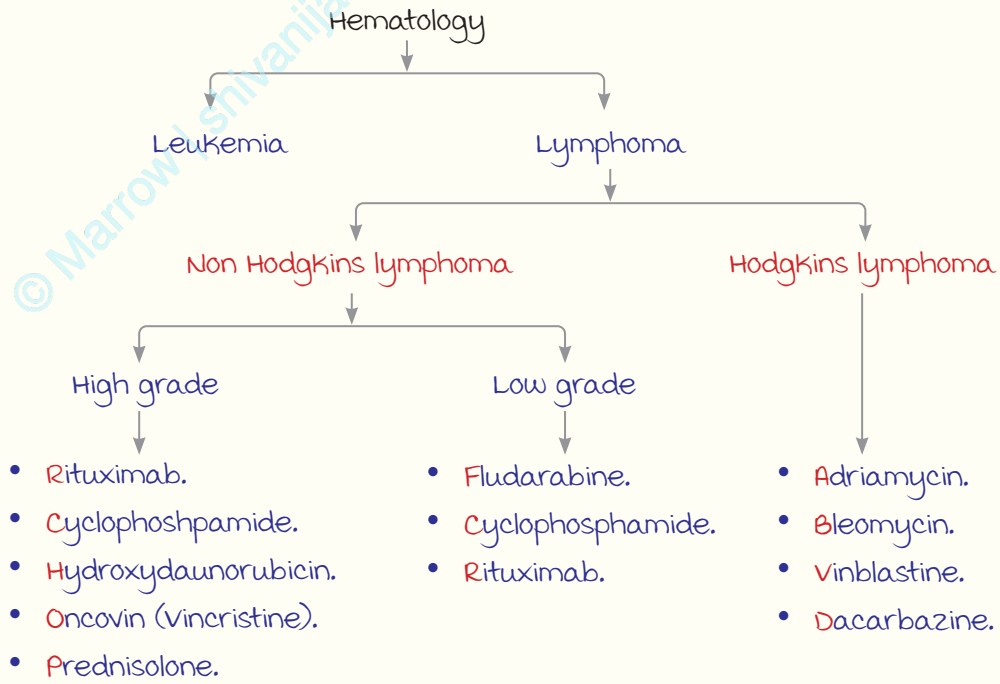


Note : Pregnancy planning :

- After 3 months of stopping SERM (Tamoxifen).
- After 7 months of stopping Trastuzumab.

Hematological cancers :

00:12:28



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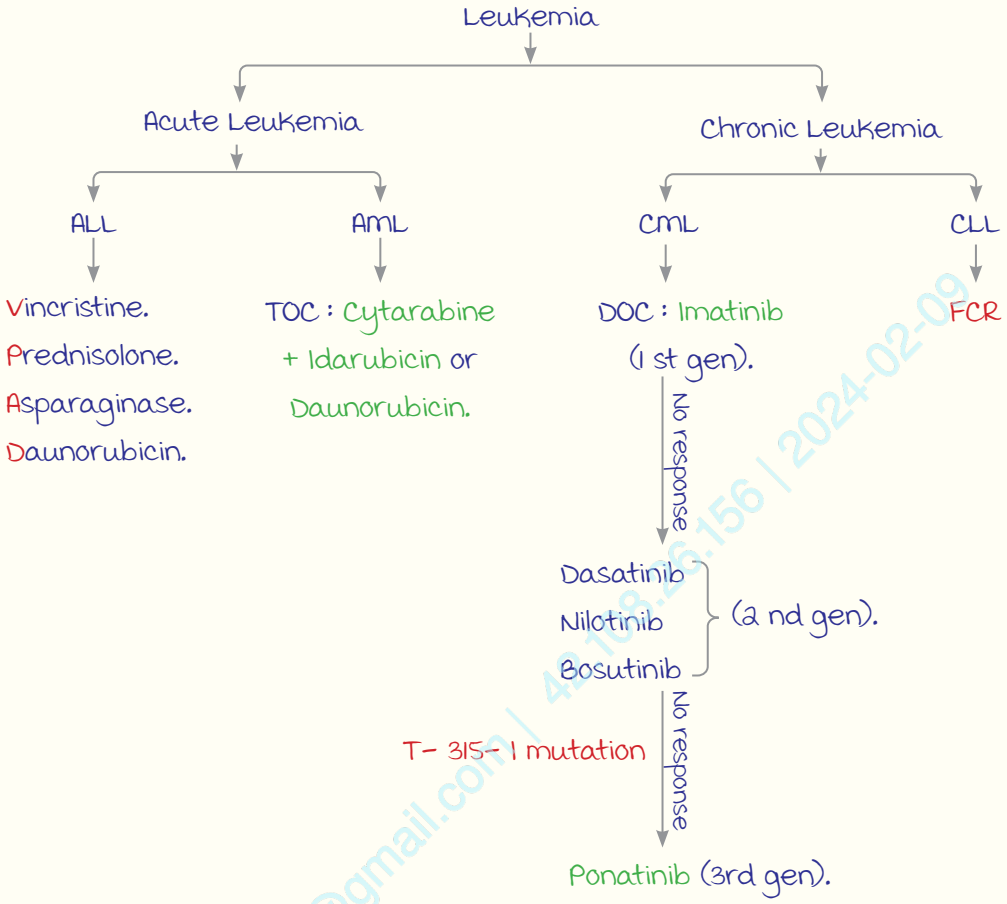


Note : The drugs used in Rx of CML are BCR-ABL Tyrosine Kinase inhibitor → Blocks the enzymatic site.

If CML is still unresponsive to 3 rd gen Tyrosine Kinase inhibitor :

- Asciminib is used (blocks BCR-ABL → allosteric site).
- Omacetaxine : Blocks BCR- ABL protein.
- Interferon alpha (rarely used).

Drug of choice in other hematological conditions :

- Hairy cell Leukemia : Cladribine.
- Sickle cell disease
- Polycythemia vera
- Essential Thrombocytosis

} Hydroxyurea.

Lung carcinoma Rx :

00:42:34 ----- Active space -----

Small Cell Carcinoma :

Cisplatin + Etoposide + Immunotherapy (Atezolizumab or Durvalumab).

Non-Small Cell Carcinoma :

Driver mutation absent :

- PDL1 expression > 50% : Immunotherapy (Pembrolizumab or Atezolizumab).
- PDL1 expression < 50% : Add Chemotherapy.
    a. For non-squamous : Cisplatin + Pemetrexed.
    b. For squamous : Cisplatin + Paclitaxel.

