Parasympathetic System

Motor nerves:

a. Somatic (voluntary Ms) → NMJ → NT: Ach; R: NM

b. Autonomic (Involuntary Ms)

Sympathetic	Parasympathetic
↓	↓
Stressful	non stressful stimuli
Stimuli	↓
↓	NT = Ach
NT = NAdr / Adr	(Cholinergic system)
↓	↓
∝/B-R	R = M muscarinic (M)

Nerve
To nerve junction
ganglia

ACH SYNTHESIS AND RELEASE 5:00

AcetylcoA + Choline
↓
Acetyl choline
↓ (-)
Ach release

Botulinum toxin (origin: clostridium)
Type A > B
MOA: SNAP - 25 (x) Fusion protein
(Irreversible (x))

2. Ach Receptors

- All R are stimulatory except M_2 / M_4
  - ↳ i. $N=N_N$ and N_M

↓	↓
Nerve - Nerve	Nerve - ms junction
Junction	all voluntary ms.

  - ↳ If. M: M_1 - M_5

M_1 = GIT (↑ acid secrerm)
CNS (↑ tremors)
M_2 = cardiac cells
M_3 = All smooth Ms glands

ACH ACTIONS 9:50

a. N_N ↑
- CNS ↑ (Memory, learning ↑)

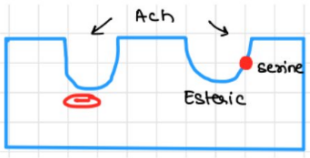
b. N_H ↑
- Ms. Contraction

c. M↑
D-Diarrhea, Dilation of blood vs (↓ BP)
↓
↑ NO → ↑ guanyl cyclase →↑ cGMP ⇒ Rxs dilatn
(nitric oxide)

U = Urination
M = Miosis and Accommodation
B = Bradycardia, Bronchospasm
E = Erection
L = Lacrimation
S = Salivation, Sweating, secretion of GIT

ACH METABOLISM 13:54

- Ach Esterase



2 active site

Drugs acting:

1. Cholinergic drugs (DUMBELSSS)
   a. Directly acting (M↑)
   b. Indirectly acting
      Ach E(x) → ↑ Ach)
      i. N_N↑
      ii. N_H↑
      iii. M↑

2. Anticholinergic (Opposite to DUMBELSSS)

ii. N_H↑
iii. M↑

a. Directly acting:
1. Bethanechol → cholinergic
   - ↑ urination
   - DOC for atonic bladder (overflow incontinence)
   - Post operative ROU

   bladder
   B → S/E: Bronchospasm
   C/I: Bronchial asthma / COPD

2. Pilocarpine (Eye drop)
   - Cholinergic drug
   - Pin point pupil (miosis)
   - ↓ pressure in eyes
   - ↑ trabecular drainage of aq. Humour

   T/t: Acute ACG
   (Acetazolamide)

   S/E:
   - Pain eyes
   - Punctum blockage (Nasolacrimal duct block)
   - Peripheral retinal detachment
   - Pin pt. pupil ↓ vision

b. Indirectly acting
(reversible blocker) ↓ AchE → ↑ Ach
a. N_n (R)
   ↑ CNS
   ↓
   T/t: Dementia

1. Dorepezil (DOC)
   - Most efficient
   - Dose modification not required in CKD/CLD

   ↳ S/E: Diarrhea

2. ↳ Rivastigmine (↓ GIT: S/E)
   used as skin patch

3. Galantamine

b. N_M : ↑ strength of voluntary Ms
   1. Pyridostigmine (long action)
      ↳ DOC: Myasthenia Gravis (M.S)
      T/t: Lambert Eaton MS
   2. Neostigmine (Fast onset)
      T/t: Cobra snake bite
      (Anti snake venom + Neostigmine)
      DOC: Reversal of skeletal Ms. Relaxant
      (Always given with atropine / glycopyrrolate)

3. Edrophonium (short action)
   - Only for diagnosis of myasthenia gravis

c. M↑↑
   (CNS / ANS)

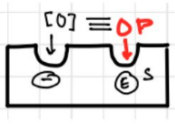
1. Physostigmine
   DOC: Atropine / Bella-dona / Datura poisoning → M (x)

- Ach E (x) (irreversible (-))
  ↓
  Poisons (organophosphate & carbamate)
  ↓
  Ach E (x)
  ↓
  ↑ Ach

M Nm ↑↑ (over stimulation)
(DUMBELSSS) ↓
↓ receptor down regulation
Deash ↓
↓ (-) Ms. Weakness
Atropine

- High dose atropine: Monitor :-
  a. Dryness of secretion
  b. Chest B/L clarity

2. Oximes
   - For OP poisoning only
   - Best to be given before irreversible blocker



AcheE

T/T OF ALZHEIMER'S DISEASE *37:00*

(Ach deficiency)

a. Symptomatic relief:-
Ach E (x)
↓
Domeprazil (DOC)
Rivastigmine (Skin patch)

b. Disease modifying
↓
1. Memantine
↓
Memory ↑↑
NMDA (x) (Glutamate receptor)

2. Aducanumab
   - β- amyloid protein (x)

3. Antioxidants
   - Coenzyme Q
   - Vit E

T/T OF MYASTHENIA GRAVIS *39:28*

- Pyridostigmine > Neostigmine + low dose Atropine
↓ not controlled
Add: Azathioprine
Mycophenolate
- Drugs avoided: SMR, local anesthetics

Aminoglycosides: NMJ (x)
Botulinum Toxin
Ca^{+} channel blocker
$MgSo_4$ (Mg^{2+} = Ca^{2+} (x))
Quinine / Quinidine / Quinolone
Immune check pt. inhibitor: ↑ Immunity

COBRABITE 43:28

Anti snake venom → Atropine → Neostigmine

II. ANTICHOLINERGIC 43:47

(opp to DUMBELSSS)

1. Constipation: Atropine (M_1 – M_5) (x)
   ↓
   M_3 (x) (peristalsis ↓)
   ↓
   2nd DOC: Non- infective diarrhea
   (& DOC: Loperamide)

2. Reflex bladder (ROU)
   - 2nd DOC: Overactive bladder
     Trospium > Darifenacin, Solifenacin > oxybutynin, Tolterodine
     ↓
     Max. Dementia & S/E

3. Mydriasis with loss of accommodation (cycloplegia)
   Atropine > Homatropine > Cyclopentolate > Tropicamide

   a. More efficient

	• Weak cycloplegic
• Strong cycloplegic	• Adult
• Children	
• Long acting	• Short acting
• T/t: Amblyopia Anterior uveitis	• T/t: Eye examination Cataract Surgery

4. Tachycardia
   ↑ AV conduction, ↑hR
   a. Atropine DOC for bradycardia, AV block
   (1 → 3 mg)
   - M_1 to M_5 (x) → (M_2) (x)

5. Bronchodilation (inhalational)
   T/t: Bronchial asthma / COPD)
   - SAMA (short acting)
     Ipatropium
     ↓
     Faster onset
     ↓
     Acute & prophylaxis of B.A / COPD → non - selective
     ↓
     S/E drymouth
   - LAMA
     Tiotropium
     ↓
     Slow onset
     ↓
     Only maintenance
     ↓
     Selective action (NO S/E)
     ↓
     DOC: COPD

6. ↓ gland secretion
   - Glycopyrolate → ↓ glands
     - Pre - anesthetic drug
     - Quarternery structure (doesn't cross Blood - brain barrier)

7. ↓ Secretion of acid → M_1 (x)
   - PIRENZIPINE
     ↓
     (Parietal cell (x))

   T/t: Peptic ulcer disease

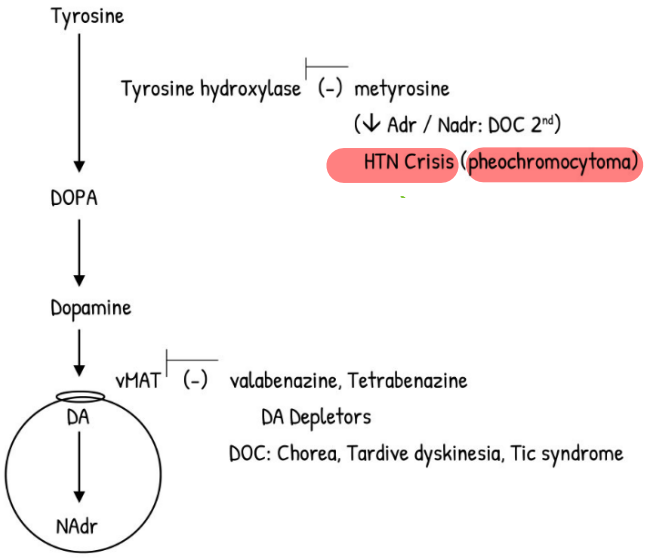
8. CNS action
   ↳ M_1 (x)
   ↓
   Benzhexol (Tri hexyphenydryl)
   ↓
   T/t: tremors (Parkinson's disease)
   ↳ hyoscine (scopolamine)
   ↓
   ↓ CNS centre →
   a. Vestibular stimulus
      DOC: motion sickness (air/sea) as skin patch
   b. Narco analysis (truth serum)

All Anticholinergics are C/I in Angle closure glaucoma (mydriasis)

Sympathetic System

- NAdr.
- 3 exceptions:-
  a. Sweat glands (Ach → ↑ Sweat)
  b. Adrenal medulla (Adr > NAdr)
  c. Blood vessel of kidney & mesentry (DA: D_1 ↑ vasodilation)

ADR / NADR SYNTH 1:57



NADR / ADR RECEPTOR 5:12

a. ∝: α_1 , α_2
b. β: β_1, β_2, β_3

α_1: PROBESS

- Prostate → ✓, B
- Blood vessel (∝ / B)
- Eyes (radial ms) (∝/A)
- Sphincter
- Seminal vesicle

α_2: ↓ CNS centre
↓ Ciliary body of eye

β_1: CNS ↑
Ciliary body of eye ↑
Cardiac ↑
Cells (JG) Renin ↑

β_2: All Ms. (Relax smooth Ms)

β_3: Adipocyte
Bladder
Cardiac

NADR / ADR METABOLISM *8:47*

- Metabolised by MAO (80%)
  COMT (20%)

ACTION COPP. TO DUMBELSSS *9:08*

E: Ejaculation (α_1)

DRUGS *10:09*

a. Adrenergic
(opp to DUMBELSSS)

b. Anti-adrenergic
(Most of action ≈ DUMBELSSS)

Directly
Acing
(α/B ↑↑)

Indirectly
acting
↓
(x) Mechanism of NAdr
↓
↑ NAdr

↑CNS
Stimulation

α/B ↑↑

- Indirectly acting
  a. Methyl - phenidate
     DOC: ADHD

  b. Modafinil
     DOC: Narcolepsy

  c. Amphetamine (NMDA)
     ↓
     Rave drugs

  d. Cocaine
     ↑ NAdr, ↑ DA
     (sniff)
     ↓
     Nasal septum perforation

  e. Old expired cheese
     ↓
     ↑ Tyramine → ↑ NAdr + Antidepressants (TCA / MAO I / SNRI)
     ↓
     NAdr metabolism
     ↓
     HTN crisis → cheese reaction

  f. Scorpion toxin
     ↑ NAdr, ↑ Ach
     - ↑ BP, ↑ HR (priapism)

T/t: Antivenom → If BP ↑↑ then prazosin (α_1 (x))

Directly acting

a. Catecholamines
   1. Dopamine (DA: µg / kg / min)
      - <2 D_1↑ → vasodilation, in kidney ↑ GFR
      - 2-10 (D_1 & β_1) ↑ → ↑ GFR & CO ↑ DOC: Cardiogenic shock oligouria
      - > 10 D_1 / β_1 α_1 ↑ → ↑ GFR, BP↑, ↑CO: 2nd DOC of all other shock

2. Adrenaline (all receptor ∝/B) ↑↑
   i. (1:1000 1mg/ml)
   DOC for anaphylactic shock
   ↓
   Antagonise histamine
   ↓
   α_1 = vasoconstriction (↑ BP)
   β_2 = Bronchodilation

   1:1000
   - Conc: 1:1000
     Dose: 0.5 mg = 0.5 ml
     Route: 1.m (vastus lateralis)

Other drugs for T/t: H_1 (x) / steroids / salbutamol

   ii. 1:10000 (0.1mg/ml)
   ↳ DOC (cardiac arrest)
   ↓
   Con: 1:10000
   Dose: 1mg = 10 ml
   Route: I.V > Intraosseous (Tibia)
   - Other drug: Amiodarone / Liganocaine

3. NAdr
   - No action on β_2 → no bronchodilation
   - Agonist of all (R)
     α_1 = ↑ BP
     β_1 = ↑ CO
     DOC: all type of shock
     Except
     3 types:
     1. Anaphylactic shock, DOC: Adr
     2. Cardiogenic shock with oliguria
        ↳ DOC: DA (2-10)
     3. Cardiogenic shock with SBP>100
        DOC: Dobutamine (β_1 ↑ → CO ↑)
4. Dobutamine: β_1 ↑
5. Fenoldopam: D_1 ↑

6. Isoprenaline: All β (R) ↑

B. Non – Catecholamines:

1. α_1 agonist
   - Phenylephrine
     ↳ DOC ↓BP after spinal anesthesia
     ↳ Eye drop: contract radial ms or iris
     ↓
     Causes mydriasis w/o cycloplegia

2. α_2 ↑↑
   - ↓ CNS
     ↓
     VMC ↓
     ↓
     ↓ BP
     T/t: HTN
     → clonidine
     S/E: Rebound HTN on discontinuation suddenly

   → ∝ - Methyl DOPA
   T/t: PIH (preg. induced HTN)
   S/E: - Sedation, drowsiness
   - Post partum depression
   - Auto immune haemolytic anemia

   - Ciliary body eye (eye drop)
   - Brim onidine (↓ Aq humor synth)
     T/t: Glaucoma
     C/I: Children / neonates
     Causes respiratory depression
     S/E: retraction of eyelid

3. β_2 agonist
   (Relax smooth muscle)
   1. Bronchodilator
      ↓
      a. SABA
      -buta-
      - Salbutamol
        ↓
        Faster acting
        ↳ DOC: Acute COPD attack
        S/E: 3T/3H
        ↓
        Tachycardia, Tremors, Tolerance
        Hyperglycemia, hypotension, hypokalemia

   2. Tocolytics
      - Ritodrine
        T/t: Preterm Labour
        S/E: Tachycardia
        Tremors
        Hyperglycemia
        Hypotension
        ↓
        Pulmonary edema

Tachycardia, Tremors, Tolerance
Hyperglycemia, hypotension, hypokalemia

b. LABA (-metero-)
- Salmeterol (slow onset)
- Formeterol (fast onset)

↓

Most preferred for acute broncho asthma ∴ ZCS

c. Verylong acting BA (VLABA)
(-terol)
Indacaterol (T/t: COPD)

iv. β_3 agonist
- Mirabegron (Relax Bladder)
DOC: urge Incontinence (overactive bladder)

ANTI-ADRENERGIC DRUGS 42:45

- α - (x)
- β - (x)

A. α - blocker

i. Prazosin
α_1 (x)
(α_1A & α_1B)

↓

- Vasodilator
- T/t: HTN, HTN crisis HTN crisis in scorpion sting
- S/E: Max risk or orthostatic hypotension

ii. Tamsulosin
- α_1A (x)
- No vasodilation
- No hypotension
- Relax prostate & urinary sphincter
- DOC: BPH
- S/E: Floppy iris syndrome (miosis

mnemonic: FIRE

retrograde ejaculation

1. α action on Eye
parasym ↑ radial ms
& Miosis

Retrograde Ejaculation

iii. Phenoxybenzamine
- (α_1 & α_2) (x)
- Irreversible blocker (covalent bond)
- DOC: HTN crisis in pheochromacytoma

iv. Phentolamine
- (α_1 & α_2)(x) reversible
- Short action
- DOC : HTN crisis: Clonidine withdrawal syndrome
  : Cheese reaction
  : Intra operative crisis of pheochromocytoma

DOC of

Nitroprusside > phentol-amine

B. β blocker

1. Generation – I
(β_1 & β_2) (x)

S/E: Bronchospasm
Vasospasm
Hypoglycemia

C/I: BA / COPD
Coronary artery disease
HTN crisis
Diabetes Mellitus – II

Indication: Non CVS Indication

- i. Propanolol (↓ CNS)

DOC: Performance anxiety
~~Asthenia~~ Akathesia
Essential tremor
Migraine prophylaxis (cause vasospasm)
Esophageal varices prophylaxis
Congenital hemangioma

- Timolol: Glaucoma

ii. Generation II — β_1 (x)

iii. Generation III — β (x) + Vasodilation

S/E: ↓hR / ↓ CO / ↓AV conductor

C/I: Bradycardia
Cardiogenic shock
Heart block

Indications:

a. HTN (↓ CO → ↓ BP)
   Ex: Labetalol
   ↳ DOC: Pregnancy Induced HTN
b. Angina
c. M.I (Lowest possible dose)
d. Arrythmia (T/t: Supra ventricular)
e. CHF: ↓ HR
   ↓ Cardiac remodelling (↑ survival)
   ↓
   ↓ JG cells → ↓ RAAS

Ex: carvedilol: $\propto$ (x) , β(x) Ca^{2+} (x), Anti oxidant

- Esmolol (gen - II shortest acting β (x))
- Rapidly metabolised by RBC esterase enzyme

ANTI-GLAUCOMA DRUGS 57:02

1. ↑ Drainage of Aq. Humor
   a. Trabecular drainage ↑
      i. Pilocarpine (T/t: Acute Angle closure glaucoma)
         S/E: 4P
      ii. Netarsudil (eye drop)
         - Rhokinase (x)
         - S/E: Corneal verticellata

   b. ↑ Uveoscleral drainage:-
      i. PGF2$\propto$ ↑
         Ex: Latanoprost
         Doc: Prophylaxis

S/E:

- Lashes ↑ (length &no)
- Tanning of iris (brown)
- Macular oedema
- Pro inflammatory drug (uveitis)
- Upper eyelid sulcus becomes deep

ii. ↓ Synthesis of Aq. Humor

a. β (x) 2nd DOC

Timolol > Betaxolol

S/E: Timolol:-

- Allergic reaction
- Blurring sensation
- ↓ corneal sensitivity
- Dryness of eye
- Duct block

C/I: BA / COPD

- Brimonidine
- Carbonic Anhydrase (x)

