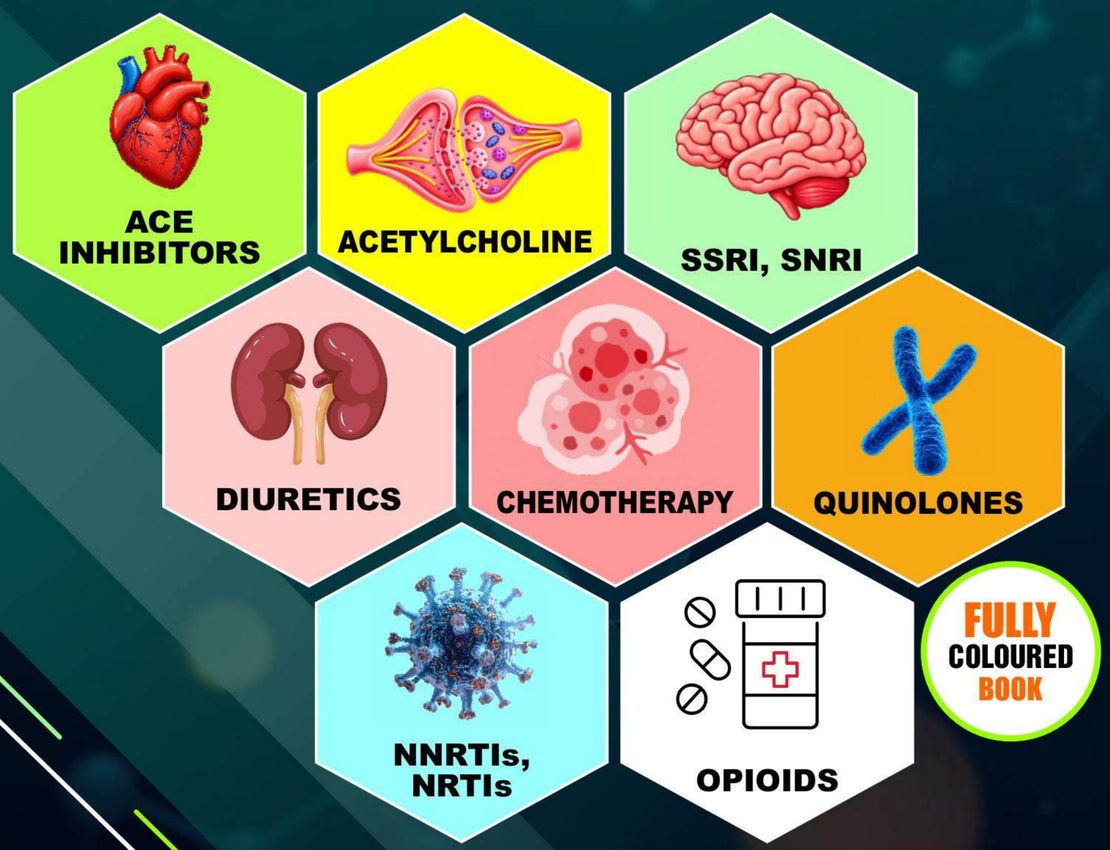
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PHARMACOLOGY TRACKER

Simplify | Memorize | Master



- MIND MAP
- DRUG CLASSIFICATIONS
- MNEMONICS
- FLOW CHARTS
- TRICKS
- CLINICAL CONCEPTS

Learn and Memorize Pharmacology in Simplified Way

PHARMACOLOGY TRACKER

SIMPLIFY | MEMORIZE | MASTER

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GENERAL PHARMACOLOGY



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INTRODUCTION TO PHARMACOLOGY

Important Scientists & Their Contributions in Pharmacology

Oswald Schmiedeberg	Father of Pharmacology
Col. Ram Nath Chopra	Father of Indian Pharmacology
Sir James Black	Father of Modern Pharmacology
Banting and Best	Discovered insulin in 1921
Hippocrates	Father of Medicine
Paul Ehrlich	Father of Modern Chemotherapy
Alexander Fleming	Discovered penicillin
Selman Waksman	Discovered streptomycin
J. N. Langley	ccncept of receptors and drug–receptor interactions
Paracelsus	Grandfather of Pharmacology

Important Concepts

Pharmacokinetics

- Drug movement in, through and out of the body.
- "What body does to the drug."