Driver mutation present :

- EGFR L858 R mutation :
    a. 1st gen : Gefitinib, Erlotinib.
    b. 2nd gen (more toxic) : Afatinib, Dacomitinib.
    c. 3rd gen (T790M mutation) : Osimertinib.
- ALK mutation :
    a. 1st gen : Crizotinib.
    b. 2nd gen (L1196M mutation) : Alecitinib, Brigatinib, Certinib.
    c. 3rd gen (G1202R mutation) : Loratinib.

Note : Some named trials in non small cell lung Carcinoma :

- Keynote 189 trial : Chemotherapy + Pembrolizumab.
- Checkmate 227 trial : Ipilimumab + Nivolumab.

----- Active space -----

Side effects of anticancer drugs.

00:19:24

Complication	Drugs responsible	Rx & its mechanism
SIADH.	Vincristine	
Ototoxicity, Maximum nausea, vomiting, Nephrotoxicity.	• Cisplatin.	Rx : 1. Nausea, Vomiting • Ondansetron. 2. Nephrotoxicity • NaCl (Chloride diuresis). • Mannitol (Diuretic). • Amifostine (Radio protective).
Diarrhoea.	• Irinotecan.	Rx : Loperamide.
Peripheral Neuropathy.	• Cisplatin. • Vincristine. • Paclitaxel.	
Hemorrhagic cystitis.	• Ifosfamide > Cyclophosphamide.	Prevention : MESNA. Cause : Acrolein.
Cardiotoxicity.	• Trastuzumab. • Doxorubicin. • Daunorubicin.	
Pulmonary fibrosis.	• Bleomycin > Busulfan.	
Hepatotoxicity.	• 6- Mercaptopurine. • 6- Thioguanine. • Methotrexate.	
Note : Methotrexate can cause Liver cirrhosis if used for treatment of psoriasis or Rheumatoid arthritis. (Long term low dose exposure).		
Hand and Foot syndrome.	• Capecitabine > 5 Fluorouracil.	Prevention : Vitamin B6.
Bone marrow suppression.	• Methotrexate. • Pemetrexed.	MOA : DHFR blockers. Prevention : • Methotrexate → Folinic acid (Leucovorin) > Folic acid. • Pemetrexed → Folinic acid + Vitamin B 12.
Flagellate dermatitis : Long streaks of hyperpigmentation.	• Bleomycin.	
Note : Side effects of Bleomycin are usually seen in skin and lungs (as the hydrolases are deficient in these sites).		

Miscellaneous anti cancer drugs

00:29:40

----- Active space -----

Identification of monoclonal antibodies function based on nomenclature.

Nomenclature	Use	Example.
tu/tum	• Tumor (Breast cancer).	Trastuzumab.
c/ci	• Circulation (block Gp IIb/IIIa).	Abciximab.
	• Antidote for Dabigatran.	Etaracizumab.
tox	• Toxin (Against Clostridium difficle toxin : toxin B) → used in Pseudomembranous enterocolitis.	Bezlotoxumab.
vi	• Virus (used in Respiratory syncitial virus).	Palivizumab.
li/lim	• Target Lymphocytes (TNF α blocker).	Infliximab.
n/ne	• Neurology.	Erenumab.
bac	• Bacteria (against anthrax).	Raxibacumab.

Identification of source of monoclonal antibodies : (before mab)

- Zu : Humanized.
- U : Human.
- Xi : Chimeric.
- O : Murine.

Kinase inhibitors :

1. Imatinib : BCR ABL Tyrosine Kinase inhibitor → Rx of CML, GIST.
2. Gilteritinib : FLT-3 Kinase inhibitor → Rx of AML.
3. Dabrafinib : BRAF inhibitor
4. Cobimetinib : MEK 1/2 inhibitor } Rx of Melanoma.
5. Idelalisib : PI-3K inhibitor (Phosphatidyl inositide)
6. Ibrutinib : Brutons tyrosine kinase blocker. } Rx of CLL.

Others :

1. Olaparib : PARP blocker (Poly ADP Ribose polymerase) → Rx of Breast Ca.
2. Bortezomib : Proteazome inhibitor → Rx of multiple myeloma.
3. Sonidegib : Hedgehog pathway blocker.
4. Retinoic acid : DOC for Promyelocytic leukemia.
5. Aspariginase : Rx of ALL.

Note :

Side effects of Asparaginase :

- Hyperglycemia.
- Hypercoagulation.
- Hypersensitivity.
- Hyperlipidemia.
- Hemorrhage.

----- Active space -----

Immune check point inhibitors and uses :

Mnemonic : New Rising Star Drugs Acting At Immune Check Point.

PD 1 blocker.	PD-L1 blocker (Programmed death cell ligand 1 blocker).	CTLA-4 blocker.
• Nivolumab. • Retifanlimab. • Dostarlumab. • Cemiplimab. • Pembrolizumab.	• Durvalumab. • Avelumab. • Atezolizumab.	• Ipilimumab.

1. PD 1 Blockers :

Nivolumab	Pembrolizumab
Mnemonic : Nivea CREAM Hydration.	Mnemonic : PEMBROLI.
• Non small cell lung Ca. • Colorectal Ca. • RCC, Urothelial cancer. • Esophageal Ca, Gastric Ca. • Adjuvant Rx. • Melanoma, Mesothelioma. • Head and neck Ca, Hodgkin's disease.	• Primary mediastinal B-cell lymphoma. • Endometrial and Cervical Ca. • Melanoma, Merkel cell cancer. • Breast Ca (triple -ve). • RCC, Urothelial Ca. • Oesophageal, Oral and Gastric carcinoma. • Liver Ca, Lung Ca, Hodgkin's lymphoma. • Intestinal CA (Colorectal).

2. PD-L1 Blocker :

Durvalumab	Avelumab	Atezolizumab
Mnemonic : Dura BL	Mnemonic : Avail RUM	Mnemonic : Ate LAMB
• Biliary tract Ca. • Liver Ca / Lung Ca (non small cell/ small cell).	• RCC. • Urothelial cancer. • Merkel cell carcinoma.	• Ca Liver, Ca Lung (non small cell). • Alveolar sarcoma. • Melanoma. • Breast Ca (triple -ve).