  Ex: Acetazolamide (oral, I.V)
  - 1st drug given in acute Angle closure glaucoma
  - Followed by pilocarpine eye drop

  Mannitol (I.V)

  T/t Acute ACG: not controlled by Acetazolamide

Respiratory System

1. DRUGS FOR BRONCHIAL ASTHMA 00:19

a. Inhalational corticosteroids

- DOC Prophylaxis

MOA:

1. ↓ DNA expression of mast cell
2. ↑ Lipocortin = ↓ PLA_2 (-) = ↓LT synthesis

Ex: Fluticasone
Beclomethasone
Budesonide
Ciclesonide

S/E:

1. Oral candidiasis (M/C)
   ↳ Prevention: Spacer
   Mouth rinse
   ↳ T/t: Local antifungal (clotrimazole > Nystatin)
   ↓ Not controlled
   Systemic antifungal
   Fluconazole (DOC)
2. Dysphonia / hoarseness
3. Systemic S/E
   ↑ CNS: ↑ICT / epilepsy
   ↑ IOP (glaucoma, cataract)
   - ↑ hR
   - ↑ BP (Na^+ / H_2O ↑)
   - Osteoporosis ↓ Ca^{2+}
   - Muscle - skin atrophy
   - Peptic ulcer disease
   - Hyperglycemia, obesity (systemic S/E)
   - ↓ hPA axis

b. Bronchodilators:

1. SAMA / LAMA
   - Ipratropium
   - Tiotropium
2. SABA / LABA
   - Salbutamol
   - Formetrol (DOC)
3. $MgSO_4$ (I.V): Block Ca^{2+} channel
   T/t: Acute B.A
4. Theophylline (oral)
   Aminophylline (I.V)
   - Enzyme and PDE inhibitor → ↑ CAMP → Bronchodilation
   - Adenosine A_1 (x) → Bronchodilation

- S/E
  - Resembles salbutamol
  - Tremors, tachycardia
  - Hyperglycemia, Hypotension

- S/E Aminophylline
  - ↑ HR
  - CNS centre (Insomnia seizure)
  - ↑ RR, HR
  - Diuresis

- 3 problems of Theophylline:
  a. Narrow therapeutic index
  b. Liver enzyme (CYP1A1/2) → Zero order kinetic
  c. Drug interactions (+) (+)

c. Other drugs

a. IgE (x)
   - Omalizumab
b. Leukotriene receptor (x)
   - Monteleukast
     → No S/E
       Rare (Mood swings)

- T/t for Bronchial Asthma
  1. Acute B.A
     Formetrol + Budesonide / Salbutamol
  2. Prophylaxis
     ↳ F+B (↑↑ severity) →↑ Dose Budesonide
  3. COPD (emphysema / chronic Bronchitis
     - Acute attack
       Salbutamol (DOC)
       ↓ not controlled
       Add: Ipatropium
     - Prophylaxis
       ↓
       Tiotropium
       ↓ not controlled
       Add: VLABA / Salbutamol

- Others drugs:
  a. N - Acetyl cysteine - mucolytics
  b. Opioids = T/t Drug complex
     Codeine / Noscapine / Levopropoxyphene
     S/E: Constipation
     Addiction
     ↓ RR

Dextromethorphan (DOC)
- +u and NMDA (x)
- Min risk of constipation / Addiction

c. Pulmonary Fibrosis: Pirfenidone
   Nintedanib
d. Cystic Fibrosis: cFTR analogue
   -caftor
   Ex: Ivacaftor

Kidney (Diuretics)

1. PCT:-

1a. Carbonic anhydrase (x)

- HCO_3^- loss
- S/E:
  1. Metabolic acidosis
  2. Hco_3^- loss

CC^- ↑ ; ↑ loss of Na^+ / K^+
↓
↑ RAS
(↑ Aldosterone)
↓
↑ Na^+ and H_2O retention } mild hyponatremia
K^+ / H^+ loss
↓
Max. incidence of hypokalemia

  3. Ca^{2+} (Alkaline in urine)
     ↓
     Ca^{2+} stones

Indication:

a. Acetazolamide
   2nd DOC for raised ICT → ↓ CSF Synthesis
b. Glaucoma
   - Oral / iv
     Acetazolamide (1st Drug in acute ACG (+) Pilocarpine)
   - E/D: Brinzolamide
     Dorzolamide
c. DOC: Acute mountain sickness (↓ Hypoxia)

Acetazolamide → metabolic acidosis → Hyperventilation
↑ (-)
CO_2 Wash out alkalosis ←

2nd DOC: Dexamethasone
Complication: pulmonary edema, Nifedipine
C/I:

- CKD (↑ Acidosis)
- COPD (↑ CO_2 → ↑ Acidosis)
- Cirrhosis (↑NH_3) - encephalopathy

IB: SGLT2 (x)

- Na^+ and H_2O loss ↑
  ↓
- ↓ congestion: T/t CHF (Empaglifozin
  Dapagliflozin)

S/E:

- Hypotension - orthostatic
  ↓
  ↑ Fall → bone injury
- Dehydration
- ↑ glucose loss
  (↓ hba1c)

T/t: Diabetes mellitus - II
↓ macroangiopathy CAD
↓ microangiopathy DKD
2nd DOC - proteinuria

S/E:

- Glycosuria
  ↑ UTI (candida)
  ↑ genital skin infection
  (Fournier's gangrene, vulvovaginitis)
  - Wt loss
- ↑ DKA
  C/I: DM-I / DM-II with h/o DKA
- ↑ risk of limb amputation

C/I: PVD and Diabetic foot ulcer

1c. Mannitol

- I.V (20% solution)
- Site: PCT > Loop of Henle descending limb
- Osmotic effect
  ↓
  Bind to H_2Oin Kidney tubule
  ↓
  H_2O reabsorption (x)

Indication:

1. DOC Raised ICT (↓ CSF synthesis)
2. Acute ACG (Refractory to Acetazolamide)
   ↓

↓ Aq humour synthesis

3. DOC: Cerebral edema

   Risk: Long term T/t or h/o cerebral haemorrhage
   TOC: 3% hypertonic saline

4. DOC: post dialysis disequilibrium syndrome

- C/I:-
  - CHF with pulmonary edema - hypervolemia

Loop Diuretics	**Thiazide Diuretics**
SOA: Asc. LH (Thick)	• Early DCT
MOA: Na+ K^+ - $2cl^-$ (x)	• Na^+ -cl- (x)
Efficiency: 20% Na+ & H_2O loss ↓ ○ Max loss of Na+ and K^+ loss ○ Less incidence of hyponatremia & hypokalemia	• 5-10% Na^+ loss (No loss of H_2O) - Max risk of hyponatremia - Medium efficacy
• High ceiling drugs	• Low ceiling drugs
• Indications: 1. ↑ Na^+ & H_2O loss DOC: CHF with pulmonary edema Pedal edema CKD with periorbital edema	• Na^+ loss (hyponatremia) T/t: hypernatremia • DOC nephrogenic D-I ↓ H_2O loss ↑↑ ↓ hCTZ
• Other ion loss:- T/t: Hypercalcemia Hyperkalemia	• ↑ Ca^{2+} retention ↑ PTH action T/t: Hypocalcemia Doc: Idiopathic hypercalciuria With nephrocalcinosis
• ↓ BP Maintenance T/t HTN ↓ Risk of dehydration	• ↓ BP (Hyponatremia) ↓ Sympathetic nerves (mild vasodilation)

HTN with CKD, HTN with CHF] ↑ H_2O retention
↓
Furosemide

S/E:
- Loss of all ions
  ↓ Na^+ / K^+ / Cl^- / mg^{2+} / Ca^{2+} / HCO_3^- / H^+
  ↓
  Parasthesia, ototoxicity
  Ms. Weakness
- All metabolic pathways ↓↓

Id: K^+ sparing diuretics
SOA: Late DCT & cortical DCT
MOA: Aldosterone receptor antagonist (-one)

S/E:
- ↑ Na^+ & H_2O loss (mild)
- ↑ K^+
- Spironolactone
  ↳ Sexual S/E - gynecomastia
  → ↑ K^+ - C/I = CKD

Indications:
a. Aldosterone (RAAS (X))
   1. CHF (↓ cardiac remodelling - Eplerenone)

b. Resistant HTN
   - Not controlled by 3 Anti HTN drug must include one diuretic
   - 4th drug ARA spironolactone

c. DKD
   Finrenone
   ↓
   ↓ Proteinuria
   DOC: ACE I, ARB

d. DOC: Ascites, edema, cirrhosis → spironolactone

Maintenance hTN
(Mild to moderate HTN - 1st line)

Ex: Chlorthalidone
Indapamide
- Min S/E (metabolic)
- Long acting drug

- Same S/E (no loss of Ca^{2+})

- Other indications:
  1. Hirsutism (Spironolactone)
  2. ↓ K^+
  3. DOC: Conn's syndrome (1° hyperaldosterone)

- Misc drugs:
  1. ADH Drugs:
     A. Analogue
        - Terlipressin (VI) ↑
          ↓
          Vasoconstriction
          - DOC: Acute bleeding
            esophageal varices
        - Desmopressin (V_2) ↑
          ↓
          ↑ water retention

          DOC: Central diabetes insipidus
          Nocturnal eneuresis
          T/t: Factor VIII ↓↓ (V_2 ↑)
          Hemophilia

     B. Antagonist
        Tolvaptam (V_2 (x))
        DOC: SIADH
        S/E: ↑ Na^+
        ↓
        Leads to osmotic demyelination syndrome

  2. ARNI
     ARB + Neprilysin enzyme (x)
     ↓
     Valsartan + Sacubitril
     ↓ ↓
     RAAS (-) ↑ ANP
     ↓ ↑ BNP
     ↓ Cardiac ↓
     Remodelling Na^+ - H_2O loss → ↓ congestion
     Max. ↓↓ Mortality
     ↓↓ hospitalisation ↑ survival in CHF

     S/E:
     - K^+: Valsartan

- Angioedema – Sacubitril

ARNI + ACEi ↑ C/I

ARNI → ACEi switching; min. 36 hours

- ↓ BP
  (C/I SBP < 100)
- C/I : Pregnancy

- Nesiritide (BNP analogue)
  I.V Acute CHF

- Omapatrilat
  ACEI + ND → ↑ Angioedema

Haematology

A. ANTIPLATELET DRUGS 0:28

- Used in presence of arterial thrombi
- Angina / STEMI / cerebral stroke / gangrene

Groups:

1. Aspirin
   - Cox - 1 (-) irreversible
   - Low dose (75 - 325 mg)
   - ↓ TxA_2 synthesis
     ↓
     ↓ thrombosis
   - 1st drug in Acute M.I
     Loading dose: 325 mg (oral, chew)
   - DOC: Pre-eclampsia prophylaxis
   - S/E: Nausea, Vomiting
     • GERD / PUD
     Hypersensitivity Reaction
     Interstitial nephritis

2. P_2Y_{12} Receptor (x); ADP receptor (x)
   - Clopidogrel
   - Ticlopidine
   - Prasugrel

   - Prodrug; Irreversible (x)
   - Action: 4 to 5 days
   - Patients undergoing surgery should stop

- Ticagrelor
  - Active drug
  - Reversible P_2Y_{12} (x)
  - Stopped before surgery

- Clopidogrel (prodrug)
  ↓ liver (CYP2C19)

Active

- Defective in 40% Asian
- PPI except pantaprazole

3. PAR – 1 (x) Thrombin receptor (x)
   - Vorapaxar

4. Gp IIb IIIa (x)
   - Abciximab (I.V route)
     ↳ Most efficient antiplatelet

5. PDE (x)
   - Dipyridamole
     S/E: Coronary steal phenomenon
     C/I: Angina, MI
   - Cilostazol

GUIDELINES *11:20*

Dual Anti platelet therapy (min. 6-12 months)
↳ Aspirin + Clopidogrel

- Stop Aspirin before surgery
  1. Chronic intake: 3 days before surgery
  2. Recent start: Don't stop

B. ANTICOAGULANT DRUGS *13:06*

- ↓ Clotting Factor pathway
- Venous thrombi
  (DVT / PE / prosthetic heart valve / Atrial fibrillation / major jt. Surgery / cancer / APS)
- In STEMI, stroke, gangrene; Antiplatelet + Anticoagulants both given

Drugs:

1. Directly acting: (more efficient)
   - Fluid phase
   - Clot lysis (thrombolytic property

2. Indirectly acting
   (↓↓ efficient = ↓ Fluid phase)

a. Xa (x)
   - Oral route (Directly acting oral anticoagulant)
   - -Xaban
     1. Rivaroxaban
        - Better absorption after food
     2. Apixaban (safe in CKD)
        Antidote: Andexanet Alpha

b. IIa (x) (direct thrombin inhibitor)
   - ↓ XIIIa ↓ clot stabilising factor
   - Va, VIIIa, Xia (x)

     ↓ platelet aggregation

- Oral route:
  - Dabigatran (DOAC)
    ↳ Antidote: Idarucizumab (for toxicity)

- I.V route:
  - Short action
  - Acute emergency

  Ex: Argatroban
  DOC: Haparin Induced Thrombocytopenia Syndrome

- Bivalirudin
  - Derived from leech
  - Used in percutaneous angioplasty (to dissolve clot)

Indirectly acting:

a. Pareneral
   - Low molecular weight heparin
     - Parin (enoxaparin)
   - Unfractionated heparin

b. Oral
   - Warfarin
   - -Coumarin-
     (Acecoumarin)

- MOA: Activate AT - III enzyme
  ↓
  Xa (x), IIa (x)
  Fondaparineux: Xa 9x) only

- Fast onset: Acute
  emergency
- Fast offset: Few hours before surgery stopped
- UFH: Macrophage metabolism
  - Safe in CKD/CLD
- LMWH: Kidney metabolised
  ↓↓ Dose in CKD
- Route: IV/S.C
- Monitoring:
  1. UFW = aPTT
  2. LMWH = aPTT/anti Xa level

  In CKD, obesity, pregnancy

- Management of toxicity
  a. Protamine sulfate
     ↓ (-)
     UFH
  b. Prothrombin complex Concentrate (II, VII, IX, X) or, Fresh frozen Plasma
     ↓ (-)
     LMWH

- Liver; VKOR (x) Competitive inhibitor)
  ↓
  II/VII / IX / X ↓↓
  - First clotting factor: ↓↓ VIIa
  - Slow onset: 7 days (peak)
  - Slow offset: 4-5 days
    ↓
    Stopped before surgery
- Metabolised by liver
  ↓
  Safe in CKD
  ↓
  CVP2C9 (Zero order Kinetic)

- Phenytoin (drug induced ++)
- Oral (100% absorption)
- INR monitoring
  (N) ≈ 1
  Toxicity > 4.5

- INR:
  1. >4.5 - ≤5.0: skip the next dose
  2. >5.0 - ≤9.0: Stop warfarin
     Restart drug

- IF INR is in desired range
- Vit K given if patient is at high risk of bleeding
  >9.0: Stop drug
  ↓
- Give Prothrombin concentrate complex > FFP
- Vit K_1

- Pregnancy safety
  Safe
  - Guidelines (>5mg / day)
- 1st trimester: LMWH
- II/III: Warfarin (oral)
- At 36 wks: LMWH
  ↓
  At 37 wks: Delivery
- S/E: UFH > LMWH
  - Aldosterone ↓
  - ↓ Ca^{2+} - osteoporosis
  - Hypercoagulation

Dose ≤ 5mg / day
Safe in all trimester
Dose > 5mg/day - unsafe

- If given in 1st trimester:
  Contradi's syndrome (Dwarf)
- At delivery: CNS hematoma (Kernicterus)
  - Skin necrosis
- (↓ protein C, S)
- First 7 days
  ↓
  Hypercoagulation
  ↳ Bridge therapy (Warfarin + LMWH)

- Guidelines:
  - Acute emergency / hospitalised patient
    ↓
  - LMWH
    ↓
  - Discharge (long term anticoagulant therapy)

a. DVT
   PE
   Atrial fibrillation
   Ex: DOAC.

b. Prosthetic heart valve, APS, Atrial Fibrillation with mitral stenosis
   ↓
   Warfarin

c. Cancer
   ↓
   LMWH / DOAC

DOAC
- ↑ efficienty
- Monitoring not required

Warfarin
- ↓ efficiency
- Always required (INR)

- Short acting (BD / TDS)
- Not approved in
  - Cardiac valve pathology
  - Pregnancy
- Long acting
- DOC: Valve pathology safe in pregnancy
  ≤ 5mg / day

THROMBOLYTICS / FIBRINOLYTICS *45:2*

MOA: tissue plasminogen activator - ↑
↓ (+)
Plasminogen ⟶ Plasmin (dissolve already formed clot)

a. Natural:
   - Streptokinase / urokinase

b. Synthetic: - teplase
   (alteplase, reteplase, tenecteplase)

Indications: STEMI
Stroke
Gangrene
Symptomatic Pulmonary embolism

Antidote: ↓ t-PA (Epsilon Amino caprioic acid (I.V))
Or,
Tranexemic acid

C/I:
a. H/o neurosurgery
b. Ongoing bleeding
c. HTN crisis

HYPOLIPIDEMIC DRUGS *48:42*

- ↓ cholesterol / ↓ LDL

A. Statins:
   - DOC
   - MOA: HMG CoA Reductase (x)
     ↓

↓ Cholesterol synthesis in liver
↓
↑ LDL receptor
↓
↑ Cholesterol uptake
↓
↓ lp (a) expression – liver

- S/E: Hepatotoxicity
  Myopathy
  Hyperglycemia
  C/I in gravid females

- Long Acting Drugs (Rosuva > Atorva)
  ↳ CYP3A4 (liver safe in CKD
  - ↑ efficiency
  - ↑ S/E
  - Given at any time of day

- Short acting drug (Fluvastatin > Pravastatin)
  - ↓↓ Efficiency
  - ↓↓ S/E
  - Given at night time preferably

  Fluvastatin – safe in CKD
  Pravastatin – safe in CLD

B. PCSK – 9 (x)
↓
Liver (x)
↓
LDL Receptor: Down regulation on liver cells (x)
↓
LDL – (R) over expressed
↓
↑ Cholesterol uptake from plasma
Ex: Evolocumab (2nd DOC)

