Contents

GENERAL PHARMACOLOGY : PART 1

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Types of Drugs

00:07:58

Orphan drugs :

Used for rare diseases → ↓Profitability (↓Development of drug).

Note : Orphan receptor → Receptor with unknown ligand.

Essential drugs :

Meets healthcare needs of the majority of a population :

- Inexpensive.
- Non-toxic.
- Easily available.
- Efficacious.
- Safe.
- Single molecule (Not fixed dose combination).

Prescription/legend drugs : Require prescription (under Schedule H).

Spurious drugs : Does not produce expected effect as drug component is falsified.

Misbranded drugs : Incorrect or missing information on drug label.

Adulterated drug : Unwanted additive in drug.

Rational Drug Use :

Use of right drug for right disease & patient; at right dose, duration & route with right dispensation & monitoring ("Right price" not included).

Movement of Drug Through the Body (ADME)

00:08:00

Note : Pharmacodynamics → Drug induced change in body via receptor binding (Drug receptor effect).

Drug Absorption

00:10:10

- M/c mechanism : Passive diffusion along concentration gradient.
  (Lipid soluble; Unionised drugs → pH of drug = pH of medium).
- Maximum absorption of drug in GIT : Small intestine (D/t large surface area).
- Poor oral absorption : Drugs with large size (Eg : Proteins → Drugs with -tide/-ase/-mab).

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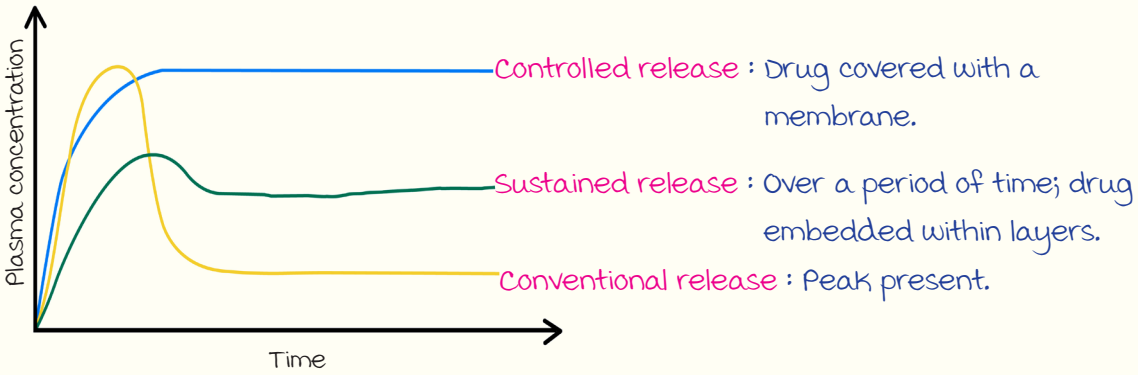
Types of Tablets/Capsules :



Uses of controlled/sustained release :

- ↑Duration of effect → ↓no. of doses. (Useful if t1/2/< 4h).
- ↓Risk of acute toxicity : D/t lower/absent peak concentration.

Enteric coated drugs :

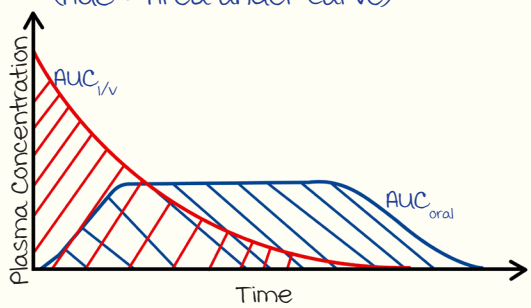
- HCl-resistant membrane coating used.
- Prevents drug breakdown in acidic pH of stomach.

Extent of Absorption :

- Amount of drug absorbed.
- AKA bioavailability.
- Formula :

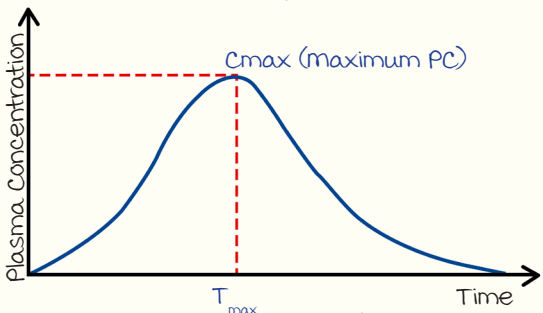
$$\text{Bioavailability} = \frac{AUC_{oral}}{AUC_{i/v}}$$

(AUC = Area under curve)



Rate of Absorption :

- Amount of drug absorbed per unit of time.
- Determined by T_{max}.



Note → R A T E : Rate → T_{max}
AUC → Extent

ATP-binding Cassette (ABC) :

AKA : p-glycoprotein/multi-drug resistance (MDR)-1 pumps.

Physiological functions :

1. Intestine/liver : Drug efflux (Eg : Digoxin).
   ↓Drug concentration in systemic circulation due to removal.
2. Blood brain barrier : Limit drug exposure to central nervous system.
   Removes drugs that cross the BBB → No central effects (Eg : Loperamide).
3. In liver : Excretion of bile acids.

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Pathological function :

Cancer cells/bacteria : use the pump to remove drug. (Confers resistance → AKA MDR-1 pump).

p-GP/MDR-1 substrates	
• Loperamide	• Digoxin
• Methadone	• Erythromycin, Clarithromycin
• Nelfinavir	• Quinidine
• Cyclosporine	• Ranolazine
• CCB (Verapamil)	• Sotagliflozin

p-GP/MDR-1 inducers
Enzyme inducers like :
• Rifampicin
• Phenytoin
• Carbamazepine

Significance :

1. pGP substrates competitively inhibit each other → ↑Toxicity of either drug.
   Eg :
   - Clarithromycin + Digoxin → Digoxin toxicity.
   - Quinidine → Loperamide induced CNS toxicity (Crosses BBB).
2. pGP inducers cause drug failure.
   Eg : Rifampicin + Digoxin → ↑Digoxin efflux → Rx failure.
3. pGP substrates can cause cholestatic jaundice :
   D/t competitive inhibition of bile acid excretion. Eg : Cyclosporine.
4. pGP inhibitors can be used to reverse drug resistance.
   m/c used : Verapamil.

Drug Distribution

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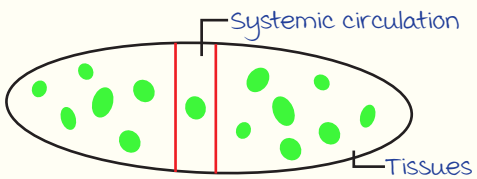
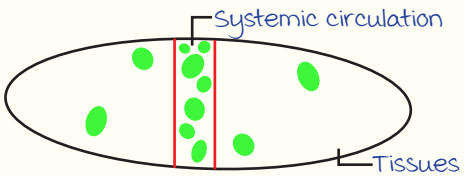
Volume of Distribution (V_d) :

High volume of distribution	Low volume of distribution
↑Extravascular concentration.	↑Intravascular concentration.
	

Formulae :

$$\text{Apparent } V_d \ (aV_d) \text{ (Liters)} = \frac{D}{C_0} = \frac{\text{Dose via IV route}}{\text{Initial PC}}$$

$$\text{Loading dose} = aV_d \times C_T \text{ (Target PC)}$$

Note : Loading dose $\propto aV_d$.

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Significance :

Dialysis : Not effective for high V_d drugs.

Drugs with ↑V_d (BAD DOC)	Antidote
Benzodiazepine	Flumazenil
β-blocker	Glucagon
Amphetamines	Ammonium chloride
Digoxin	Digibind
Opioids	Naloxone
Organophosphates	Atropine
Calcium channel blockers	Calcium gluconate

Plasma Protein Binding :

Proteins :

Albumin (m/c)	Alpha-1-acid glycoprotein
Binds to acidic drugs	Binds to basic drugs
• Aspirin • Anti-coagulant (Warfarin) • Anti-epileptics/Anti-psychotics/ Anti-depressants • Antibiotics (Sulfonamides)	• Opioids • Tricyclic anti-depressants • β-blockers • Anti-arrhythmics (Amiodarone/Lidocaine)

Significance :

1. Liver cirrhosis :
   ↓Albumin production → ↓Drug binding → ↑Free drug → ↑Toxicity.
2. Nephrotic syndrome/Chronic kidney disease :
   ↑Albumin excretion → ↑Drug excretion → Drug failure.
3. ↑Alpha-1-acid glycoprotein :
   Seen in RA, IBD, MI → ↓Free drug → Drug failure.

Drug Metabolism

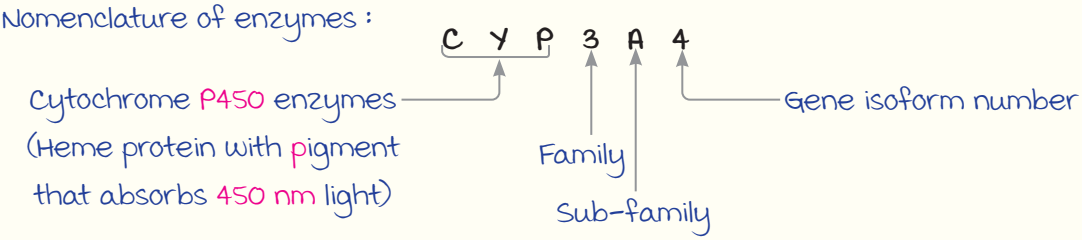
00:45:12

Phase I vs. Phase II Reactions :

	Phase I reactions	Phase II reactions
Purpose	Drug inactivation	Make drug water soluble
m/c reaction	Oxidation	Glucuronidation
m/c enzyme	CYP3A4	Glucuronyl transferase (GT)

Note :

- Nomenclature of enzymes :



- Crigler-Najjar syndrome : ↓GT → ↑Toxicity of → Irinotecan (Anti-cancer).
  → Atazanavir (Anti-HIV).

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Drug – Enzyme Interaction :

	Enzyme inducers	Enzyme inhibitors
Effect	Cause drug failure	Cause drug toxicity
Examples	Mnemonic : GRAB PC • Griseofulvin • Rifampicin • Alcohol (Chronic consumption) • Benzopyrene • Phenytoin, Phenobarbital, Primidone • Carbamazepine, Cigarettes	Mnemonic : QuICK VEG, DISK • Quinidine • Isoniazid, Protease inhibitors • Cimetidine, Chloramphenicol, Ciprofloxacin • Ketoconazole, Itraconazole, Fluconazole • Valproate Erythromycin, Clarithromycin • Grapefruit juice • DEC, Delavirdine, Disulfiram
Important drug interactions	Rifampicin : • OCP failure • C/I in HIV with TB	• Erythromycin → Theophylline toxicity • Clarithromycin → Statin toxicity

Drugs Metabolised by Plasma Esterase :

Quick action of plasma esterase → Short $t_{1/2}$ of drugs.

Examples : Plasma Esterase Can Readily Metabolise Short Acting drugs.

- Procaine, cocaine.
- Esmolol.
- Clevidipine.
- Remifentanil, Remimazolam.
- Mivacurium.
- Succinylcholine.
- Acetylcholine.

Drug Excretion

00:54:52

M/c organ : Kidney (Drug needs to be ionized & water soluble).
→ (Acidic drug → Basic media and vice versa).

Significance :

Drug toxicity :

- Acidic drugs (Aspirin, Phenobarbital) → Alkalinisation of urine with bicarbonate.
- Basic drugs (Amphetamines) → Acidification of urine with ammonium chloride.

Mechanisms :

- Filtration : Only free drug excreted.
- Tubular secretion : Free + plasma protein bound drug excreted.

Calculations :

Rate of drug elimination : Amount of drug excreted per unit of time.

Rate = P.C. x clearance (In mg/hr)

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Infusion rate (IR) : Amount of drug to be administered per unit of time.

IR : Rate of drug elimination = P.C. x clearance

Maintenance dose : Dose required to maintain steady state of drug P.C.

MD = P.C. x clearance x time

Half-life :

$$t_{1/2} = \frac{0.693 \times V_d}{\text{Clearance}} = \frac{0.693}{K_{elimination}}$$

Note : Infusion rate & maintenance dose ∝ Clearance.

Order of Kinetics :

	Zero order kinetics	First order kinetics
Definition	Constant amount eliminated per hour	Constant proportion eliminated per hour
Effect of ↑sing dose	• $T_{1/2}$ ↑ • Clearance ↓ • P.C. : Disproportionate ↑	• $T_{1/2}$ constant • Clearance constant • P.C. : Proportionate ↑
Risk of toxicity on overdosing	Higher	Lower
Examples	Zero ATP Has Made Weak : • Alcohol • Theophylline, Tolbutamide • Phenytoin • Heparin • Methanol • Warfarin	Most drugs

GENERAL PHARMACOLOGY : PART 2

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Drug $\xrightarrow{\text{Binds to}}$ Receptor $\xrightarrow{\text{Causes}}$ Effect.

Factors Affecting Pharmacodynamics :

Affinity :

- Tendency of a drug to bind to its receptor.
- Marker of dose $\left[\text{Affinity } \alpha \frac{1}{\text{Dose}}\right]$.

Efficacy :

- Maximum clinical effect produced by a drug (most important factor).
- Marker of effect of drug.

Potency :

- Relative dose of a drug required to produce particular effect.
- Potency $\alpha \frac{1}{\text{Dose}}$.

Dose-Response Curve (DRC)

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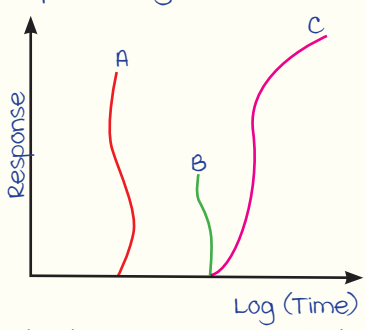
Graded Curve :

Response is graded.



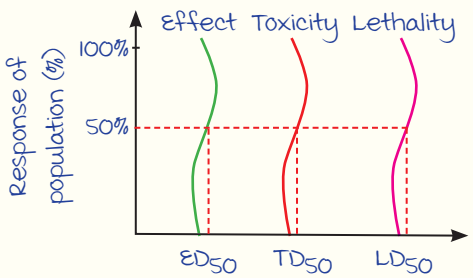
Individual responses noted.

- Efficacy : Height of curve.
  - C > A > B.
- Potency : Left shift.
  - A > B > C.

HELP

- Affinity :
  Compared only if acting on the same receptor.
  - Parallel graphs = Same receptor.
  - A > B.

Quantal Curve :



- Response : Binary (Yes/No) → Eg : Sedation.
- Population response noted.
- In 50% population, dose required to cause :
  - Effect : ED_{50} (marker of potency).
  - Toxicity : TD_{50}
  - Lethality : LD_{50}

marker of toxicity.

Note : Lethality checked only in animals.

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Therapeutic Index (TI) :

- Marker of drug safety.
  1. In humans : TI = TD_{50} / ED_{50}.
  2. In animals : TI = LD_{50} / ED_{50}.
- Significance : Small change in dose → Toxicity (Eg : Lithium has ↓TI).

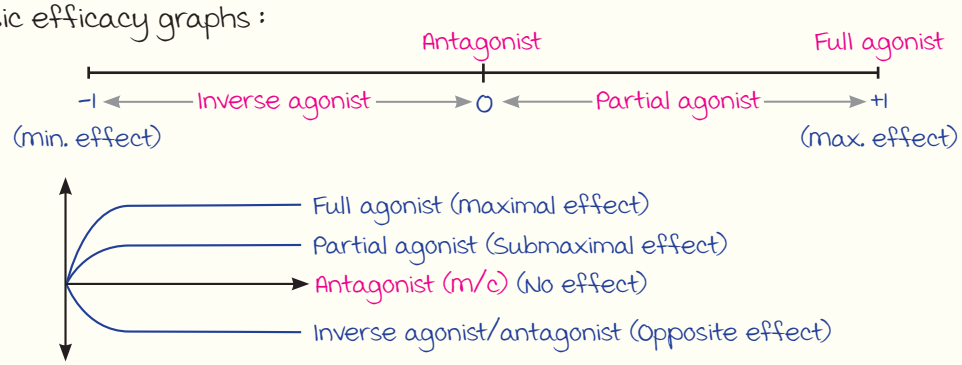
Therapeutic Window/Range :

More important indicator of toxicity than TI.

Drug Receptor Interaction

00:20:23

Intrinsic efficacy graphs :



Type of Antagonism :

1. Physical/Pharmacokinetic antagonism :
   - Affected by physical binding of antagonist.
   - Eg : Charcoal in alcohol toxicity (Adsorbs alcohol → Preventing absorption by intestine).

2. Chemical antagonism :
   - Chemical reaction causes antagonism.
   - Eg :
     - Heparin (Negative charge) – Protamine sulphate (Positive charge).
     - Iron – Desferrioxamine (Chelation).

3. Physiological antagonism :
   - Opposite effect caused by binding on different receptors.
   - Eg :
     - Histamine via H_1 → Bronchoconstriction.
     - Adrenaline via β_2 → Bronchodilatation.

4. Competitive and Non-competitive antagonism :

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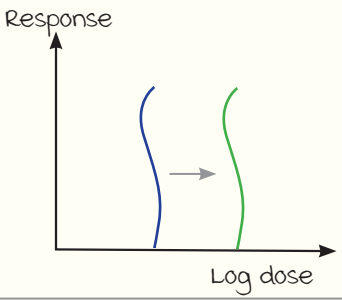
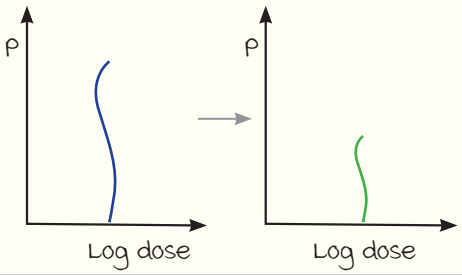
	Competitive inhibition	Non-competitive inhibition
Graph		
Change in graph	Right shift in DRC	↓Height of DRC
Change in reaction	• Vmax : Constant • Efficacy : Constant • ↑Km • ↓Potency	• ↓Vmax • ↓Efficacy • Km : Constant • Potency : Constant

RECEPTORS

Type of receptor	Sub-types	Examples
Ligand gated ion channel	-	• $GABA_A$ • Glutamate (NMDA, AMPA, Kainate) • Nicotinic • $5HT_3$
Enzymatic	Tyrosine Kinase receptors	• EGFR • Insulin, IGF-1 • Toll-like receptors • VEGFR • Her-2
	Serine/threonine Kinase receptors	TGFR
	Janus Kinase receptors (JAK)	• Cytokine receptors (Eg : Leptin) • Prolactin receptor • Growth hormone receptor
	Guanylyl cyclase linked receptor	ANP & BNP (Vasodilatation)
Nuclear	Located in nucleus (TREP)	• Thyroid • Retinoic acid • Retinoid X • Estrogen • Progesterone • PPAR
	Located in cytoplasm	• Mineralocorticoid • Glucocorticoid • Androgen • Vitamin D

Note : Insulin & IGF-1 are present in areas of ↑rate of growth.