3. CTLA-4 Blocker :

----- Active space -----

Ipilimumab
Mnemonic : IP MEN Like Chinese Restaurant.
• Melanoma, Mesothelioma. • Esophageal Carcinoma. • Non small cell lung Carcinoma. • Lung Carcinoma. • Colorectal carcinoma. • RCC.

Endocrinology

00:45:04

Antidiabetic drugs :

Note : Drugs which cause Hypoglycaemia → Insulin > drugs which cause increase in insulin release.

Drug.	MOA & uses.	Side effects & C/I.
1. Insulin.		
a. Shortest and fastest acting.	Inhalational route. Afrezza : Control post prandial hyperglycaemia. has 3 colors : Blue → 4 units. Green → 8 units. Yellow → 12 units.	• Cough. • Lung cancer. C/I : • COPD. • Asthma. • Smokers.
b. Short acting insulin.	Subcutaneous route : m/c site → Anterior Abdominal wall except periumbilical region. • Use 60 min before food : Regular insulin (slow acting). • 15 min before food : Glulisine, Aspart, Lispro (fast acting). Also called monomeric. Use : control post prandial hyperglycaemia, DKA, Hyperkalemia.	• Hypoglycemia (m/c). • Hypokalemia. • Lipodystrophy.
c. Intermediate acting insulin.	Subcutaneous route. • NPH (cloudy white) • Lente (30 % Semilente + 70 % Ultralente).	
d. Long acting insulin.	Subcutaneous route. • Glargine : forms white crystals if combined with other insulin. • Degludec : Longest acting.	

----- Active space -----

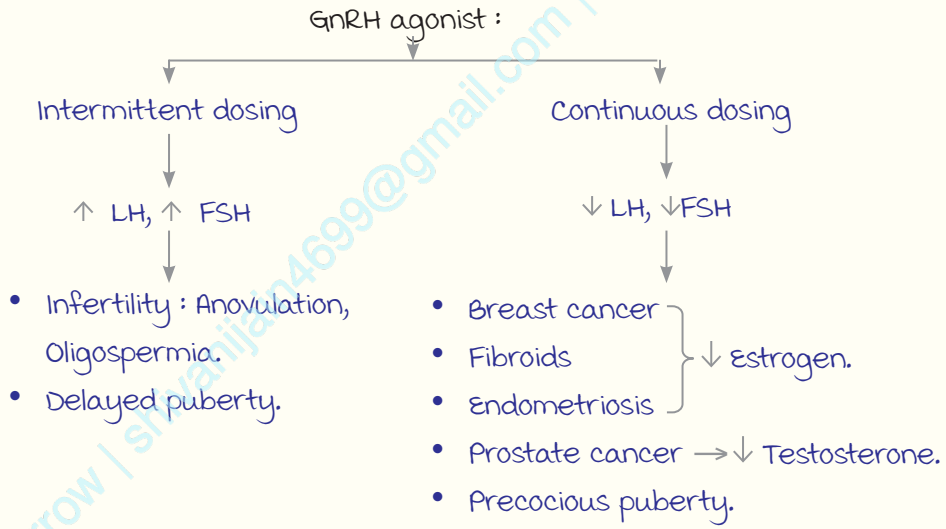
Drug.	MOA & uses.	Side effects & C/I.
2. ↑ Insulin release.		
a. Sulfonylureas : • Glyburide. • Glimepride. • Gliclazide.	Inhibit ATP sensitive K^+ channels.	• Hypoglycaemia. • Weight gain.
b. Meglitinides : • Repaglinide. • Nateglinide. • Mitiglinide.		
Note : Hypoglycaemia and Weight gain : Sulfonylureas > Meglitinides.		
c. DPP-4 inhibitors : • Sitagliptin. • Saxagliptin. • Alogliptin. • Linagliptin.	↑ GLP-1 : increase insulin release.	• Weight neutral. • Respiratory infection.
Note : All DPP-4 inhibitors are C/I in Renal failure except Linagliptin (Liver excretion).		
d. GLP-1 agonist : • Liraglutide • Dulaglutide • Albiglutide • Semaglutide	Subcutaneous route (peptides). • Release insulin. • Delays gastric emptying. • Type II DM for maintanence.	• Pancreatitis. • Weight loss : Semaglutide > Liraglutide (DOC in obesity). • Hypoglycaemia.
Note : Semaglutide can also be given via oral route.		
3. ↓ Hepatic Glucose production.		
Biguanides : • metformin	• Stimulates AMPK : blocks Hepatic glucone-ogenesis. • DOC : Type 2 DM, Metabolic Syndrome, PCOS.	• Weight loss • Decrease Vit B12 • Lactic acidosis Contraindication : • Elderly. • Renal/ Hepatic failure. • Chronic alco-holic. • CHF, Severe Respiratory dis-tress.
Note : Smoking is not a risk factor for use of Biguanides.		
4. ↓ Insulin resistance :		
Thiazolidenidiones : • Pioglitazone. • Rosiglitazone.	• Stimulate PPAR-γ. • ↓ Insulin resistance.	Edema , CHF, Mac-ular edema, Bone fractures in female , Hepatotoxicity.

----- Active space -----

Drugs	MOA/ uses	Side effects and C/I
5. Blocks glucose absorption :		
α Glucosidase inhibitors : • Acarbose. • Voglibose. • miglitol.	• Inhibit breakdown of starch and disaccharide. • Use : post prandial hyperglycemia. (drug taken after few bites of food).	• Flatulence • Diarrhoea.
6. Urine glucose excretion : SGLT-2 inhibitor.		
7. Miscellaneous drugs :		
Amylin analog : • Pramlintide.	• Delays gastric emptying. • Use : Post prandial hyperglycemia.	• Nausea. • Vomiting. • Weight loss (Not FDA approved).
• Colesevelam. • Bromocriptine.		

GnRH related drugs :

00:56:52



GnRH agonist :

- Goserelin.
- Buserelin.
- Nafarelin.
- Leuprolide.

Side effects :

When used as intermittent dosing →
- Multiple gestation
- Carcinoma ovary
- Ovarian cyst

----- Active space -----

When used as continuous dosing →
- Osteoporosis
- Vaginal atrophy
- Hot flushes

} d/t ↓ Estrogen.

- Osteoporsis
- Impotence
- Gynaecomastia

} d/t ↓ Testosterone.

GnRH Antagonist :
- MOA : ↓ LH and FSH
- Action and side effets same as GnRH agonist at continuous dose.