Route: S.C

Dosage: once - twice/month

C. Ezetimibe
- Enterocyte acting
  ↓
- Stop cholesterol absorption from food
  ↓
- Efficiency ↓↓

d. Bile acid Binding Resin
  ↓
  Chole -
  Ex: Cholestyramine

↓ Triglyceride / ↓ VLDL
- Fibrates (Femo Fibrate)
  ↓
  Min. Drug interaction
- MoA: PPaR - ∝ ↑↑
  (↑ LPL enzyme)
  ↓
  Shifts Triglyceride from plasma to organs / adipose tissue
- S/E: HMG S/E + gall stones

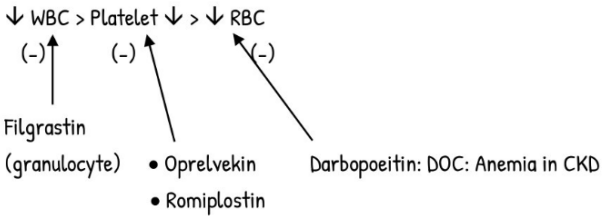
Niacin (Outdated)
- Max. risk of hMG
- Diabetic complication ↑↑ Acanthosis Nigrans

V. IRON OVERLOADING *59:30*

- Iron chelating agents
  a. I.V: Desferroxamine
     DOC: in Symptomatic patients
  b. Oral: Defarivox
     Deferipone
  - In asymptomatic patients

VI. BONE MARROW SUPPRESSION

1:00:46



Anti HTN Drugs

I. Diuretics
- High efficiency (loop diuretics) = Furosemide (T/t HTN with CHF / CKD)
- Medium efficiency, Thiazide diuretics chlorthalidone / Indepamide
  ↳ Long action min. S/E → 1st line drug
- Low efficiency
  Aldosterone receptor antagonist (K^+ ↑↑↑) S/E
  T/t: Resistant HTN
  Ex: Spirono lactone

II. ANS:-
- ∝ blockers: Prazosin
  S/E ↑: Maximum risk of orthostatic Hypotension
- β-blockers
  - Gen II/III best
  - Ex: labetalol, Esmolol
- $\propto_2$ agonist (↓ VMC → ↓ BP)
  - Clonidine
  - ∝-m-DOPA

III. RAAS
a. Direct Rennin Inhibitor
   ↳ Aliskiren (S/E ↑K^+)
b. ACE inhibitor (-pril)
c. ARB (Angiotensin II Receptor blocker) [-sartan]
   • AT_1 (R)(x)

IV. Vasodilators
a. Calcium channel blockers (-dipine)
   ↳ 1st line drug
b. No Donors -nitro-
c. K↑↑↑
d. D_1 ↑ - Fenoldopam (used in HTN with oliguria)

ACE INHIBITORS / ARB 10:29

- ↓ RAAS

a. HTN (1st line drug)
   - Preferred in young pt. (<55 yrs)
   - Min. sexual dysfunction
   - Min risk of orthostatic Hypotension

b. HTN crisis – Captopril
   Enalaprilat

c. ChF (↓ Cardiac remodelling /↓ mortality)
   (ARNI > ACEI > ARB)
   ↳ Valsartan + Sacubitril

d. Diabetes keto acidosis / proteinuria / DM Nephropathy – DOC
   - ACEI / ARB > SGLT – 2 (x) > ARA (finrenone)

e. DOC for scleroderma acrisis (↑ BP / glomerulosclerosis)
f. DOC HTN with U/L Renal artery stenosis
g. Losartan – Antiplatelet (↓ TxA2 (R))
   – Antigout (uricosuric)
h. Candesartan – migraine Prophylaxis
   Or,
   Lisinopril
i. Telmisartan – Anti-DM property
   ↓
   PPaR-γ (R) ↑ → ↑ glucose uptake

#PK:-

a. All are prodrug except:
   - Captopril (short acting)
   - Lisinopril (long acting)

b. ↓↓ Dose in CKD except:-
   Fosinopril
   Moexipril } liver
   Telmisartan

S/E and C/I:

C: Cough and Angioedema (only with ACEi) d/t ↑: bradykinin
A: Anemia (↓ erythropoietin)
P: Potassium ↑
T: Taste change (captopril)
O: Orthostatic hypotension (mm risk)
↳ Increased risk with diuretics / dehydration
P: C/I in Pregnancy (Kidney & lungs ↓)
R: C/L: B/L Renal artery stenosis
I: Increase serum creatinine; avoided > 2.5 level
L: Local skin rashes (red) = captopril
S: Sprue like enteropathy (olmesartan)

VASODILATORS *22:33*

a. CCB (Calcium channel blocker)
   1. Dihydropyridine (DHP) - dipine
      - Strong vasodilator
        ↳ DOC: HTN Crisis (Nicardipine)
        1st line drug in prophylaxis of HTN (Amlodipine)
        DOC in reflex vascular spasm after SAH (Nimodipine)
        DOC in PVD (Peripheral vascular disease - Raynaud's)

- DOC: Vasospastic Angina
- DOC: Pulmonary artery Hypertension (Vasore active test (+))
- DOC: Preterm labour (tocolytics)
  ↓
  Nifedipine

PK:

Liver metabolised
Safe in CKD

S/E:

- ↓ BP
- Reflex HR ↑
- Pedal edema
- Headache (m/c)

B. Nondihydropyridine

a. Verapamil

- Non selective action
- Block Ca^{2+} (x) entry in heart

  ↓

  ↓ Nodal Automacity

  T/t Antiarrythmia
  - ↓ SA node: Sinus tachycardia (β blockers)
  - ↓ AV node: PSVT (Adenosine)

  ➔ Thus its 2nd DOC

PK: liver (CYP3A4)
P-glycoprotein inhibitor
Drug interaction maxm

#S/E: ↓hR/AV conduction • ↓ Co
#C/I: ChF (↓Co)
Along with β(x)

B. No Donors

- Nitroprusside
  - Most potent
  - DOC: Intraoperative HTN crisis
  - S/E: Cyanide toxicity

    ↑ (-)

    Vit B_{12} (hydroxycobalamin)

- Nitroprusside
  - Most potent
  - DOC: Intraoperative HTN crisis
  - S/E: Cyanide toxicity

    ↑ (-)

    Vit B_{12} (hydroxycobalamin)

- Nitroglycerine:
  - Venodilator > coronaries > arteriole
  - T/t: HTN crisis with coronary artery disease

- S/E: Methemoglobinemia
  ↑ (-)
  Methylene blue

K+CHANNEL OPENERS *31:53*

1. Hydralazine
   T/t: PIH
   S/E: SLE

2. Diazoxide
   T/t: Insulinoma
   DOC: Hypoglycemia

3. Minoxidil
   - T/t: Alopecia

Guidelines

a. HTN without comorbidity

<55 years → ACE 1 / ARB → ↓ not controlled → ↑ Dose

> 55 years → Calcium channel blocker → Not controlled ↓ → ↑ Dose

Not controlled
↓
ACE I + CC B
↓ not controlled
Diuretics (thiazide)
↓ not controlled
Resistant HTN

4th drug: ARA (Aldosterone receptor antagonist)

b. HTN with CHF
   - Furosemide not controlled → ACEi/ARB not controlled → CCB
   - Metolazone

c. HTN with DM
- ACEi / ARB —not controlled→ CCB —not controlled→ Thiazide (Telmisartan)

d. HTN with CKD

1. Proteinuria (+)
- ACE I / ARB
  ↓ not controlled
- CCB (non DHP > DHP)
  ↓ not controlled
- Furosemide

2. Proteinuria absent

↓ Edema:

Present → ↓ Furosemide → ↓ Not controlled → ↓ ACEi / ARB → ↓ Not controlled CCB

absent → ↓ ACE / ARB or CCB

e. PIH
- Safe: labetalol (DOC)
  ∝ - m - DOPA
  Hydralazine
  Nifedipine
  Prazosin
  Clonidine

- C/I: RAAS (-)
  Diuretics

f. HTN crisis
- Nicardipine + labetalol: TOC
- 7 exceptions:-
  1. Scorpion sting: Prazosin
  2. CNS cheese reaction: Phentolamine
  3. Pheochromocytoma: Phenoxybenzamine
  4. PIH: labetalol
  5. Aortic dissection: Esmolol
  6. Intraoperative crisis: Nitroprusside

g. Pulmonary artery HTN:
- CCB (DOC): If vasoreactive test (+)
- If vasoreactive test (-)

1. Oral drugs: Mild to moderate route
   - Endothelin (R) Antagonist

   ↳ Bosentan: ETA & ETB (R) (x)
   S/E: hepatotoxicity

   ↳ Ambrisentan: ETA (x)
   No hepatotoxicity

   - PDE - V (x): ↑cGMP

     - Sildenafil S/E: blue vision
     - Tadalafil (longest acting) S/E: Back pain
     - Avanafil (Fastest)

- DOC for erectile dysfunction
- Common S/E: ↓BP/Reflex HR↑ / Headache / Diarrhea
  Rare S/E: Hearing loss

- Riociguat:
  ↑ guanyl cyclase = ↑ cGMP
- PGI_2 ↑ :Tresprostenil- ↑ cGMP

2. Non oral route (severe cases)
   - PGI_2 analogue
     - Epoprostenol (I.V pump)
     - Treprostenil (I.V Inalational)
   - NO (Inhalational)
     ↳ Pediatric patients

Drugs for Angina, CHF, Arrhythmia

ANGINA PECTORIS 00:22

A. Nitrates
- DOC: Acute anginal attack
- Nitroglyceride > Isosorbide dinitrite
- Sublingual > I.V route
- T/t: Maintenance Angina
  ↓
  This is associated with risk of tolerance
  ↓
  Therefore nitrate free period of 8-10 hrs min.
  b/w 2 doses is kept

B. B Blockers:
- ↓ hR: DOC Maintenance of classical symptoms

C. Calcium channel Blockers (-dipine)
- Vasodilator
- DOC: Maintenance vasospastic symptoms

D. Nicorandil
- K^+ channel opener

E. Ivabradine
- Inhibitor of funny current in SA node
  ↓
  Causes bradycardia
- T/t: Angina, MI, CHF

F. Fasudil
- Rhokinase inhibitor
- Coronary vasodilator

G. Ranolazine
- Late Na^+ current (x) > PFOX (x) partial fatty acid oxidation inhibitor

H. Trimetazidine
- Outdated
- PFOX (x)

Nitrates

MOA: ↑ NO: vasodilator
↓
Venodilator > coronaries > arteries
Major epicardial vs. > minor vs
↑ pooling of blood in veins - ↓ preload

- Indications: Angina
  CHF
  MI
  - Relax GIT muscle
  - Anti platelet
  - Amylnitrite (cyanide toxicity T/t)

- PK:
  - High first pass metabolism (except isosorbide mono nitrate)
  - Lipid soluble - cross BBB

- S/E:
  - Headache (m/c)
  - ↓ BP
  - Bradycardia / Tachycardia
  - Tolerance

- C/I: PDE - V (x) → ↑ cGMP (maintain time gap)

DRUGS FOR CHF *11:30*

A. Acute CHF
1. ↓ preload, ↓ congestion (venodilator)
   a. Furosemide (DOC)
   ↓
   ↑ PGE_2 Synthesis > Diuretic

b. Morphine
c. Nitroglycerine
d. Nestritide (BNP Analogue)

2. Inotropic drugs
Used if EF < 35 – 40%
a. With oliguria – dopamine
b. With systolic BP < 90 – nor Adrenaline
c. With SBP > 90 – Dobutamine
d. With Arrhythmia – digoxin

3. Vasodilators

B. Maintenance CHF:-
- HFγEF (systolic hF, EF = 40%)
1st line drugs:-
a. ↓ cardiac remodelling (↓ mortality)
ARNI > ACEI > ARB
b. ↓ congestion
Furosemide
c. ↓ Tachycardia
β. Blockers – carvedilol, or metoprolol, Bisprolol

- 2nd line drugs
  - Add on / Aternate:-
a. ↓ mortality: ARA (eplerenone), IDN + Hydralazine
b. ↓ congestion: SGLT2 (x) (Empa / Dapagliflozin)
c. ↓ Tachycardia: Ivabradine
d. ↓ CO: Inotropic (Digoxin – oral route)

2. HFpEF, Diastolic HF, (EF>50%)
- Only diuretics given to prevent congestion:-
  - Furosemide
  - SGLT2 (x)
  - ARA

Digoxin

- MOA: Muscle (Na^+ K^+ ATPase (x) ↑Ca^{2+})
  ↓
  Inotropic → ↑CO → T/t: CHF
  CNS (Vagal): M_2 = ↓ Node T/t: SVT
- C/I: Wolf Parkinson white syndrome
  Hypertrophic Cardiac myopathy
- S/E:
  - G/T toxicity (m/c)
  - Gynaecomastia (rare)
  - Yellow vision
  - Inhibit nodes (↓ hR / heart block)
  - ↑ Ca^{2+} over loading loads to arrhythmia
    → m/c ventricular arrhythmia
    Ventricular Bigeminy

- Toxicity: Non PSVT with heart block
  ↳ T/t: Digibind
- Rare S/E: Neuralgia, Delirium
- Risk factors:
  1. Reduced drug elimination from kidney
     - CKD
     - Old age
     - Any drug which is p-glycoprotein pump inhibitor
       - Clarithromycin
       - Cyclosporine
       - Amiodarone
       - Verapamil
       - Erythromycin
       - Quinidine

  2. ↑ T_3 / ↓T_3

3. Cardiac Muscle disease:-
   - Na^+K^+ ATPase already blocked
   - Ex: MI, Myocarditis, Myopathy

4. Electrolyte imbalance
   - ↑ Ca^{2+} / ↓ Mg^{2+} / ↓K^+

DRUGS FOR ARRHYTHMIA *28:16*

Classification:

a. Class 0: Funny current inhibitor
↓
↓ SA node
↓
T/t: Sinus Tachycardia
Ex: Ivabradine

b. Class I: Na^+ channel blocker
T/t: Muscle arrhythmia
   a. Ia: Na^+ (x) > K^+ (x)
      - Procainamide
      - Quinidine
        - Cause delay in depolarisation & repolarisation
        - S/E: QT prolongation – Torsades de pointes
   b. Ib – lignocaine
   c. Ic

c. Class – II: β blocker; DOC: Sinus tachycardia

d. Class III:
   - K^+ channel blocker
   - Broad spectrum
   - Amiodarone

e. Class IV:

- Calcium channel blocker
  - Verapamil
  - 2nd DOC for sinus tachycardia / PSVT
  - M/c SE: constipation

f. class V: Miscellaneous drugs.

- Digoxin
- MgSO4
- Adenosine

Lignocaine	**Amiodarone**	**Adenosine**
• Class 1b	Class III	Class V
• MOA: Na (x)	• Na (x) / B (x) / K (x)	• A_1 receptor
• Indications: - Ventricular arrhythmia (1st line Drug)	• Atrial fibrillation / flutter • 1st line for VA	•
• Dose: 1.5mg / kg ↓ 0.75 mg/kg	• 300mg → 150mg	• 6 mg ↓ 12 mg
• PK: - High first pass metabolism - I.V route - Oral not given	• Oral / I.V • P-gp inhibitor • High drug interactions	• Short t ½ = 10 sec in RBC • I.V Bolus with saline push in central vein

- S/E:
  - CNS toxicity: tremors, seizures
- Pigmentation (blue)
- Corneal deposit
- Pulmonary, liver fibrosis
- ↑ T_3 / ↓ T_3
- Optic neuritis (rare)
- Bronchospasm
  ↓
  C/I B.A or COPD
  ↳ DOC: Verapamil

1. Sinus tachycardia
   ↑ (-)
   β-blocker > Verapamil

2. Atrial Flutter / Fibrillation
   (-)

   Amiodarone → not controlled → Sotalol, Ibutilide

3. Ventricular arrhythmia
   ↑ (-)
   Amiodarone, lignocaine

4. PSVT
   ↑ (-)
   Adenosine, Verapamil

GIT

A. DRUGS FOR PEPTIC ULCER DISEASE 00:30

1. Proton Pump inhibitor

A MOA: H^+ K^+ ATPase (-)
Irreversible (-)
Action: 2-3 days

2. H_2 Receptor Antagonist

- MOA: H_2 receptor
(reversible competitive (-))
- Short action

Except: Famotidine
Reversible
(Non competitive (-))
- Most potent drug

b. More efficient drug:
↓
↓ PAO / ↓ BAO
DOC: All types of PUD
Stress ulcer
Zollinger Ellison Syndrome
T/t: H. Pylori

- Less efficient drugs
↓ BAO →
Same indication as PPI
Except: ZES / H. pylori

c. Acid sensitive drugs
(enteric coating)

- ↑ First pass metabolism
Low oral bioavailability

- After food: ↓ absorption
(given 30-45 mins before food)

- Can be taken before / after food intake

- CYP2C19 liver metabolised
↓
Except pantoprazole

- Kidney eliminated

- S/E:
  a. ↓ PAO: ↓Ca^{2+} /Mg^{2+} / Fe or Vit B_{12}
  b. ↓ BAO: ↓GIT immunity (pseudocolitis)
  (↑ LRTI)
  c. Interstitial nephritis

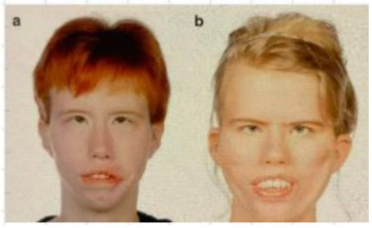
- S/E
  a. Cimetidine
  ↑ gynecomastia
  ↑ prolactinemia
  b. Ranitidine
  If stored > 6 months cancer risk
  ↑

d. Dementia

Others drugs

a. M_1 blocker
Pirenzipine (act on parietal all)

b. PGE_1 analogue (misoprostol)
- ↓ acid production
- ↑ mucus and HCO_3^- secretion
- Ulcer protective
- Pregnant female
  ↳ Moebius syndrome in baby



VI / VIII nerve not developed

c. Antacids (Directly neutralise $\bar{a}$)
- $Al(OH)_3 + Mg(OH)_2$
- Fastest acting
- Not absorbed in circulation
- Safest in pregnancy

Cation containing drugs

d. Ulcer protective drugs
- Sucralfate Bismuth
  → may cause Al^{3+} toxicity or black tongue & teeth

e. Antibiotics (mostly for H. pylori)
1. Clarithromycin sensitive
   Triple regimen
   CAMP
   - Clarithromycin
   - Amoxicillin / metronidazole
   - PPI