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G-Protein Coupled Receptors (GPCRs) :

GPCR	MOA	Examples	Drugs
G_s	$\uparrow \alpha_s$-GTP → ⊕ Adenylate cyclase → ↑cAMP → Cardiac & skeletal muscles → Contraction; Smooth muscles → Relaxation	β_2-receptor	• Salbutamol • Ritodrine
		β_1-receptor	• Dobutamine
G_q	$\uparrow \alpha_q$-GTP → ⊕ Phospholipase C → ↑IP_3 (2° messenger) → ↑Ca^{2+} production → Smooth muscle contraction.	α_1, m_1, m_3	• Oxytocin • Angiotensin
$G_{i/o}$ (Inhibitory)	• ↓cAMP • ↓Ca^{2+} • Open K^+ channels } Relaxation	m_2 (Heart)	-
$G_{12/13}$	⊕ Rho-Kinase → Smooth muscle contraction		Rho-Kinase ⊖ : • Fasudil → Angina (Vasodilator) • Netarsudil → Glaucoma • Belumosudil → Immunosuppression (Targets B-cells)

Drug Safety

00:41:50

Pre-clinical trials : Only on animals.

Clinical Trials :

Investigational New Drug (IND) : Drug under trial.

Phases of a clinical trial :

Phase	Features studied	Target population
I	• Toxicity • Maximum tolerable dose • Pharmacokinetics, Pharmacodynamics	• 20 to 100 healthy volunteers • 1 to 2 years • Open label trial
II	• Therapeutic exploratory trial/Efficacy trial • Efficacy determined • Dose range/Dose safety	• 100 to 500 patients • 2 to 3 years • Randomized Control Trial (RCT)

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Phase	Features studied	Target population
III	• Therapeutic confirmatory trial • Efficacy & safety confirmed ↓ Drug marketed.	• 500 to 3000 patients • 3 to 5 years • Drug approved by : – CDSCO – India – FDA – USA • RCT/RUCT
IV	Post marketing surveillance (If ADR is rare/long term)	• Many thousands of pt. • No specific duration • Open label trial.

Note :

- Phase I & phase II done together for toxic drugs like anti-cancer/anti-HIV.
  - Patients are taken up directly.
  - 20 to 100 patients involved.
- Non-mandatory phase :
  - Phase 0 (microdosing) : 100 mcg of drug given.
  - Phase V (Pharmacoepidemiology) : Case control study, cohort study etc.

Adverse Drug Reactions (ADR) 00:49:40

Types of ADR :

Mnemonic : ABCDE.

Type	Features	Examples
A : Attenuated	• Enhanced effect of drug • Dose dependent	Antihypertensive causing hypotension
B : Bizarre	• Dose independent • Immune mediated	Drug causing hypersensitivity (Eg : Penicillin causing rash)
C : Chronic	Dose & duration dependent	↑Steroids → ↑HPA suppression
D : Delayed	Delay in time from exposure to ADR	Drugs causing teratogenicity (Eg : NTDs d/t valproate)
E : End-of-use/ withdrawal	D/t stoppage of dose	Opioid withdrawal (HTN d/t clonidine withdrawal)

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Pharmacovigilance :

Flow of ADR information

Vigibase : Largest database of pharmacovigilance (In Sweden).

Therapeutic Drug Monitoring (TDM)

00:55:00

Principle : Plasma concentration (PC) correlates to effect/side-effect.

Indications :

1. Clinical effect not easily quantified.
2. Drugs having low therapeutic index :
   - Aminoglycosides.
   - Antiepileptics.
   - Lithium.
   - Theophylline.
   - Digoxin.
   - Cyclosporine.
   - Tacrolimus, Tricyclic antidepressants.
3. Drugs with variable metabolism.
   Eg : metabolised by acetylation.

Dosage examples :

1. Digoxin :
   - 0.5 to 0.9 ng/mL : Therapeutic range.
   - >0.9 ng/mL : Effect constant, ↑risk of toxicity.
   - >2 ng/mL : Toxicity.
   - >1.2 ng/mL : Increased mortality in atrial fibrillation.
2. Lithium :
   - 0.6 to 1.0 mEq/L : Mania prophylaxis
   - 1.0 to 1.5 mEq/L : Mania treatment

   } Therapeutic range.
   - >1.5 mEq/L : Toxicity.
   - >4 mEq/L : Dialysis needed.
3. Theophylline :
   - 5 to 15 mg/L : Therapeutic range.
   - >15 mg/L : Toxicity.

Miscellaneous

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Pharmacogenetic Conditions :

ADR caused in certain individuals d/t genetic difference.

1. Acetyl transferase polymorphism
   - NAT 1 gene : Fast acetylators.
   - NAT 2 gene : Slow acetylators.

2. Malignant hyperthermia :
   D/t lignocaine, halothane, succinylcholine.

Drugs metabolized by acetylation
Mnemonic : HIPS Dance • Hydralazine. • Sulfonamides. • Isoniazid. • Dapsone. • Procainamide.
All can cause drug induced SLE

3. G-6-PD deficiency associated hemolysis : Dr. MANISh
   - Dapsone.
   - Nitrofurantoin.
   - Methylene blue.
   - Isoniazid.
   - Antimalarial : Primaquine > Chloroquine > Quinine.
   - Sulfonamides.
   - Nalidixic acid.

4. Glucuronyl transferase polymorphism : Causing irinotecan toxicity.

5. CYP450 enzyme polymorphism :
   - CYP2C19 : Activates clopidogrel.
   - CYP2C9 : Metabolizes warfarin.
   - CYP2D6 : Metabolizes → Antidepressants. / Opioids.

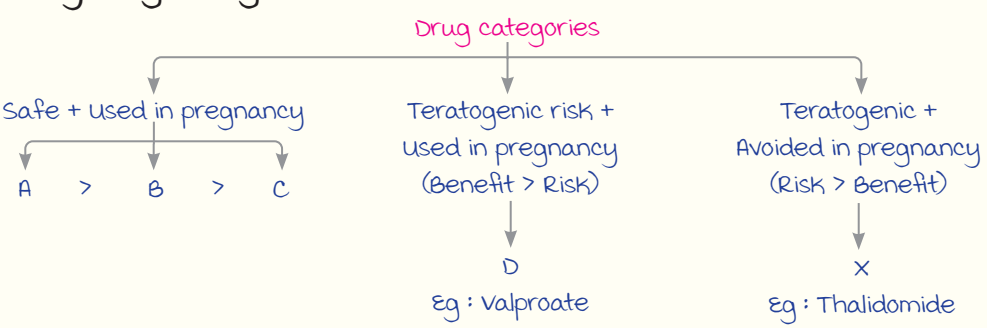
   } Polymorphism → Variable drug effects.

6. VKORC 1 gene (For Vitamin K oxidoreductase) : Variable metabolism of warfarin.

7. Succinylcholine associated prolonged apnea (D/t atypical pseudocholinesterase).

8. Thiopurine methyl transferase polymorphism :
   Causing toxicity of Azathioprine, 6-mercaptopurine & 6-thioguanine.

Pregnancy Drug Categories :



Note : Schedule X drugs.
- High abuse potential.
- Narcotropics (Amphetamine, Ketamine etc).

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DRUGS ACTING ON AUTONOMIC NERVOUS SYSTEM

Regulation of ANS :

	Parasympathetic NS	Sympathetic NS
Receptor	Muscarinic (m/c : M_3) or nicotinic	α or β
Neurotransmitter	Acetylcholine (ACh)	Norepinephrine (NE) Exceptions : • Dopamine $\xrightarrow{D1}$ Renal blood vessels : Vasodilation (Diuresis) • ACh in adrenals & sweat glands

Sweating :

- Regulated by sympathetic NS.
- Mediated via ACh to muscarinic receptors.
- Atropine/Datura poisoning blocks M_3 → ↓ Sweating → Hyperthermia.

Drugs Acting On ACh

00:03:40

1. Aminoglycosides ⊖→ Presynaptic voltage gated Ca^{2+} channels → ↓ ACh.
2. Botulinum toxin ⊖→ ACh release ⊖→ Muscle contraction → Respiratory paralysis.

Drugs Acting On NE/Dopamine

00:05:18

VMAT2 inhibitor → ↓Dopamine (used in movement disorders).

- Tetrabenazine 💊 : DOC for → Tics a/w Tourette syndrome.
  → Huntington's chorea.
- Deutetrabenazine, Valbenazine 💊 : DOC for Tardive dyskinesia. (Longer acting)

	Parasympathomimetic	Parasympatholytic	Sympathomimetic	Sympatholytic
CNS	• ↑Cognition • Donepezil (DOC) 💊 in Alzheimer's disease/dementia	• ↓Cognition • Scopolamine : For narcoanalysis (DOC : Thiopentone 💊)	-	β-blocker s/e : • Depression • Insomnia • Nightmares
Pupil	Active miosis	Passive mydriasis	Active mydriasis	Passive miosis

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	Parasympathomimetic	Parasympatholytic	Sympathomimetic	Sympatholytic
Pupil	Pilocarpine (DOC) : Closed angle glaucoma	Drugs : • Tropicamide • Atropine • Homatropine • Cyclopentolate	Drugs : • Phenylephrine • Ephedrine	Drugs : • Phenoxybenzamine • Prazosin
		• Ocular fundus exam. • In uveitis/corneal ulcers → Prevent synechiae • C/I : Closed angle glaucoma → Ppt → Acute congestive glaucoma		
		Cycloplegic function : • ↓Iridocyclitis pain • Refractive error testing	No cycloplegic function	
Oro-pharyngeal secretions	↑	↓	–	–
	Pilocarpine, Cevimeline For xerostomia (Sjogren syndrome)	Glycopyrrolate (Does not cross BBB) > Atropine : As pre-anaesthetic medication (Prevent aspiration)	–	–
Bronchi	Bronchoconstriction	Bronchodilatation (M_3 ⊖)	Bronchodilatation (β_2 ⊕)	Bronchocnstriction
	C/I : Bronchial asthma (BA) & COPD	For COPD : • Tiotropium (DOC) } LAMA (OD) • Umeclidinum • Revefenacin • Aclinidium → LAMA (BD) • Ipratropium → SAMA (QID).	β_2 – agonists (S/e : Hyperglycemia) • SABA – Salbutamol – Terbutaline – Pirbuterol } BA/COPD • LABA – Formeterol – Salmeterol } BA/COPD • VLABA – Olodaterol – Vilanterol – Carmoterol } COPD only	–
			SABA & formoterol are relievers (Fast acting)	
Heart	• ↓ HR • ↓ AV conduction	• ↑ HR • ↑ AV conduction	• ↑ HR • ↑ AV conduction • ↑ Contraction	• ↓ HR • ↓ AV conduction • ↓ Contraction
	–	Atropine (DOC) : • AV Block • Bradycardia (Max 3 mg) 1 mg → (3–5 min) 1 mg → (3–5 min) 1 mg	Epinephrine : • Bradycardia (In children) • Cardiac arrest	β-blockers (DOC) : • Atrial fibrillation/ flutter • HOCM • Aortic dissection

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	Parasympathomimetic	Parasympatholytic	Sympathomimetic	Sympatholytic
Blood vessels & GIT	↑ HCl secretion ↑ Contraction	↓HCl secretion ↓Contraction	Vasoconstriction (α-agonist)	Vasodilation (α-blocker)
	Bethanecol, Neostigmine : • Gastroparesis • Post-operative ileus	Pirenzepine, Telenzepine : Peptic ulcer disease	Spinal anaesthesia induced hypotension : • ↓ HR : Ephedrine • Normal HR : Phenylephrine	Pre-op HTN in Phaeochromoytoma : Phenoxybenzamine (DOC) (F/b β-blocker : Prevents arrhythmia)
		Anti-spasmodics : • Glycopyrrolate, • Dicyclomine (m/c) • Scopolamine	Postural hypotension : Midodrine (DOC)	Phentolamine (IV) : DOC • Cheese reaction (MAO ⊖ + Cheese/wine) • Clonidine withdrawal HTN. • Intra-op HTN in pheochromocytoma
			Cardiogenic, septic, neurogenic shock : Norepinephrine (DOC)	HTN with BPH : Terazosin, Doxazocin, Prazosin (DOC : Scorpion bite)
			Anaphylactic shock : Epinephrine (DOC) • Im route : 0.3 to 0.5 mg (1 : 1000 dilution) • IV route : ↑ Risk for V-fib	β-blockers : HTN in young age
Bladder detrusor	Contraction (m_3 ⊕)	Relaxation (m_3 ⊖)	Relaxation (β_3 ⊕) Bladder sphincter : Contracts (α)	-
	Bethanechol, Neostigmine : • Post-op urinary retention • Bladder atony/ overflow incontinence.	Overactive bladder (Urge incontinence) : • Fesoterodine • Darifenacin • Oxybutinin • Solifenacin → m_3 selective • Tolterodine, Trospium (⊗ BBB) • S/E : Dementia (Via m_1); Least in : Darifenacin/ Solifenacin, Trospium	• Overactive bladder (Urge incontinence) : Mirabegron (DOC) (β_3 agonist) • Stress incontinence : Duloxetine (SNRI)	-
Skeletal muscles	Contraction	Relaxation	Contraction	Relaxation

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

	Parasympathomimetic	Parasympatholytic	Sympathomimetic	Sympatholytic
Skeletal muscles	Edrophonium (DOC) 💊 : • Tensilon test : For Dx of myasthenia gravis (MG) • Myasthenic vs. cholinergic crisis (Dx)	NDMR (NM receptor blocker) : Muscle relaxants	β_2 agonists : • Tremor : S/e • Clenbuterol : Performance enhancer (Banned)	β-blockers : ↓ Exercise tolerance
	Neostigmine : Dx & Rx of MG – Cobra bite – NDMR reversal			
	Pyridostigmine (DOC) 💊 : Mx of MG			
	Pre-medication atropine before edrophonium/neostigmine : Prevent muscarinic s/e			

Side Effects Of Drugs

00:30:30

Drugs	Symptoms	Treatment
Cholinergic poisoning	• Miosis : Pin-point pupil • Salivation, Sweating ↑ • Involuntary urination/defecation • Bradycardia	• Atropine + Pralidoxime : OP poisoning • Atropine only : Carbamate poisoning
Anticholinergic poisoning (Atropine, Datura)	• Mydriasis • Dry mouth • Urine retention/constipation • Tachycardia • Hyperthermia, dry skin	Physostigmine
β-blockers	• Bronchospasm • Bradycardia • Insomnia, nightmares • Blocks hypoglycemia symptoms • Exercise intolerance	Glucagon (Source of cAMP for the heart)
α-blockers	• Postural hypotension • Ejaculation abnormality • Floppy iris	–

Miscellaneous

00:32:33

Cardioselective β-blockers : Mr. BEAN Cardiologist.

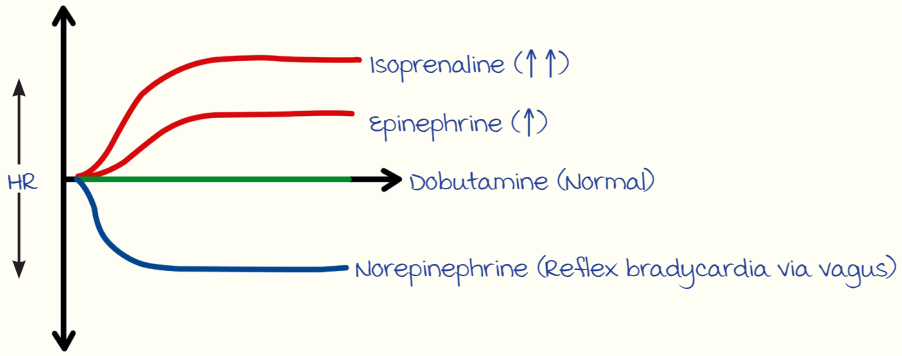
- Metaprolol.
- Betaxolol, Bisoprolol.
- Esmolol (Shortest acting).
- Atenolol, Acebutolol.
- Nebivolol ⟶ Most cardioselective, Antioxidant action ⊕.
- Celiprolol.

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

β-blockers With :

1. α-blockers (vasodilatation) : Carvedilol, Labetalol (m/c).
2. No release : Nebivolol.
3. Calcium channel blocker : Carvedilol.
4. Longest action : Nadolol.

Effect Of Catecholamines On HR :



Note : NE with atropine/transplanted heart = ↑↑HR.

Dopamine :

Use similar to NE

Dose dependant action :

Continuous IV infusion.

Dose (mcg/kg/min)	Effect (Receptor)
0-2	Diuresis (D_1)
2-10	↑Contraction of heart (β_1)
>10	Vasoconstriction (α_1)

Epinephrine Dilution :

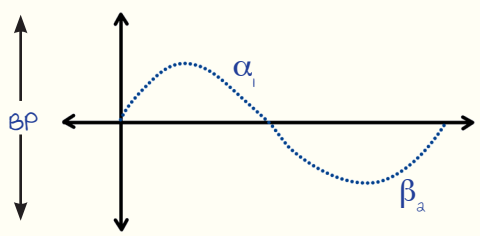
Dilution	Route of administration
1 : 1000	S/c, Im; Endotracheal
1 : 10,000	IV; Intraosseous, Intracardiac (Not used)
1 : 100,000	Local; vasoconstriction
1 : 100,000 or 1 : 200,000	Local (With lignocaine)

Blood Pressure Effects

00:38:44

Dale's phenomenon :

Threshold concentration of epinephrine for $\alpha_1 > \beta_2$.



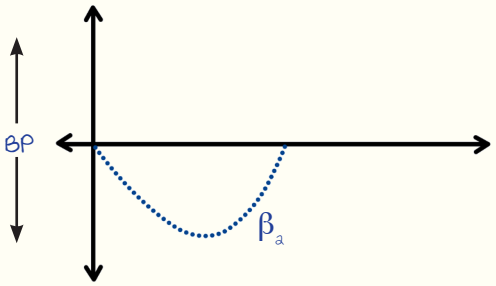
Biphasic response :

Initial high conc : ↑BP (α_1 mediated) —Drug metabolism and excretion→ Later, low conc : ↓ BP (β_2 mediated)

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

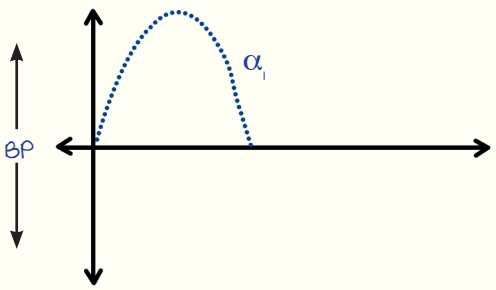
Vasomotor reversal of Dale :

- Epinephrine + α blocker in living system.
- Only ↓ in BP d/t unopposed β2 action



Vasomotor re-reversal of Dale :

- Epinephrine + β-blocker in living system.
- Steep ↑ in BP d/t unopposed α_1 action.