Contraceptive drugs :

00:59:35

Regular contraception	Mechanism
Combined OCPs	• Inhibit ovulation.
Mini pills	• Increase cervical mucus viscosity. • Decrease sperm penetration. • Inhibit blastocyst implantation.
Mifepristone	• Blastocyte detachment.

Emergency contraceptives	Dose
Levonogestrel (DOC)	0.75 mg 2 tab 12 hrs apart or 1.5 mg single dose within 3 days.
Ulipristal (SPRM)	30 mg 1 tab within 5 days.
mifepristone	600 mg 1 tab within 3 days.

Note : SPRM → Selective Progesterone Receptor Modulator.

Growth Hormone (GH) related drugs :

01:00:46

GH analogs :

Somatrem/Somatropin.

Use : DOC for treatment of Dwarfism.

Side effects and contraindication : Mnemonic → CHILDREN.
- C : Carpel Tunnel syndrome.
- H : Hyperglycemia.
- I : ICT is raised.
- L : Leukemia.
- D : Diabetes.

Contraindication
- Re : Retinopathy
- N : Neoplasia

----- Active space -----

GHRH analogs : → Sermorelin, Macimorelin, Tesamorelin → Diagnosis of dwarfism.

Somatostatin analogs	Use	Side effects
• Octreotide. • Lanreotide. • Pasireotide.	Drug of choice : • Acromegaly. • Secretory diarrhoea. • Glucagonoma. • Somatostatinoma. • VIPoma. Also used in : • Thyrotrope adenoma. • Acute variceal bleeding.	• Hypothyroidism (can also ↓TSH). • Gall stones.

Note : Gall stones are caused by → Somatostatin analogs and Fibrates.

GH receptor antagonist :

Pegvisomant.

Use : Treatment of Resistant Acromegaly.

Osteoporosis related drugs :

01:03:48

Drugs decreasing Bone resorption :

Drugs	MOA/uses	Side effects
Bisphosphonates : • Zoledronate/ Pamidronate : Parenteral route. • Alendronate/ Risedronate : Oral. Note : Zoledronate → Longest acting and most potent.	• Inhibit farnesyl pyrophosphate synthase. • Block ruffled border synthesis by the osteoblast. DOC : • Pagets disease. • Osteoporosis. • Hypercalcemia of malignancy (IV drugs).	• Hypocalcemia. • Esophagitis (prevented by taking the drug with full glass of H_2O on empty stomach and not to lie down for 30 min). • Osteonecrosis of jaw. • Femoral Chalk stick fracture.
Note : • Prefer to begin with oral drugs for Rx of Osteoporesis (3–5 yrs). • Hypocalcemia is fastest with Calcitonin and maximum with Bisphosphonates.		

----- Active space -----

Drugs	MOA/uses	Side effects
Denosumab.	Blocks RANK ligand. Use : Post meopausal osteo-porosis (When bisphosphonate intolerance (+) with high risk of fracture).	• Osteonecrosis of Jaw. • Femoral fracture. • Hypocalcemia.
Raloxifene (SERM).	Use : In treatment of postmeno-pausal women with osteoporosis and having a high risk of breast cancer.	• Hot flashes. • Thrombosis.
Calcitonin.	MOA : Inhibits resorption. Use : • Pagets disease. • Osteoporosis prophylaxis.	• Liver cancer. • Breast cancer.

Drugs increasing bone formation :

Drug and Route of Administration	MOA/ Uses	Side effects
• Teriparatide (PTH analog). • Abolaparatide (PTHRP analog).	Stimulate osteoblast mediated bone formation. Use : • Post menopausal osteoporosis. • Bisphosphonate intolerance with high risk of fractures.	• Osteosarcoma (max use limited to 2 years). • Hypotension. Note : Contraindicated in Pagets disease (risk factor for osteosarcoma).
Note : Teriparatide used for Bisphosphonate induced fracture.		
• Romosozumab.	• Stimulate bone formation. • Blocks sclerostin. Use : • Post menopausal osteoporesis. • Bisphosphonate intolerance with high risk of fractures.	

Drugs decreasing bone resorption and increasing bone formation :

Drug and Route of administration	MOA/ Uses
Strontium ranelate.	• ↓ Bone resorption. • ↑ Bone formation.

Steroid drugs :

01:09:44

----- Active space -----

Steroids	Half life	Uses
Hydrocortisone : (Derived from cortisol).	8- 12 hrs.	• Replacement : Addisons disease.
Prednisone. Prednisolone.	12-36 hrs.	• Supress Immune system. • Supression of inflammation (RA, Vas-culitis, Gout).
Methylprednisolone.		
Triamcinolone.		
Dexamethasone. Betamethasone.	36-72 hrs.	

Note :

- Least potent and shortest acting steroid : Hydrocortisone.
- Most potent and longest acting steroid : Dexa/Betamethasone.
- Triamcinolone and Dexa/Betamethasone → Also called pure glucocorticoids.
- Cushings disease → Side effect of steroids.

Thyroid related drugs :

01:13:23

Hyperthyroidism :

Drugs	MOA /uses	Side effects
• Propylthiouracil : (Short acting → Need multiple dosing).	Inhibit Thyroid peroxidase.	• Hepatotoxic. • Agranulocytosis.
• Carbimazole, Methimazole : (Both are Long acting → OD dosing.)		• Teratogenic : Choanal and esophageal atresia, cutis aplasia. • Agranulocytosis.
Note : Universal DOC → Carbimazole/ Methimazole. DOC for Hyperthyroidism in pregnancy. • 1st Trimester : Propylthiouracil. • 2nd & 3rd Trimester : Carbimazole / Methimazole.		
• Potassium iodide. • Lugols iodine (fastest acting antithyroid drug).	• Inhibit thiol endo-peptidase → block release of T3/ T4. • ↓ Thyroid size and vasculogenesis. (Use in preopertive preperation : make thyroid gland firm and small.	

----- Active space -----

Drugs	MOA /uses	Side effects
• Potassium iodide. • Lugols iodine (fastest acting antithyroid drug).	• Inhibit thiol endopeptidase → block release of T3/ T4. • ↓ Thyroid size and vasculogenesis. (use in preopertive preperation : make thyroid gland firm and small.	
• Propranolol. • Propylthiouracil. • Amiodarone. • Steroids.	Block peripheral conversion of T4 → T3.	
Note : • Thyroid storm → DOC : Propylthiouracil. c. 1 st drug to be started → Propranolol. d. In Bronchial asthma/COPD → DOC : Verapamil/Diltiazem.		
Radioactive Iodine : I^{131}	Destroys Follicular cells by beta and gamma rays. Use : • Thyroid cancer. • Recurrent Graves disease. • Hyperthyroidism in elderly.	• Secondary cancers • Permanent hypothyroidism. Contraindicated in Pregnancy.