2. Clarithromycin resistant

Quadruple regimen

TOMB

- Tetracycline
- Omeprazole
- Metronidazole
- Bismuth

B. DRUGS FOR GERD *13:46*

- ↓ Acid production
  a. PPI (DOC)
  b. H2RA

- ↓ Food storage
  (prokinetic drugs - ↑ perisistalsis)
  1. D_2 (x)
     ↑ Ach in GIT
     - Metoclopromide
     - Domperidone
  2. $5hT_4$ receptor ↑↑
     - ↑ GIT neuron
       ↓
     - ↑ peristalsis
       - Cisapride (QT prolongation S/E)
       - Mosapride
  3. Macrolides
     - Motilin receptor ↑
       Ex: Erythromycin

C. ANTIEMETIC DRUGS *16:26*

a. CINV (Chemotherapy induced nausea vomiting)

- Max risk with cisplatin

1. <24 hrs [Early onset]
   - DOC $5HT_3$ (x) ↑ (-)
   - Seteron

   Ex: Palorosteron
2. >24 hrs (late onset)
   ↑ (x)

   DOC: NK_1 (-)
   - Substance P inhibitor

Graniseteron
Ondansetron (least eFF)
↓
DOC: PONV
Opioid Induced NV
S/E: Headache m/c
Constipation
QT ↑ (rare)

- pitant

a. Aprepitant
↓
(3 day schedule)
b. Fosaprepitant Rolapitant
- 1 day schedule
- Long action

S/E: QT ↑↑

3. Other drugs: Dexamethasone
Olanzapine

- Regimen for Cisplatin Induced CINV:
Day 1: $5hT_3$ (x) + NK_1 (x) + Dexamethasone + Olanzapine
Day 2/3: NK_1 (x) (If aprepitant) + Dexa + olanzapine

b. Motion Sickness
- Hyosine | Promethazine

c. Morning sickness
- Doxylamine (H_1 (x))
- Pyridoxine (Vit B_6)

d. Other Vomiting
- $5HT_3$ (x)
- D_2 (x)
  ↳ Metoclopramide
  S/E: Extrapyramidal symptom
  ↳ Domperidone
  (No CNS S/E)

D. DRUGS FOR DIARRHOEA 24:37

a. Infective diarrhoea
DOC: Fluorquinolone
b. Non-infective diarrhoea
DOC: Loperamide / Atropine

c. Traveller's diarrhoea
Flouroquinolone / Rifaximine
d. Secretary diarrhoea
DOC: Ocreotide (somatostatin analogue
T/t: Glucagonoma
Vipoma
Carcinoid
S/E: CCK (-): biliary sludge
Gall stone

E. DRUGS FOR IBS *26:39*

a. Constipation
1. Prucalopride 5hT4 ↑
   - Tegaserod
2. Lubiprostone: ↑CL^- channel
3. Linaclotide, Plecanatide ↑ guanyl cyclase - C receptor
4. Tenapanor : (-) of Na^+ H^+ Exchanges pump
5. Isapaghula
6. Polyethynl glycol

b. Diarrhea
- Loperamide (tu)
- Rifaximine
- Anticholinergics
- Isapghula

F. DRUGS FOR ESOPHAGEAL VARICES *29:46*

- Acute bleeding
  Terlipressin (DOC)
  Ocreotide
- Prophylaxis
  - Generation 1 β-blocker
    - Nadolol
    - Sotalol
    - Propranolol

Autacoids

1. NSAIDS
   - MOA: Cox inhibitor
     a. Non-selective cox-1 and cox-2 inhibitor
     b. Preferential cox-2 > cox-1 inhibitor
     c. Selective cox-2 inhibitor

- a = Aspirin (antiplatelet) = 75 mg to 325 mg
  C/I in gout, viral fever (cause Reye's syndrome)
  Toxicity: Metabolic acidosis
  ↓
  Treatment forced alkaline diuresis
  = Indomethacin (multiple MOA)
  - Cox (-)
  - CNS pain pathway ↓↓

  S/E: Vertigo / Insomnia / headache
  = Piroxicam
  - Long acting NSAID
  - Enterohepatic circulation

S/E: (NSAIDS) = Nausea, Vomiting
= PUD / GERD

- Papillary necrosis in kidney
- Interstitial nephrosis

C/I:

- CKD
- With PCM and opioids use
- CHF (causes water retention)

b= Preferential Cox-2 > cox -1 inhibitor

Advantage:

- ↓ PUD / GERD
- ↓ Papillary necrosis

1. Nimesulide
   S/E: hepatotoxicity
   C/I: children < 12 yrs

2. Diclofenac, Aclofenac
   T/t: Joint pain

c. - Coxib
- No advantage
- Disadvantage: ↑ platelet aggregation
  ↑risk of coronary heart disease

II. PCM (ACETAMINOPHEN) 9:51

- ↓ fever
- ↓ pain
- Mild /moderate anti inflammatory
- Over the counter
- Safe in pregnancy / children
- No S/E
- PCM toxicity ↑↑: Liver toxicity
- < 4 hours: gastric lavage
  > 4 hrs /: N - acetyl cysteine (antidote) symptom

- When a child is born with patent ductus arteriosis, for its closure
  ↓
  We use: PCM + NSAIDS (Ibuprofen + Indomethacin)

II. PROSTAGLADIN ANALOGUE 12:18

1. P4E, analogue
   a. Misoprostol
      - MTP (1st trimester)
      - PUD
        (Moebiens syndrome)

   b. Gemeprost
      - MTP (1st trimester)

c. Alprostadil
DOC: to keep ductus arteriosus patent

2. PGE_2
- Dinoprostone
- DOC: cervical ripening

c. PGF2 $\propto$ analogue
a. Eye drops:
- Latanoprost (DOC: glaucoma)
↓
(↑ uveoscleral outflow)

b. I.V:
- Carboprost (T/t PPH)
- DOC: Carbentocin = 100mg I.V over 1 mins

d. PGI_2 Analogue
T/t: Pulmonary artery hypertension
↓
Treprostnit

III. DRUGS FOR GOUT *16:50*

- ↑ Uric $\bar{a}$

a. Acute gout
1. DOC: NSAIDS
2. 2nd DOC: Colchicine
- MOA: Inhibit β-tubulin protein
↓
(-) Spindle formation
↓
↓ Multiplication of WBC in lymph nodes
- Inhibit migration of cells at site

S/E: Diarrhea (m/c)
Myopathy
Neuropathy

3. Steroids (Refractory)

b. Maintenance T/t gout

- Urate lowering drugs

1. ↓ uric acid synthesis
2. (-) Xanthine oxidase
   - Uricosuric drugs = ↑ uric acid elimination
3. ↑ uric acid metabolism

1. Allopurind (DOC)
   S/E: hypertension reacⁿ
   Febuxostat
   S/E: MI/stroke

2. Losartan
   Sulfinpyrazone
   Benzbromanone
   Probenocid

3. Recombinant uricase I.V
   - Pegloticane
   T/t: Chronic tophaceous gout
   C/I: G6PD deficiency

IV. RHEUMATOID ARTHRITIS 23:10

- Maintenance: DMARD's

a. HCQs (Hydroxine Chloroquine sulfates)

- Safe in pregnancy
- S/E: Bull's eye Retinopathy

b. Sulfasalazine (Folic $\bar{a}$ (-)
S/E: pregnancy
Oligospermia
Bone marrow suppression
C/I: G6PD deficiency
Porphyrias

c. Methotrexate (DOC)
MOA: Dihydrofolate reductase inhibitor (↓ Folic acid)

↑ Adenosine (anti inflammatory)
DOC / Route: <25 mg/week
Subcutaneous route (best)
Oral (m/c)
Pharmacokinetics: C/I: CKD as eliminated in kidney

S/E: Nausea, vomiting, diarrhea
Liver / pulmonary fibrosis

T/t: Folic $\bar{a}$
↓ not controlled
Folinic $\bar{a}$

- Methotrexate Refractory
  - Not responding to T/t for 3-6 months

a. TNF - $\propto$ blocker added - parenteral
   - Adalimumab
   - Golimumab
   - Etanercept

b. Oral triple regimen
   - Methotrexate + hcQs + sulfasalazine

c. Add IL-6 inhibitor (I.V)
   - Tocilizumab
   - Sarilumab

d. Add / Alternate
   JAK inhibitor

   - Baricitinib } other drugs
   - tofacitinib }

Other drugs
- Anakinra (IL-1 (-))
- Rituximab (CD20 (-))

- Leflunomide (liver metabolised)
- Abatacept (CTLA4 ↑)
  ↓
  Suppresses immune system

V. DRUGS FOR MIGRAINE *33:32*

a. acute migraine
   1st line Drugs
   1. PCM
      ↓
   2. NSAIDS
      ↓
   3. Triptans (Sumatriptan) - act on 5hTIB / ID ↑
      ↓
   4. Rizatriptan / Dihydroergotoxin / opioids

Other drugs
- Lasmiditan (5HTIF↑)
  - ↓ pain pathway
  - No vasoconstriction
- Ergot derivative
  - 5hTIB/ID ↑↑
  - S/E nausea / vomiting
- Direct CGRP Inhibitor
  - Gepant (gene peptide antagonist)
    (ex: Ubrogepant)

Maintenance migraine
a. Propranolol (DOC)
b. Flunarizine (T-type Ca^{2+} channel blocker)
c. Antiepileptic drugs
   1. Sodium valproate (wt. gain)
   2. Topiramate (Wt. loss)
d. Antidepressant drugs:
   - TCA
   - SNRI (venlafaxine)

S/E Ergot derivatives

E - Euphoria

R - Retroperitoneal Fibrosis

G - GIT Toxicity

O - Optic hallucination

I, S - Ischaemia

M : Mothers (pregnancy) → abortion

Tumor lysis syndrome

- ↑ uric acid
- Ca^{2+} / $PO4^{3+}$ stones

  TOC: I.V Fluids + Drugs

  Low risk: Allopurinol / Feboxostat

  High risk or KFT ↓↓ - Rasburicase (I.V)

  C/I: G6PD deficiency

Endocrine

DRUGS GIVEN FOR DIABETES MELLITUS

00:30

A. Insulin

1. Rapid acting:
   Glulisine — Fast onset given before meals
   Aspart
   lispro
2. Short acting
   ↓
   Regular insulin (I.V) DOC: DKA
   Semilante (Zinc amorphous)
3. Intermediate acting
   - NPH
     (30% Semilante + 70% ultralante)
4. Long acting insulin
   - Action lasts for 18 hrs
     - Ultralante (Zinc crystalline)
   - Action > 24 hrs
   - Glargine • Detemir • Degludee (given once aday)
     ↳ longest acting

- DOC: DM - 1 /GDM / DKA
  - 1st line drug for acute hyperkalemia; DOC: Ca^{2+} gluconate
    Route: Subcutaneous route (pens > syringe)
    m/c site: Anterior abdominal wall leaving periumblical area

II. Insulin secretogogues

- β-cells ↑↑ → ↑ Insulin release

IIa: K^+ channel blockers:-

↳S/E: hypoglycaemia
Wt gain
↑ risk of CAD

a. Sulfonylureas
Gli-
- Long acting
(control post prandial and fasting blood sugar)
- Sulfa drug
↓
- Hyper sensitivity reaction is a S/E

b. Meglinitide
-glinide
- Short acting
(control post prandial sugar)
- Not a sulfa drug

IIb. Incretin pathway drugs
- Do not cause hypoglycaemia
- ↓ glucagon fed state

1. GLP-1 analogues
-glutide
- Peptide structure
(S.C route)
↓
Except semaglutide
↓
Oral / S.C
- No effect on GLP-1 / GIP level
- No effect of glucagon in fasting state
- CNS entry (↑ satiety centre)
- Wt loss ++
- T/t of obesity

2. DPP-4 (x)
-gliptin
- Oral route
- ↑ GLP - 1 / GIP level
- ↑ glucagon in fasting state
- No CNS entry
↓
Wt. neutral

Ex: Liraglutide
Semaglutide
- ↓ Macro/microangiopathy
(↓ CAD ↓ Retinopathy
- Long acting drugs
Dulaglutide (1/week)
- Safe to use in CKD except exenatide

- No such effect
- Short acting BD / TDS
- ↓ Dose in CKD except Linagliptin (safe in CKD)

- M/C S/E:
  - Nausea, vomiting
- Rare:
  - Gastroparesis
  - gall stone
- ↑ risk of pancreatitis
- Acc to animal studies
  ↓
  ↑ Risk of medullary thyroid
- Unique S/E: absent

- Inflammation (S/E
  - M/C: nasopharyngitis
    Precipitate IBD
    Skin ulceration
    Myalgia / arthralgia
- ↓ risk of pancreatis
- ↑ risk of MEN syndrome
- Saxagliptin: ↑ CHF
  Vildagliptin] ↑ liver toxicity
  Alogliptin]

III. ↓ Insulin Resistance:

a. Metformin
b. Pioglitazone (PPar - γ) ↑ - ↑ glucose uptake
   ↳ ↑ risk of Bladder, Bone Ca
   ↑ CHF
   ↑ Wt. gain
   ↳ Outdated

Metformin: DOC for DM - II

- Cause mild wt loss
- ↓ Microangiopathy (CAD)
- T/t: PCOD

- S/E:
  - Nausea (M/C)
  - Vit B_{12} ↓
  - Wt loss
  - Rare - lactic acidosis

IV. ↑ Glucose Elimination

a. Kidney (PCT)
↓
SGLT - 2 (x)
- gliflozin

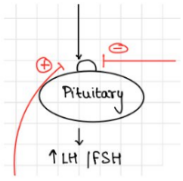
b. Small Intestine
↓
∝ - glucosidase (x)
↓
↓ glucose absorption
- Voglibose
- Acarbose

S/E: Abdominal pain
Bloating
Flatulence
- Precipitate IBD

DRUGS ACTING ON REPRODUCTIVE PATHWAY 21:56

A. Pathway common to both Female / male

Hypothalamus
↓
GnRH



GnRH Antagonist (-relix)
↓
Cetrorelix
Gamarelix
Degarelix

GnRH (R) Analogues (-relin)

- Buserelin
- Guserelin
- Nafarein
- Lenaprolide (prodrug)
↓
- Given in pulsatile manner on a daily basis (↑ LH / FSH)

↓

DOC: Delayed puberty

Hypogonadotropic hypogonadism

- Continuous manner (S.C route)

↓

Down regulation of receptor: ↓LH / ↓FSH

↓

DOC: Precocious puberty

DOC: Prostate Ca

T/t : Endometrial / Breast Ca

: Fibrinoids / endometriosis

- Avoided in symptomatic pt.
- High efficiency

B. Act on Male pathway:

1. Testosterone Synthesis ↓
   - Abiraterone acetate

   MOA: 17 ∝ hydroxylase ↓

   T/t: Prostate Ca.

2. 5∝Reductase

   (Testosterone → DHT)

   (-ride)
   - Finasteride
   - Dutasteride

T/t: BPH (↓ size of prostate) min 6 months

DOC: Androgenetic alopecia

3. Androgen receptor inhibitor (-lutamide)
   - Bicalutamide
   - Nilutamide

S/E: hepatoxicity

Seizures

C. Estrogen Drugs

1. Analogue:-

- Ethinyl estradiol (most efficient) OCP
- Conjugated Equine estrogen
  ↓
  m/c used for hRT
- Tibolone: DOC for hot flashes

2. Modulators: 1 SERM

- Raloxifene
- Post menopausal
  - For osteoporosis
- S/E: hot flashes
  Thromboembolism
  No risk of Ca

- Ormilexifine
  - OCP (once/week pill)
    Ex: Chaya, Saheli

- Clomifene
  T ½ : 2 weeks (long)
  - Multiple ovulation
  - Teratogenic } S/E
  - Poor birth

- Tamoxifen
  DOC: Breast Cancer
  ↓
  T/t & prophylaxis
  ↓ ↓
  Pre/post Menopausal — DOC (pre-menopausal)
  T/t (post menopausal)

S/E: ↑ risk for endometrial Ca
Thromboembolism
Cataract

Menopausal symptoms ↑

3. Antagonist:- /SERD
- Fulvestrant
- T/t Breast@ Ca
- Aromatase Enzyme (-) (AEI)
  ↓
  a. Irreversible
  - Exemestane
  b. Reversible
  - Anstrazole
  - leterozole

  } T/t Breast Ca

- DOC for both pre and post menopausal women.
  Who are ER +ve
  DOC for: Breast Ca prophylaxis

- No risk for Endometrial Ca

- **Leterozole**
  - DOC for ovulation in PCOD
  - T½ : 2 days (short)
  - ↑ Birth success rate
  - Not teratogenic
  - No multiple ovulation

d. Progesterone drugs:
1. Analogues
- OCP
- Levonorgesteral
  M/c used for emergency contraception 1.5mg < 72 hrs of unprotected intercourse
  S/E: Nausea, vomiting
  ↓
  If occurs < 3 hrs - repeat druga
  OTC: ipill / pill 72

2. Modular / SPRM
- Ulipristal

- Most efficient drug for emergency contraception
  ↓
  30 mg stat within <120 hrs of unprotected intercourse

3. Antagonist:
   - Mifepristone (MTP: 1st trimester)
     1st day: 200 mg (oral)
     ↓
     >24 hrs < 48 hrs)
     ↓
     Misoprostol (PGE_1): 200 µg x 4 tablets
     (Buccal / vaginal route)

ANTITHYROID DRUGS *47:18*

For grave's disease

1. Hormone Synthesis (x) inhibitors
   - MAO: Thyroid peroxidase (x)
     a. Carbimazole
     b. Methimazole
        ↓
        ↓↓ Synthesis
        ↓
        No effect on already formed T4
        ↓
        Slow onset of action
        ↓
        DOC: Maintenance
        ↓
        Long ti/2
   - C/I: Pregnancy 1st trimester
     ↓
     Causes: Aplasia cutis
     (scalp defect)
   - But, safe in IInd / IIIrd trimester – DOC
   - Agranulocytosis – S/E

     c. Propylthyrouracil
        ↓
        ↓↓ synthesis, also inhibits peripheral conversion of T_4 → T_3
   - Fast onset
   - DOC: Thyrotoxicosis
   - Safe in 1st trimester – DOC
   - ↑ Fulminant hepatitis in IInd / IIIrd Trimester → C/I
   - S/E: hepatotoxicity
   - Pk: t ½ short

2. Hormone release inhibitors
   - Iodides
     - NaI / K1 / Lugol's Iodide / Na Ipodate
   - Thyrotoxicosis – T/t

- ↓ Blood supply / size of gland ↓
- Can be used before gland surgery
- S/E:
  - Teratogenic
  - Mucositis (Salivation / rhinorrhea)