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DRUGS ACTING ON CARDIOVASCULAR SYSTEM : PART 1

Anti-arrhythmic Drugs

00:00:14

SVT & PSVT

- Arising from atrium.
- Aim : Block AV node (Prevent conduction into ventricles).

Drugs : ABCD

IV drugs :
- Acute attack
- ↓BP

- A : Adenosine
- B : Beta blocker
- C : CCB (Diltiazem/Verapamil)
- D : Digoxin

Oral (Chronic mx)

Order of preference

mx :

a. SVT/PSVT :

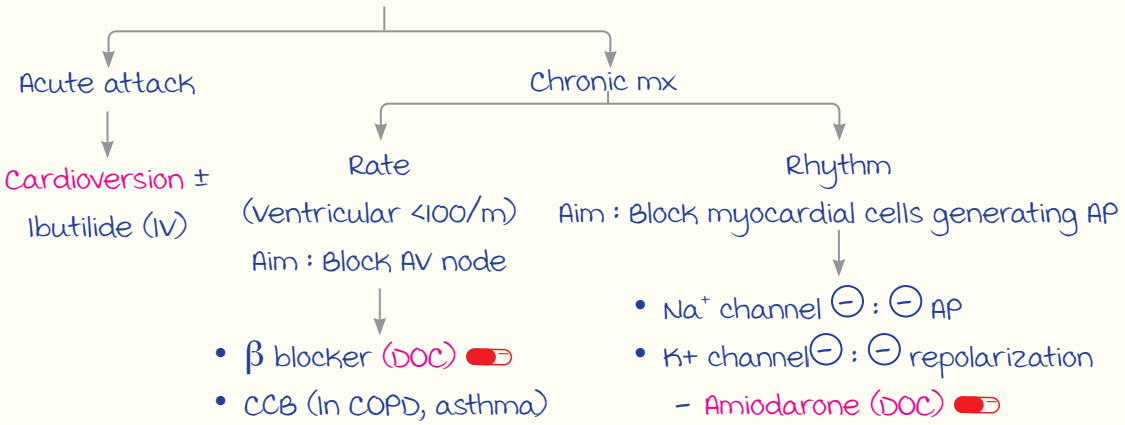
- ↓BP (Unstable) → Cardioversion
- Normal BP (Stable) → Carotid massage (↑Vagal)
  - H/o asthma/COPD
    - Absent → Adenosine (DOC)
      - IV rapid push.
      - Adults : 6 mg.
      - Children : 0.1 mg/kg
    - Diltiazem/Verapamil

Note :

- Adenosine, β blocker : S/e → Bronchoconstriction (C/I : Asthma).
- Adenosine : S/e → A. fibrillation.
- Digoxin indication : SVT/PSVT + Chronic CHF.

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

b. Atrial fibrillation :



VENTRICULAR FIBRILLATION & TACHYCARDIA

V. tachycardia : Block myocardial cells.

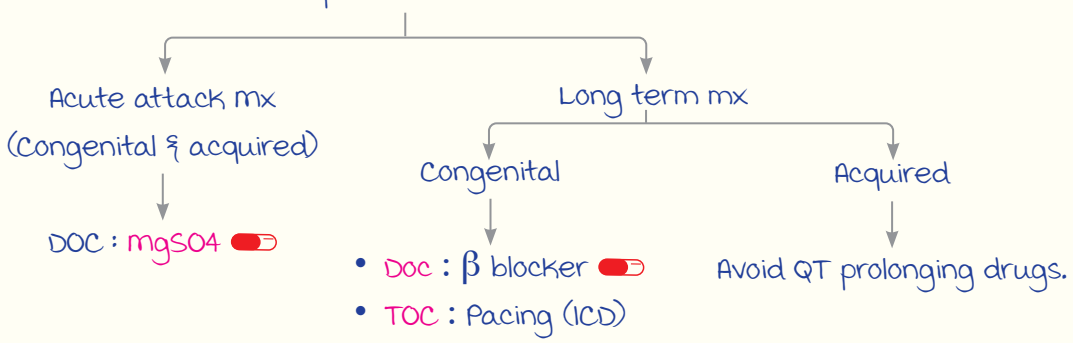
- Na^+ channel ⊖
- K^+ channel ⊖
  - Amiodarone (DOC)
    - Exception

Digoxin/Ischemia-induced V. tach/V. fib : DOC Lidocaine

V. fibrillation : Defibrillation (TOC).

LONG QT SYNDROME

Can cause Torsades de pointes (Fatal).



WPW SYNDROME

Cause : Anatomical accessory pathway.

- Acute mx : IV Procainamide.
- Long term mx :
  - DOC : Flecainide (S/E → most arrhythmogenic).
  - TOC : Radiofrequency ablation of accessory pathway.

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

Drugs in Heart Failure

00:27:30

ACUTE

m/c cause : MI (m/c of LV).

Mx :

- ↓LV contraction → DOC : IV Dobutamine (maintains N HR, No ↑O_2 demand) → No response → PDE 3 ⊖ : Milrinone (Inodilator)
- Pulmonary edema → DOC : IV Furosemide → Alternative :
  - Nitroglycerine.
  - BNP analogues.

BNP analogue :

- Nesiritide (IV).
- Metabolized by : Neprilysin (Neutral endopeptidase).

Neprilysin ⊖ : (↑BNP)

- Sacubitril
- Formulation : Sacubitril + Valsartan
- Rx : Chronic CHF
- S/E : Angioedema → C/I : ACEI.

Omapatrilat :

- NEP ⊖ + ACE ⊖
- Not used (Banned).

CHRONIC

Drugs :

- For symptomatic Rx:
  - Furosemide
  - Digoxin
- To ↓mortality : SHIVA Beta
  - Sacubitril .
  - Spironolactone.
  - SGLT 2 ⊖ (-gliflozines).
  - Hydralazine.
  - Ivabradine.
  - Vericiguat (↑cGMP).
  - ACEI/ARB.
  - β blocker.

Mx of new case orally :

1st : Furosemide (symptomatic) → x 1 week → 2nd : ACEI/ARB

OR

Sacubitril + Valsartan (Preferred) → 3rd : β blocker (BCMN)

- Bisoprolol
- Metoprolol
- Carvedilol
- Nebivolol

Hypertension

00:41:50

Mild to moderate HTN :

	<55 yr (Young)	≥55 yr (Old)
Pathology	• Normal vessel • ↑Renin	• Calcified, atherosclerotic (Stiff) • ↓Renin
Drugs	• DOC : ACEI/ARB • Beta blocker	• DOC : CCB (Amlodipine) • Diuretics (Thiazides) : Chlorthalidone

Mx :

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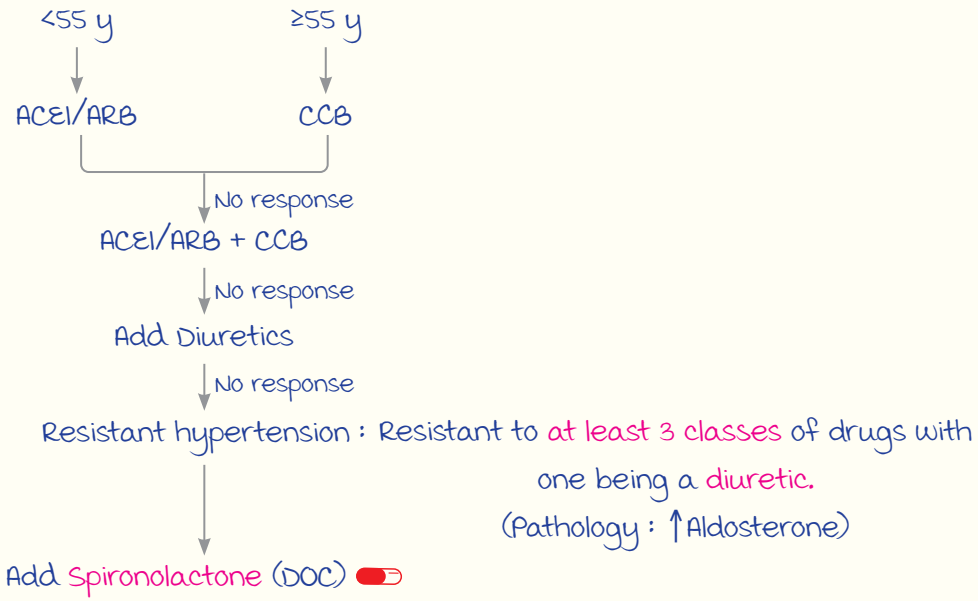


Drugs for HTN with co-morbidities (Irrespective of age) :

- DM.
- CKD.
- Nephrotic syndrome.
- Scleroderma.

→ ACEI/ARB

- Osteoporosis
- Renal stones/colic

→ Thiazides (↑Ca^{2+} absorption from tubules)

- Migraine.
- Hyperthyroidism.
- Stable angina.
- Anxiety disorder.
- Essential tremor.

→ Beta blocker

- Raynaud's disease.
- Cyclosporin induced HTN.

→ CCBs

- BPH → α ⊖ : Prazosin

Severe Hypertension :

	Hypertensive emergency	Hypertensive urgency
BP	↑	≥220/125 mmHg
End organ damage	⊕	⊖
Drugs	IV drugs : HELEN Dance • Hydralazin • Esmolol • Lasix • Labetalol : (DOC pregnancy) • Enalapril • NTG • Nitroprusside • DHP – Clevidipine – Nicardipine (DOC)	Oral drugs • DOC : Clonidine • ACEI/ARB • CCB

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

DRUGS ACTING ON CARDIOVASCULAR SYSTEM : PART 2

Drugs Used in Angina

00:00:06

STABLE & PRINZMETAL ANGINA

Acute angina Rx : S/L NTG (DOC).

Long term mx :

- Stable (↓Preload)
  - ↓Acute attack
    - CCB
    - Long acting nitrates
    - Beta blockers (Best)
    - Ivabradine
    - Ranolazine
    - Nicorandil
    - Trimetazidine
  - ↓Mortality
    - Statins
    - Aspirin
    - ACEi/ARB
- Prinzmetal (Coronary vasospasm)
  - DOC : CCB
  - Long acting nitrates : S/E → Postural hypotension

Ivabradine :

- MOA : (−) Funny channel/IF current
  - (−) SA node
  - ↓HR, normal contraction. (Bradycardiac drug)
- S/E :
  - Luminous phenomenon. (Colored halos)
  - ↑A-fib.

Ranolazine :

- MOA : (−) Late inward Na^+ channel.
- S/E :
  - ↓Resistance to insulin (↑HbA1c).
  - ↓Risk of A-fib.

Trimetazidine : (Antimetabolite)

MOA : (−) Partial FA oxidase (P-Fox)

- (−) TG metabolism
- ↑Glycolysis (Less ATP)
- ↓Oxygen demand.

Nicorandil : K^+ channel opener

Fasudil : (−) Rho-Kinase

} Vasodilator

Side Effects of Anti-anginal Drugs

00:08:24 ----- Active space -----

Amiodarone :

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

- Pulmonary fibrosis : C/I in ILD; baseline CXR done.
- Corneal microdeposits : Whorl-like, asymptomatic.
- Blue colored skin (Ceruloderma) : Sunscreen.
- Myocarditis.
- Liver toxicity : Baseline LFT done.
- Neuropathy.
- Alpha receptor ⊖ causes hypotension.
- Photosensitivity (Brown skin) : Sunscreen.
- Thyroid (Hypo > hyper) : Baseline TFT done.

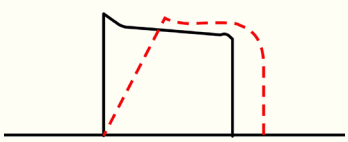
Note : Anti-arrhythmics

- Longest acting : Amiodarone.
- Shortest acting : Adenosine.

Anti-Arrhythmics Causing QT Prolongation/Torsades :

Class Ia :

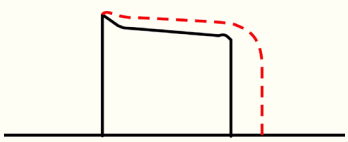
- Quinidine.
- Procainamide.
- Disopyramide.



- Na^+ & K^+ channel ⊖.
- Delay in repolarisation & depolarisation.

Class III :

- Sotalol.
- Amiodarone.
- Dronedarone.
- Dofetilide.
- Ibutilide.
- Vernakalant.



- Only K^+ channel ⊖.
- Delay in repolarisation.

Note : Drugs causing ↑QT.

- Quinidine.
- Quetiapine.
- Methadone.
- Moxifloxacin (Max. QT prolongation among FQs).
- Macrolides.
- Mycobacterial drugs : Bedaquiline, Delamanid.
- Muscarinic (H_1) receptor ⊖ : Aztemizole, Terfenadine.

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

DIGOXIN

S/E :

Mnemonic : DIGOXIN.

- Dialysis, defibrillation C/I.
- Increases K^+.
- Gynaecomastia.
- Ocular S/E : Green halos.
- Xanthopsia : Yellow vision.
- Increases risk of arrhythmia (m/c : V. bigeminy).
- Nausea/vomiting

Antidote : Digibind

MOA : Blocks Na^+/K^+/ATPase.

C/I :

- Increased risk of toxicity.
  Mnemonic : KMC in Manipal Rocks
  - $\downarrow K^+$.
  - $\downarrow Mg^{a+}$.
  - $\uparrow Ca^{a+}$ (Increase).
  - MI.
  - Renal failure.
- WPW syndrome :
  AV node ⊖ → ↑WPW pathway.
- HOCM :
  ↑Contraction worsens LV outflow tract obstruction.

RAAS INHIBITORS

ACEi :

- Angioedema
  (Laryngeal edema → Tracheostomy).
- Dry cough.

DRI :

- Aliskiren.
- Direct renin ⊖.

ARB :

Losartan :

Mnemonic : PUT

- PPARr ⊕ : ↓insulin resistance.
- ↑Uric acid excretion :
  HTN with gout 💊 DOC.
- Thromboxane A_a ⊖ : Antiaggregant.

Telmisartan :

Max insulin resistance : HTN with DM 💊 DOC

C/I of RAAS ⊖ :

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

CALCIUM CHANNEL ⊖

- Headache.
- Ankle edema d/t amlodipine.
  ↓
  Prevention : + ACEi/ARB
- Constipation : Verapamil.
- AV block : Diltiazem/Verapamil.
  ↓
  💊 C/I with beta blockers
  (Causes total conduction block → Asystole)

Hypolipidemic Drugs

00:26:31 ----- Active space -----

Aims :

1. ↓LDL (In atherosclerotic CVD).
   - Statins 💊 DOC
     ↓ Inadequate response
   - Bempedoic acid.
   - Ezetimibe.
   - Inclisiran.
   - PCSK-9 ⊖.
   - Bile acid binding resins.
   - Lomitapide.
2. ↓TG (To avoid pancreatitis)
   - Fibrates.
   - Icosapent.
   - Omega 3 fatty acid.
3. ↑HDL
   Niacin : Max ↑HDL
   (Last drug to ↓LDL, VLDL).

STATINS

- Most potent : Pitavastatin > Rosuvastatin 💊
  ↓ Ceiling effect ↓ DOC (max ↓LDL).
- Longest acting : Rosuvastatin > Atorvastatin.
- All metabolized by CYP450 except : Pravastatin 💊.
  ↓
  DOC : Protease inhibitors causing dyslipidemia
  (Enzyme ⊖ → Statin toxicity)

MOA :

- Hypolipidemic effect :
  (⊖ HMG CoA reductase).
  - ↓LDL, VLDL, TG.
  - ↑HDL, Lipoprotein-A.
- Pleiotropic effects : (All except ↓LDL)
  - Antiaggregant, anticoagulant.
  - Anti-inflammatory, antioxidant.
  - ↑NO.
  - Plaque stabilization.

Uses :

- DOC : 💊
  - Type II hyperlipoproteinemia.
    (Familial hypercholesterolemia).
- Primary & secondary prophylaxis of MI and stroke (ASCVD).
- Night time dosing, except :
  - Rosuvastatin. } Very long acting.
  - Atorvastatin. }

S/E :

- Myopathy.
- Hepatotoxicity.
- Insulin resistance.

C/I :

- Pregnancy.
- Children :
  - <10 yrs.
  - <8 yrs (Pravastatin).

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

Drugs	MOA (Imp)	Uses	S/E
Bempedoic acid	⊖ ATP citrate lyase : • ↓Cholesterol synthesis. • ↓LDL.	Add on to statins	-
Bile acid binding salts : • Cholestyramine. • Colestipol. • Colesevelam.	⊖ Enterohepatic circulation of bile acid : ↓LDL	• Add on • Preferred : - Pregnancy. - Children.	• Hypertriglyceridemia. • Hyperchloremic acidosis. • GI upset. • ↓Absorption of other drugs. • Least with Colesevelam.
PCSK-9 ⊖ : • Evolocumab. • Alirocumab.	Prevent LDLr degradation : • ↓LDL (max). • ↓Lipoprotein-a.	Add on	-
↓PCSK-9 synthesis : Inclisiran.	Is a small interfering RNA → Breaks PCSK-9 mRNA : ↓LDL		
Evinacumab	Blocks angiopoietin like protein 3 & LPL : ↓LDL, TG.	Familial hypercholesterolemia	-
Lomitapide	Block MTP (microsomal triglyceride transport protein).		
Fibrates : • Clofibrate. • Fenofibrate. • Bezafibrate. • Gemfibrozil.	⊕ PPAR-α, ↑LPL synthesis : • ↓TG, chylomicrons. • ↓VLDL.	DOC : • Hypertriglyceridemia. • Chylomicronemia syndrome.	• Cholelithiasis. • Myopathy.
Icosapent	• ↓TG rich VLDL synthesis by liver. • ⊖ Platelet aggregation → ↓CVS mortality.	• Hypertriglyceridemia. • Add on to statins.	-
Niacin	↓Hormone sensitive lipase synthesis.	Dyslipidemia with ↓HDL.	Toxicity : • Hepatotoxicity. • Insulin resistance. • Flushing. ↳ DOC : Aspirin
Ezetimibe	• ⊖ NPC_1L_1 receptor (Small intestine). • ⊖ Cholesterol absorption.	Add on to statins.	-

Note : Lipoprotein-A
- ↑ : Statins.
- ↓ : Niacin, PCSK 9 ⊖.