Hypothyroidsim :

Drugs	MOA/ Uses	Side effects
Levothyroxine : T4 salt (Long acting).	• DOC for replacement : Oral route → in empty stomach. • Thyroid cancer. • Myxedema coma : IV route.	• Osteoporosis • Atrial fibrillation : Decrease the dose of drug.
Liothyronine : T3 salt.	• Before Radioactive Iodine therapy in thyroid cancer (oral route) → Increase I^{131} uptake. • Myxedema coma : IV route.	

PHARMACOLOGY REVISION 8

Active space

Autacoids

00:00:15

First generation	Second generation
H1blockers: Cross BBB (Sedative).	Do not cross BBB (Non sedative).
C/I : Elderly, children, drivers & pilots.	
Uses : • Non allergic rhinitis. • Used as anti muscarinic in : a. Extra pyramidal symptoms b. Motion sickness c. Meniere's disease. Note : Max muscarinic block seen with 1. Promethazine 2. Diphenhydramine 3. Dimenhydrinate	Uses : • DOC for urticaria. • Rx of allergic rhinitis (DOC is Intranasal steroids : Fluticasone).
Important drugs : 1. Doxylamine + Vitamin B6 : DOC for morning sickess. 2. Chlorpheniramine : • Least sedative 1st generation anti-histamine. • Preferred for day time use. 3. Doxepin : Used as TCA. 4. Cyproheptadine : 5-HT2 blocker → DOC for Serotonin syndrome. 5. Hydroxyzine : Used for pruritis.	Important drugs : 1. Cetirizine : Most sedating 2nd gen antihistamine (Since it is derived from hydroxyzine). 2. Levocetirizine 3. Fexofenadine 4. Loratadine 5. Desloratadine 6. Rupatadine : Blocks Platelet activating factor (Anti inflammatory). 7. Topical antihistamines (Only) : • Olopatadine • Levocarbastine • Ketotifen • Azelastine • Astemizole

----- Active space -----

NSAIDs :

Non selective COX inhibitors :

They cause ↑gastric ulcer, ↑nephrotoxicity.

1. Acetaminophen/paracetamol :
   - Good analgesic & antipyretic.
   - Poor anti inflammatory .
   - m/c cause of drug poisoning.
   - m/c cause of drug induced liver failure.
   - Liver toxicity :
     Caused d/t NAPQI metabolite (Depletes glutathione).
     At >150–250 mg/kg or ≥10g (Fatal dose : ≥20g).
     m/c in chronic alcoholics & during fasting.
     HPE : Centrilobular necrosis with periportal sparing.
     To predict toxicity : Rumack Matthew nomogram is used.
     Antidote : N-Acetyl Cysteine (Replenish glutathione & blocks NAPQI).

Note : For vancomycin nephrotoxicity, Matzke nomogram is used.

2. Aspirin :
   - Different doses have different effects :

Dose	Action
Low dose (50–325 mg OD)	Antiaggregant
Moderate dose (325–650 mg SOS)	Antipyretic & analgesic
High dose (3–4g/d, divided doses)	Anti inflammatory

   - S/E : Reye's syndrome.
   - C/I :
     a. Viral fever in children.
     b. Gout.

Active space

Non selective COX inhibitors	Important points
3. Indomethacin	• MOA : Blocks a. COX. b. Phospholipase A. c. Lymphocyte proliferation and chemotaxis. • Uses : a. DOC for acute attack of gout. b. Closure of PDA.
4. Ibuprofen	• DOC for closure of PDA. • M/c cause of drug induced aseptic meningitis. • C/I with aspirin (One drug ↓ efficacy of other).
5. Piroxicam	• Long acting drug (Undergo enterohepatic circulation). • Used in chronic pain.
6. Nimesulide	• Hepatotoxic • C/I for use > 15 days in adults. • In India, banned in children < 12 years.
7. Ketorolac	Used in : • Post operative pain. • Eye drops (Ocular pain).

Selective COX inhibitors :

They are cardiotoxic (Can cause MI).

Selective COX-2 inhibitors	Important points
Celecoxib Etoricoxib	Usesd as 3rd line drugs for pain/ inflammation.
Parecoxib	Post operative pain.
Lumiracoxib	Banned due to hepatotoxicity.
Valdecoxib Refecoxib	Banned as both cause MI.

----- Active space -----

Prostaglandins :

Prostaglandin	Analogues	Uses
Prostaglandin E_1	Misoprostol	• Abortion. • NSAID induced gastric ulcer. • Maintain patency of DA.
	Alprostadil	• Maintain patency of DA. • Erectile dysfunction.
Prostaglandin E_2	Dinoprostone	• Abortion. • Cervical ripening. • PPH.
Prostaglandin $F_{2\alpha}$	Carboprost	• Abortion. • PPH.
	Latanoprost/Bimatoprost	Open angle glaucoma.
Prostaglandin I_2	Synthetic PGI2 : Epoprosterenol PGI2 analogs : Iloprost PGI2 receptor agonist : Selexipag	Pulmonary hypertension.

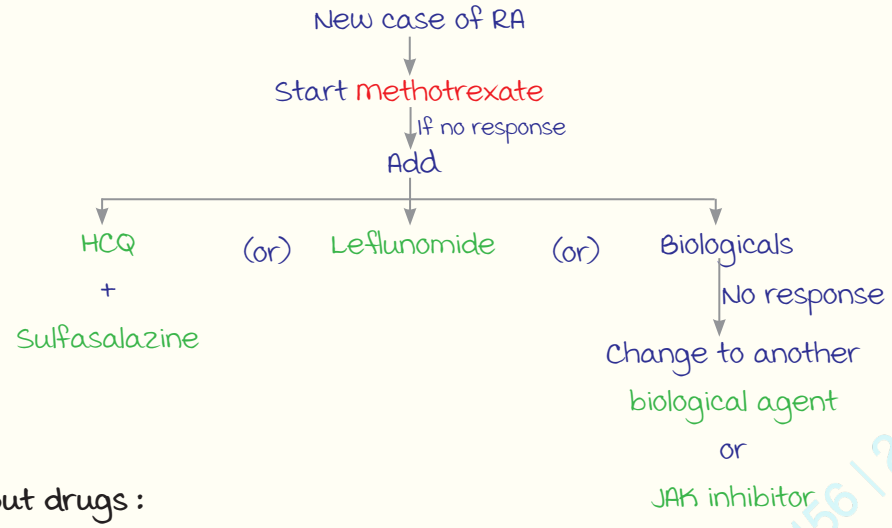
Disease Modifying Anti Rheumatic Drugs (DMARDs) :