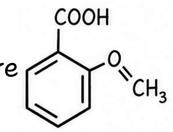
Pharmacodynamics

- Physiological & biochemical effects of drugs and their mechanisms of action.
- "What the drug does to the body."

Drug Nomenclature

Chemical Name

Indicates the chemical structure of the drug



Examples: Acetylsalicylic acid, N-acetyl-p-amisophenol

Generic Name

Official/common name assigned by a competent scientific authority



Examples: Aspirin, Paracetamol (Acetaminophen)

Brand Name

Trade name given by the drug manufacturer



Examples: Dignrin, Ecosprin, Crocin, Metacin, Tjienol

Drugs Administered by Various Routes

Transdermal route – Nitroglycerine, nicotine, fentanyl, hyoscine.

Sublingual route – Nitroglycerine, isosorbide dinitrate, clonidine, nifedipine.

Nasal route – Nafarelin (GnRH agonist), calcitionin and desmopressin.

Inhalational route – Salbutamol, ipratropium, montelukast etc.

Rectal route – Diazepam.

Routes of Drug Administration

- **Systemic**
  - **Enteral**
    - Oral
    - Sublingual
    - Rectal
    - Trick → ORS
  - **Parenteral**
    - **Injections**
      - Others
        - Intra-arterial
        - Intrathecal
        - Intramedullary
      - Intradermal
      - Subcutaneous
      - Intramuscular
      - Intravenous
      - Intraperitoneal
    - **Inhalation**
      - Liquids (Eg: GA, Bronchdilators)
      - Gases (Eg: GA, Oxygen)
      - Powders (Eg: Bronchodilators)
    - **Transdermal**
      - Adhesive units
      - Intrathoracic
      - Jet injection
- **Local (Topical)**
  - **Skin**
    - Ointment
    - Cream
  - **Mucous membrane**
    - Eye, ear drops
    - Nasal spray
    - (local, systemic)

Essential Medicines

"Papa Eats Cheap Apples Daily Quality Is Awesome"

P – Public health relevance
E – Efficacy & safety
C – Cost-effectiveness
A – Succiner
D – Dosage form
Q – Quality & stability
I – Information
A – Affordable price