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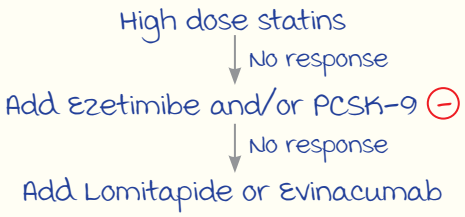
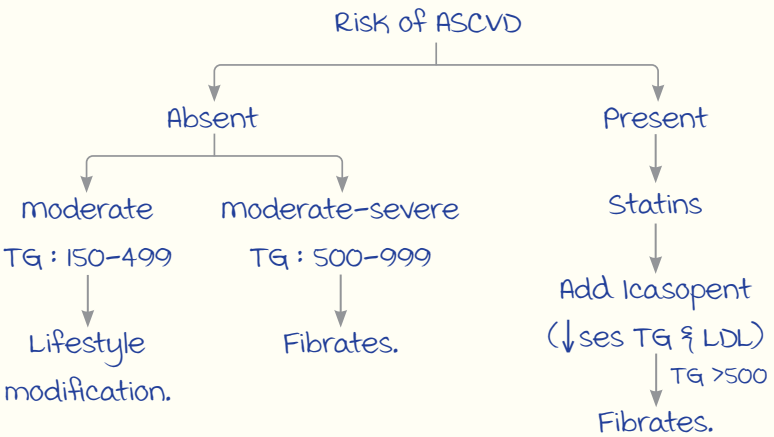
mx :

High LDL :

Familial hypercholesterolemia :



Hypertriglyceridemia :



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DRUGS ACTING ON KIDNEY

Diuretics

00:00:05

	MOA & site	Uses	Side effects	
Carbonic anhydrase inhibitors	Blocks carbonic anhydrase in PCT.	• Acetazolamide (DOC) 💊 : Acute mountain sickness. • Acetazolamide/Dichlorphenamide : Familial hypokalemic periodic paralysis.	• $\downarrow K^+$. • Metabolic acidosis. • Renal stones ⊕. • Hypersensitivity : Rash, BM suppression. • $NH_3\uparrow$: C/I in liver cirrhosis.	
Loop diuretics (C/I with amino-glycosides)	• Blocks Na^+-K^+-$2Cl^-$ pump in thick ascending limb. • Indirect vasodilators : ↑Prostaglandins.	• Furosemide 💊 : DOC for pulmonary edema, renal insufficiency. • Torsemide : Longest acting. • Bumetanide : Most potent. • Ethacrynic acid : Most ototoxic. • Most useful drugs when GFR <40.	• $\downarrow K^+$. • Metabolic alkalosis. • ↑Uric acid. • ↑Glucose. • $\downarrow Mg^{2+}$.	• $\downarrow Ca^{2+}$: Rx of hypercalcemia • Ototoxic : C/I with aminoglycoside.
Thiazides	• Blocks Na^+-Cl^- cotransporter in DCT. • Direct vasodilators • Open K^+ channels.	• DOC for : – HTN with edema. – Nephrogenic DI. – Other edema (As add on). • Chlorthalidone 💊 : Long acting, preferred in HTN. • Indapamide : Hepatic excretion. • Metolazone : Effective if GFR <40, add-on to furosemide		• $\uparrow Ca^{2+}$: Rx HTN with osteoporosis/ renal stones. • C/I in HTN with DM/gout (↑Uric acid & glucose)
Potassium sparing diuretic	• Spironolactone/ Eplerenone : Blocks aldosterone. • Amiloride : Blocks ENaC in collecting duct.	Spironolactone/Eplerenone 💊 : • DOC in resistant HTN & cirrhotic edema (+ Furosemide). Amiloride 💊 (DOC) : • Lithium induced DI. • Liddle syndrome.	• $\uparrow K^+$. • Metabolic acidosis. • Spironolactone : Gynecomastia.	
Osmotic diuretics	Solute free water loss : PCT & loop.	Mannitol 💊 (Mnemonic : ABCDE) • Acute congestive glaucoma. • Braking of diuretics. • Cerebral edema. • Dialysis disequilibrium. • Expected renal failure (Impending).	• $\uparrow/\downarrow K^+$. • $\uparrow/\downarrow Na^+$. • Pulmonary edema. • C/I in existing renal failure.	

Vasopressin Related Drugs

00:15:00

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

Drug	Uses	Side effects
Vasopressin antagonist :		
• Conivaptan (IV). • Tolvaptan • Mozavaptan } Oral.	SIADH : 3rd line → Vasopressin antagonists. Rx : • Free H_2O restriction : 1st line. • Saline infusion : 2nd line.	• Hypokalemia. • Hepatotoxicity (Tolvaptan).
Vasopressin analogs :		
• Vasopressin	Not preferred due to ↑toxicity	-
• Terlipressin	DOC in acute variceal bleed	-
• Desmopressin	• Central DI. • Nocturnal enuresis. • vW disease → ↑vWF. • Hemophilia A → ↑Factor VIII.	-

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

DRUGS ACTING ON CENTRAL NERVOUS SYSTEM

Anti-Epileptic Drugs

00:00:10

Epilepsy	DOC
• GTCS • Myoclonic seizure (JME)	Valproate
Absence seizure	Ethosuximide (Alternative → Valproate)
• Partial seizure • Rolandic epilepsy	Carbamazepine
Mixed seizure syndrome : • Lennox Gastaut Syndrome (LGS) • Dravet Syndrome (DS)	Valproate
Seizure in neonates	Phenobarbital
Alcohol withdrawal	Lorazepam
Status epilepticus	
Infantile spasm with Tuberous Sclerosis (TS)	Vigabatrin
Infantile spasm without TS or Salaam spasm (West syndrome)	ACTH

Valproate

MOA :
- ⊖ Ca^{2+} channel.
- ⊖ Na^{+} channel.
- ⊖ GABA transaminase → (↑GABA).

Cannabidiol

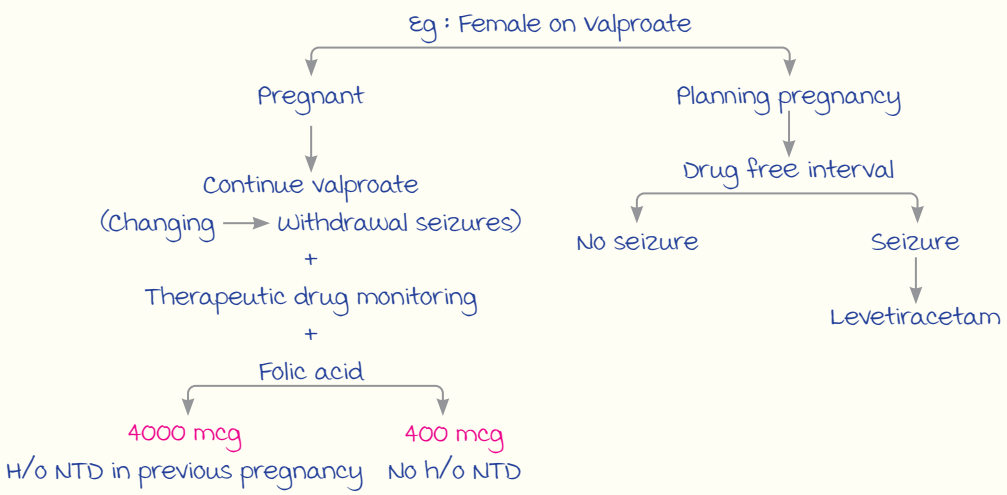
- Uses : LGS, DS, TS.
- S/E : Hepatotoxic.
- C/I : Children <2 yr.

In Pregnancy :

Teratogenicity

- Min : Levetiracetam (DOC) < Lamotrigine.
- Max : Valproate (A/w neural tube defects).

Mx :



Psychiatric Drugs

00:07:52

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MANIA

Mania	DOC
• Acute mania • Mania in pregnancy	Atypical antipsychotic : Aripiprazole
• Mania prophylaxis • Bipolar disorder • Hypnic headache	Lithium (Also used to Rx leucopenia)
Rapid cycler (BPD pt. with >4 episodes of mania/depression in 1 yr)	Valproate
Most teratogenic in BPD	Valproate
Least teratogenic in BPD	Lamotrigine

Acute mania mx : Aripiprazole + lithium.

DEPRESSION

Depression	DOC
Depression	1st line : SSRI/SNRI
With insomnia or erectile dysfunction	Mirtazapine (NASSA)
With suicidal tendency	Mnemonic : Life can end • Lithium • Clozapine • ECT
Novel antidepressant	• Vilazodone • Vortioxetine (MSAA)
	Post partum depression : • Brexanolone : (Continuous IV 60 hrs) • Zuranolone : Oral • Ketamine : Intranasal

Withdrawal :

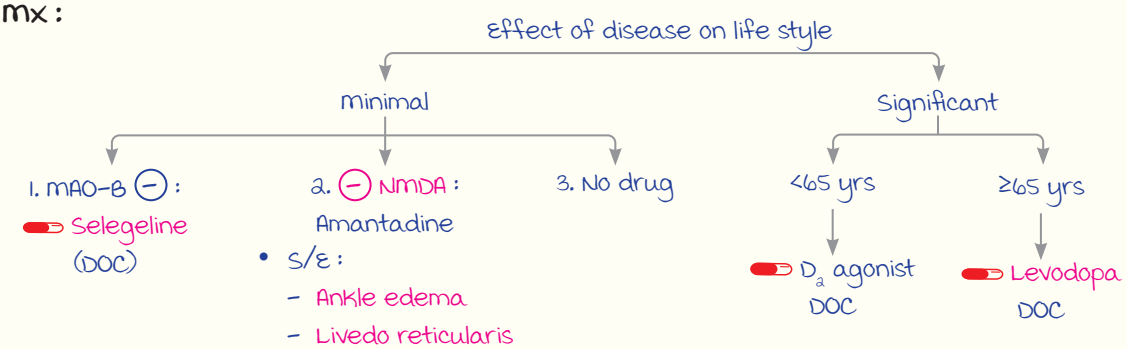
- Seen with :
  - Venlafaxine (SNRI).
  - Paroxetine (SSRI).
- Not seen with :
  - Fluoxetine (SSRI)
    (Longest acting : 10d)

Degenerative Disorders

00:15:00

PARKINSONS DISEASE

Mx :



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

D_a Agonists :

- Oral drugs :
  - Pramipexole.
  - Ropinirole.
  - Rotigotine (Transcranial patch).
- S/E :
  - Fatigue.
  - Compulsive sexual activity.
  - Compulsive gambling.

Levodopa :

- With Carbidopa (⊖ peripheral DOPA decarboxylase).
- C/I : Psychosis (Absolute).
  Angle closure glaucoma (Relative).
- On-off phenomenon :
  💊 DOC Entacapone (COMT ⊖).
- S/E : Mnemonic DOPA
  - Dyskinesis → DOC : Amantadine. 💊
  - Orthostatic hypotension.
  - Psychosis → DOC : Pimavanserin. 💊
  - Angle closure glaucoma (D/t mydriasis).

ALS

Management :

- Muscle spasticity.
- Drugs (Mnemonic : REST Bed).
  - Riluzole (DOC).
  - Edaravone.
  - Sodium phenylbutyrate taurursodiol (SP-T).
  - Tofersen (Only in SOD-1 gene mutation).

  } ⊖ neurodegeneration.
  - Baclofen (GABA B ⊕).

  } Symptomatic relief.

ALZHEIMERS

- DOC : Donepezil 💊
  ↓ No response
  Add Memantine 💊 (NMDA ⊖).
  ↳ Never used as monotherapy.
- New : ⊖ β amyloid proteins (Mild disease)
  - Aducanumab.
  - Lecanemab.
  - Donanemab.

MISCELLANEOUS

Disorder	DOC
Trigeminal neuralgia	Carbamazepine
• Post herpetic neuralgia • Spinal cord injury • Restless leg syndrome	Pregabalin/gabapentin (use : Peripheral neuropathy)
Psychosis	Atypical antipsychotic (Except Clozapine, olanzapine) ↓ Another atypical antipsychotic ↓ Typical antipsychotics (Suffix : -zine/-peridol)

Disorder	DOC
ADHD	Methylphenidate
ADHD with Tourette syndrome	Clonidine
ADHD with family h/o drug abuse	Selective NE reuptake ⊖ : Atomoxetine, Reboxetine
Tics a/w Tourette syndrome Huntington's chorea	Tetrabenazine

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

Migraine & Sleep Disorders

00:31:30

MIGRAINE

Prophylaxis :

- Propranolol (DOC) 💊.
- Topiramate.

Treatment :

1. SHT 1B/1D ⊕
   - (DOC) → Oral : Sumatriptan, Rizatriptan (Fastest oral drug).
     → S/c : Sumatriptan (Overall fastest).
   - C/I : Angina (D/t vasoconstriction).
2. Ergotamines :
   - Very potent vasoconstrictor → Gangrene of organs with end arterial disease.
3. New drugs :
   - SHT 1F ⊕ : Lasmiditan.
   - CGRP ⊖ :
     - Eptinezumab.
     - Fremanezumab.
     - Galcanezumab.

     } S/c for prophylaxis.
   - CGRP receptor ⊖ :
     - Erenumab.
     - Olcegepant 💊.
     - Rimegepant.
     - Ubrogepant.

     } Oral for either Rx/prophylaxis.

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

SLEEP DISORDERS

Narcolepsy : Modafinil DOC.

Insomnia : DOC

- H/o drug abuse/elderly
  - DORA : ⊖ wakefulness
    - Suvorexant
    - Daridorexant
- Others
  - Z compounds :
    - Zolpidem
    - Zaleplon
  - Ramelteon : melatonin ⊕
    - Only sleep induction

Sleep induction & maintenance

Opioids

00:40:56

Condition	Drug	
Opioid dependence	↓withdrawal symptom : • Methadone • Buprenorphine	Prevent relapse : • Naltrexone
Labour analgesia	• Morphine (DOC) → C/I : Head trauma (↑ICP) • Pethidine	
Opioid induced constipation	Methyl naltrexone : DOC	
Post-op ileus	Alvimopan : DOC	
Post anesthetic chills	α_a ⊕ : • Pethidine/meperidine (DOC) • Tramadol	
Opioid contraindicated in MI	Pentazocin	
Opioid toxicity	Naloxone	
Opioid with : Partial agonist (PA) at μ & antagonist at Kappa	Buprenorphine	
PA at μ & full agonist at Kappa	Pentazocine	
5-HT & NE reuptake ⊖	Tramadol	
MAO ⊖	Pethidine	
Rett syndrome	Trofinetide	
Fredrich's ataxia	Omaveloxolone	

Note :

- Constipation.
- Convulsion.
- Constriction of pupil (miosis).

} No tolerance for these side effects.

Mx of Dependencies

00:45:06 ----- Active space -----

ALCOHOL DEPENDENCE

FDA approved Rx :

a). Anti-craving drugs :

LFT
- <3 times ↑ → 1. Naltrexone : Doc (Hepatotoxic)
- ≥3 times ↑ → 2. Acamprosate

b). Aversive Rx :

3. Disulfiram :

⊖ Aldehyde dehydrogenase

↑Acetaldehyde (Toxic)

(Aversion to alcohol)

Non-FDA approved :

- Anti-craving drugs.
- Benzodiazepines.
- Clonidine.
- Topiramate.
- Baclofen.
- Ondansetron.

SMOKING

First Line :

Drugs :

- Bupropion : Anti-depressant.
- Varenicline :
  - Partial agonist at NE receptor ($\alpha_4\beta_2$)
  - most effective.

Nicotine replacement :

- Nasal spray :
  - Needs prescription (Schedule 4).
  - most effective.
- Patch.
- Gums. } Need alkaline saliva for absorption
- Lozenge. }

↓

Do not drink anything 15 min before usage.

Mx :

Maintainence :

- Varenicline.
- Bupropion.
- Nicotine patch.

↓break through cravings :

- Nicotine spray.
- Gum.
- Lozenge.

Second Line :

- TCA.
- Clonidine.
- Cystine.

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

Side Effects of CNS Drugs

00:51:56

ANTI – EPILEPTICS

Valproate : (mnemonic VALPROIC).

- Vomiting & nausea.
- Alopecia.
- Liver toxicity.
- Pancreatitis.
- Rash.
- Obesity : PCOS.
- Increase ammonia.
- Carnitine : Antidote for hepatotoxicity & hyperammonemia.
- Tab : Tremor, teratogenic max.

Phenytoin : (mnemonic HYDANTOIN).

- Hirsutism.
- Hyperplasia of gum.
- Lymphadenopathy.
- Diplopia.
- ↓Vit D (Hypocalcemia).
- Ataxia ⟶ Therapeutic drug monitoring & adjust dosage.
- Nystagmus.
- Teratogenic : Facial clefts.
- Osteomalacia.
- Increased bleeding in Newborn (↓Vit K).

Carbamezapine : (mnemonic HEADS).

- Hyponatremia :
  - Delayed S/E.
  - m/c in elderly.
- Hypersensitivity :
  - Eosinophilia.
  - Aplastic anemia.
  - Agranulocytosis.
- Ataxia.
- Diplopia.
- SJS : HLA B1502 gene.

Oxcarbazepine/Eslicarbazepine :

- ↓Hypersensitivity.
- ↑Hyponatremia.

Lamotrigine :

SJS (Rash) : Started at low dose.

Topiramate : (mnemonic RAM eat less).

- Renal stones.
- Angle closure glaucoma : Eye examination before starting.
- Metabolic acidosis.
- Weight loss.

  Use : Obesity.

ANTI – DEPRESSANTS

Drugs		S/E
SSRI/SNRI	5-HT_2 ⊕	• Anxiety • Insomnia • Vivid dreams • Erectile dysfunction • Delayed ejaculation • Anorgasmia
	5-HT_3 ⊕	Nausea, vomiting
	5-HT_4 ⊕	Loose stools
TCA "Pramine" "Triptaline"	Muscarinic ⊖	• Constipation, dry mouth • Urine retention, mydriasis
	H_1 ⊖	Obesity, sedation
	α_1 ⊖	Postural hypotension

SSRI/SNRI :

- Transient anxiety & insomnia Rx : Benzodiazepines (1 month).
- Secondary use : Premature ejaculation.

TCA :

- C/I :
  - BPH.
  - Glaucoma.
- Toxicity : Bicarbonate.

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

Drugs	S/E
SNRI	-
Mirtazapine H_1 ⊖	Sedation, obesity
Bupropion	Seizure, max anxiety
MAO ⊖	• Cheese reaction • Serotonin syndrome
Trazodone	Priapism

MAO ⊖ :

- Cheese reaction Rx : IV Phentolamine.
- Serotonin syndrome Rx : Lorazepam → Cyproheptadine.