Drugs used in rheumatoid arthritis (RA) :

Conventional DMARDs	Biological DMARDs	Targeted DMARDs
1. Methotrexate (DOC) : • Anchor drug. • MOA in RA : Increases adenosine. 2. Hydroxychloroquine 3. Sulfasalazine 4. Cyclophosphamide 5. Immunomodulators : • Azathioprine • Cyclosporine • Mycophenolate mofetil • Leflunomide	1. TNF-alpha inhibitors : • Downregulate lympho-cytes. • S/E : ↑ risk of infections. • C/I : Hep B & CHF. • Drugs : a. In : Infliximab b. C : Certolizumab c. A : Adalimumab d. G : Golimumab e. E : Etanercept 2. Rituximab : Anti CD 20. 3. Abatacept : Anti CD 80/86. 4. Anakinra : IL 1 antagonist . 5. IL-6 inhibitors : • Tocilizumab • Sarilumab	JAK inhibitors : • Tofacitinib • Baricitinib • Upadacitinib S/E : ↑ risk of infections.

Active space

Treatment of Rheumatoid Arthritis (RA):



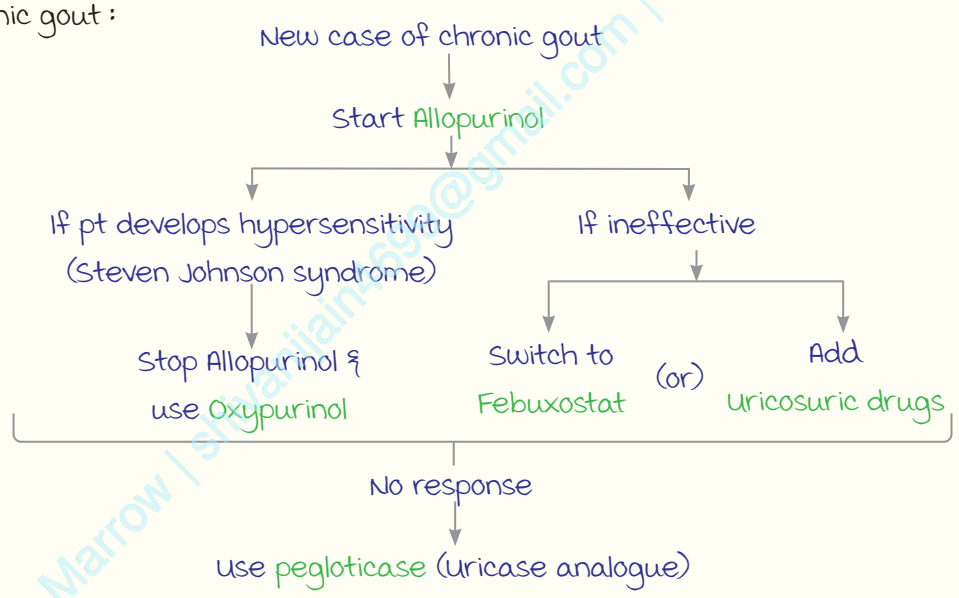
Anti gout drugs :

Acute gout :

DOC : Indomethacin > Colchicine.

Colchicine MOA : Blocks microtubules ⟶ Blocks chemotaxis.

Chronic gout :



Xanthine oxidase inhibitors :

Drugs :

1. Allopurinol
2. Oxypurinol
3. Febuxostat

S/E : Xanthine stones.
SJS (Allopurinol).

Uricosuric drugs :

Increase uric acid excretion.

Drugs :

1. Sulfinpyrazole } Not effective in renal failure
2. Probenecid }
3. Benzbromarone } Effective in renal failure
4. Lesinurad }

S/E : Urate stones.

----- Active space -----

Hyperuricemia in tumor lysis syndrome :

- Solid tumors : DOC Allopurinol
- Leukemia : DOC Rasburicase

Respiratory system

00:29:00

Anti asthmatic drugs :

Drugs	Uses	Side effects
Beta-2 agonists & Anti cholinergics	-	-
Methyl Xanthines : • Theophylline • Aminophylline New PDE-4 inhibitor approved for COPD : Roflumilast	• Bronchodilatation d/t adenosine A1 antagonism, PDE 3 > 4 block. • Anti inflammatory d/t PDE 4 block, histone deacetylase stimulation, ↑ IL-10.	Adenosine A1 block : • Seizures • Arrhythmias • Diuresis PDE-4 block : • GIT upset • Headache
Inhaled corticosteroids (ICS) : Fluticasone (most potent) Soft steroids : • Ciclesonide • Beclomethasone	• DOC : Persistent asthma • TOC in acute attack : ICS + Formoterol	• Hoarseness of voice (m/c). • Oropharyngeal candidiasis.
Systemic steroids	For Rx acute exacerbation (↑ Beta-2 agonist effect)	
LOX inhibitor : Zileuton LT C4/D4 inhibitors : Montelukast	Persistent bronchial asthma add on EIA	Hepatotoxic
Mast cell stabilizers : • Cromolyn sodium • Nedocromil	Prophylaxis of allergen induced asthma	Safest drugs
Anti Ig E : Omalizumab	Severe persistent bronchial asthma	Not effective in atopic dermatitis
Anti IL 5 : • Reslizumab • Mepolizumab Anti IL 5 receptor : Bendralizumab Anti IL 4 receptor : Dupilumab	Severe eosinophilic asthma	

Active space

Anti-tussives :

Centrally acting drugs :

Opioids	Non opioids
For mild/moderate dry cough : • Codeine • Pholcodine • Hydrocodone For severe cough (eg. bronchial Ca) : • Methadone • Morphine	• Dextromethorphan : 1. NMDA antagonist 2. S/E : Hallucinations (Has abuse potential). • Diphenhydramine • Noscapine • Levopropoxyphene

Expectorants :

Guaifenesin : Cause oscillatory movement of the bronchi leading to expulsion of products.