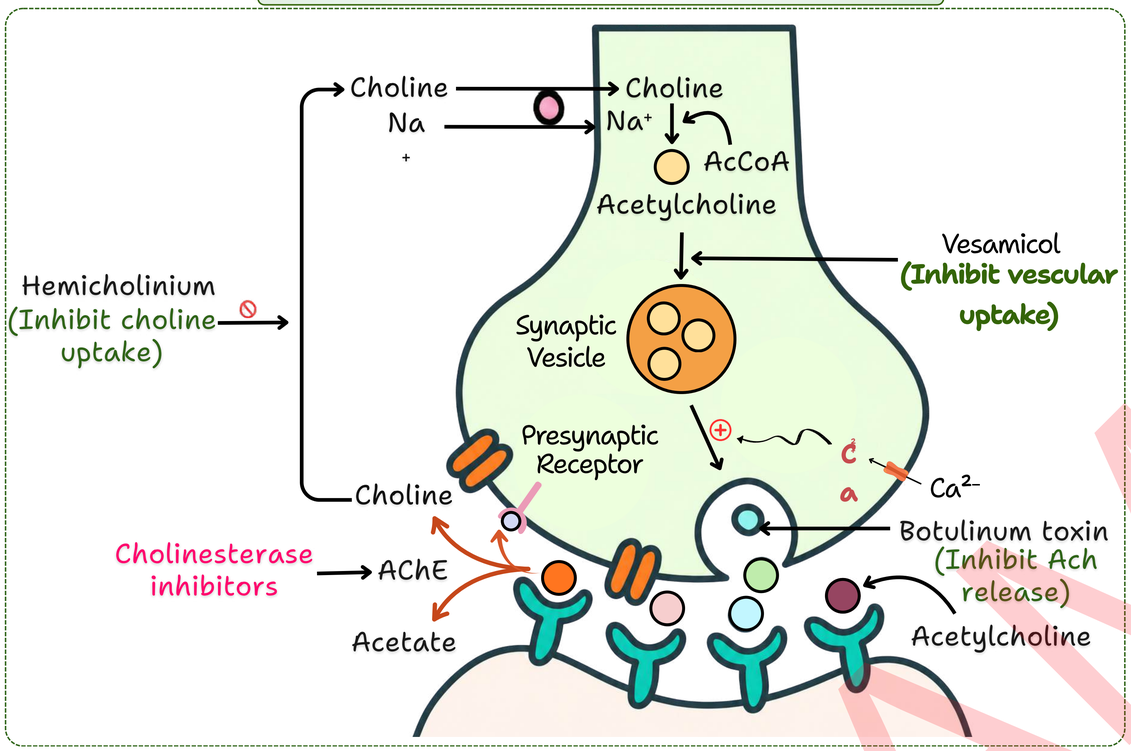


SAMPLE

CHOLINERGIC SYSTEM AND DRUGS

Acetylcholine (ACh) is a major neurohumoral transmitter at autonomic, somatic as well as central sites.
Acetylcholine (ACh) is the principal NT at NMJ as well at all preganglionic fibres.

Synthesis, Storage and Destruction of Ach



Cholinergic Receptors

- **Nicotinic (N)**
  - **N_M**
    - Ganglia
    - Adrenal medulla
  - **N_N**
    - Neuro-muscular junction
- **Muscarinic (M)**
  - **M_1**
    - Autonomic ganglia
    - Gastric glands
    - CNS
  - **M_2**
    - Heart
    - CNS
  - **M_3**
    - Eye
    - GIT
    - Bladder
    - Bronchus
    - Glands
    - CNS
  - **M_4 & M_5**
    - CNS

Characteristics of Nicotinic Receptor Subtypes

	N_M Receptor	N_N Receptor
Location & function	• **Neuromuscular junction:** depolarization of muscle end plate → contraction of skeletal muscle	• **Autonomic ganglia:** depolarization → postganglionic impulse • **Adrenal medulla:** catecholamine release • **CNS:** site-specific excitation or inhibition
Agonists	Phenyl trimethyl ammonium (PTMA), Nicotine	Dimethyl phenyl piperazinium (DMPP), Nicotine
Antagonists	Tubocurarine, α-Bungarotoxin	Hexamethonium, Trimethaphan

Characteristics of Muscarinic Receptor Subtypes

	M_1	M_2	M_3
Location and function subserved	• **Autonomic ganglia:** Depolarization (late EPSP) • **Gastric glands:** ↑ acid secretion • **CNS:** Learning, memory, motor functions	• **SA node:** Vagus stimulation → Hyperpolarization, ↓ rate of impulse generation ↓ heart rate (bradycardia) • **AV node:**↓ velocity of conduction • **Atrium:** Shortening of APD, ↓ contractility • **Ventricle:**↓ contractility (slight) • **Cholinergic nerve endings:** ↓ ACh release • **CNS:** Tremor, analgesia • **Visceral smooth muscle:** contraction	• **Visceral smooth muscle:** contraction • **Iris:** constriction of pupil • **Ciliary muscle:** contraction • **Exocrine glands:** secretion • **Vascular endothelium:** release of NO → vasodilatation
Agonists*	MCN-343A, Oxotremorine	Methacholine	Bethanechol
Antagonists *	Pirenzepine, Telenzepine	Methoctramine, Tripitramine	Solifenacin, Darifenacin

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Drugs that Prolongs Q–T Interval (Have potential to precipitate Torsade's de pointes)

Antiarrhythmics
- **Qu**inidine
- **Proca**inamide
- **Propa**fenone
- **Dis**opyramide
- **A**miodarone

(**Trick** → **Qu Proca** aur **Propa Disco A**aaye)

Antimicrobials
- **Halo**fantrine
- **Arte**misinin
- **Me**floquine
- **Spar**floxacin
- **Gati**floxacin
- **Qu**inine

(**Trick** → **Halo Arte Me Spark** se **Gati Qu**b aya)

Antihistaminic
- **T**erfenadine
- **E**bastine
- **A**stemizole

(**Trick** → **TErA** byte)

Antidepressants
- Amitriptyline and other tricyclics

Antipsychotics
- **Th**ioridazine
- **Ris**peridone

(**Trick** → **Th**oda **Ris**k hai)

Prokinetic

Loratadine
- Long-acting
- Metabolized to desloratadine.