ANTI-PSYCHOTICS

D2 Receptor Block :

- EPS.
- Hyperprolactinemia.
- Max : Risperidone.
- Min : Clozapine.
- Zero : Pimavanserin ⊖ SHT_2 (Only drug not acting on D_2).

Other Receptors :

Muscarinic :

- Constipation, urine retention.
- Dry mouth.
- Mydriasis.
- Max : Clozapine > Olanzapine.

H_1 : Sedation.

H_1 & SHT : Obesity.

α_1 :

- Postural hypotension.
- metabolic (Dyslipidemia & hyperglycemia).

Zero S/E (Wt : Neutral)

Mnemonic "ABCZ"

- Aripiprazole.
- Brexpiprazole.
- Cariprazine.
- Ziprasidone.

} Partial agonist : SHT_2 & D_2

Clozapine :

- DOC : Resistant hypertension.
- S/E : Mnemonic SAMOSA.
  - Sialorrhea (Wet pillow).
  - Agranulocytosis.
  - Myocarditis.
  - Obesity.
  - Sedation.
  - Angle closure glaucoma.

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

EPS

EPS	Symptom	Cause	DOC
Akathesia: m/c	Restlessness	Unknown	• Beta blockers : DOC • Benzodiazepines
Acute dystonia (Earliest)	• Abnormal posturing • Facial grimacing	• D_2 ⊖ • metoclopramide inj.	Anticholinergics : DOC • Trihexyphenidyl (Benzhexol) • Benztropine • Biperiden Antihistaminics : Promethazine
Parkinsonism	• Tremor • Bradykinesia		
Tardive dyskinesia (most late)	• Facial dyskinesia : – Tongue protrusion – Lip smacking • Limb dyskinesia : – Piano finger movement – Foot tapping	D_2 upregulation	VMAT-2 ⊖ : • Valbenazine • Deutetrabenazine
Neuroleptic malignant syndrome (most lethal)	• Muscle rigidity • Hyperthermia • ANS instability	D_2 ⊖	• Dantrolene DOC → ⊖ Ryr • Bromocriptine → ⊕ D_2 (most specific drug)

Lithium

01:10:50

Side effects : (Mnemonic HOTHEAD)

- Hypothyroidism.
- Obesity.
- Tremor :
  - Fine : Normal plasma conc.
  - Coarse : Toxicity.
- Hypercalcemia (↑PTH).
- Ebstein anomaly : C/I pregnancy (1st trimester).
- Acne.
- Diabetes insipidus (Thirst).

Interaction :

- Thiazide > K^+ sparing diuretic.
- Vomiting, diarrhea.
- Fasting.

} ↓S. Na → ↑Li tubular reabsorption.

Therapeutic drug monitoring:

- Sample taken 12 hrs after last dose + 6th day of Rx.
- Doses (mEq/L) :
  - Prophylaxis of mania : 0.6 – 1.
  - Acute mania : 1 – 1.5.
  - Toxicity : >1.5.
  - Dialysis : >4.

Side Effects of Opioids

01:14:40 ----- Active space -----

μ receptor effects (mnemonic : MUSCARINE).

- Miosis.
- Urine retention.
- Sedation.
- Constipation, convulsion.
- Analgesia.
- Respiratory depression.
- Increase muscle rigidity.

} Opposite → Withdrawal symptoms.

- No bile flow : Contraction of sphincter of Oddi.
- Euphoria.

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

ANTIBIOTICS : PART 1

Cell wall synthesis ⊖ : (Bactericidal)
- Beta lactams :
  - Penicillins
  - Cephalosporin
  - Carbapenems
  - Monobactams
- Vancomycin (Glycopeptide)
- Bacitracin
- Cycloserine
- Fosfomycin

Protein synthesis ⊖ : (Bacteriostatic)
- Tetracyclins
- Macrolides
- Clindamycin
- Linezolid
- Streptogramin
- Aminoglycosides (Cidal)

Antibiotics

Acting on cell membrane : (Bactericidal)
- Colistin
- Daptomycin (Lipopeptide)

Antifolate :
- Sulfonamides (Static)
- Cotrimoxazole (Cidal)

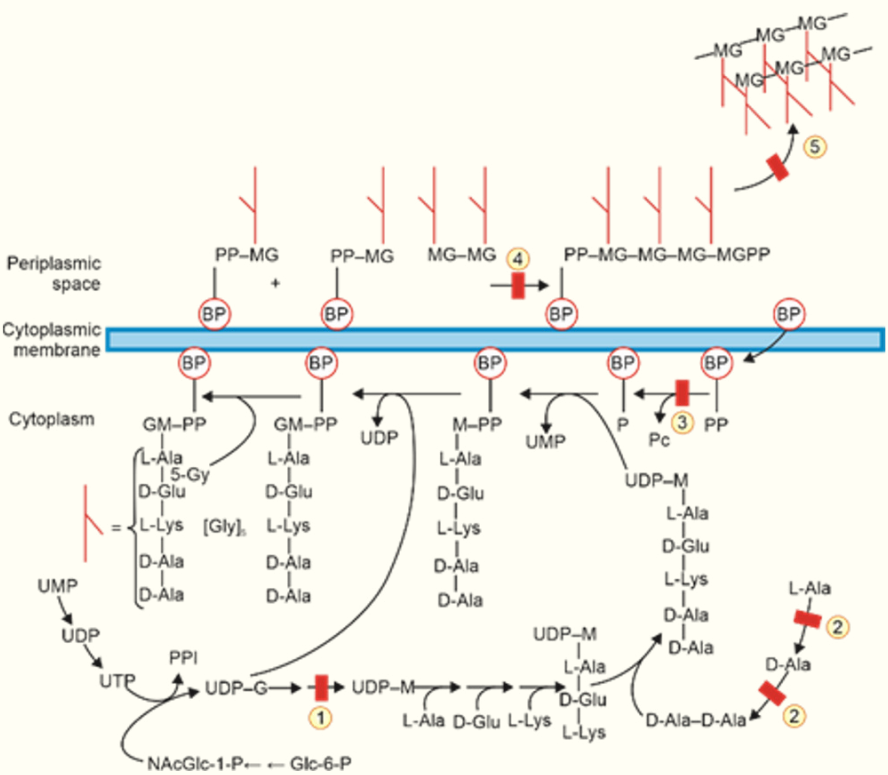
Fluoroquinolones :
Ciprofloxacin (Bactericidal)

Preference : Beta lactams —Resistance→ Vancomycin —Severe Infection→ Add on : Aminoglycoside.

Cell Wall Synthesis Inhibitors

00:04:32

1. Fosfomycin :
   UDP-G ⊘→ UDP-M.
2. Cycloserine :
   L-alanine ⊘→ D-alanine.
3. Bacitracin :
   ⊖ bactoprenol phosphorylation.
4. Vancomycin :
   ⊖ polymerization.
5. Beta-lactams :
   ⊖ crosslinking.



Cell wall synthesis

BETA – LACTAMS

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

Penicillins :

Drug	Use
Benzathine penicillin G : 💊 • I/m • Longest acting (28 days)	DOC : Mnemonic SLY GRAM +ve • Streptococcus • Syphilis • Leptospirosis • Yaws • Gas gangrene • Rat bite fever • Actinomycosis • Meningococcus
Amoxicillin	• Respiratory infection • UTI
Ampicillin 💊	Listeria meningitis (DOC)
Piperacillin	Pseudomonas

Penicillin resistance :

- mediated by β – lactamases (Penicillinase)

Penicillinase resistant penicillin (PRPs) :

Cloxacillin, Methicillin

(⊖ β-lactamase/penicillinase)

↓ Counteracted by : Altered PBP (mec-A gene)

MRSA

↓

💊 Vancomycin DOC

(⊖ d-alanine)

↓ d-alanine → d-lactate

VRSA

↓

💊 Daptomycin DOC.

Note : Rationale for regimes in severe infections.

Eg : Endocarditis → Ampicillin/Vancomycin + Gentamicin (Aminoglycoside).

(Cell wall synthesis ⊖)

CEPHALOSPORINS

Drugs	Uses
1st gen :	
Cefazolin 💊	DOC : Surgical prophylaxis
3rd gen :	
Ceftriaxone 💊 (Paraenteral)	DOC : • Typhoid • Meningitis (Empirical) • Gonorrhea
Cefixime	Typhoid (Oral DOC)
Ceftazidine	Pseudomonas (DOC)
Cefoperazone	Pseudomonas
4th gen :	
• Cefepime • Cefpirone	• Pseudomonas • Enterobacter • ESBL • Typhoid • Meningitis • Gonorrhea (Extended Spectrum β – lactamase)
5th gen	
• Ceftobiprole 💊 • Ceftaroline	• MRSA • Typhoid • Meningitis • Gonorrhea

Note :

- 2nd gen cephalosporins not used.
- Severe pseudomonas Rx : Ceftazidine + Gentamicin

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

CARBAPENEMS

Imipenem 💊 :

- Combined with Cilastatin → ⊖ renal dihydropeptidase (↓ imipenem metabolism).
- DOC :
  - ESBL.
  - Acinetobacter.
  - Serratia.
  - Enterobacter.

MISCELLANEOUS

Drug	Use
Bacitracin (Ointment)	Staph. nasal carriers
Cycloserine	Second line TB
Fosfomycin	UTI

Note : Last line drugs (Resistance)

- Linezolid : VRE.
- Streptogramin : Reserved for last.
- Daptomycin : VRSA.

} Gram positive.

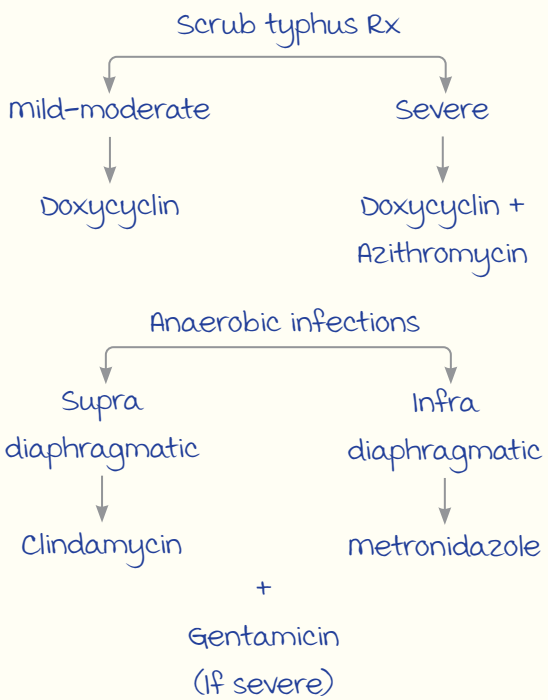
- Colistin : MDR gram -ve organisms.

Protein Synthesis Inhibitors

00:24:24

Drugs	Uses
Tetracycline	
Doxycycline : • Least nephrotoxic. • C/I pregnancy & children.	Mnemonic : My Pink RBC. • Mycoplasma (STD). • Plague prophylaxis. • Rickettsia : Scrub typhus. • Borrelia, Brucella. • Chlamydia, Cholera.
Macrolides	
Erythromycin 💊	DOC : • Pertussis. • Diphtheria.
Azithromycin 💊	DOC : • Chlamydia. • Legionella. • Mycoplasma. } Atypical pneumonia. • Campylobacter. • Chlamydia, cholera in pregnancy. • Cholera in children.

Note :



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Drugs	Uses
Clindamycin	• Toxic shock syndrome DOC : (Cidal drugs ↑toxin release). • Anaerobes.
Aminoglycoside As monotherapy, not active against : • Anaerobes. • Typhoid. • Gram positive organisms.	• monotherapy : Gram negative. • Add on for : – Gram positive/negative. – Aerobe/anaerobe. • DOC : – Tularemia, Plague } Gentamycin or streptomycin

Antifolate drugs

00:35:42

Well concentrated in urine : UTI.

Used against protozoa.

SULFONAMIDE

Drugs	Uses
Sulfadiazine + Pyrimethamine (Teratogenic)	DOC : Toxoplasmosis
Sulfadiazine (Topical)	DOC : • Burn prophylaxis • Fungal keratomycosis
Cotrimoxazole : Trimethoprim + Sulphamethoxazole (1:5 ratio)	DOC : Mnemonic : (Cautery PINS) • Cystitis • Cyclospora • Cepacia burkholderia • Pneumocystis • Isospora • Nocardia • Sarcocyst • Stenotrophomonas

Note:

- Toxoplasmosis in pregnancy : Spiramycin.
- Stenotrophomonas Rx : Cotrimoxazole + ticarcillin.
- Cepacia burkholderia Rx :
  - Cotrimoxazole.
  - Ceftriaxone.
  - Carbapenems.
  - C/I : Colistin.

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

Fluoroquinolones

00:39:54

⊖ DNA gyrase.

Well concentrated in urine & stool.

Ciprofloxacin : 💊

- DOC :
  - Pyelonephritis (Urine).
  - Traveler's diarrhea.
  - Typhoid carrier.
  - Shigella.

  } (Stool).
- Contact of meningococcal meningitis.

Respiratory fluoroquinolones :

- Gemifloxacin.
- Levofloxacin : Max oral bioavailability.
- Moxifloxacin
  - Max $t^{1/2}$.
  - Max mycobacterial activity.
  - Max QT prolongation, seizure.
  - Max hepatic excretion
    (Safe in renal failure; not used in UTI).

Note : Regimen for CAP

Amoxicillin + Azithromycin (G+ & G−) (Atypical org) → (If penicilin resistance) → Respiratory fluoroquinolones → Lefamulin. (Last line)

Side Effects

00:46:20

Drugs	S/E & C/I
Tetracyclines	• S/E : Mnemonic → Tetra PACKET – Photosensitivity – Acute renal failure – Calcium binding (↓bone growth) – Kidney : ↑Urine, Diabetes insipidus – Esophagitis – Teeth : Yellow • C/I : Pregnancy, children, antacids
Aminoglycosides	• S/E : – Nephrotoxicity – Neuromuscular toxicity – Ototoxicity (Outer hair cell : Irreversible) Auditory : Amikacin Vestibular : Streptomycin (+minocycline) • C/I : Pregnancy
Erythromycin (Can be used in pregnancy)	• S/E : Mnemonic → Macro SD Card – Motilin receptor ⊕ : Hypertrophic pyloric stenosis – Skeletal muscle weakness – Diarrhea – Cardiac : QT prolongation – Cholestatic jaundice

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

Drugs	S/E & C/I
Fluoroquinolones	• S/E : Mnemonic → PQRST – Photosensitivity – QT prolongation – Rash – Seizure – Tendonitis, tendon rupture
Linezolid	• S/E : Mnemonic → Bone Marrow – Bone marrow suppression (Monitor platelets) – MAO ⊖ – Mitochondrial toxicity : Optic neuritis, lactic acidosis • C/I : Along with Anti-Ca drugs
Beta lactams : 3rd gen cephalosporin > Amoxicillin	• S/E : – Pseudomembranous colitis – Hypersensitivity a. Type 1 : Rash, anaphylaxis b. Type 2 : Hemolysis
Beta lactams Mnemonic : PMT • Cefoperazone • Cefamandole • Moxalactam • Cefotetan	• S/E : – Disulfiram like reaction – Hypoprothrombinemia (Bleeding)
Imipenam	• S/E : Seizures
Sulfonamides	• S/E : Mnemonic → Folic Acid makes RBC – Fetal Kernicterus – Acute intermittent porphyria – Methemoglobinemia (Cyanosis non responsive to O_2) – Rash – Bone marrow suppression – Crystalluria
Vancomycin	• S/E : – Red man syndrome (Histamine release → Flushing) – Ototoxicity – Nephrotoxicity : Use Matzke nomogram for dosing, based on creatinine clearance

Note :

- Staphylococcal nasal carrier : Mupirocin.
- Pseudomembranous colitis : Fidaxomicin.

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

ANTIBIOTICS : PART 2

Non-Retroviral Drugs

00:00:14

Drugs	Uses	Side effects
Oral Valacyclovir > Acyclovir	DOC : HSV/VZV	-
Topical Acyclovir	Local infections	-
IV Acyclovir	DOC : HSV encephalitis	Crystalluria → Renal failure
Oral Valganciclovir > Ganciclovir	DOC : CMV retinitis	Bone marrow suppression
IV Ganciclovir	DOC : CMV pneumonia	-
Foscarnet	Resistant herpes (Non-responsive to VZV/HSV)	Electrolyte imbalance
Intralesional Cidofovir	DOC : Recurrent laryngeal papillomatosis	-

Disease	DOC	Other drugs
Anti-influenza : A/B/Bird flu	Oseltamivir (Oral) (−) Neuraminidase ↓ Resistance/No response • Inhalational Zanamivir • Rx : 5 days; Prophylaxis : 7 days	New drug : Baloxavir : • (−) RNA polymerase (Endonuclease) • Only Rx : One dose
Anti-hepatitis B :	Tenofovir : • No limited duration • Avoided in hepatic decompensation	IFN-α : • Only 48 weeks (Toxic) • Used in hepatic decompensation
Anti-hepatitis C :	Direct acting agents (Oral) : • Sofosbuvir : NS 5B (−) • Velpatasvir : NS 5A (−) • Paritaprevir : Protease (−)	-
RSV	Ribavarin (DOC)	Prophylaxis : • Palivizumab • Nirsevimab

Antiretroviral Drugs

00:08:06 ----- Active space -----

NRTI

1. Lamivudine → Derivatives → Emtricitabine (Hence not used together) :
   S/e : Pigmentation of palms and soles.
2. Tenofovir :
   - S/e : Nephrotoxic
   - C/I :
     - -Renal failure
     - -Safety unknown in <10 yrs, <30 kg
       → Abacavir used
       (S/E : SJS a/w HLAB5701)

NNRTIs

Nevirapine
DOC : Prevent Perinatal HIV transmission in neonates

Entry Inhibitors

- Ibalizumab (IV) : CD4 ⊖ (HIV I)
- Maraviroc : CCR5 ⊖ (HIV I & 2)
- Fostemsavir : Gp 120 ⊖ (HIV I)
- Enfuvirtide (S/c) : Gp 41 ⊖ (Fusion ⊖)

Integrase inhibitors

- Dolutegravir
- Elvitegravir
- Raltegravir

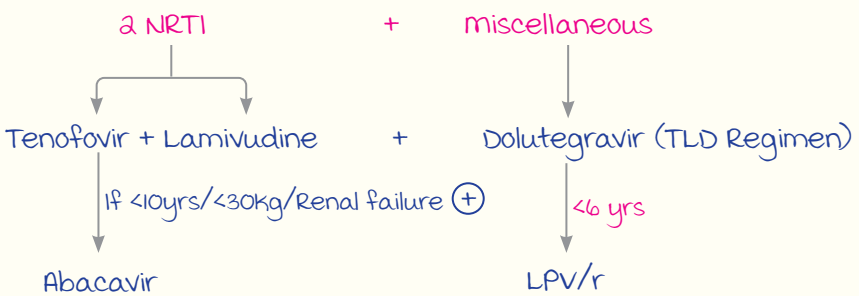
Protease inhibitor

- Used <6 yrs
- Lopinavir :
  Used as LPV/r = 90% LPV + 10% Ritonavir
- Ritonavir :
  - Most potent enzyme ⊖
  - Used as booster : ⊖ metabolism
  - Do not boost : Nelfinavir
- Atazanavir : No dyslipidemia
- Indinavir
  S/e : Renal stones
- Tipranavir
  S/e : Intracranial bleed

Note :

Cobicistat : Used as a booster with → Atazanavir, Darunavir, Elvitegravir.