3. Peripheral conversion inhibitor:

- T4 —x→ T3
- Fast onset
- T/t: Thyrotoxicosis

- Propylthyrouracil
- Propranolol
- Prednisolone call steroids)

T/t of thyrotoxicosis / Thyroid storm

↑hR, ↑BP, arrhythmia, Tremors, ↑T_3

a. PTU (DOC) + propanol (sympatholytic - fastest relief)
   ↓ not controlled
b. Add Iodides (Na Ipodate)
   ↓ not contolled
   Add steroids: hydrocortisone

- Calcium channel Blockers (Diltiazem) - Refractory cases
- In COPD and BA patients we use esmolol & labetalol

DRUGS FOR OSTEOPOROSIS *57:49*

a. Anabolic
   - ↑ osteoblast action
   - Teriparatide (PTH analogue)
     ↓
     - Given in pulsatile manner
     - T/t of severe osteoporosis where Tscore >-3.5

   - Romosozumab
     - Given to mothers (post menopausal O⁺ osteoporosis)
     - MOA: Sclerostin protein (x) ↑ osteoblast survival

b. Antiresorption drugs

- ↓ osteoclast activity
  1. Bisphosphonates (DOC)
     S/E: Esophagitis
     ↳ avoided by upright posture
     - GERD / PUD
     - ↓ Ca^{2+}
     - Bone pain (over reactivity of drug)
       ↳ Stop medicine: minimum 2 to 3 years
       ↓
       ↳ ↑ risk of Bone fracture / osteonecrosis of jaw

- (-dronate) suffix
- Strontium (S/E: ↑MI)
- Denosumab (MOA: RNAK ligand (x))
- Raloxifene (SERM)
- Calcitonin (↑ risk of CA)

c. ↑ Minerals to bone
   - Ca^{2+} supplements
   - Vit-D
   - Calcitonin

DRUGS FOR ACROMEGALY *1:03:54*

a. Somatostatin analogues
   ↓ GH release
   - Lanreotide (subcutaneous depot)
     Or
   - Ocreotide

b. GH receptor antagonist
   Peguisomant - 2nd DOC

c. D_2 Receptor agonist
   - Cabergoline (↓ GH release)

DRUGS FOR CUSHING'S DISEASE *1:06:00*

- ↑ Cortisol

a. Ketoconazole (DOC)
   - ↓ cortisol synthesis
   - S/E: hepatotoxicity

b. Metyrapone: 2nd DOC
   - Safe in pregnancy

c. Mitotane (3rd DOC)

DRUGS FOR PROLACTINOMA *1:07:09*

D_2 ↑↑
- Cabergoline: DOC: non pregnancy states
- Bromocriptine: DOC pregnancy

TOCOLYTIC DRUGS *1:07:40*

- T/t for preterm labour

a. High efficiency drugs
   1. Nifedipine (DOC)
      S/E: Reflex ↑ HR
   2. Ritodrine (2nd DOC)
      S/E: Tremors
      Tachycardia
      Hyperglycemia
      Hypotension
      Pulmonary edema

b. Low efficiency drugs
   - Atosiban
     ↓
     Oxytocin (R) inhibitor
     - No S/E
   - Mg SO4
     - Neuroprotective

Antiepileptic Drugs

Indications:

1. Epilepsy (EEG Shows Spikes)
   a. Generalised seizures (both hemispheres)
      1. GTCS (m/c)
      2. Myoclonic (JME, LGS, Dravet's)
      3. Atonic (LGS)
      4. Absence: Atypical < 2.5 Hz
         Typical 3 Hz
         → DOC: Ethosuximide,
         Or, SV > LTG

   DOC:
   Sodium valproate >
   Lamotrigine

2. Focal seizures (EEG: One hemisphere)
   - Simple
   - Complex

   DOC: LTG > OXCBZ > CBZ

- Guidelines:
  a. Withdrawal therapy: After 2 years of seizure free interval
     ↓
  b. Gradual (3-4 months)

  If drug S/E (+): Stop abruptly (+) Start other AED (↑ Dose)

3. Pregnant Female

   Safe: Levitiracetam
   Lamotrigine
   Oxcarbazepine
   Carbazepine

   Unsafe: Sodium Valproate → causes neural tube defect
   Phenytoin → hydantoin syndrome

- If already on T/t - continue T/t
- If planning to conceive and on Antiepileptic drug; stop and wait for 4 months → no recurrence → don't start medicine

d. Breast feeding

Unsafe: Levetiracetam > Lamotrigine

Safe: Sodium valproate > phenytoin

e. CKD, CLD, old age, stroke, CHF, polytherapy

- Levetiracetam (safe) - no S/E

f. childhood epilepsy:

1. Absence seizures

Typical - Ethosuximide

Atypical - Sodium valproate > Lamotrigine

2. febrile seizures

Stabilisation (BZD)

i. Hospital: I.V LZ > DZ or I.M MDZ

ii. Not - hospitalised: D2Z (Rectal) or MDZ (N.S)

3. Infantile spasm: DOC: ACTH

I.S + Tuberculosis: DOC - Vigabatrin (GABA transaminase (-))

↓

S/t: Visual defect

g. Status epilepticus

- Stabilise patient: BZD (I.V) LZ > DZ

↓ Or

I.M MDZ

Bolus dose (braod spectrum drug)

- Bolus dose (broad spectrum drug)
- Fosphenytoin / Levetiracetam / sodium valproate

↓ Recurrence

- Repeat drug (↑ Dose) / Alternate drug

↓ Recurrence

Refractory S.E

IV. fusion MDZ / Propofol / Barbiturates

h. ↓ pain pathway (CNS)

DOC: Trigeminal neuralgia OXCBZ>CBZ

2nd DOC: DM Neuralgia Pregabalin > gabapentin

T/t migraine prophylaxis sodium valproate > Topiramate

i) Psychiatry drugs:
DOC Acute attack of anxiety disorder BZD
Bipolar disorder:- • Mania: S.V > CBZ
• Depression: LTG

P/K 20:23

a. Absorption: Phenytoin (orally bioinequivalent)
Gabapentin (Zero order kinetic)

b. Distribution
Narrow therapeutic Index → Therapeutic drug monitoring
- Phenytoin - 10-20
- CBZ - 4-12 } mg/L
- Barbiturates - 20-40

c. Metabolism
S.V $\xrightarrow[\text{oxidase}]{\text{liver}}$ free radical ↑

- ↑ dose
- Children < 2 yr age
- Enzyme Inducer (oxidase) ↑↑

d. Liver enzyme ↑↑ except S.V
1. CBZ: C4P3A4 ↑↑
• Metabolised by same enzyme (auto inducer)
2. Barbiturates: ↑ ALA synthase
↓
Precipitates porphyria symptoms
↓
C/I porphyria

3. Phenytoin: Metabolised by CYP2Ca
↓
Zero order kinetics
(Warfarin metabolism)
↓
S/E + + +

- S/E:
  1. Valproate
     - Weight gain
     - Ataxia
     - Liver toxicity
     - Pancreatitis
     - Rashes
     - ↓ Ovulation (PCOD)
     - Alopecia
     - Tremors
     - Encephalopathy

  2. CBZ > OXCBZ
     - Liver toxicity
     - Epilepsy
     - SIADH (M/C OXCBZ)
     - SLE like symptom
     - Cerebellar ataxia
     - Agranulocytosis
     - Sexuality ↓↓
     - HSN reaction

  3. Phenytoin
     - 3 fibrosis
       - Gum hypertrophy
       - Pseudo lymphoma
       - Acne

     - 3 Vit ↓
       B_9, K, D ↓
       - Megaloblastic anemia
       - Bleeding
       - Osteomalacia

     - 3 Hyper ↑
       - HSN reaction
       - Hyperglycemia

- Hypertrichosis (hirsutism)

4. Topiramate
   - CA (-) → Metabolic acidosis
     Renal stones
   - M (X) → Mydriasis
     Glaucoma
     Dryness

- Wt loss
- Language & speech disturbance
  M/C S/E: Drowsiness, sedation
  ↳ Levetiracetam: no significant S/E

DRUGS FOR INSOMNIA *34:00*

1. $GABA_A$ receptor ↑↑ : CL - ↑ influx
   BZD / Barbiturates / Z Drug (Zolpidem - DOC)
   (-) (-)
   Antidote: Flumazenil
   : Forced alkaline diuresis → (-) Barbiturates

- BZD (properties)
  1. Indications: Chlordiazepoxide
     ↓
     DOC: Alcohol withdrawal syndrome
     - Diazepam (MS. relaxant)
  2. ↓ Dose in CLD except lorazepam, oxazepam, (long, short acting)
  3. All BZD are long acting except:
     T - Temezepam
     T - Triazolam
     O - Oxazepam
     M - Midazolam

4. Wide T. Index; No Drug Indication
5. S/E Flunitrazepam (Date rape Drug)

- Orexin receptor antagonist
  - Lemborexant
  - Suvorexant

- Melatonin receptor agonist
  - Improve sleep disturbances (T/t)
    - Shift workers } Ramelteon
    - Jet lag
    - Depression - Agomelatin

Psychiatry Drugs

ANTIPSYCHOTIC DRUGS

00:35

- For schizophrenia, Delusion disorder, mania with bipolar disorder
- ↑ 5hT / ↑DA

- Drugs
  a. First generation antipsychotics
     - Typical
     - MOA: D_2 receptor (x)

     ➢ Haloperidol (high potency)
     ➢ Chlorpromazine, Thioridazone (low potency)

  b. Second generation antipsychotics
     - Atypical
     - MOA: $5hT_2$ (x) > D_2 (x)

     ➢ Clozapine (↑ efficiency)
     ➢ Aripiprazole ($5hT_2$ (x) > partial D_2 ↑)
     ➢ Pimavanserin (only $5hT_2$ (x))

Indications

- Psychotic disorder (SGA > FGA)
  ↳ Safe in pregnancy
- Clozapine (D_4 receptor (x)) - only drug to control suicides in psychosis
- DOC for refractory schizophrenia
- Best drug to control its negative symptoms

- PK: Route : M/c oral
  : I.M Depot (2 track technique to prevent direct injection in plasma
  Asenapine (sub lingual route): Fastest onset
  ↓
  Acute emergency

  :Dose: needs to be reduced in CLD except Paliperidone
  (Kidney elimination)

:S/E: 1. Unique

a. Thioridazone – Brown vision
b. Quetiapine – Cataract
c. Clozapine – Sialorrhoea, myocarditis (dose related)

(–) ↓
PCC > 350 ng/ml
Glycopyrrolate

➢ Agranulocytosis (autoimmune S/E, no relation with dose)

2. Common
   - Clozapine, Risperidone: Seizures
   - D_2 (x): Extrapyramidal symptoms, ↑prolactin
   - H_1 (x): Sedation / Drowsiness
     Wt. gain, ↑ lipid, DM-II
   - α_1 (x): ↓ BP
   - M (x): Anticholinergic side effect
   - QT↑: Torsades de pointes

- First generation antipsychotics:
  a. D → Max: haloperidol
     Min: CPZ / thioridazone
  b. H Max: CP2; thioridazone
  c. A Min: haloperidol
  d. M
  e. Q

- Second generation antipsychotics:
  - Maximum with clozapine, except:
    1. Extrapyramidal symptoms (min)
    2. QT ↑↑ (zipraridone)
  - Min with Aripiprazole

- Types of EPS:
  1. Acute Muscle dystonia – torticollis
  2. Parkinson like disease – tremors
  3. Akathesia (Restlessness)

4. Tardive dyskinesia (rabbit)

- Prevention of Acute Ms dystonia and Parkinson like symptoms:
  ↓
  DOC: Benzhexol (Trihexyphenydryl)
  2nd DOC: Promethazine

- Acute symptoms: I.V promethazine
- Akathesia DOC: propranolol
- Tardive dyskinesia DOC: Valbenazine – VMAT (x)
  – ↓ DA storage
  ↓ Stable patient
  Clozapine (min. EPS)

ANTIDEPRESSANT DRUGS *21:06*

a. Typical drugs:0
   - SSRI
   - SNRI
   - TCA

   S/E: Sexual dysfunction

b. Atypical drugs:-
   - No sexual dysfunction
     a. Mirtazipine (No drug interaction)
     b. Agomelatine (↑ melatonin); S/E: hepatotoxicity
     c. Bupropion
        T/t: Nicotine deaddiction
             Obesity
        S/E: Seizures

c. Serotonin modulators
   - $5hT_1$ – 5hT↑ receptors ±
   - S/E: Sexual dysfunction
     1. Trazodone
        S/E: Priapism
     2. Nefazodone
        S/E: hepatotoxicity

3. Vilazodone
4. Vortioxetine (only antidepressant that improves cognition)

SSRI	SNRI	TCA
• ↑ 5ht	↑ 5ht / ↑ NAdr	↑ NAdr > ↑ 5ht
• DOC For: ○ Depression ○ Anxiety disorder ○ Fibromyalgia ○ Pre mature ejaculation	• Same as SSRI ↓ Except PME • Duloxetine is DOC for :- • DM Neuralgia • Stress Incontinence ↓ Venlafaxine • Cataplexy T/t: Migraine	• Same indications as SNRI • DOC for post herpetic neuralgia Nortryptiline
• Liver metabolism ↓ Liver enzyme (-) ↓ Drug interaction ↑ ↓ Except Escitalopram (No. Drug Int.)	• Kidney elimination ↓ Except Duloxetine (liver)	• Liver (CYP2D6) ↑ (-) SSRI (Fluoxetine, Paroxetine)
• Safe in pregnancy (DOC) except paroxetine ↓ Congenital heart disease	• Unknown	• Pregnancy safe
• Long acting except:- Fluvoxamine Paroxetine	• Long acting except VenlaFexine	• Long acting except Amoxapine

- They are cause Discontinuation syndrome and thus prevented by using sustained release tablet
- S/E:
- GO-SSRI:
  - GIT S/E (m/c)
  - Osteoporosis
  - Sexual dysfunction (Anorgasmia)
  - Serotonin syndrome
  - Recurrence of symptoms (short acting)
  - Insomnia / vivid dreams
- ↑ 5hT
  ↓
  40-SSRI
  And
  NAdr ↑
  ↑hR / ↑ BP
  ↓
  Sympathetic S/E
- HAMQ - S
  -S: Seizures
  ↓ Sexuality
  - For toxicity
  metabolic acidosis
  ↑ (-)
  $NaHCO_3$

Unique S/E

1. Paroxetine
   ↓
   H_1 (x)
   M (x)
2. Venlafexine
   ↓
   Seizures
3. Amoxapine
   ↓
   ↑Prolactin
   ↑ Galactorrhea

DRUGS FOR BIPOLAR DISORDER 37:04

- Mood Stabilisers
  ↓

a. Lithium: antimanic + antidepressant
   - Only drug which control suicides

b. SGA: antimanic + Antidepressant
   - Lurasidone
   - Olanzapine
   - Aripiprazole

c. Antiepileptic drug: For mania: Sodium Valproate, Carbamezepine
   - For depression: Lamotrigine

d. SSRI: Depression (only)

DOC for BPD

a. Maintenance
   - Lithium > SGA
   - If pregnant: SGA > Lithium
     S/E: Ebstein's anomaly
   - If suicidal tendency – only lithium
   - If CKD (SGA only; Lithium C/I)

b. Acute attack
   1. Acute Mania
      S.V > Lithium (slow onset)
      (+)
      SGA
   2. Acute hypomania: only SGA
   3. Acute depression: SGA (lurasidone)
      ↓
      Not controlled
      ↓
      SSRI + olanzapine

Lithium:

Indication: BPD (Acute mania)
Maintenance BPD – DOC
Unipolar depression T/t
SIADH
Neuralgia

PK:

- Only given by oral route $LiCO_3$ – m/c form
- Interfere with cardiac conduction (ECG charges)
- Less lipid soluble (slow onset)
- (–) Plasma protein bound = successful hemodialysis
- Kidney elimination (C/I: CKD)
  (Steady state level = 4–5 days)
- Narrow therapeutic Index (0.5 – 1.5 mg/L)
  ↓
  Therapeutic drug monitoring
  Plasma monitoring > urine dipstick test

S/E:

L, I ↑ leukocyte count

T – Fine tremors (m/c)

H – hormonal ↓

I – Increase weight

U – U wave appearance in ECG

M – Ebsteins anomaly in mother

Toxicity: Acute overdose

↓

No CNS symptoms

↓

Only GIT symptoms (N/V/D)

: Acute on chronic toxicity

- CNS symptoms
  (tremors, ataxia, vertigo)

DOC: I.V fluids

If 3meq/L ↑ life threatening symptoms – hemodialysis

Risk factors

- Low Na^+ diet / fasting / Diuretics / Ace I / ARB
- NSAID's = ↓ GFR = ↑ Water retention
- Amiloride (Protective)

Opioids and Drug Deaddiction

- Analgesics
- DOC: Cancer /colicky / post operative / RTA pain
  ↓
  μ./K/δ - Inhibitory

a. Spinal cord (Dorsal horn)
   ↓
   μ>K>δ
   ↓
   ↓ pain pathways
   ↓
   Epidural > subarachnoid
   (No risk of Respiratory suppression)

b. Brain
   ↓
   (μ>K)
   ↓
   ↓ pain centres
   ↓
   Systemic route
   ↓
   Risk of ↓ RR

CLASSIFICATION 4:30

a. Full Agonist

+μ (high efficiency)

- Morphine: T/t CHF with pulmonary edema
- Methadone: 1st line drug for opioid deaddiction (risk of addiction)
- Mepiridine (pethidine : ↑ temp (via hypotharamus)
  DOC: post - operative - shivering
- Fentanyl (Su - /Remi - AL-) : Intraoperative analgesic
  ↳ most potent
- Loperamide - Relax GIT wall ↑ sphincter tone
  - high efficiency opioid
  DOC: non infective diarrhea
  C/I: Biliary colic

b. Partial Agonist (± μ)

i. Codeine

↓ cough

Converts to morphine in liver by CYPD6
↓
↓ pain

ii. Buprenorphine

- 1st line opioid deaddiction (↓ risk of addiction)
  ↓
- Given w/o supervision
- Longest acting

c. Mixed action opioids

- -μ ; +K/δ
- Low ceiling

- Pentazocine : ↑ hR S/E
- Nalbuphine
- Butorphanol

d. Antagonist
- CNS (-μ\K\δ) ↓
- Naloxone (Fast action) DOC opioid toxicity
- Naltrexone (slow action) DOC: Alcohol / opioid - Relapse prevention