Cetirizine
- Active metabolite of hydroxyzine
- Cause sedation.
- Levocetirizine → its more potent L-isomer.

Terfenadine
- overdose or interaction with CYP3A4 inhibitors (ketoconazole, erythromycin, clarithromycin, itraconazole) → may cause QT prolongation and torsades de pointes.
- Rapid-acting
- Active metabolite is fexofenadine → lacks this cardiac toxicity.



5-HYDROXYTRYPTAMINE & ITS ANTAGONISTS

Serotonin
Vasoconstrictor released during blood clotting.

Enteramine
Smooth muscle-contracting substance in intestinal enterochromaffin cells.

Synthesis of 5-HT
- 5-HT is β-aminoethyl-5-hydroxyindole.

Tryptophan
↓ hydroxylase
5-hydroxytryptophan
↓ decarboxylase
5-hydroxytryptamine
↓ drhydrogenase / MAO
5-hydroxytryptophol; 5-hydroxy indole acetic acid (5-HIAA)

Serotonergic (5-HT) Receptors

5-HT$_1$
- CNS
- Cranial blood vessels

5-HT$_2$
- Platelets
- Smooth muscle
- Cerebral cortex (5-HT$_{2A}$)
- Fundus of stomach (5-HT$_{2B}$)
- Choroids (5-HT$_{2C}$)

5-HT$_3$
- CTZ
- NTS
- parasympathetic nerve terminals (GIT)



5-HT$_4$
- GIT
- CNS

Serotonergic (5-HT) Agonists

5-HT$_4$ (used in GERD)
Metoclopramide, Cisapride, Renzapride

5-HT$_{1A}$ (used in antianxiety)
Buspirone, Isapirone, Gepiron

5-HT$_{1B/1D}$ (used in acute migraine attacks)
Sumatriptan, Naratriptan

5-HT$_2$
α-Methyl 5-HT

5-HT$_3$
2-Methyl 5-HT

SAMPLE

Dipeptidyl Peptidase -4 (DPP-4) Inhibitor

- Inhibit DPP-4 (Dipeptidyl Peptidase-4) enzyme → Prevent the degradation of GLP-1 (Glucagon-Like Peptide-1).
  - ↑ plasma GLP-1 concentration, leading to
    - ↑ glucose-dependent insulin secretion.
    - ↓ glucagon secretion.
    - Improved control of fasting and postprandial hyperglycaemia.
- Do not cause nausea or weight loss
- Most common adverse effect
  - Nasopharyngitis



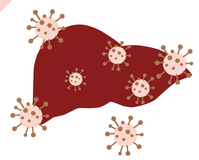
  - Upper respiratory tract infections



- Causes
  - Allergic reactions (with sitagliptin)



  - Hepatotoxicity (with Vildagliptin)



Onswik (insulin efsitora alfa-gobe)

- Once-weekly long-acting basal insulin analog
- Contraindicated in type 1 diabetes

Merilog (Insulin Aspart)

- First rapid-acting insulin biosimilar (biosimilar to Novolog)
- Glycemic control in adult and pediatric diabetes mellitus

Tzield (teplizumab)

Decline of insulin production in pediatric patients ages 8 through 17 with recently diagnosed Stage 3 type 1 diabetes.

Desmopressin

Drug of choice for neurogenic Diabetes Insipidus

Acarbose

Reduce carbohydrate absorption and cause flatulence.