Regimen (Rx & post exposure prophylaxis) :



Pre-exposure : Tenofovir + Lamivudine.

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

Antifungal Drugs

00:19:44

Amphotericin-B S/e :

- Hypokalemia : KCl for prevention.
- Nephrotoxic :
  - Load pt. with 1-2L NaCl.
  - Combined with liposome.

Candidiasis Rx :

- Oral candidiasis : Clotrimazole.
- Systemic, Non-albicans } Echinocandins (Caspofungin).
- Recurrent vaginal candidiasis :
  - Oteseconazole (Azole).
  - Ibrexafungerp (-β glucan synthase).

Mucormycosis :

- Posaconazole.
- Isavuconazole.
- Amphotericin B.

Drug		DOC
Amphotericin B (IV with 5% dextrose)		• Kala-azar • Mucormycosis • Cryptococcal meningitis
Azoles	Fluconazole	Candida : • Mucocutaneous infection (Except oral) • Albicans
	Itraconazole	• Taenia cruris • Taenia corporis
	Voriconazole	Aspergillosis
Griseofulvin		T. capitis (Oral with fatty food)
Natamycin		Fungal corneal ulcer
Terbinafine		Onychomycosis

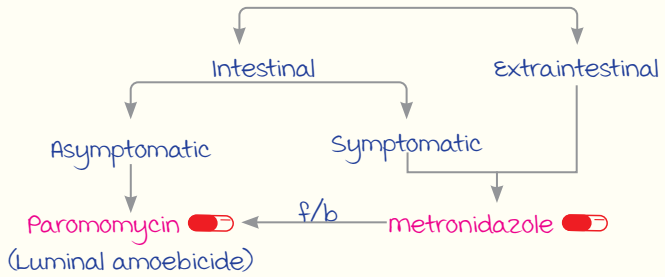
Antihelminthic Drugs

00:27:06

	DOC : Albendazole	Other drugs DOC
Nematodes	• Roundworm, Whipworm, Hookworm } Soil transmitted • Enterobius vermicularis • Trichinella spiralis	• Strongyloides, O. volvulus } Ivermectin • Loa loa : DEC • Filariasis : IDA (Ivermectin, DEC, Albendazole) • Dracunculus : Metronidazole
Cestodes	• Neurocysticercosis 1st drug : Prednisolone (↓edema) • Echinococcus	• Intestinal T. solium, T. saginata, H. nana, D. latum } Praziquantel
Trematodes	-	• Others flukes and schistosoma : Praziquantel • Fasciola hepatica : Triclabendazole

Antiprotozoal Drugs

00:30:52 ----- Active space -----

Disease	mx
Amoebiasis	
Leishmaniasis	Visceral (Kala azar) : • IV : Liposomal amphotericin B • Oral : Miltefosine → DOC : PKADL Cutaneous : • Na^+ Stibogluconate
Trypanosomiasis	African (IV drugs) : • West African : Oral Fexinidazole (DOC) American (Chagas Disease) : • Benznidazole
Cryptosporidiosis	Nitazoxanide : ⊖ PfoR
Babesiosis	Atovaquone + Azithromycin
Toxoplasmosis	Sulfadiazine + Pyrimethamine
• Giardiasis • Amoebiasis • Trichomoniasis • Bacterial vaginosis	DOC : Metronidazole

MALARIA

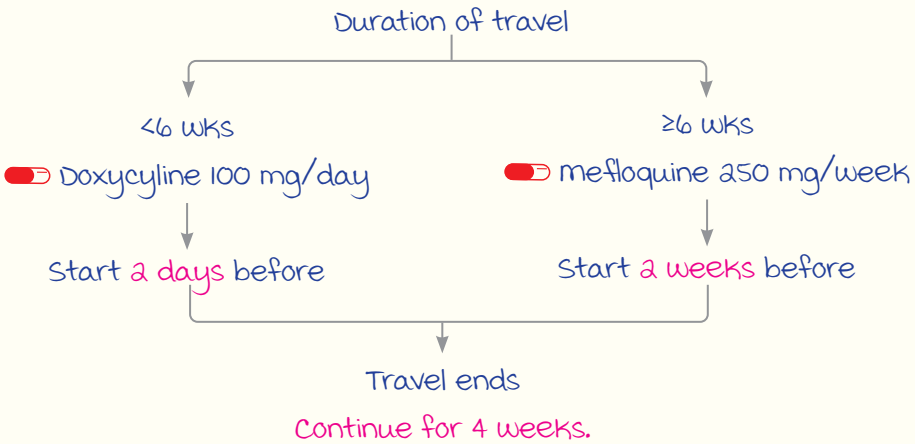
Severe Falciparum malaria :

Doc : IV Artesunate (48 hrs)

	P. vivax	P. falciparum/Resistant P. vivax (ACT)
Uncomplicated malaria	DOC : Chloroquine x 3 days + Primaquine x 14 days OR Tafenoquine x once	• Artesunate + Sulfadoxine + pyrimethamine • Artemether + Lumefantrine : North east India • Quinine + Tetra/Doxy/Clindamycin
Uncomplicated malaria in pregnancy	Chloroquine	• 1st trimester : Quinine + Clindamycin • 2nd trimester : ACT

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

Prophylaxis :



Antitubercular Drugs

00:41:20

FIRST LINE

	Isoniazid	Rifampicin	Pyrazinamide	Ethambutol
MOA	• Activated by catalase peroxidase • ⊖ mycolic acid synthesis	⊖ RNA polymerase	-	-
Action	Cidal	Cidal (max)	Cidal	Static
Target type bacteria	Replicating	Non-replicating/Persisters		Replicating
	Intra + Extracellular		Intracellular	Extracellular
Excretion	Liver	Liver (max) (Safest in RF)	Liver	Kidney (C/I in RF)

Side effects :

Isoniazid (↓Vit B6)	Rifampicin	Pyrazinamide	Ethambutol
• ↓GABA : Euphoria, hallucination, psychosis, neuropathy • ↓Haeme : Anemia • Rx : Vit B_6 • Toxicity : Seizure ↓ – Rx : IV pyridoxine – 1 g for 1 g Isoniazid – max 5 gm	• Red orange secretions/urine (Avoid contact lens) • Respiratory symptoms (Flu-like) with continuous dosing • Permanently stop : – Purpura (↓ Platelet) – Pulmonary syndrome	• Most hepatotoxic • Hyperuricemia • Hip joint pain (Arthralgia)	• Optic neuritis • Red – green color blindness (green > red)

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

SECOND LINE DRUGS

	Bedaquiline	Delamanid	Pretomanid
MOA	⊖ ATP synthase	Free-radical production	
About	Bactericidal, taken with food (↑Absorption)		
Side effects	QT prolongation (C/I : Arrhythmia)		-
Pharmacokinetics	• Sequestered in tissues • $T_{1/2}$: 165 days • Dosing is intermittent : 3d/week	• 99% Plasma protein bound • Metabolised by albumin • C/I : Albumin <2.8	-

Note : Ethionamide (S/e : Hypothyroidism).

Antileprosy Drugs

00:54:38

Ist line :

- Rifampicin : most cidal.
- Dapsone : m/c side effect → Haemolysis in G6PD deficiency.
- Clofazamine side effect → Skin pigmentation, ichthyosis.

2nd line :

- Minocycline.
- Clarithromycin.
- Fluoroquinolones (Cidal).
  - Moxifloxacin.
  - Ofloxacin.

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

DRUGS ACTING ON ENDOCRINE SYSTEM

Antidiabetic Drugs

00:00:10

BASED ON MOA

↑ Insulin Release :

Can cause hypoglycemia (S/e).

1. Sulfonylureas : Glyburide, Gliclazide.
2. Meglitinides : Repaglinide, Nateglinide.
3. GLP-1 agonists :
   Liraglutide (S/c); Semaglutide → DOC for obesity (S/c or oral).
4. DPP-4 inhibitors :
   Sitagliptin, Saxagliptin, Linagliptin (Hepatic excretion → Safe in renal failure).

↓ Insulin Resistance :

MoA : Stimulation of PPAR-γ (Nuclear receptor)

Drugs : Pioglitazone, Rosiglitazone.

Side effects :

- Retention of Na^+ & H_2O → Edema, CHF.
- Bone : Fractures in females.
- Bladder cancer.
- Hepatotoxic.

↓ Hepatic Glucose Production :

Drug : Metformin (Anchor drug for Type 2 DM).

MoA : Activates AMPK → (−) Gluconeogenesis.

Other uses :

- PCOS : for anovulation (But, Doc : Letrozole).
- Non-alcoholic steatohepatitis (NASH).

Side effects :

- Loose stools (Diarrhea).
- Low B_{12}.
- Lactic acidosis.

↑ Urinary Glucose Excretion :

1. SGLT-2 inhibitors : Canagliflozin, Dapagliflozin, Empagliflozin.
2. SGLT-1 & 2 dual blocker : Sotagliflozin.

Side effects of SGLT-2 blockers :

- ↓ BP
- Dehydration
- Diuretic effect

(D/t loss of glucose, Na^+ & water in urine)

(Can be used in CHF)

- ↑Risk of UTI/vaginal candidiasis(D/t glycosuria).
- Rare :
  - Diabetic Ketoacidosis (DKA).
  - Bone fractures (No sex predeliction).

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

↓ Glucose Absorption :

MOA : α-Glucosidase inhibitor (↓ Starch & disaccharide breakdown).

Drugs : Acarbose, Voglibose, Miglitol.

Side effects : Flatulence (m/c), diarrhoea (D/t undigested starch & disaccharide).

Insulin :

Duration of action	Insulin & features	Side effect
Shortest & fastest acting	Afrezza (Inhalational)	Cough, ↑Risk of lung cancer (C/I in asthma, COPD)
Short acting	• Route : S/c • Use : Post-prandial hyperglycemia • Regular : Slow acting (60 min before food) • Glulisine, Aspart, Lispro } Fast acting (15 min before food)	• Hypoglycemia (↑Risk with short acting) • Hypokalemia • Lipodystrophy
Intermediate acting	• Route : S/c • Use : Maintenance • NPH (Cloudy white) • Lente (30% short acting semilente/powder + 70% long acting ultralente/crystal)	
Long acting	• Route : S/c • Use : Maintenance • Glargine : White crystals on combining with other insulin • Detemir • Degludec : Longest acting (OD/BD)	

Insulin Regimen :

1 fast acting (Postprandial ↑glycemia) + 1 long acting (Maintenance).

Amylin Analog :

Drug : Pramlintide

Use : Type 1 DM and Type 11 DM (For postprandial hyperglycemia).

Miscellaneous :

Drugs :

- Colesevelam
- Bromocriptine

} In Type 11 DM.

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

GnRH Related Drugs

00:18:28

GnRH agonists (m/c) : Goserelin, Buserelin, Nafarelin & Leuprolide.

GnRH antagonists : Ganirelix, Abarelix, Cetrorelix & Elagolix.

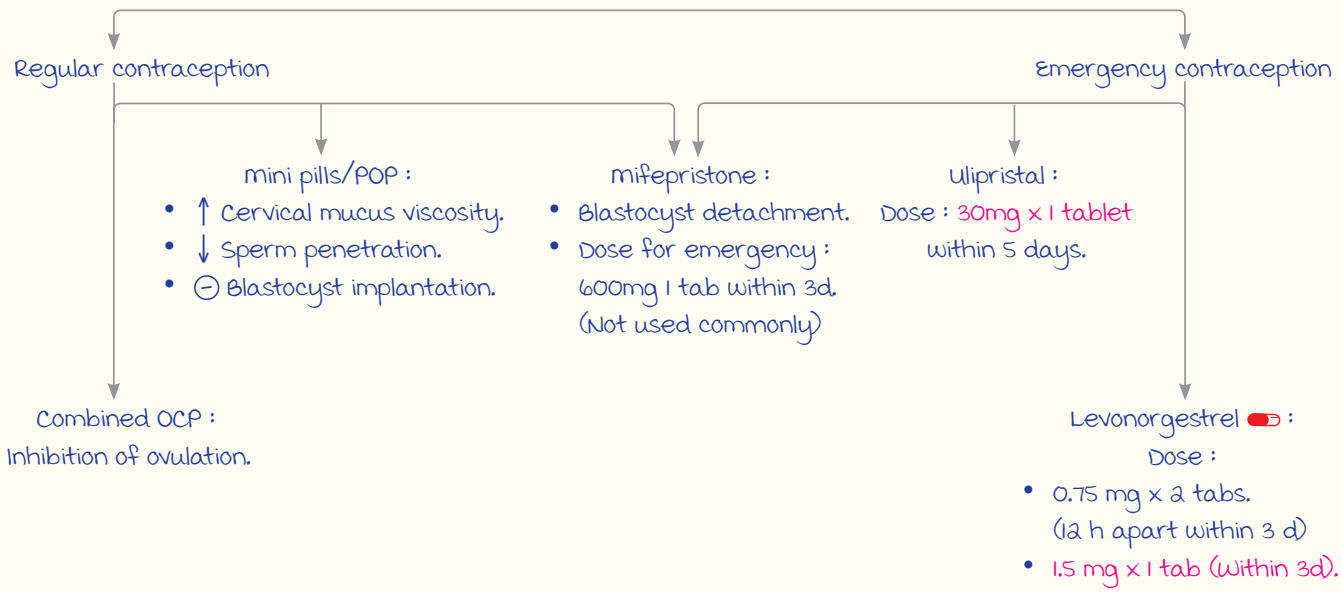
Dosing, Uses and Side Effects :

GnRH agonists produce different effects when dosed intermittently vs. continuously.

	GnRH agonists (intermittent)	GnRH agonists (Continuous)/GnRH antagonists	
MoA	↑ LH/FSH	↓ LH/FSH (↓ Estrogen/Testosterone)	
Uses	• Infertility (Anovulation/ Oligospermia) • Delayed puberty	↓ Estrogen • ER +ve breast Ca • Endometrial fibrosis • Endometriosis	↓ Testosterone • Prostate cancer (DOC) • Precocious puberty
Side effects	• Multiple gestation • Ovarian cyst • Ovarian cancer	• Osteoporosis • Vaginal atrophy • Hot flashes	• Osteoporosis • Impotence • Gynecomastia

Drugs for Contraception

00:21:52



Growth Hormone Related Drugs

00:23:30 ----- Active space -----

Classification & drugs	Uses	Side effects
GH analogs : Somatrem/Somatotropin	• DOC in dwarfism d/t GH deficiency • ↑Proliferation & growth.	Mnemonic : CHILDREN • Carpal tunnel syndrome • Hyperglycemia • ICT is raised. • Leukemia • Diabetes • C/I : – Retinopathy in DM – Neoplasia.
GH releasing hormone (GHRH analog) : • Sermorelin • Macimorelin • Tesamorelin	• Diagnosis of dwarfism. • ↓Abdominal fat of lipodystrophy in HIV patients (Tesamorelin).	-
Somatostatin analogs : • Octreotide • Lanreotide (long acting) • Pasireotide	• Route : S/c • DOC for : – Acromegaly. – Secretory diarrhea. – Glucagonoma/VIPoma/ Somatostatinoma. • Other uses : – Thyrotrope adenoma. – Acute variceal bleeding.	• Hypothyroidism • Gall stones
GH receptor antagonist : Pegvisomant	Drug resistant acromegaly ↓ (Octreotide/Lanreotide resistant)	↑Size of pituitary adenoma (monitor : MRI; visual field exam)

Note : Gall stones also caused by fibrates.

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

Drugs Used in Osteoporosis

00:28:23

Drugs	MOA & uses	Side effects
↓Bone resorption		
Bisphosphonates : • Oral : – Alendronate 💊 – Risedronate • IV – Zolendronate 💊 (most potent, longest acting) – Panidronate	• MOA : – ⊖ Faresyl pyrophosphate synthase ↓ Induce apoptosis of osteoclasts. – Block ruffled border synthesis. • Uses (DOC) : – Osteoporosis (Oral preferred) Duration : 3y (IV) to 5y (Oral). – Paget's disease/hypercalcemia of malignancy (IV preferred).	• Esophagitis (Oral drugs) : Prevention : Full glass of water + empty stomach + avoid lying down (↓Reflux). • Osteonecrosis of jaw. • Femoral chalk stick fracture (D/t brittleness of bone).
Denosumab	Blocks RANK Ligand	• Osteonecrosis of jaw • Femoral fractures
Raloxifene	• MOA : Selective Estrogen Receptor Modulator (SERM). • Indication : Post menopausal osteoporosis with ↑risk of breast cancer.	• Hot flashes • Thrombosis
Calcitonin (Not preferred)	• MOA : Inhibits resorption. • Use : Paget's; Prophylaxis of osteoporosis.	• Liver cancer. • Breast cancer.
↑Bone formation		
Teriparatide 💊 (PTH analogue)	• MOA : Stimulate osteoblast mediated formation. • Use : Bisphosphonate induced fracture. • Duration : Max. 2 yr.	• Hypertension. • Osteosarcoma ; C/I in Paget's disease.
Romosozumab	Blocks sclerostin	–

Note : Strontium ranelate 💊
- MOA : ↓Bone resorption + ↑Bone formation (Only drug).
- Use : Osteoporosis.
- Not FDA approved.

Steroid Hormone Related Drugs

00:35:10 ----- Active space -----

	Potency	Half-life	Uses	
Hydrocortisone (Similar to cortisol)	Glucocorticoids(GC)↑ x 1 Mineralocorticoid (MC)↑x 1	8 – 12 hours	DOC for replacement : • Addison's disease. • Congenital adrenal hyperplasia (CAH).	
Prednisone/ Prednisolone	GC↑ x 4 MC↑ x 0.8	12 – 36 hours	-	• ↓Inflammation • ↓Immunity
Methylprednisolone	GC↑ x 5 MC↑ x 0.8			
Triamcinolone	GC↑ x 5 MC = 0			
Dexamethasone/ Betamethasone	GC↑ x 30 MC = 0	36 – 72 hours	• Surfactant maturation • CAH pregnancy.	