• No CNS actin -μ ↓ Alvimopan
• Methylnaltraxone
• Nalogol ↓ T/t: opioid induced constipation

Other drugs:

1. Tramadol / Tapentadol
   +μ and ↑ NA dr / ↑ 5hT ↓ α_2 / 5hT1B/10 ↑ - ↓ pain pathways
   S/E: Serotonin syndrome ↑hR

2. Dextromethorphan
   DOC: Dry cough

Receptors

1. μ.
   P - Physical dependence
   M - Miosis - Muscle Rigidity (Fentanyl)
   C - Constipation
   A - Analgesic
   R - ↓ Respiratory centre
   E - Euphoria
   S - Sedation

2. K: Diuresis Dysphoria
3. δ
   • ↓ GIT

- Tolerance (seen against all actions) except constipation, miosis

Drug deaddiction:

a. Deaddiction / Craving and withdrawal
   - Methadone

- Buprenorphine

b. Prevent Relapse
   - Naltrexone

c. Toxicity
   - Naloxone

Alcohol

- Deaddiction craving
  - Naltrexone (DOC)
  - Acamprosate

- Prevent relapse
  - Naltrexone
  - Disulfiram

- Aldehyde dehydrogenase (non competative block) 2 days to 2 weeks

- Withdrawal
  1. Chlordiazepoxide
  2. If delirium tremors: Lorazepam / Diazepam
  3. Vit B_1

- Toxicity:
  - Symptomatic T/t
  - Vit B_1

Nicotine deaddiction

- Motivated enough: Nicotine replacement therapy (2 forms together) → Skin patch + lozenges
  - Not motivated
    Oral varencline (12 weeks)
    ↓
    Partial agonist NN ($\alpha_4 \beta_2$)
  - Bupropion
    S/E: Wt loss
    Seizures

Antivirals

1. HIV.
   - Entry inhibitors
     - Gp41 (x) (Fusion - Inhibitor) → En Fuvirtide HIV -1 only
     - CCR5 (x) co-receptor → Maraviroc
       S/E: ↑ Risk M.I

- Enzyme Inhibitors:

NRTI	NNRTI	II	P.I
• Vudine	• Virine	• Tegravir	• Navir
• Require 3 PO_4^{3-} For activation except Tenofovir (Nt RIT)	• Active	• Active	• Active
• HIV-I/II	• HIV - I	• HIV-I/II	• HIV I/II
• Kidney elimination → No Drug interaction	• Liver • D.I ++	• Liver • D.I ++	• Liver → Liver enzyme ↓↓ (Max. Ritonavir Drug booster)
S/E (Common) • Lipidystrophy • Neuropathy • Pancreatitis (min - Lamivudine)	• HSN Reaction • Nevirapine (liver toxicity)	• Dolutegravir → Wt gain hepatoxicity Insomnia	• Lipodystrophy except Atazanavir

- Ziduvudine
- BM ↓↓
- Megaloblastic
- ↑ pigmentation of nail beds

- Effavirenz CNS toxicity (seizures)

- Reltegravir ↓ Mood swings myoglobinuria

- Indinavir ↓ ↑ Bilirubin Renal stone

- Emtricitabine ↑ pigmentation of palms / soles

- Tenofovir ↓ Nephrotoxicity osteoporosis fanconi's anemia

- Abacavir ↓ HSN Reaction

T/t for HIV:

T+L+D

Tenofovir	+ Lamivudine	+ Dolutegravir
300mg	300mg	50mg
(OD)	(life time intake)	

- Post exposure prophylaxis:
  (T+L+D) x 28 days = <2 hrs; max 72 hrs
  ↓
  Vertical Transmission

- Mother ART (+)
  ↓
  Nevirapine / Ziduvudine
  For 6 wks
- ART (-)

- If HIV + Co-infection
  - Start T/t for co-infection first
  - Ex HIV + TB
    ↓
    Start ATT → 2 weeks Later → ART
    - Rifampicin → liver enzyme ↑↑ → Dolutegravir ↑↑ Metabolism (Add 50 mg)

HEPATITIS 15:40

a. Hep - B (DNA)
↓
Only chronic Hep - B

1. DNA polymerase (x): oral, monotherapy, continues > 5 years T/t
   ↓
   Tenofovir DOC (both pregnant & non pregnant)
   Lamivudine
   Emtricitabine
   Entecavir (2nd DOC - non pregnant)
   Talbivudine

2. Interferon - ∝:
   - Subcutaneous
   - S/E: hepatotoxicity
   - C/I: -cirrhosis
   - MOA: Multiple; except DNA polymerase

b. Hep - D + Hep -B
↑ (-)
Interferon - ∝ (DOC)

c. Hep - c (acute, chronic) T/t

- RNA pol (x)
  ↓
  -buvir
  ↓
- Protease inhibitor
  -previr
  (Simeprevir)
- Direct RNA packing (x)
  -asvir
  Ombitasvir
- Interferon - ∝
  ↓
  Ribavarin

SoFosbuvir + Ledipasvir

Given in oral form + combination

HERPES VIRUS 21:00

HSV - I
HSV - II
HZV
Chicken pox
Shingles

- DOC: Acyclovir
  Valacyclovir (long acting)

- CMV
  HIV (+)
  Bone marrow transplant

  TOC: Ganciclovir I.V
  Prophylaxis: Oral valganciclovir

  # Cedofovir, Foscarnet = used in acyclovir, ganciclovir refractory patients
  S/E of Tenofovir, Cedofovir, Foscarnet
  - Nephrotoxicity
  - Osteoporosis
  - Fanconi's anemia

  # S/E Foscarnet is genital ulceration / BM ↓↓

MISC. VIRUS 27:36

a. COVID - 19: Remdesivir (I.V)
   MOA: RNA dependent RNA polymerase (x)
   T/t: Mild to moderate COVID - 19

b. RSV (Bronchiolitics) = Ribavirin ↓ RNA
   Palivizumab (Virus attachment (x))

c. Influenza virus (swine flu HINI / H3N2); Bird Flu H5NI
DOC - Nueraminidase (x): Oseltamivir (oral route)
T/t: 75 mg BD x 5 days
- Baloxavir (endonuclease (x) in oseltamivir refractory patients.)

Anti Fungal

1. Liposomal Amphotericin -B (LAMB)
   MOA: • Pores in cell membrane - nutrients leak out
   Indication: • Most efficient antifungal
   1. DOC: Mucormycosis
      (LAMB + Posaconazole)
   2. DOC: Cryptococcal meningitis (HIV +)
      ↓
      LAMB + Flucytosine
      ↓ if stable
      LAMB + FCZ
      S/E: BM ↓↓ (MOA: DNA polymerase)
   3. DOC: All other serious systemic fungal infection
      (LAMB + FCZ / ITZ)
      2 exception (2nd DOC)
      - Invasive Aspergillosis (VCZ)
      - Coccidial meningitis (FCZ)
   4. DOC (Kala Azar; Visceral leishmaniasis)
      IF only skin manifestation: miltefosine
      S/E: a. nephrotoxicity
      ($K^{\downarrow}$+ / Mg^{2+})
      ↓
      Neurotoxicity / ototoxicity
      T/t: IV fluids → Rapid flushing
      b. Hypersensitivity reaction
      T/t: Antihistaminics

2. Azoles:
   MOA: Cell membrane inhibitor
   14∝ - Demethylase (x) → ↓ ergosterol synthesis
   PK:
   - Acidic media for absorption (lime water)
   - Elimination:
     Liver: KTZ
     VCZ
     ITZ
     Kidney: FCZ
     Small intestine: PCZ
     } Safe in CLD

Indications:
a. FCZ → DOC: Candida Albicans
   Coccidial Meningitis
   Cryptococcus prophylaxis

DOC: T. Versicolor

b. ITZ: DOC: Tinea: Cruris
Corporis
Pedis
Untilum (nail)
DOC: sporotrichosis
DOC: histoplasmosis

c. VCZ: DOC Aspergillosis

d. PCZ (Isavuconazole): T/t: mucomycosis

e. Clotrimazole, Miconazole } Local route

S/E: a. KTZ: ↓ cortisol synthesis DOC: cushing disease
↓ Testosterone = gynecomastia

b. ITZ: ↓ Aldosterone : ↑ K^+
↓ Na+
↓ BP

c. VCZ: Neurotoxicity : seizures
retinitis

Other drugs

a. Terbinafine
2nd DOC Tinea
Where ITZ DOC
S/E: hepatotoxicity
MOA: ↓ cell membrane (squalene peroxidase)

b. Griesofulvin
DOC: T. capitis
S/E: Alcohol (Disulfiram reacⁿ)
MOA: Direct DNA (x)
B tubulin protein (x)

c. Echinocandida – I.V Route
T/t: Candidiasis (caspofungin)
MOA: β-1, 3-glucan synthesis cell wall enzyme

Anti Protozoal

1. ANTI MALARIAL DRUGS 00:16

- Plasmodium
  Vivax - CQ sensitive
  Falciparum - CQ Refractory
  a. Malaria prophylaxis
    - For visitors
      < 6 weeks
      ↓
      Doxycycline
      If pregnant / children <7-8 yrs
      Progunial
    - > 6 weeks
      Mefloquine
      S/E: Mood swings
      C/I: Pilots

  T/t: Malaria
  a. P. vivax

- Chloroquine (600 → 600 → 300 mg)
  ↓ Schizonss (RBC) = ↓ clinical symptoms
  And
  ↓ Gametocidal - ↓ transmission

- Primaquine (15mg) x 14 days
  (x) hypnozoite → Relapse of Malaria (radical cure)
  C/I: pregnancy / G6PD ↓↓
- If pregnant / G6PD↓↓ = only chloroquine (long time) = 9 to 10 days
  Quinine: 2nd DOC P.vivax

T/t for P. Falciparum
Artesunate (3 days)
+
Pyrimethamine + Sulfadoxime (1 day)
Or,
Primaquine (45 mg = single dose)

- If pregnant:
  1st trimester = Quinine

IInd / IIrd = ACT

- If North Eastern State if India
  ACT (lumefantrine + Arte|ether) + PQ
  ↳ After Fatty meal

- Complicated malaria (P.Falciparum) =cerebral
  I.V Artesunate

- Other drugs:
  - Amoebiasis
  - Giardiasis
  - Trichomonas vaginalis

  } DOC = Metronidazole

  - Toxoplasmosis:
    Pyrimethamine (DOC) + Sulfadiazine
  - Babesiosis = Azithro + Atovaquone
  - Cryptosporidium parvum: DOC Nitazoxanide

Antibiotics: Classification & Beta Lactam Antibiotics

1. CELL WALL INHIBITORS 00:29

a. Fosfomycin → NAG
↓ ↓ ✕
UTI NAM

Pregnancy safe

3gm sachet stat

b. Glycopeptide Antibiotics (Vancomycin)

MOA: Transglycolase (x)

↓

Inhibit peptidoglycan chain elongation ($P_1 - P_2 - P_3 - P_4$)

c. β - lactam Antibiotics)

- Penicillin, Cephalosporin, Carbapenems, Monobactam

  MOA: Transpeptidose (x)

  ↓

  (x) cross linking between peptide chains

II. CELL MEMBRANE INHIBITOR 4:27

a. Colistin, Daptomycin

III. PROTEIN SYNTHESIS (X) 4:49

- Act on ribosomes

  → On 30s

  - Aminoglycosides

    ↓

    (x) γRNA chain (x)

    (x) mRNA reading

  - Tetracyclines

    (x) tRNA

- 50s
  - Streptogrammin

- Erythromycin
- Lincosamides
- Linezolid (23s subunit; inhibit γRNA chain)
- Chloramphenicol

IV. FOLIC ACID PATHWAY INHIBITOR 7:22

- Sulfonamides
- Cotrimoxazole

V. NUCLEAR PATHWAY INHIBITORS 7:48

a. DNA gyrase
Inhibitor
↓
Fluoroquinolones

b. RNA polymerase (x)
- Rifampicin
- Fidaxomicin

c. Direct DNA (x) (Free radicals)
- Metronidazole
- Nitro Furantoin
  - UTI
  - Bacteriostatic

S/E: Neurotoxicity
Fibrosis

d. Anaerobic metabolic pathway 9x)
- Metronidazole

Bacteriocidal
- Cell wall (x)
- Cell membrane (x)
- Nuclear pathway (x)

Bacteriostatic

- Folic acid (x)
- Protein synthesis (x)

- 3 exceptions: Cotrimoxazole
  Streptogrammin
  Aminoglycosides

Safe to use in CKD

1. β - Lactam: Naficillin
   Ceftriaxone
   Cefoperazone

2. Tetrocycline: Doxycycline
   Tigecycline

3. FQ: Moxiflox
   Pefloxacin

4. 50s Ribosome except clarithromycin (liver toxicity seen)

A. β - LACTAM ANTIBIOTICS *13:49*

1. MOA: cell wall (x) (Transpeptidase)
2. Bacteriocidal
3. PK:
   a. Penicillin G (Parenteral route)
      i. Aq Pen G (Benzyl Pen G)
         - I.V
         - Fastest
      ii. Procaine Pen G
         - Intermediate onset (alternateive)
      iii. Benzathine Pen G
         - I.M
         - Slow onset
         - Long action
         - Maintenance

b. Pen G+ Probenicid: ↓ Pen G elimination (prolongs action)

c. Imipenem + cilastatin: Dehydropeptidase (x) in Kidney
↓
Prolongs action

4. Resistance:
   - M/c method: β Lactamase
     ↓
     Opens β - lactam ring
   - Ex: Staph aureus
     ↑
     Cloxacillin
     Oxacillin
     Nafacillin
     Dicloxacillin
     Methicillin
   - Other bacteria
     - Amoxyclav
     - Piperacillin + Tazobactam
   - Gram -ve bacteria (Klebsiella) → Resistant β - Lactamase
     (Ambler Classification)

(-)
A: ESBL ├── DOC: Carbapenem

B: Metallozyme (Super Bug NDV)
↑(-)
DOC colistin / Tigecycline

(-)
C: Amp - C ├── DOC Gen IV cephalosporin
D: Oxa - D (x)

- 2nd method: Modification of Target
  PBP - 2a → PBP - 2a'

Staph aureus MRSA
↓
- Mupirocin (ointment)
  DOC: Carrier state
- Rifampicin
- Streptogrammins
- Septran (cotrimoxazole)
- Anti MRSA cephalosporin (Gen – V)
- Vancomycin DOC
- Daptomycin
- Delafloxacin
- Tigecycline
- Linezolid

S/E:

a. Hypersensitivity reaction

β – lactam ⟷ Azithromycin ⟷ cotrimoxazole

↓

I.V – Vancomycin — oral

– Sulfasoxazole

b. Superinfection (Pseudomembranous colitis)
DOC: fidaxomicin > Vancomycin / MTZ
Max . Clindamycin > β – lactam

c. Cefoperazone:
1. Vit K oxido reductase (x) – Bleeding
2. ↓ Aldehyde dehydrogenase (DisulFiram reaction (x))

d. Imipenem, Cefepime } CKD patients = causes seizures

Indications

1. Penicillin
   - Narrow spectrum
     - Pen G (I.V / I.M)
     - Pen V (Oral)

DOC for GRASS (Mnemonic)

Gas gangrene
Rat Bite Fever
Actinomycetes
Streptococcus (RHD)
Syphilis

- For Staph Aureus
  ↓
  Skin infection (T/t)

- Broad spectrum
  - Amoxyclav
    DOC: Otitis medial
    Dental surgery prophylaxis
    1st line AB: Skin infection / UTI / Community acquired pneumonia

- Ampicillin
  DOC: Enterococcus
  Listeria

- Antipseudomonal penicillin
  - Piptaz
  - Ticarcillin
  - Carbencillin

2. Cephalosporin
   a. Gen – I
      - Cefazolin
        -M/c for surgery prophylaxis
      - Cefalexin – Skin infection T/t

   b. Gen – II
      - Gram –ve + anaerobic
        ↓
        Cefuroxime T/t: Abdominal infection
        Sinusitis

c. Gen - III
   - Gram -ve
     ↓
     Ceftriaxone
     DOC: Gonococcus
     Meningococcus
     H. Influenza
     S. typhi
     Pneumococcus
     Cefixime (oral) - gonococcus STD
     Ceftazidime - T/t: pseudomonas
     Cefoperazone

d. Broad spectrum: Gen - IV
   a. -pi-
      T/t: pseudomonas
      DOC: amp-c β - lactamase
   b. -rol-
      - For T/t MRSA

3. Carbapenems
   - Broad spectrum
   - Anaerobic
   - Pseudomonas

   DOC : ESBL (Type A)
   : Acinetobacterium
   : Burkholderia
   : Serratia
   : Enterobacter

4. Monobactam
   - Aztreonam = T/t: Pseudomonas

Antibiotics - Other Antibiotics

1. Vancomycin
   - DOC: MRSA
   - 2nd DOC: Pseudomembranous colitis (oral)

   S/E: ↑ histamine (red man syndrome)
   Nephrotoxicity

2. COLISTIN: DOC: Type B β - lactamase (-)
   (metallozyme)
   T/t: pseudomonas

3. DAPTOMYCIN: T/t MRSA
   DOC: VRSA
   T/t: VRI

Cant be given for lower respiratory tract infection (sensitive to surfactant)

4. Aminoglycosides:
   - Injectable
   - Require O_2 for action = (x) anaerobic bacteria
   - S/E: Nephrotoxicity
     Ototoxicity - C/I loop diuretics
     Neurotoxicity - NMJ (x) C/I: Myasthenia Gravis
     Teratogenic - C/I pregnancy
   - Indications:-

     DOC: Plague
     T/t: Pseudomonas
     DOC: Tularemia
     T/t: TB

5. Tetracycline (Doxycycline)

   DOC for:
   Rich - Ricketssia (Typhus)
   Reliance - Relapsing Fever
   Brothers - Brucellosis
   Love - LGV (Chlamydia)

Cool – Cholera
Green – granuloma Inguinale
Park – Prophylaxis :