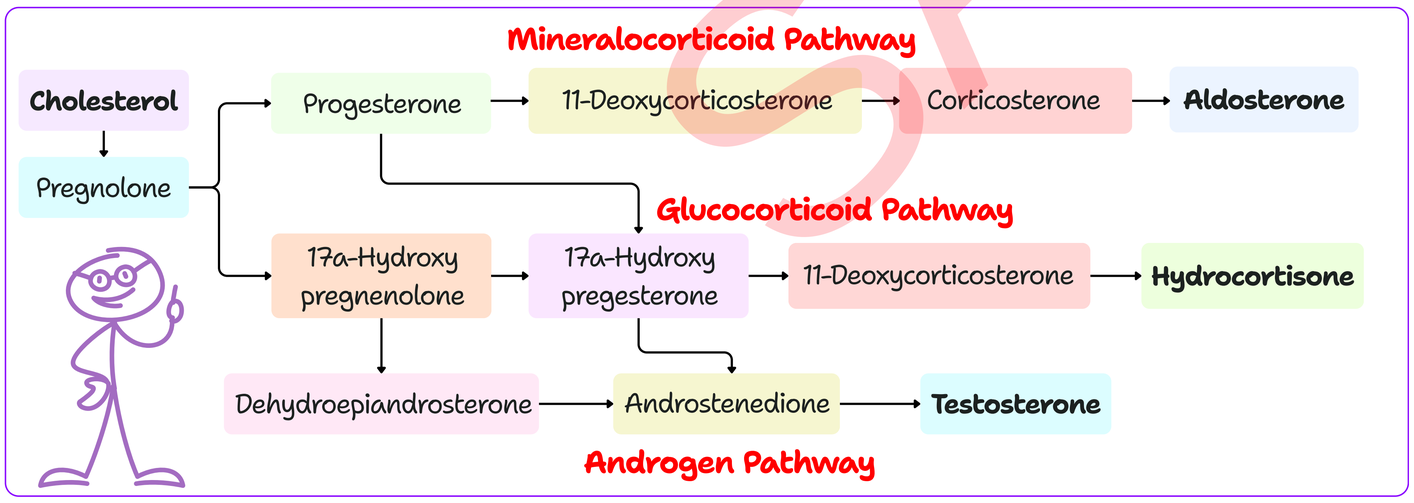
Complex oligosaccharide

Dapagliflozin

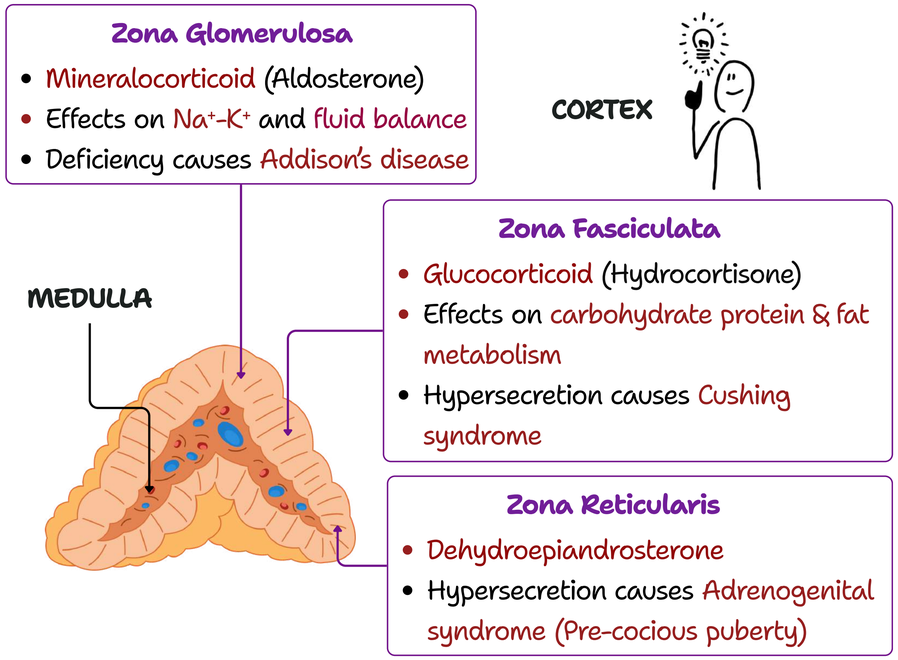
Inhibit SGLT-2 in renal proximal tubule → inhibit glucose absorption → glycosuria, ↓ blood glucose level

CORTICOSTEROIDS

Pathways of Adrenal Steroid Hormone Biosynthesis



Sources of Corticosteroids, their Functions and Disorders



SAMPLE

Adverse Effects and Contraindications of Steroids

Trick - GLUCOCORTICOIDS

- **G – G**laucoma (on topical use)
- **L – L**imb muscle atrophy
- **U – U**lcer (peptic ulcer)
- **C – C**ushing syndrome
- **O – O**steoporosis
- **C – C**ataract (on systemic use)
- **O – O**steonecrosis (avascular necrosis)
- **R – R**enal failure (Contraindicated)
- **T – T**uberculosis (particularly ileo-caecal) (Contraindicated)
- **I – I**mpair healing
- **C – C**HF (Contraindicated)
- **O – O**edema
- **I – I**nfections (due to immuno suppressant action)
- **D – D**iabetes mellitus
- **S – S**uppression of HPA-axis