Note : Triamcinolone, Dexamethasone & Betamethasone : Pure glucocorticoids.

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

Thyroid Related Drugs

00:41:47

Hyperthyroidism :

	MoA	Uses	Side effects
Propylthiouracil (multiple doses)	Inhibits thyroid peroxidase.	DOC for : • Hyperthyroidism in 1st trimester. • Thyroid storm (β-blocker used to prevent A. Fib).	Hepatotoxic
Carbimazole methimazole (OD)		DOC for Hyperthyroidism : Overall & 2nd & 3rd Trimester.	Teratogenic : • Choanal/Esophageal atresia. • Cutis aplasia.
Potassium iodide Lugol's iodide	• ⊖ Thiol endopeptidase ↓ ⊖ T_3, T_4 release. • ↓Thyroid size. • ↓Vasculogenesis/Bleeding.	Pre-operative preparation of thyroid gland for surgery.	-
Propranolol Propylthiouracil Amiodarone Steroids	Inhibit peripheral conversion of T_4 to T_3.	First line in thyroid storm Propranolol > CCB (Treatment of A. Fib).	-
Radioactive iodide (I^{131}) (I^{123} : used in Imaging)	Destroy follicular cells (Thyroid ablation) by β & γ rays.	• Thyroid cancer. • Recurrent Grave's disease. • Hyperthyroidism in elderly.	• Secondary cancer. • Permanent Hypothyroidism. • C/I : In pregnancy

Hypothyroidism :

	MoA	Uses	Side effects
Levothyroxine	T_4 salt (Long acting)	• Oral route (On empty stomach, 30m before food) : – DOC : Replacement. – Thyroid cancer (d/t ↓TSH). • IV route : – Myxedema coma.	• Osteoporosis. • Atrial fibrillation (↓ Dose used if pre-existing arrhythmia ⊕). • Thyrotoxicosis Symptoms.
Liothyronine	T_3 salt	• Oral route : T_3 given and stopped before radioactive iodine treatment ↓ TSH → ↑I^{131} uptake. • IV route : Myxedema coma.	-

AUTACOIDS

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

Anti-Histaminics

00:00:10

H 1 blockers.

	First generation	Second generation
Cross blood-brain barrier	Crosses (Sedating) : m 1 ⊖ effect. C/I in → Children. → Elderly. → Drivers/pilots.	Does not cross BBB (Non-sedating).
Drugs and their uses	1. Antihistamine with muscarinic ⊖ effect : – Promethazine, diphenhydramine, and dimenhydrinate. – Used in : Acute dystonia, meniere's disease and motion sickness. 2. Doxylamine : For morning sickness. Formulated with Vit. B_6 → ↑GABA (Calming effect). 3. Chlorpheniramine : Least sedative. 4. Doxepin : Currently under TCA. 5. Cyproheptadine : Currently under 5HT2 ⊖. 6. Hydroxyzine : – For pruritis. – Used in non-allergic rhinitis (D/t antimuscarinic effect).	• Cetirizine, Levocetirizine } Most sedative 2nd gen drugs. • Astemizole, Terfenadine } Cause QT prolongation. • Fexofenadine : Least sedative overall. • Loratadine. • Desloratadine : Most potent. • Rupatadine : Inhibits Platelet Activating Factor (PAF) → ↓inflammation. • Olopatadine, Levocabastine, Ketotifen, Azelastine, Astemizole } Topical anti-histaminics. • Azelastine (Nasal spray) : Allergic rhinitis. • Oral drugs : DOC for urticaria.

Motion Sickness :

1. Scopolamine 💊 : Transdermal patch.
   - DOC.
   - Apply patch night before travel.
   - Reapplication : 2 to 3 days.
2. Promethazine :
   - Oral tablet.
   - 1 hour before travel.
   - Highly sedative.

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

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) 00:07:58

NON-SELECTIVE NSAIDS

Acetaminophen (Paracetamol) :

Use : Analgesic & antipyretic effect.

Side effect :

Hepatotoxic (m/c cause of poisoning worldwide).

- ↑risk in chronic alcoholics/fasting.
- HPE : Centrilobular necrosis + periportal sparing.
- Cause : metabolite NAPQI —Depletes→ Glutathione.
- Toxic dose :
  - 150 – 250 mg/kg or 10 g total : Hepatotoxic.
  - >20 g : Fatal.
- Treatment :
  - DOC : N-acetyl cysteine → Blocks NAPQI.
    → Replenishes glutathione.
  - If no response : Fulminant liver failure → Emergency liver transplantation.

Aspirin :

Dose dependent effects :

- 50 – 325 mg OD : Anti-aggregate.
- 325 – 650 mg SOS : Pain/fever Rx.
- 3 – 4 g/day (Divided dose) : Anti-inflammatory (Eg. RA).

Side effects :

- Reye's syndrome : Hepatic encephalopathy.
  - C/I in viral fever in children.
- ↑Uric acid : C/I in gout.

Management of toxicity :

- Bicarbonates (Alkalinize urine → ↑excretion).
- If pulmonary edema developed : Dialysis.

Indomethacin :

MOA :

- Inhibits COX.
- Blocks leukocyte migration.

Use :

- DOC for acute gout.
- Closure of patent ductus arteriosus(PDA).

Ibuprofen :

DOC for closure of PDA in India.

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

Piroxicam :

Long-acting : D/t enterohepatic circulation —used for→ Chronic pain.

Nimesulide :

Hepatotoxic : C/I in → Children <12 y.
→ Adults for >10 d.

Ketorolac :

Uses → Post-operative pain (↑Potency).
→ Eye pain.

SELECTIVE COX-2 INHIBITORS

Features :

- ↓risk of gastric ulcer.
- ↑risk of myocardial infarction (MI) : Not preferred.

Celecoxib, Etoricoxib : Last line for pain & inflammation.

Lumiracoxib : Hepatotoxic (Banned).

Parecoxib : Post-operative pain.

Valdecoxib, Rofecoxib : ↑Risk of MI (Banned).

Prostaglandin Analogs

00:18:20

Prostaglandin	Analog	Uses
Prostaglandin E1	Misoprostol	• Abortion (+ Mifepristone) • NSAID induced gastric ulcer • Maintain patency of DA
	Alprostadil	• Maintain patency of DA • Erectile dysfunction
Prostaglandin E2	Dinoprostone	• Cervical ripening (DOC) • PPH
Prostaglandin F2 alpha	Carboprost	PPH
	Latanoprost/Bimatoprost	Open angle glaucoma
Prostaglandin I 2	• Epoprostenol (Synthetic) • Iloprost • Beraprost • Treprostinil (Analogs) • Selexipag : Receptor agonist	Pulmonary HTN

Pulmonary HTN : Rx

Stage II/III :

- Endothelin ⊖ : Bosentan, Ambrisentan.
- Alternative : PG I 2 analogues ; PDE 5 ⊖ (Sildenafil) ; inhalational NO.
- CCBs may be used only if vasoreactive test ⊕.

Stage IV : Epoprostenol.

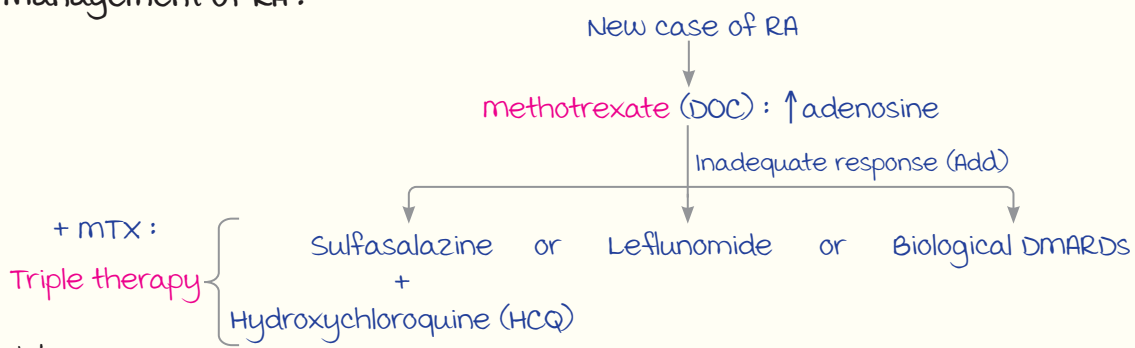
Note : DOC for PPH → Oxytocin.

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

Disease Modifying Anti-Rheumatoid Drugs (DMARDs) 00:21:40

Conventional DMARDs	Biological DMARDs	Targeted DMARDs
1. Methotrexate (DOC) : Anchor drug (D/t universal use) 2. Hydroxychloroquine 3. Sulfasalazine 4. Cyclophosphamide 5. Immunomodulators – Azathioprine – Cyclosporine – Mycophenolate mofetil – Leflunomide : Block pyrimidine synthesis (⊖ Dihydroorotate dehydrogenase)	Route : Parenteral 1. Anakinra : IL 1 ⊖ 2. Rituximab: CD 20 ⊖ 3. TNF – α blockers : Block lymphocyte activity (CAGE) – Certolizumab – Adalimumab – Golimumab – Etanercept – Infliximab 4. IL-6 ⊖ : • Sarilumab • Tocilizumab 5. CD80/86 ⊖ : Abatacept	Last line drugs : JAK inhibitors Route : Oral 1. Baricitinib 2. Upadacitinib 3. Tofacitinib

Management of RA :



Note :

S/e of HCQ : Corneal deposits (Whorled) & bull's eye retinopathy → Routine eye exam.

Anti-gout Drugs 00:29:34

Acute Gout :

- Aim : ↓Inflammation.
- DOC : Indomethacin.
- Alternative : Colchicine → ⊖ microtubules → ⊖ chemotaxis.

Chronic Gout :

- Aim : ↓Uric acid (UA).

Xanthine Oxidase Inhibitors :

- MOA : ⊖ UA synthesis.
- Drugs :
  1. Allopurinol (DOC).
  2. Oxypurinol (If SJS with Allopurinol).
  3. Febuxostat (most effective).
- Side effects :
  - Xanthine stones.
  - Steven Johnson syndrome (SJS).
  - Acute gout.

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

Uricosuric drugs :

- MOA : ↑UA excretion.
- Drugs :
  1. Sulfinpyrazone
  2. Probenecid
  3. Benzbromarone

  } monotherapy + add on drugs.

  4. Lesinurad : Only as add-on } Effective in renal failure.
- S/e : Urate stones, acute gout → Add indomethacin/colchicine.

Uricase analogs :

- MOA : metabolize UA.
- Drug : Pegloticase (Last line).
- Rasburicase is used to prevent tumor lysis syndrome.

Note : Tumor lysis syndrome.

- ↑UA d/t chemotherapy induced cell death.
- Risk : Solid tumor < leukemia.
- DOC : Allopurinol. Rasburicase.

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

DRUGS ACTING ON RESPIRATORY SYSTEM, GIT AND BLOOD

Asthma

00:00:10

Histamine : Bronchoconstriction & inflammation.

Drugs	Action/use	S/E
Methylxanthines : • Theophylline • Aminophylline	• Bronchodilation : – Adenosine A_1 ⊖ – PDE 3 > 4 ⊖ • Anti-inflammatory : – PDE 4 ⊖, ↑IL-10 – Histone deacetylase ⊕ (Similar to steroids)	• Adenosine AI ⊖ : Seizure, arrhythmia, diuresis • PDE 3 ⊖ : GIT upset, headache
ICS : • Fluticasone : most potent • Ciclesonide • Beclomethasone } Soft steroids – Inactive orally ; activated in the lungs. – ↓risk of oropharyngeal candidiasis	• DOC : Persistent BA • TOC : Acute attack (ICS + formoterol)	• Hoarseness of voice (m/c) • Oral candidiasis
Systemic steroids (Oral/IV)	Acute exacerbation of BA : ↑β_2 receptor density in bronchi → ↑agonist effect	–
LOX ⊖ : Zileuton	–	–
LTC4/D4 ⊖ : Montelukast	Persistent asthma (Add-on)	Hepatotoxic
Mast cell stabilizers : • Cromolyn sodium • Nedocromil	–	Safest
Anti IgE : Omalizumab	Severe persistant BA	Not effective in atopic dermatitis
• Anti IL-5 : – Reslizumab – Mepolizumab • Anti IL-5 R : Benralizumab • Anti IL-4 R : Dupilumab	Severe eosinophilic BA	–

Mx of acute asthma attack :

- ICS + formoterol.
- Salbutamol $\xrightarrow{5\ min}$ ICS (when taken separately).
- Salbutamol $\xrightarrow{1\ min}$ Repeat (if >1 puff required).

New drugs COPD :

- Roflumilast : PDE_4 ⊖.
- Ensifentrine : PDE_3 ⊖.

Antitussives

00:06:54 ----- Active space -----

1. Dry Cough :

Centrally acting agents (⊖ medullary centre) :

- **Opioids :**
  - **Mild-moderate :**
    - Codeine
    - Pholcodine
    - Hydrocodone
  - **Severe (Eg : Bronchial Ca)**
    - Methadone
    - Morphine
- **Non-opioids :**
  - Dextromethorphan (m/c)
    NMDA ⊖ → S/E : Hallucinations (↑r/o abuse)
  - Diphenhydramine
  - Noscapine
  - Levopropoxyphene

2. Productive Cough :

1. Expectorant : Guaifenesin.
2. Mucolytics : Liquifies mucous.
   a. N-acetyl cysteine : Break disulfide bond.
   b. Ambroxol/bromhexine : Depolymerize mucopolysaccharide.

Mx : Syrup Guaifenesin + ambroxol/bromhexine + salbutamol.

Peptic Ulcer Disease

00:10:32

Aim : Ulcer healing → ↓HCl secretion.

Drugs	Uses	S/E
PPI 💊 : • Omeprazole → Esomeprazole (Isomer; long acting) • Pantoprazole • Lansoprazole • Rabeprazole	DOC : • PUD • GERD • ZES • H. pylori • Barrett's esophagus (Life long)	• GIT upset • Pneumonia • Pseudomembranous colitis • Iron, B_{12}, Ca^{2+} deficiency → Osteoporosis (Hip #) • Hypergastrinemia
Vonoprazan : • K^+ competitive acid blocker (PCAB) • Blocks basal + food induced acid secretion	H. pylori	-
H_2 ⊖ : • Cimetidine • Ranitidine • Famotidine	DOC : Prophylaxis of aspiration pneumonia (Post op patients)	Cimetidine 💊 : • Females : Galactorrhea (↑prolactin) • males : (⊖ androgen) – Impotence – Gynaecomastia
Misoprostol (PGE_1 analogue)	NSAID induced gastric ulcer (most specific)	• Diarrhoea • Abdominal cramps
Sucralfate	• PUD • Rectal ulcer	• Constipation • Gastric bezoars

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

Drugs	Uses	S/E
Bismuth subsalicylate/ subcitrate	• H. pylori • Traveller's diarrhea	• Constipation • Black colour stool & tongue
Antacids : Salts of • Al (Constipation) • Mg (Diarrhea)	• PUD • Dyspnea • GERD	↓absorption of other drugs

Note : With sucralfate.

- Antacid : 30 min after.
- Food : 1 hr before.
- Other drugs : 2 hrs before.

Prokinetics

00:17:50

Use : Gastroparesis.

a. D_2 Antagonists :

Also used as anti-emetics.

1. Metoclopramide :
   - Also → $5HT_3$ ⊖ ; $5HT_4$ ⊕.
   - S/E : Acute dystonia (Crosses BBB); hyperprolactinemia.
2. Domperidone : No EPS.

b. Other Drugs :

- $5HT_4$ agonists : Mosapride, itopride, prucalopride.
- Motilin receptor agonists : Erythromycin, mitemcinal.
- CCK 1/A receptor antagonist : Dexloxiglumide.

Anti-emetics

00:19:20

Drugs for chemotherapy induced nausea/vomiting :

Group	Drugs
$5HT_3$ antagonists (DOC)	• Ondansetron (Shortest) • Palonosetron (Longest, most potent)
NK1R antagonists	• Aprepitant • Rolapitant • Netupitant
CBR1 agonists (2nd line)	• Dronabinol • Nabilone } S/E : Hypotension, blood shot eyes
Other	• Dexamethasone • Metoclopramide • Olanzapine

Other uses :
- Morning sickness.
- Post-op vomiting.
- Radiation induced vomiting.

Laxatives

00:20:47

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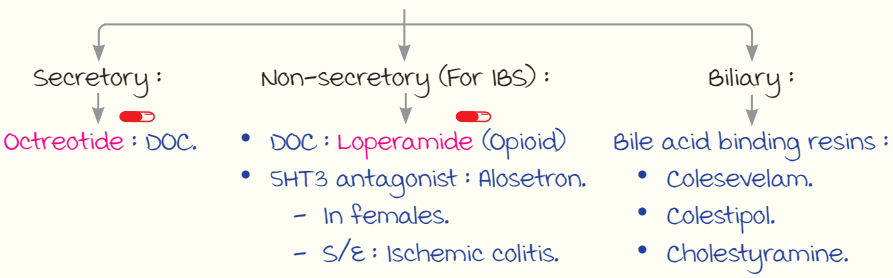
↑water in intestine	↑intestinal contraction	↑stool bulk	↑stool softening (Least effective)
1. Osmotic laxatives : – Mannitol – 2nd line for constipation – Hepatic encephalopathy • Polyethylene glycol (PEG) DOC : IBS + constipation	1. Bisacodyl, senna, cascara : – ↑low grade inflammation of large intestine → ↑contraction – Effect : After 6–8 hrs (Night dose) – Max 10 days (Short term Rx) – Senna : a. Melanosis coli b. Pink/Yellow brown urine	1. Probiotics : Beneficial microbes ↓ – Lactobacillus – Saccharomyces – B. clausii	1. Docusate sodium (Surfactant)
2. Chloride secretory agents : – Lubiprostone : (⊕ Type II chloride channels) – Linaclotide : (⊕ Guanylate cyclase) ↑cGMP → ⊕ CFTR	2. 5HT-4 agonists : – Mosapride – Prucalopride	2. Prebiotics : Dietary fibers ↓ – Methylcellulose – Psyllium husk – Bran	2. Docusate calcium
3. Tenapanor : ⊖ Na^+– proton exchanger			

Anti-Diarrheal Agents

00:23:48



Blood

00:24:46

ANTI-AGGREGANTS

Drugs	Uses	S/E
COX-1 inhibitor : Aspirin (↓TXA_2)	Primary prophylaxis : MI & stroke	Bleeding
PAR-1 blocker : Vorapaxar	Primary prophylaxis : MI	Intracranial bleed (C/I : Stroke/TIA)
GP IIb/IIIa blocker : • Abciximab • Tirofiban • Eptifibatide	• PCI in MI • Unstable angina	• Bleeding • Thrombocytopenia

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AD/PAYIA Blockers :

Irreversible :

1. Clopidogrel 💊 :
   Primary prophylaxis : MI and stroke.
2. Ticlopidine (Toxic) :
   S/E : Agranulocytosis, TTP-HUS, Thrombocytopenia.
3. Prasugrel (most potent) :
   - Causes : Intracranial bleed → C/I : Stroke/TIA.
   - Use : PCI in MI.