Mucolytics :

N-acetyl cysteine : Breaks disulfide bonds in the mucus.

Ambroxol/Bromhexine : Depolymerise mucopolysaccharides.

Management of productive cough :

Syrup : Ambroxol/Bromhexine + Salbutamol + Phenylephrine.

Gastrointestinal system

00:35:00

Peptic ulcer disease :

Drugs	Uses	Side effects
Proton pump inhibitors : • Omeprazole • Pantoprazole • Lansoprazole • Rabeprazole	DOC in : • Peptic ulcer disease (PUD). • GERD. • Zollinger Ellison syndrome. • H.pylori. • Barret's esophagus (Life long Rx with PPI).	• GIT upset. • Pneumonia. • Pseudomembranous enterocolitis. • Osteoporosis. • Iron, B12 deficiency. • Hypergastrinemia.
H2 blockers : • Cimetidine • Ranitidine • Famotidine	Same as PPI, for Rx. DOC for prophylaxis of aspiration pneumonia in postoperative patients .	Cimetidine : • Impotence. • Gynecomastia. • Galactorrhea.

----- Active space -----

Drugs	Uses	Side effects
Misoprostol	Most specific for NSAID induced ulcer.	• Diarrhoea. • Abdominal cramps.
Sucralfate	• PUD. • Rectal ulcer.	• Constipation. • Gastric bezoars. • C/I with food, antacids & other drugs.
Bismuth subsalicylate/sub-citrate	• H.pylori. • Traveler's diarrhoea.	• Constipation. • Black discoloration of stool and tongue.
Antacids (Salts of Al^{3+} and mg^{a+}) Al^{3+} : Causes constipation mg^{a+} : Causes diarrhea.	• PUD. • Dyspepsia. • GERD.	Decrease absorption of oth-er drugs.

Note :

- PPI's sholud be consumed 30 mins before food.
- Antacids should be given 30 min after sucralfate.
- Food should be consumed 1 hr before sucralfate.
- Any other drug should be consumed 2hrs before sucralfate.

Prokinetics :

Classification	Drugs /side effects
D2 antagonists	1. Metoclopramide : • Crosses BBB. • Causes EPS. • Hyperprolactinemia. 2. Domperidone : No EPS.
5-HT4 agonists	1. Mosapride 2. Itopride 3. Prucalopride
Motilin receptor agonists	1. Erythromycin 2. Mitemcinal
CCK1/A receptor agonist	1. Dexloxiglumide

Active space

Antiemetics :

Drugs	Uses	Side effects
5-HT3 antagonists : • Ondansetron : Shortest acting. • Palonosetron : Longest acting, most potent	• DOC : Chemo/radiation/postoperative nausea or vomiting. • Morning sickness.	
NK1R antagonists : • Aprepitant • Rolapitant • Netupitant	Chemo induced nausea & vomiting	
CB 1R agonists : • Dronabinol • Nabilone	Chemo induced nausea & vomiting (As an add on drug).	• Hypotension (monitor BP). • Blood shot eyes .
Dexamethasone	Chemo induced nausea & vomiting	

m/c used drugs in chemo induced nausea and vomiting :
Ondansetron + Aprepitant + Dexamethasone.

Laxatives :

Increase water in intestine	Increase intestinal contraction	Increase stool bulk	Softening of stool
1. Osmotic laxatives : Mannitol : • Used as second line in constipation (Costly). • Used in hepatic encephalopathy as well. Polyethylene glycol : DOC for IBS associated constipation.	Bisacodyl, Senna, Cascara : • Promote low grade inflammation of large intestine → increase contraction. • Taken at night. • Used for short term treatment of constipation. • Senna causes melanosis coli and pink/yellow brown discoloration of urine.	Probiotics : Beneficial micro organisms • Lactobacillus • Saccharomyces • B. clausii	Docusate Na^+ : They increase surface tension of stool → Collapses stool.

----- Active space -----

Increase water in intestine	Increase intestinal contraction	Increase stool bulk	Softening of stool
2. Chloride secretory agents : 1. Lubiprostone : Stimulates type II chloride channels. 2. Linaclotide : Stimulates guanylate cyclase, cGMP, which stimulates CFTR.	5-HT4 agonists : • Mosapride • Prucalopride	Prebiotics : Dietary fibers • methyl cellulose • Psyllium husk • Bran	Docusate Ca^{2+} : They increase surface tension of stool → Collapses stool.
3. Tenapanor : Inhibitor of sodium-proton exchanger.			

Anti diarrheal agents :

Drugs	MOA/uses
Alosetron	5-HT3 antagonist. IBS associated with diarrhea in females.
Loperamide (opioid)	DOC for non secretory diarrhea (IBS associated diarrhea).
Octreotide	DOC for secretory diarrhoea.
Bile acid bending resins	Biliary diarrhoea

Hematology

00:47:03

Antiaggregants :

Drugs	Uses	Side effects
COX-1 inhibitor : Aspirin : ↓ TXA2 synthesis	Primary prophylaxis of MI & stroke.	Bleeding
PAR 1 blocker : Vorapaxar	Primary prophylaxis of MI.	C/I : Cerebrovascular disorders (Intracranial bleed)
GP IIb/IIIA blockers : • Abciximab • Tirofiban • Eptifibatide	PCI in MI. Unstable angina.	Bleeding Thrombocytopenia

Active space

AD/PaYIa blockers :

Irreversible	Reversible
1. Clopidogrel : Primary prophylaxis of MI and stroke. 2. Ticlopidine : S/E : Agranulocytosis, TTP-HUS, thrombocytopenia. 3. Prasugrel : • Causes intracranial bleed. • C/I in stroke/TIA. • Use : PCI in MI.	1. Cangrelor : • Adenosine analog : IV & short acting. • Use : PCI in MI. 2. Ticagrelor : • Oral • Use : Acute coronary syndrome, prophylaxis of MI and stroke.