- Malaria (< 6 wk)
- Plague
- Leptospirosis

Tigecycline: MRSA
VRSA
VRE

C/I: Pregnant / children < 7 – 8 yrs
Ca^{2+} Binding = Teeth / Bones ↓

6. Macrolides
   1. Erythromycin
      DOC; T/t; prophylaxis of Diptheria
   2. Azithromycin
      - DOC:
      - Chancroid
      - Cat scratch disease
      - Cholera (pregnant / children)
      - Campylobacter jejuni
      - CAP
      - Leigonella
      - Atypical pneumonia (mycoplasma)
      - Whooping cough

   ➢ Antiprotozoal: Babesiosis
   ➢ Antimycobacterial: MAC

3. Clarithromycin → Same indication as Azithromycin:
   H. Pylori
   TB

S/E: QT ↑↑↑
Diarrhoea

7. Linezolid and Tedizolid
   - Oral route > 90% absorption
     T/t: MRSA, TB
     DOC: VRE
     S/E: BM ↓
     Serotonin syndrome
     Neuropathy
     Lactic acidosis

- Tedizolid: More potent
  ↓↓ S/E

8. Cotrimoxazole
   Combination of Trimethoprim: Sulfamethoxazole
   1 : 5
   - Dose reduced in CKD / CLD
   - ↓ Folic acid pathway → S/E: Bone marrow ↓↓
     HIV Drug = risk of BM ↓ High
   - DOC Pneumocystis pneumonia (HIV+)
   - DOC prophylaxis in : PCP, Toxoplasma — HIV+ CD4 < 2400
   - DOC: Nocardiasis
   - DOC: Stero|phomonas maltophidia (Cystic Fibrosis)
   - MRSA
   - CAP (pediatric pts)
   - 1st line drug
     - UTI
     - Skin infection
     - CAP

S/E: ↓ Folic acid: BM ↓↓
Teratogenic
Oligospermia
Sulfonamides : Hypersensitivity Reaction
↑ Bilirubin (C/I < 2 months)
C/I: G6PD deficiency
Porphyrias
↑ K^+ (hyperkalemia)

9. FQ

PK:

- Good absorption ↑↑
  Ofloxacin, Levofloxacin = 100%
- Cation drugs - ↓ absorption
  ↓
  Min. time gap 120 mins
- Ciplox: Liver enzyme ↓

S/E:

- N/V
- Neurotoxicity: Neuropathy
  Seizures
  Rhinitis
  FQ + NSAIDS / Theophylline = ↑ Seizures
  - ↓ Tendon / Cartilage growth
  - C/I pregnant
  - Avoided: Children / old patients

Indication:

- 1st line Ab - UTI
  - Infective diarrhea
- CAP
- TB (Moxi / Levofloxacin)
- DOC: E. coli, Shigella, S. typhi
- Delaflox: MRSA
- Ciplox = Pseudomonas
  DOC for anthrax, dysentery
- Moxi: anaerobic

10. Metronidazole

i. Antibiotics:

DOC: Bacteriodes
Fusobacterium
Clostridium Tetani
Bacterial vaginosis

Abscess
2nd DOC: Clostridium perfringes
3rd DOC: P. colitis

ii. Antiprotozoal
- Giardiasis
- Amoebiasis
- Trichomonas vaginalis

} DOC

MTZ
- Liver enzyme (-)
- Pregnant females given with caution

S/E: Neurotoxicity
Disulfiram like reaction

Anti TB Drugs

- 1st line drugs

H	R	Z	E
Isoniazid	Rifampicin	Pyrazinamide	Ethambutol
MOA: Cell wall (-)	RNA pol (-)	Cell wall (-)	Cell wall (-)
B.cidal	B.cidal	B.cidal	B.static
Liver elimination	Liver	Liver + Kidney	Kidney
Resistance:	Rpo-B	Pnc-A	Emb
m/c cat-G inh - A			
Indication:	TB T/t	TB T/t	TB T/t
• TB T/t	Leprosy		MAC (HIV+)
• TB / prophylaxis	MRSA		R-Rifabutin E - Ethambutol C - Clarithromycin
- Patients living with + HIV and neonates (delay BCG)	Meningitis prophylaxis DOC: H.Inf		
- 3 month: INH+ Rifampicin (weekly) Or, 6 months INH daily	2nd DOC: Mengiococcal meningitis Brucellosis (Rifa + Doxy)		

S/E:

Liver toxicity
SLE
Vit B_6 ↓
↓
- Neuropathy
- Seizures
- Optic neuritis (Peripheral)

Liver toxicity Flue like symptom
Orange discoloration HSN Reaction
(BM ↓)

Liver toxicity
↑ uric acid

- ↑ uric acid
- Neurotoxicity
- Central optic neuritis

Rifampicin	Rifabutin
• Liver enzyme ↑↑ Orange secretion urine	Not Yellow (Skin / Sclera) Pseudojaundice
• Mild flu like	Severe inflammation cuveitis
• T/t TB leprosy	T/t MAC

Anti TB Drugs

Topic Notes: 2

- Class A medicines
  a. Aminoglycosides: Injectables
     Amikacin
     Streptomycin
     Kanamycin
  b. FQ (Moxi / Levoflox) = Bactericidal
  c. Bedaquilline: ATP synthase (x)
     B. cidal
     S/E QT ↑↑
  d. Delamanid: Cell wall (x)
     B. cidal
  e. Linezolid
  f. Ethionamide
  g. Cycloserine

- TB T/t Regimen
  - 2 months HRZE + 4 months HRE
  - MDR TB - (H + R) (X)
  - XDR TB - [H+R + 1FQ + 1-2 class A] (X)

Anticancer Drugs

- Common S/E
  a. m/c – GIT toxicity
     i. N/V (Nausea, vomiting)
        - Maximum cisplatin
        - Early DOC – $5hT_3$ (x)

        Delayed – NK_1 (x)

     ii. Diarrhea

     Doc: Loperamide

  b. Bone marrow suppression (m/c) dose limiting toxicity

     Except: Vincristine
     Bleomycin

     (WBC > Platelets > RBC)
     (+) (+) (+)

     Filgrastin Oprelvelkin Darbropoeitin
     Romiplostin

  c. Tumor lysis syndrome:

     TOC: IV Fluids + Drugs

     Low risk: Allopurinol
     Febuxostat

     High risk: Rasburicase

  d. Pulmonary fibrosis (Type I pneumocytes) ↓↓

     (Type II and fibroblast ↑↑)

     Ex: Nintedanib
     Pirfenidone

- Targetted Chemotherapy drugs:
  a. Trastuzumab = hER \ 2Nu (x)

     DOC: ER –ve Breast cancer

     ↓ If progresses

     Lapatinib = hER / 2 Nu kinase (x)

And

EGFR Kinase (x)

Imatinib = abL: bcr TK (x) = DOC for CML

↓ If refractory

Dasatinib

Nelotinib

Poratinib

Or, Erlotinib, Geftinib, Afatinib — EGFR Kinase (x) → given for non small cell carcinoma of lung

In mutation like threonine 790 methionine – Osimertinib given

D. Bevacizumab, Ranibizumab, Pegaptinib — VEGF (x) ↓ Angiogenesis

- Cancer immunotherapy:
  - Immune check point (x)

i. CTLA-4 (x): Iplimumab

ii. PDL-1 (x) = Atezolizumab
PDL-2 Nevolumab

iii. PDR-1 (x) = Pembrolizumab

iv. LAG – 3 (x) = Relatlimab

- T/t Cancer:
  Anticancer drugs + Immunecheck pt (-)

- S/E:
  a. Cyclofosfamide = Hemorrhagic cystitis
  Ifosfamide (d/t Acrolein)
  ↑ (-)
  MESNA
  b. Methotrexate = Nausea, vomiting, diarrhea (pulmonary/liver fibrosis)
  ↳ Prevention: Leucovorin
  TOC: Forced alkaline diuresis

c. 5-Fu capecitabine
↳ Hand & foot syndrome

d. 6-mercaptopurine → metabolism
(toxicity ↑↑) Xanthine oxidase
(-)
↑
Allopurinol

e. Doxorubilin → Cardiotoxicity
Dilated cardiomyopathy
↑ (-)
Dexrazoxane

f. Cisplatin: Nephrotoxicity (-)
↓ electrolytes
Neurotoxicity ← IV fluids mannitol Amifostine
Ototoxicity

g. Bleomycin → Pulmonary fibrosis
Bacterial flagellate ↑ pigmentation
Raynaud's phenomenon

h. Asparginase → coagulation problem

- **Indication:**
  a. Temozolamide: DOC: Glioblastoma multiforme
  b. Maintenance: DOC for chorio carcinoma
  = ↑↑ Dose osteosarcoma
  = Intrathecal Route for T/t fo All

3. 5FU+Folinic ā = T/t colon ca
4. Cladribine: DOC Hairy cell leukemia
5. Mitomycin-c : Local fibrinolytic drug
: Used for tracheobronchial stenosis
: Pterygium surgery
6. Hydroxyurea: DOC for sickle cell anemia

L - glutamine
Crizamlizumab

Immunopharmacology

A. KIDNEY TRANSPLANT 00:20

- Induction therapy (2-3 months)
  a. Antithyrocyte globulins ATG
  b. Basiliximab (CD25 (x))
     IL-2 → ↑ CD25 → ↑ T_4 cell
  c. Alemtuzumab (CD52 (x))
     - Precursor of WBC ↓

- Maintenance therapy (lifelong)

Prednisolone	+	Mycophenolate	+	Tacrolimus
↓		↓		↓
↓IL, 1, 2, 3		(x) IMP Dehydrogenase		↓ calcineurin
↓ TNF - ∝		(↓ purine synthesis)		↓ IL - 2 synthesis
↓ NK-cell		↓		↓
		↓ B/T-cell multiplication		↓ T cell / B cell

S/E: hyperkalemia
Hypertension
Hyperlipidemia
↑ uric ā
Hyperglycemia

Nephrotoxicity
Ototoxicity
Neurotoxicity
Bone marrow toxicity

Alternative drugs

- MTOR (x): Sirolimus, Everolimus } Alt of steroids
- DNA pol (x): Azathioprine (Alt of mycophenolate)
- Calcineusin 9x): Cycloporine (Alt of Tacrolimus)
  ↳ Same S/E
  - Causes - Hirsutism / gum hyperplasia
    - ↑ Risk skin Ca

- Bile stasis ((-) MDR gene)

- Balatacept: ↑ CTLA - 4 (↑ Immune check pt)

Kidney Rejection

- Prednisolone (Methyl) I.V
- Plasmapheresis
- I.V Ig
- Rituximab (CD 20 (x))
- Eculizumab (C5a) (x)
- Bortezomib (Proteosome (x))

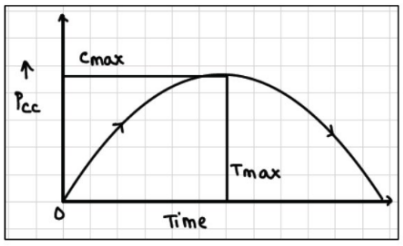
→ Thalidomide : Immunity ↓
↑ IL - 10

S/E:

a. ↓ T_3
b. Constipation
c. Hypercoagulation (LMWH given with it)
d. Teratogenic = phocomelia

Pharmacokinetics

1. Absorption:
   Time Vs Plasma concentration



Cmax: amount of drug in plasma

Tmax: rate of absorption

Area under curve: Bioavailability (rate & extent of absorption)

↓

Fraction of drug that reaches plasma in unchanged form

$$\text{B.A [F] (n)} = \frac{\text{AUC (x)}}{\text{AUC (I.V)}}$$

Factors on which drug absorption depends:

1. Lipid solubility ↑ = cross membrane = ↑ BA
   (passive diffusion)
2. ↓ molecular size (lipid insoluble)
   ↓
   Filtration (+) (Intercellular spaces)
   (BBB = (X) intercellular spaces) - lipid insoluble
   If meningitis = ↑ permeability

3. PH of surrounding media
   ↳ Acidic in acidic media - non ionic (lipid soluble)
   Acidic drug → upper part GIT

Stomach	Duodenum
(More non ionic)	(less non ionic)
Thick mucosa	Thin mucosa
(x) Villi	Villi (↑ surface area)

Basic drug → lower part GIT

Small Intestine	>	large intestine
Villi (+) - Jejunum More than ileum		Villi ↓

4. Vascularity of absorbing surface

I.M	Vs.	S.C
↑ Vascular		↓ Vascular
↑ ROA		↓ ROA
Fast		Slow

C/I - Anticoagulants (forms hematoma)

5. GIT motility
   - Healthy
   a. Young → ↑ peristalsis → ↑ ROA
   b. Old / pregnant →↓ peristalsis → ↓ ROA
   - Disease (GIT disease) → ↓ absorption

6. First pass metabolism (liver) = ↓ bioavailability
7. Route of administration:-
   I.V ≈ 1 B.A
   Other route ≈ <1

II. Distribution

- $Vd = \frac{Dose}{Pcc}$

  Dose = Vd x PCC

1. Obese : lean
   Adult: Child
   Pregnant: Non pregnant
   (↑ BSA: ↓ BSA)
   } Physiological

2. Pathological
   Chf
   Edema } Vd↑
   Ascites
   Dehydration Vd ↓

3. Drug related factor
   - Lipid soluble ↑↑ Vd
   - Plasma protein binding size ↑ Vd ↓

- Plasma protein binding
  ↓
  Bound portion (size ↑)

- (X) Filtered from glomerulus
- (X) Entry in liver for metabolism
- (X) Hemodialysis

- Plasma proteins
  1. Albumin (acidic drugs)
     ↓
     Weak acid
     ↓
     Ex: Methotrexate
     Aspirin
     Probenecid

  2. α_1 acid glycoprotein
     ↓
     Basic drug (weak base)
     Ex: Amphetamine

Morphine
Atropine
Local anaesthetic

- Hemodialysis – not successful for (X) protein bound (organ entry ↑)
  Amphetamine – TOC forced acidic diuresis
  Anti depressants – $NaHCO_3$
  BZD – Flumazenil
  β (X) – glucagon
  CCB – Ca^{2+} gluconate
  Digoxin – Digibind
  Opioid – Naloxone

III. Metabolism (Liver)

a. Phase – I reaction
(Non-conjugative reaction)
- Microsomal enzyme (CYP450)
  m/c reaction – oxidation

b. Phase II – conjugative reaction
|
Non-microsomal enzyme except glucuronide conjugation

- Types of CYP450
  1. CYP450 → 3A4
     ↓
     CYP3A4
     - Atorvastatin (safe in CKD)
     - CBZ (Auto inducer)
     - Verapamil (↑ drug interaction)
  2. CYP2D6 (2^{nd} M/C) ⊢(-) SSRI
     - Codeine → morphine →↓ pain
     - Metoprolol
     - RCA
     - Tamoxifen → active metabolite

3. CYP1A1/2: Theophylline
4. C4P2C9: Warfarin
   Phenytoin
   - Low $conc_n$
   - Zero order kinetic
5. CYP2C19: Clopidogrel activation
   PPI
   partially defective enzyme

- In phase II reaction
  ↓
- Medicines metabolised by acetylation
  S – Sulfonamide
  H – Hydralazine
  I – INH
  P – Procainamide
  D – Dapsone

IV. Elimination (Kidney)

1. Net elimination

Filtered from glomerulus + secreted in PCT − Reabsorption of drug (tubule)

↑ RBF → ↑ Filtration
↑ plasma protein binding → ↓ filtration
ATP pump → ↓ Drug interaction → + +
↓ lipid solubility → ↑ rate
ph of urine urine → acidic in acidc

Fast elimination
(Forced alkaline diuresis)
$NaHCO_3$
TOC: Methotrexate / Aspirin / PB

2. Rate of Elimination:

$$\frac{\text{Amt of Drug elimination}}{\text{Unit of time}}$$

3. Clearance : $\frac{ROE}{PCC}$ (Assessment of Kidney Function)

4. $T_{½} = \frac{\ln 2}{k}$; K (elimination constant)

$$K = \frac{CC}{Vd}$$

$$= 0.693 \times \frac{Vd}{cl}$$

5. Steady state level : Repeat same dose after every fixed interval
   : 4-5 t ½
   : ROA = ROE
   ↓ (Cl x Pcc)
   Dose x F
   Dosing interval

1. SSC (PCC): $\frac{\text{Dose x F}}{\text{D.1 x CL}}$
2. MD (Dose): $\frac{\text{CL x Pcc x D.I}}{\text{F}}$

   If I.V Route; F = 1
   If I.V infusion, D.I = per unit time
   M_D = CL x Pcc

6. Loading dose: Starting of T/t
   Higher than usual dose
   To achieve desired conc^n in short span of time

   1. Acute emergency
   2. Drug t ½ ↑
      L_D = Vd x PCC

7. 1° and zero order

   K / t ½ / CL = constant
   ROE = variable
   ROE ∝ Pcc

   K/t ½ / CL - variable
   K/t ½ / CL - $\propto \frac{1}{\text{PCC}}$
   ROE constant
   W - Warfarin
   E - Ethanol
   P - Phenytoin
   T - Theophylline

Pharmacodynamics

- Drug targets
  1. M/c receptors
  2. Enzymes inhibitor → Reversible (Electrostatic bond)
     a. Competitive Block: K_m = ↑↑ V_{max} = same
     b. Non-competitive block = K_m = Same
        V_{max} = ↓↓
        - Irreversible (Covalent bond)
          - Aspirin
          - PPI
          - Exemestane
          - OPO_4^{3-}
  3. Ionic channels
  4. Transport proteins

Receptors

- Nucleus: T_4 / T_3
  Vit A
  PPaR - $\propto_1 \gamma$
  Estrogen
- Cytoplasm = All steroid hormones -Vit-D
  - Glucocorticoids / Mineralocorticoids
  Sex steroids (estrogen)

- Membrane (Kinase)
  ↓
  (GLP - 1)
  ↓
  Growth hormone (JAK)
  Growth factor (TK)
  Leptin (Cytokine)
  Prolactin (JAK)
  Insulin (TK)

- GPCR (all drugs)
  - 7 helical stage
  - G ∝ (GTP)
    a. G ∝ s
       - Stimulater adenyl cyclase →↑ cAMP → Stimulating action
         ↓
         $\beta_1/\beta_2/\beta_3$
         V_2 / H_2 / D_1

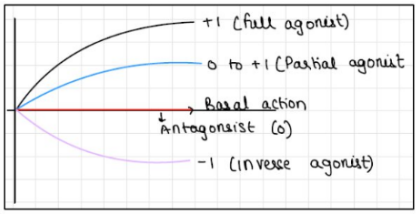
b. Gαi - ↓cAMP → Inhibitory → M_2 / M_4 / α_2 / $5HT_{1A}$ / ID / IF, μ, K, γ