Reversible :

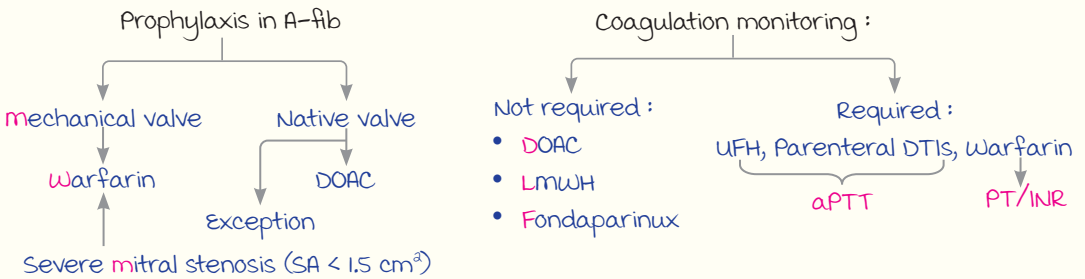
1. Cangrelor :
   - Adenosine analog.
   - IV, short acting.
   - Use : PCI in MI.
2. Ticagrelor :
   - Oral.
   - Use : Acute coronary syndrome, MI, stroke prophylaxis.

Anti-Coagulants

00:27:21

Drugs	Uses	Extra
Direct Oral AC (DOAC) : • Oral DTI : Dabigatran • Oral Xa ⊖ : – Apixaban – Edoxaban – Rivaroxaban	• DVT Rx • DOC : DVT prophylaxis • DOC : Prophylaxis of thrombosis in non-valvular atrial fibrilliation (Native valve)	1. No monitoring required 2. Antidotes : • Dabigatran : Idarucizumab • Oral Xa ⊖ : Andexanet alfa
Warfarin : ⊖ VKOR • ↓factors 2, 7, 9, 10 (Last ← → First) • ↓Protein C & S (2nd)	• DVT Rx & prophylaxis • DOC prophylaxis of thrombosis in valvular atrial fibrillation (mechanical valve)	1. S/E : • Skin necrosis : Protein C & S↓ • Purple toe • Teratogenic : – Mid facial hypoplasia – Stippled epiphyseal calcification – CNS defects 2. Antidote : • 4 factor prothrombin complex > FFP • Vit K
Parenteral DTI (PEDTI) : • Argatroban 💊 : DOC • Desirudin • Bivalirudin • Lepirudin	Heparin induced thrombocytopenia	Monitor aPTT

Note :



ANTICOAGULANTS : INDIRECT THROMBIN INHIBITORS

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UFH	LMWH	Fondaparinux
• Large size • ⊖ Xa = IIa	• Smaller • ⊖ Xa > IIa	• Smallest • ⊖ Xa only
• S/c : Prophylaxis (Low bioavailability) • IV : Rx	S/c : Prophylaxis & Rx	
Short acting : Multiple doses (Removed by macrophages)	Single dose ↓ DOC : Thrombosis, MI, DVT, pulmonary embolism	
Safe in renal failure	Avoid in renal failure (Excreted unchanged by Kidney)	

S/E : Mnemonic → HOT

- Hyperkalemia, hair loss.
- Osteoporosis.
- Thrombocytopenia (HIT) — Risk → Max : UFH > LMWH.
Zero : Fondaparinux.

Fibrinolytics

00:37:45

t-PA analogues :

- Alteplase.
- Reteplase.
- Tenecteplase (most specific).

Uses :

- MI (Only STEMI).
- Pulmonary embolism.

S/E : Bleeding.

↓

Antidotes :

- Tranexamic acid (DOC).
- ε-Aminocaproic acid (EACA).

Hematopoetic Agents

00:40:28

Group	Drug	Uses	S/E
Erythropoiesis : Erythropoietin analogues.	• Epoetin alpha • Darbepoetin (Long acting)	• Anemia of CRF • Anemia by chemotherapy • Zidovudine anemia • Anemia of dialysis	• Pure red cell aplasia (most dangerous) • Hypertension • Thrombosis • Iron deficiency
Granulopoiesis : 1. G-CSF analog	• Lenograstim • Filgrastim • Lipegfilgrastim – Long acting – Given once during a CT cycle	• Neutropenia (DOC : Lipegfilgrastim) • HIV • Chemotherapy	Bone pain
2. GM-CSF analogue	Sargramostim		

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Group	Drug	Uses	S/E
Thrombopoiesis : 1. IL-11 analog	• Oprelvekin	Thrombocytopenia by CT	-
2. Thrombopoietin agonist	• Eltrombopag • Romiplostim	ITP (New drug : Spleen tyrosine Kinase ⊖) → Fostamatinib)	
3. Other	• Lusutrombopag • Avatrombopag	↓bleeding in liver cirrhosis patients planned for procedures (Eg : Dental extraction)	

ANTI NEOPLASTIC DRUGS & IMMUNOMODULATORS

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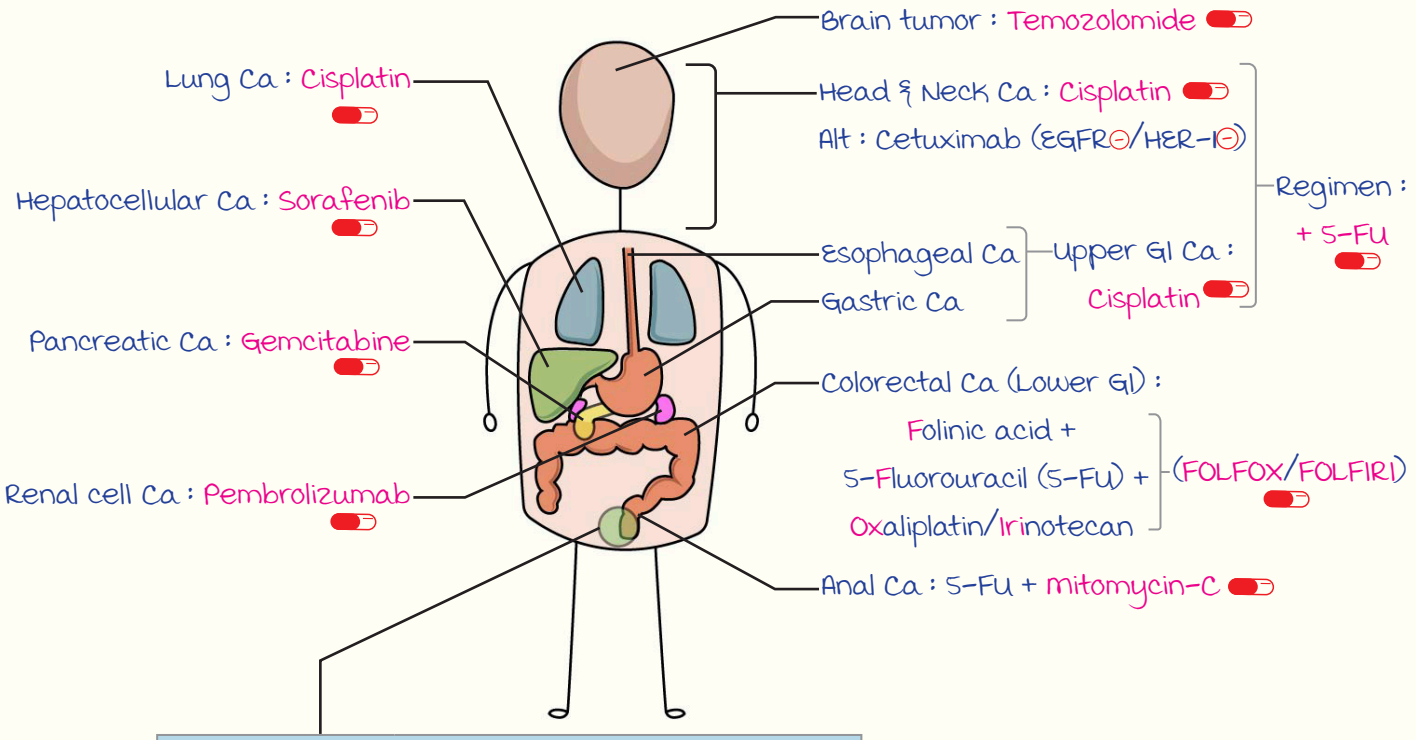
Anti Cancer Drugs

00:00:30

DOC of cancers :

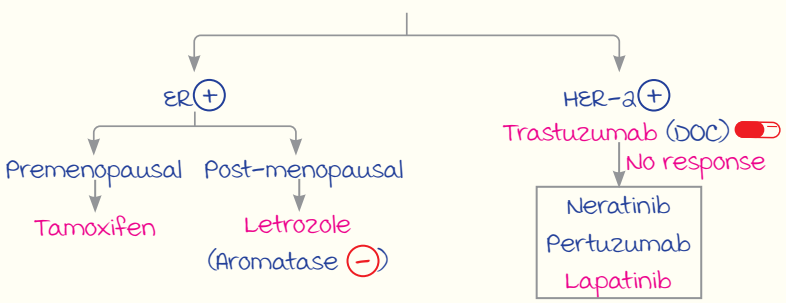


Urogenital Ca (DOC : Cisplatin)	
Cancer	Add on Rx (for regimen)
Uterine/Ovary Ca	Paclitaxel
Bladder Ca	Gemcitabine
Cervix Ca	(Only Cisplatin)
Testicular Ca	BEP (Bleomycin + Etoposide + Cisplatin)

→ If relapse Pembrolizumab.

Note : Mitomycin-C → Prevents laryngo-tracheal stenosis.

Ca Breast :



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Leukemia :

- **Acute**
  - **ALL : VPAD regimen**
    - Vincristine
    - Prednisolone
    - Asparaginase
    - Daunorubicin
  - **AML :** Cytarabine + Daunorubicin/ Idarubicin
- **Chronic**
  - **CML :** BCR-ABL Tyrosine Kinase ⊖
    - 1st gen : Imatinib (DOC)
    - ↓ No response
    - 2nd gen :
      - Dasatinib
      - Nilotinib
      - Bosutinib
    - ↓ No response
    - 3rd gen : Ponatinib
    - ↓ If T-315 I mutation in enzymatic site
    - Asciminib : ⊖ Allosteric site
    - Omacetaxine : ⊖ BCR-ABL protein
  - **CLL :** FCR regimen
    - Fludarabine
    - Cyclophosphamide
    - Rituximab

Note :

- Hairy cell leukemia : Cladribine (DOC).
- Sickle cell disease : Hydroxyurea (DOC).

Lymphoma :

- **Hodgkin lymphoma : ABVD regimen**
  - Adriamycin
  - Bleomycin
  - Vinblastine
  - Dacarbazine
  - ↓ If relapsed
  - Nivolumab (Immune checkpoint ⊖)
- **Non-Hodgkin lymphoma**
  - **Low grade :** FCR regimen
  - **High grade : R-CHOP regimen**
    - Rituximab
    - Cyclophosphamide
    - Hydroxydaunorubicin
    - Oncovin (Vincristine)
    - Prednisolone

Side Effects of Anti-Cancer Drugs

00:17:25

Side-effect	Causative drug
SIADH	Vincristine
Cerebellar Toxicity (Ataxia, dysarthria)	Cytarabine
Cardiotoxicity	• Doxorubicin • Daunorubicin • Trastuzumab } D/t iron-induced free radicals → Prevention : Dexrazoxane (Iron-chelation)
Pulmonary fibrosis	Bleomycin > Busulfan
Hepatotoxicity	Methotrexate
Hemorrhagic cystitis	Ifosfamide > Cyclophosphamide (Prevention : MESNA)
Hand & foot syndrome : Bright red discoloration	Capecitabine > 5-FU (Prevention : Vitamin B6)
Peripheral neuropathy	Vincristine, Cisplatin, Paclitaxel
Diarrhea	Irinotecan (Rx : Loperamide)
Flagellate dermatitis (On back) : Longitudinal hypopigmented strips	Bleomycin

MISCELLANEOUS ANTI-CANCER DRUGS

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Kinase Inhibitors :

1. Imatinib : BCR-ABL TK ⊖ (CML).
2. Gliteritinib : FLT-3 kinase ⊖ (AML).
3. Dabrafenib : BRAF ⊖. } melanoma
4. Cobimetinib : MEK 1/2. }
5. Idelalisib : PI-3 K ⊖.
6. Ibrutinib : Bruton's TK ⊖ (B-cell Lymphomas).

Asparaginase :

- For leukemia.
- S/E :
  - Hyperglycemia.
  - Hyperlipidemia.
  - Hypercoagulation.
  - Hemorrhage.
  - Hypersensitivity.

Olaparib :

- Poly-ADP ribose polymerase (PARP) ⊖
- For Ca breast.

Bortezomib :

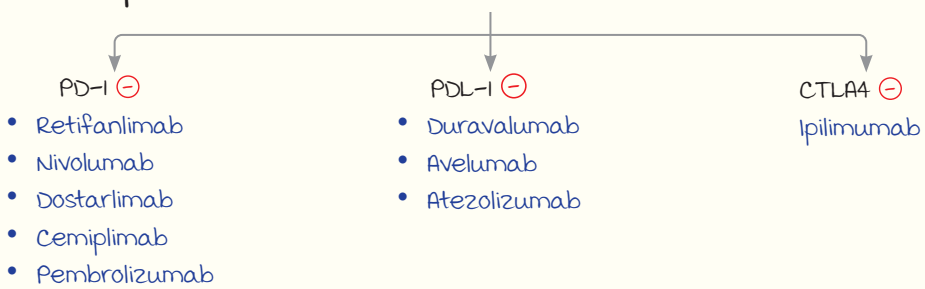
- Proteasome ⊖
- For multiple myeloma.
- ↑Risk of herpes infection/reactivation (Prevent : Acyclovir).

Sonidegib : Hedgehog pathway ⊖

Retinoic acid (ROC) : Pro-myelocytic leukemia.

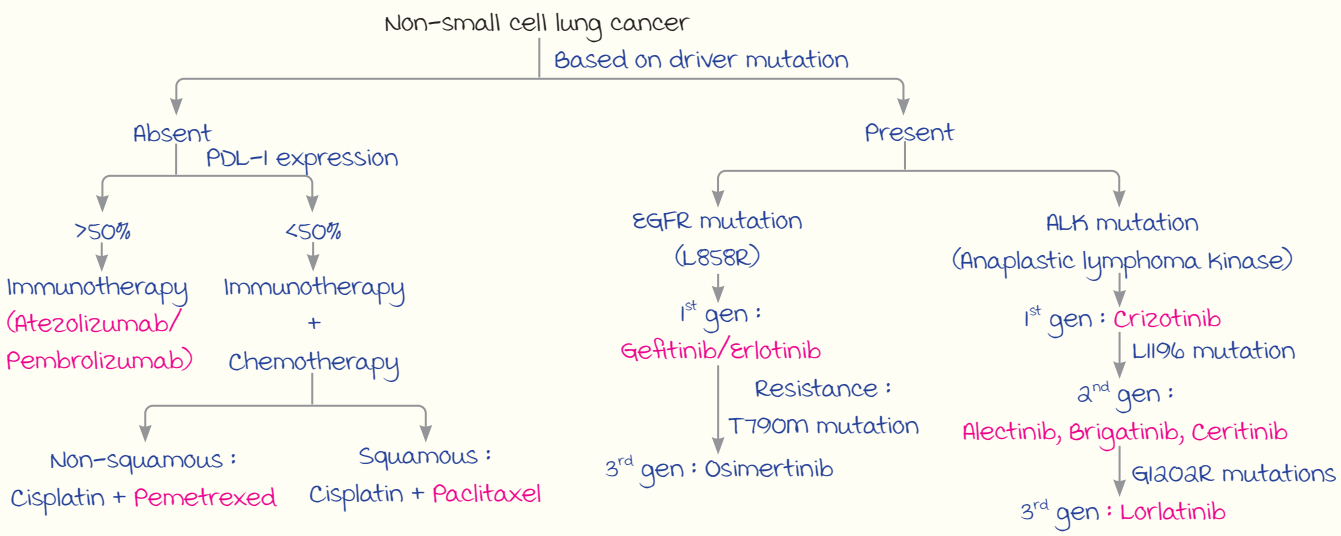
Nomenclature of monoclonal antibodies
Suffix -mab : Monoclonal antibodies.
Source :
• -u/-zu-mab : Human.
• -xi-mab : Chimeric.

Immune Check-point Inhibitors :



Drugs for Lung Cancer

00:29:40



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Small cell lung cancer :

Cisplatin + Etoposide + Immunotherapy (Atezolizumab/Durvalumab).

Note :

Named trials in NSC Lung Ca :

- Keynote 189 : Chemotherapy + Pembrolizumab.
- Uncheckmate 227 : Ipilimumab + Nivolumab.

Immunomodulators

00:32:40

Immunomodulator	MOA & Uses	Side Effects
• Cyclosporine • Tacrolimus	• Calcineurin inhibitors : ↓Transcription of IL-2 in CD4 cells • 1st line drugs → GVHD	• Common to both (Tacrolimus > Cyclosporine) : – Nephrotoxicity – Neurotoxicity – Hyperkalemia – HTN – Hepatotoxicity – Hyperglycemia • Cyclosporine only : – Hirsutism – Hyperlipidemia – Hyperplasia of gums – Hyperuricemia
• Everolimus • Sirolimus	m-tor inhibitors	Hypokalemia
Azathioprine	Prodrug of 6-mercaptopurine	Hepatotoxic, bone marrow suppression (Rarely used)
Belatacept	CD80/86 inhibitor	–
Alemtuzumab	CD52 inhibitor	–
Belumosudil	Rho Kinase ⊖	–
Thalidomide	• Anti-inflammatory • Anti-angiogenic • Anti-neoplastic • Immunosuppressant	Phocomelia : ⊖ Cereblon & tubulin ↓ ⊖ Vasculogenesis; ↑free radicals ↓ ⊖ Fetal development (Short limbs)
Basiliximab	Block IL-2 receptors/CD25 (Prophylaxis of acute graft rejection)	–
Muromonab	Blocks CD3 (Rx of acute graft rejection)	Cytokine release syndrome
Mycophenolate mofetil	Block IMP dehydrogenase	GIT upset
Leflunomide	Blocks dihydro-oratase dehydrogenase	BM suppression, hepatotxic