Anticoagulants :

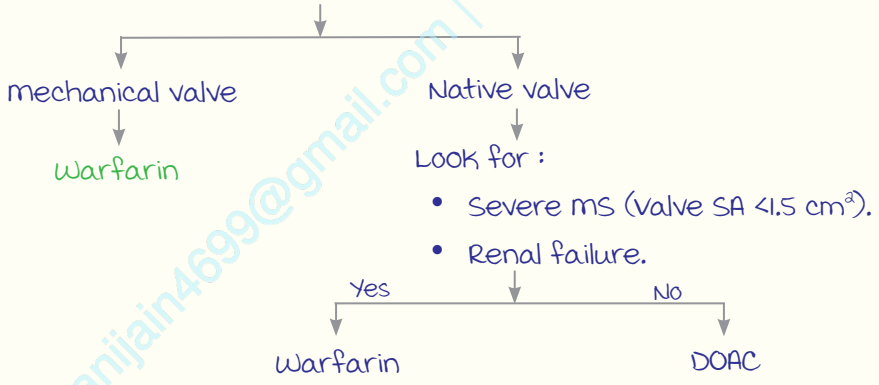
Drugs	Uses	Comments
Direct acting oral anticoagulant (DAOC) : • Oral DTI : Dabigatran • Oral Xa inhibitors : 4. Apixaban 5. Rivaroxaban 6. Edoxaban	• DVT Rx. • DOC DVT prophylaxis. • DOC prophylaxis of thrombosis in non valvular atrial fibrillation (Native valve).	No monitoring required. Incase of bleeding (D/t overdose) : • Dabigatran : Idarucizumab • Oral Xa inhibitors : Andexanet alfa
Warfarin : • Blocks VKOR . • Decreases levels of factors II,VII,IX,X & proteins C and S.	• DVT Rx & prophylaxis. • DOC for prophylaxis of thrombosis in valvular atrial fibrillation (mechanical valve).	• Skin necrosis : Due to rapid ↓ in proteins C and S. • Purple toe syndrome : Cholesterol embolus. • Teratogenic : Mid facial hypoplasia, stippled epiphyseal calcification, CNS defects. Antidote : Vitamin K & 4 factor prothrombin complex > FFP

----- Active space -----

Drugs	Uses	Comments
Parenteral DTI (Direct thrombin inhibitor)	Common use : Heparin induced thrombocytopenia (HIT) DOC : Argatroban (> Fondaparinux) Desirudin Bivalirudin	Monitor aPTT

Does not need monitoring	Needs monitoring
D : DOAC L : LMWH F : Fondaparinux	UFH & Parenteral DTI (Argatroban) : aPTT Warfarin : PT/INR

Prophylaxis of thrombosis in atrial fibrillation :



Active space

Direct thrombin inhibitors :

Unfractionated heparin (UFH)	Low molecular weight Heparin (LMWH)	Fondaparinux
Inhibits Xa = IIa	Inhibits Xa > IIa	Inhibits only Xa
S.c route : Only for prophylaxis (Poor bioavailability). IV route : For Rx.	Both Rx and prophylaxis given by s.c route. (Good bioavailability)	
Short acting (metabolized by macrophages) : Need multiple doses	Long acting, can be given as single dose/OD.	
Can be used in renal failure.	C/I in renal failure.	
Protamine sulfate has good efficacy as an antidote.	Protamine sulfate has some efficacy as an antidote.	Protamine sulfate has no efficacy as an antidote.
↑risk of heparin induced thrombocytopenia (HIT)	Less risk of HIT	No risk of HIT
	DOC for thrombosis (In MI, DVT, Pulmonary embolism, cancer induced thrombosis)	

S/E of heparin :

- H : Hyperkalemia, Hair loss.
- O : Osteoporosis.
- T : Thrombocytopenia.

Fibrinolytics :

Plasminogen $\xrightarrow{\text{t-PA}}$ Plasmin $\longrightarrow$ Breaks fibrin

t-PA analogs :

1. Alteplase
2. Reteplase
3. Tenecteplase (most clot specific).

Given in IV form.

Use : STEMI

S/E : Bleeding (DOC for bleeding : Tranexemic acid > Epsilon aminocaproic acid).

----- Active space -----

Hematopoietic agents :

Erythropoiesis	Granulopoiesis	Thrombopoiesis
Erythropoietin analogs : 1. Epoietin alfa 2. Darbopoetin alfa (Long acting). Uses : • Anemia of CRF. • Anemia causes by chemotherapy/drug. • Anemia of dialysis. S/E : • Pure red cell aplasia. • Hypertension. • Thrombosis. • Iron deficiency.	G-CSF analog : 4. Lenogastrim 5. Filgastrim 6. Lipefilgastrim (Long acting, given once in a chemotherapy cycle, more preferred). GM-CSF analog : Sargamostim Uses : • Neutropenia • HIV • Chemotherapy S/E : • Bone pain	IL-11 analong : Oprelevekin Use : Thrombocytopenia due to chemotherapy. Thrombopoietin agonist : 1. Eltrombopag. 2. Romiplostim. Use : ITP 1. Lusutrombopag 2. Avatrombopag Use : To decrease bleeding in liver cirrhosis planned for procedure.

Immunosuppressants

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Active space

Immunomodulators	MOA and Uses	Side effects
Cyclosporine Tacrolimus	Calcineurin inhibitors : ↓ IL-2 transcription. Ist line drug for GVHD.	Common : Hepatotoxicity, Hyperkalemia, Hypertension, Nephrotoxicity, Neurotoxicity, Hyperglycemia. Cyclosporine : • Hirsutism. • Gums hyperplasia. • Hyperlipidemia. • Hyperuricemia.
Everolimus Sirolimus	mTOR inhibitors : Inhibit CD8 proliferation at G1-S phase.	Hypokalemia
Azathioprine	Prodrug of 6-mercaptopurine .	Bone marrow suppression & hepatotoxicity
Basiliximab	Blocks IL-2 receptor/CD 25. Used for prophylaxis of acute graft rejection.	
Mycophenolate mofetil	Blocks IMP dehydrogenase → Blocks purine synthesis.	GIT upset
Leflunomide	Blocks dihydro-orotate dehydrogenase → Blocks pyrimidine synthesis.	Bone marrow suppression Hepatotoxicity
Muromonab	Blocks CD 3. Uses : • Rx of acute graft rejection. • Rebound rejection.	Cytokine release syndrome
Belatacept	CD 80/86 inhibitor	
Alemtuzumab	CD 52 inhibitor	
Belumosudil	Rho Kinase inhibitor	
Thalidomide	Anti inflammatory Anti angiogenic Anti neoplastic Immunosuppressant	Phocomelia mechanism : Blocks cereblon & tubulins → Blocks vasculogenesis & ↑ free radicals → blocks fetal organ development.