- Can also open K^+ ↑↑

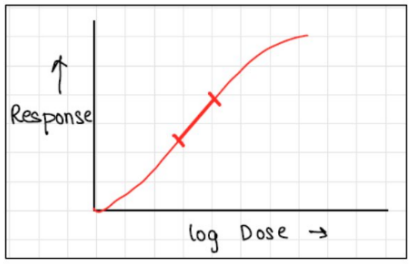
c. G ∝ q10 → ↑ phospholipase 3 → ↑ IP_3 - DAG →↑ Ca^{2+} → Action (α_1, M_1 M_3, M_5) (AT_1)

DRUG ACTIONS 9:37

- Intrinsic activity (efficacy)
- -1 to +1

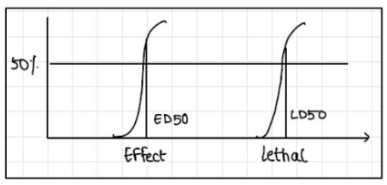


Log DRC - Dose response curve



- Sigmoid shape
- Middle part = straight line
  ↳ Response ∝ Dose (predictable)

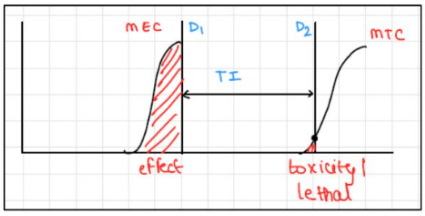
a. LD50 and ED50



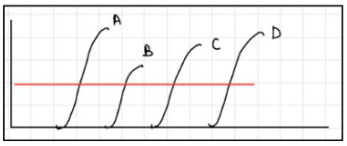
b. Therapeutic Index (Safety index) = $\frac{LD50}{ED50}$

>2 = Wide T1
<2 = narrow T1

c. Minimum effective concentration: most of patient respond to T/t (>99%)
d. Minimum toxic concentration: most of pt. not having toxic effect <1%)

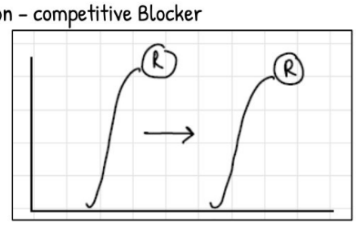


4. Efficacy and potency
   - Helps to compare durgs
   - Efficacy: Y axis (max response)
   - Potency: X axis (min dose req to produce a certain response)

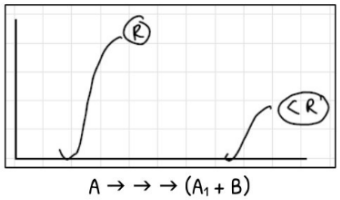


D>A>C>B – Efficacy
A>B>C>D – Potency

5. Competitive Vs Non – competitive Blocker



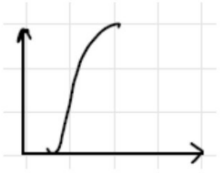
$A \rightarrow \rightarrow A_1 + B$
Rt shift of DRC (competitive block)



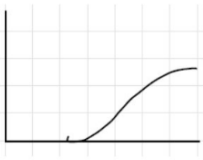
$A \rightarrow \rightarrow \rightarrow (A_1 + B)$

Flattening of DRC
Non - competitive blocker

6. Slope of DRC



Steep slope
↑ Dose → ↑ Toxicity



Flat slope
↑↑↑ Dose → ↓ Toxicity

Clinical Pharmacology

1. Drug discovery
   Approach: Target based
   ↓
   Pre-clinical trials (animal studies)
   ↓
   IND application
   India – CDSCO
   ↓
   Permission to start clinical trial
   ↓
   Clinical Trials

- Rules and Regulations: Schedule Y
- Drug and cosmetics Act, 1940

a. Phase I / Safety / Toxicity study
   - Healthy human volunteers
   - P_K / P_D
   - Max tolerated drug
   - (x) therapeutic dose
   - Size < 100
   - Non blinded > single
   - (x) Anticancer, Immunosuppressive drugs

b. Phase 2 / Proof of concept / Drug efficacy
   - Patient
   - PK/PD
   - Therapeutic dose
   - Size 100-200
   - Single > Double blinded
   - Given first in patient
   - Max drug failure

c. Phase 3
   - Patients (multi centric trial)
   - PK/PD
   - Therapeutic dose (cross checking)
   - Toxic dose not calculated
   - Size > 1000
   - Double > Triple blinded
   - Minimum error
   - Best to calculate all PK/PD parameters
   - Comparison of drugs

- Max time / Resources

↓

New Drug application (permission to launch drug in market)

↓

Phase – IV post marketing surveillance
Sampler – any commoner
Aim: reporting of adverse drug reaction
Reporting: Govt (Pharmacovigilance dept)

- Special population (Pregnant, children, old patients) are part of trial
  - No specific sample size
  - No time limit
  - Drug – drug interaction studied

↓

Patent (exclusive marketing rights)
(For 3 years – 5 years)
Exception: Orphan drugs (10 years rights)
↳ Given for rare diseases
→ current major public health problem

↓

Expiry of patent (generic drug)
(Prove only same bioavailability as parent drug = bioequivalent)

↓

Cost ↓↓

Drug and Cosmetic act, 1940
Schedule A-Y

a. Schedule H = prescription drug
   (OTC → without prescription)
b. Schedule H_1 = Antibiotics / Drug (Resistance easy)
   Ex TB Drugs
c. Schedule X = Abuse liability
   (Narcotics / Psychotropic)
d. Schedule C = Vaccines / Sera
   (Special storage conditions)
e. Schedule P – Shelf life (Expiry date)

f. Schedule M =Manufacturing practices
g. Schedule G: Drugs taken under direct supervision
(I.V fluids, Antibiotics)

Illegal Activities

a. Misbranded drugs:
- Any pre-requisite is absent
- Anything extra information (Tag line / image)

b. Adulterated drugs
- Contains anything hazardous to health
- Non - permissible color

c. Spurious drugs
- Name same / resemble other famous drugs
- Company name / Address wrong / doesn't exist
- Contains something as alternative of drug
- Wrong calculation

- If patient dies or has a permanent disability:- Min 10 years imprisonment / min 10 L fine.
- No death - 7 years imprisonment / 3L fine

1. **Which of the following receptor associated with opening of Potassium channel without involvement of secondary messanger?**
   A. Nn
   B. M2
   C. M3
   D. M4

2. **In ACLS protocol, starting dose of atropine for treatment of bradycardia is?**
   A. 0.1 mg
   B. 0.5 mg
   C. 1.0 mg
   D. 0.6 mg

3. **A 5-year-old boy went to the temple in a village with his grandmother. He was crying inconsolably on the way back. He was taken to the emergency department within 3 hours. He had altered sensorium, cold clammy extremities, increased salivation, and excessive sweating. On examination, he was pale and had priapism with the following vitals - BP - 140/78 mmHg, HR - 152/min, RR - 36/min SPO2 of 96%. Which of the following would you use in his management?**
   A. Anti venom
   B. Prazosin
   C. Adrenaline
   D. Neostigmine

4. **Which of the following drug will worsen myasthenia gravis?**
   1. **Lidocaine**
   2. **Meropenem**
   3. **Quinidine**
   4. **Alpha blockers**

   Select the correct answer from the given below code:
   A. 1 and 3 only
   B. 1 and 2 only
   C. 1, 2, 3, 4
   D. 1 only

5. **Patient came with acute glaucoma with red eye. IOP was 38mmHg. Anterior chamber shows aqueous flare and keratic precipitates. What should not be given?**
   A. Beta blocker
   B. Mannitol
   C. Acetazolamide
   D. Prostaglandin analogues

6. **A patient with organophosphate poisoning was given atropine and pralidoxime. Patient developed high grade fever after 2 hours of treatment due to?**
   A. PAM side effect
   B. OP poisoning late manifestation
   C. Aspiration pneumonia
   D. Atropine side effect

7. **Which of the following is centrally acting alpha2 agonist drug given as muscle relaxant?**
   A. Diazepam
   B. Tizanidine
   C. Guanfacine
   D. Bromocriptine

8. **A 35 year old patient who is a k/c/o COPD, has undergone orthopedic surgery. Post surgery he has complaints of urinary retention. Which of the following can be given**

as most suitable drug to manage above problem:

A. Neostigmine
B. Bethanechol
C. Tamsulosin
D. Imipramine

9. Beta blocker should be avoided in all given conditions except?

A. Glaucoma
B. Hypothyroidism
C. COPD
D. Diabetes

10. Drug useful to provide fastest symptomatic relief in patients of BPH (benign prostate hyperplasia)

A. Finasteride
B. Tamsulosin
C. Sildenafil
D. Bethanechol

11. Which of the following drug is not used to slow down the progression of diabetic kidney disease?

A. Enalapril
B. Finerenone
C. Furosemide
D. Dapagliflozin

12. Best therapy for mountain sickness?

A. Spironolactone
B. Furosemide
C. Acetazolamide
D. Mannitol

13. Sacubitril mechanism of action?

A. Inhibit sodium reabsorption in PCT
B. Neprilysin inhibitor
C. Natriuretic peptide
D. Relaxes mesangium

14. Best Drug given for treatment of hyponatremia?

A. Terlipressin
B. Desmopressin
C. Tolvaptan
D. Demeclocycline

15. Diuretics useful for CHF are all except?

A. Furosemide
B. Spironolactone
C. Mannitol
D. Metolazone

16. Sprue like enteropathy can be the side effect of which ARB?

A. Olmesartan
B. Losartan
C. Candesartan
D. Temisartan

17. Which Pk/PD property of ARBs is wrong:

A. Telmisartan undergoes exclusive hepatic clearance
B. Irbesartan undergoes combined hepatic and renal clearance
C. Losartan is antagonist of TxA2 receptor and attenuates platelet aggregation
D. Candesartan is not used in mild to moderate hepatic insufficiency but used in renal insufficiency

18. Which of the following indicated for the treatment of SAH?

A. Nicardipine
B. Clevidipine
C. Nimodipine
D. Verapamil

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19. **Which antianginal drug is also used for arrythmia and CHF?**
    A. Ranolazine
    B. Fasudil
    C. Trimetazidine
    D. Ivabradine

20. **Drug need to be given to a patient of ventricular arrhythmia after MI?**
    A. Lignocaine
    B. Verapamil
    C. Procainamide
    D. Propranolol

21. **Hepatotoxicity is not a side effect with:**
    A. Bosentan
    B. Ambrisentan
    C. Macitentan
    D. Sitaxsentan

22. **Drug avoided to be used in PIH**
    A. Nifedipine
    B. Atenolol
    C. Methyldopa
    D. Labetalo

23. **A 65 yr old patient, known case of CKD with protienuria, comes to you with BP 160/100 and requires anti hypertensive treatment. Which treatment is best to start?**
    A. Enalapril
    B. Amlodipine
    C. Atenolol
    D. Furosemide

24. **A 60 yr old severe bronchial asthma patient is planned to put on monoclonal antibody therapy. Which of the following drug requires monitoring of herpes zoster virus infection?**
    A. Omalizumab
    B. Reslizumab
    C. Mepolizumab
    D. Zileuton

25. **Match the side effects of the drug; (Column – (A) with Column – (B)):**

Column – (A)	Column – (B)
a. Amiodarone	1. Blepharoconjunctivitis
b. Hydroxychloroquine	2. Angle closure glaucoma
c. Systemic steroids	3. Retinopathy
d. Digoxin	4. Optic neuritis
	5. Yellow vision
	6. Cataract

Select the correct answer using the code below:
    A. a = 4 / b = 3 / c = 6 / d = 5
    B. a = 3 / b = 4 / c = 6 / d = 5
    C. a = 5 / b = 1 / c = 3 / d = 4
    D. a = 6 / b = 5 / c = 1 / d = 3

26. **Which of the following mechanism is involved in diuretic effect of theophylline:**
    A. Phospholipase A2 inhibtion
    B. Adenosine receptor blocking
    C. Phosphodiesterase inhibiton
    D. Increase in cAMP level

27. **Rate Of Absobtion of drug depends on**
    A. T max
    B. Cmax
    C. AUC
    D. Vd

28. **Dose of a drug depends on all except:**
    A. Plasma concentration required to achieve
    B. Volume of distrubution in body

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C. Surface area of body
D. Half life of drug

29. Which G protein subtype associated with IP3/DAG activity?
A. G alpha S
B. G alpha Q
C. Beta gamma subunit
D. G alpha I

30. SSRIs can result in reduced efficiency of:
A. Tamoxifen
B. Phenytoin
C. Carbamazepine
D. Atorvastatin

31. Phase 1 clinical trial is done for:
A. Dose
B. Safety
C. Pharmacokinetics
D. Efficacy

32. All statements are true about H2 receptor antagonist except:
A. Famotidine is non competitive blocker of H2 receptor True
B. Drugs are associated with high oral bioavailability
C. Given once daily high dose for healing of PUD
D. Ranitidine stored for more than 6 month can increase the risk of cancer

33. Side effects of PPI are all except?
A. Dementia
B. Interstitial nephritis
C. Retinopathy
D. Hypomagnesima

34. Anti emetic proved to be useful in delayed chemotherapy induced vomiting?
A. Ondansetron
B. Dolasetron
C. Granisetron
D. Palonosetron

35. Antiemetic associated with problems of body movement disorder?
A. Aprepitant
B. Domperidone
C. Cisapride
D. Metoclopramide

36. Baricitinib mechanism of action?
A. IL-1 INHIBITON
B. IL-6 INHIBITION
C. Co stimulation (CTLA 4-Ig) blockade
D. JAK/STAT kinase inhibiton

37. A newborn with diagnosed with transposition of great arteries should be administered the following drugs to maintain the patency of Ductus Arteriosus:
A. Alprostadil
B. Ibuprofen
C. Indomethacin
D. Epoprostenol

38. Which of the following can increase risk of MI and stroke?
A. Allopurinol
B. Febuxostat
C. Raspuricase
D. Probenicid

39. Which of the following drug is useful for the treatment of tumor lysis

syndrome with declined kidney function?

A. Allopurinol
B. Febuxostat
C. Rasburicase
D. Probenicid

40. Which of the following is PGE2 analogue?

A. Misoprostol
B. Dinoprostone
C. Carboprost
D. Alprostadil

41. All of the following are side effects of ergot derivatives except:

A. Gangrene
B. Valvular damage
C. Vomiting
D. Depression

42. All are side effects of salbutamol except:

A. Hypoglycemia
B. Hypokalemia
C. Hypotension
D. Tachycardia

43. Patient comes to you with arrythmia and you have decided to start digoxin as an anti arrythmic drug. What is the main mechanism of action in controlling arrythmia?

A. Na+ K+ ATPase inhibition
B. H+ K+ ATPase inhibition
C. Vagomimetic effect
D. Na Ca exchanger pump activation

44. Patient comes to you with arrythmia and you have decided to start digoxin as an anti arrythmic drug. What is the therapeutic plasma range need to maintain to control arrythmia?

A. 0.2 to 2.0
B. 0.2 to 1.2
C. 2.0 to 20.0
D. 2.0 to 12.0

45. Patient comes to you with arrythmia and you have decided to start digoxin as an anti arrythmic drug. Digoxin has half life of 40 hrs. What does it signifies?

A. Its Vd is large
B. Its plasma clearance is less
C. Need to be given in loading dose
D. Dose need to be repeated after every 1.5 days

46. Patient comes to you with arrythmia and you have decided to start digoxin as an anti arrythmic drug. Digoxin toxicity can be precipitated by all except?

A. Hypomagnesimia
B. Hypokalemia
C. Hypocalcemia
D. Hypercalcemia

47. Which is the most efficient drug for early onset vomiting?

A. Dexamethasone
B. Palonosetron
C. Dronabinol
D. Aprepitant

48. Which drug should be used in low dose along with aprepitant?

A. Dexamethasone
B. Palonosetron
C. Dronabinol
D. Aprepitant

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49. Which drug given for 3 day schedule?
A. Dexamethasone
B. Palonosetron
C. Dronabinol
D. Aprepitant

50. Single dose regimen of Netupitant is in combination with?
A. Dexamethasone
B. Palonosetron
C. Dronabinol
D. Aprepitant

51. Which is best drug to manage HTN crisis in pre operative stage?
A. Phentolamine
B. Propranolol
C. Phenoxybenzamine
D. Na nitroprusside

52. Which is best drug to control intraoperative crisis?
A. Phentolamine
B. Propranolol
C. Phenoxybenzamine
D. Na nitroprusside

53. Which drug has no role in treatment of pheochromocytoma?
A. Phentolamine
B. Propranolol
C. Phenoxybenzamine
D. Na nitroprusside

54. Which drug is used for diagnosis of pheochromocytoma
A. Phentolamine
B. Propranolol
C. Phenoxybenzamine
D. Na nitroprusside

55. Which drug is given by nasal powder?
A. Flunarizine
B. Ergometrine
C. Sumatriptan
D. Topiramate

56. Which drug is 5 HT 1b/1d receptor agonist?
A. Flunarizine
B. Ergometrine
C. Ubrogepant
D. Topiramate

57. Which is pure calcium channel blocker is approved for migraine?
A. Flunarizine
B. Ergometrine
C. Sumatriptan
D. Topiramate

58. Which drug is best for migraine associated with obesity?
A. Flunarizine
B. Ergometrine
C. Sumatriptan
D. Topiramate

59. Patient is diagnosed to be suffering from moderate to severe RA. Which is best drug to start treatment?
A. Methotrexate
B. Leflunomide
C. Tofacitinib
D. TNF alpha blockers
E. Triple regimen: MTx + HCQS + sulfasalazine

60. Above patient is found to refractory to above drug. What is the best option to be used as add on therapy?

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A. Methotrexate
B. Leflunomide
C. Tofacitinib
D. TNF alpha blockers
E. Triple regimen: MTx + HCQS + sulfasalazine

61. Above patient wants oral drug therapy for his disease. What is the best option to be chosen?

A. Methotrexate
B. Leflunomide
C. Tofacitinib
D. TNF alpha blockers
E. Triple regimen: MTx + HCQS + sulfasalazine

62. After many years of treatment patient get fed up with multiple drugs on daily basis and wants monotherapy which can be oral or parentral. What is the best option to be chosen

A. Methotrexate
B. Leflunomide
C. Tofacitinib
D. TNF alpha blockers
E. Triple regimen: MTx + HCQS + sulfasalazine