Synthesis Inhibitors & Receptor Antagonists

Glucocorticoid Synthesis Inhibitors

- **M**etyrapone
- **A**minoglutethimide
- **M**itotane
- **Tri**lostane
- **K**etoconazole

(Trick → MAM TriK)

Corticosteroid Receptor Antagonist

- Mifepristone
- Spironolactone and Eplerenone
- Drospirenone

(Trick → SpEeD Miter)

Mifepristone
Used in the treatment of Cushing's syndrome

Budesonide
Nonhalogenated glucocorticoid with high topical activity.

Metyrapone
Inhibits 11 β hydroxylase enzyme
↓
reduced glucocorticoid activity.
Safe in pregnancy

Aminoglutethimide
Inhibits the enzyme aromatase and is useful in breast carcinoma

Trilostane
Inhibits 3 β hydroxysteroid dehydrogenase enzyme

ANDROGENS AND DRUGS FOR ERECTILE DYSFUNCTION

Androgens (Male Sex Hormones)

Natural

- **Te**stosterone
- **A**drosterone
- **D**ihydrotestosterone

(Trick → Tele AD)

Synthetic

- **Me**thyltestosterone
- **Me**sterolone
- **Flu**oxymesterone

(Trick → MeMe Flu)

Testosterone
↓ 5-α reductase
Dihydrotestosterone (DHT)
↓ Aromatase
Estradiol

Less potent androgens
- Androstenidione
- Dehydroepiandrostenidione (DHEA)

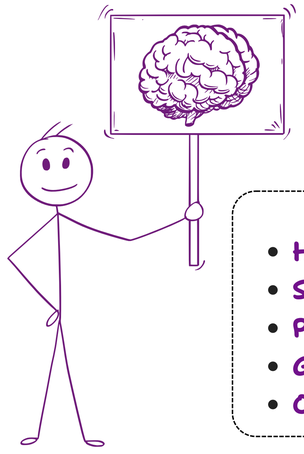
Testosterone
19 carbons containing compound

Secreted from
Leydig interstitial cell of testes

Uses of Androgens

Trick - THAI HAlwa

- **T – T**esticular Failure
- **H – H**ypopituitarism
- **A – A**IDS-related Muscle Wasting
- **I – I**diopathic Male Infertility
- **H – H**ereditary Angioneurotic Edema
- **A – A**geing



Adverse Effects of Androgens

Trick - Hello SP GOPAL in CurV

- **H – H**epatic Carcinoma/ Headache
- **S – S**alt Retention & Edema
- **P – P**recocious Puberty
- **G – G**ynaecomastia
- **O – O**ligozoospermia
- **P – P**ainful Erections
- **A – A**cne
- **L – L**ipid Changes (↓ HDL & ↑ LDL)
- **C – C**holestatic Jaundice
- **V – V**irilization (Hirsutism)

SAMPLE

Halothane

- Causes malignant hyperthermia (treated with dantrolene)
- Hepatotoxic
- For induction 2–4% and for maintenance 0.5–1% is delivered by the use of special vaporizer
- ↓ses Heart Rate
- Causes bronchodilation preferred in asthmatics
- Myocardial depression intracellular Ca^{2+}, reducing myocardial contractility

Thiopentone

- Principal mechanism limiting anesthetic duration after single dose → redistribution
- Produces unconsciousness in 15–20 sec.
- Poor analgesic
- Highly lipid soluble hence has a rapid onset and short duration (5–8 minutes) of action.
- Ultrashort acting thiobarbiturate
- Injected I.V. (3.5 mg/gm) as 2.5% solution thiopentone sodium.

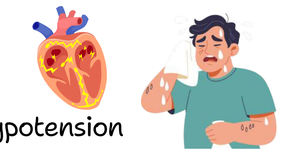
Nitrous oxide

- Used with O_2 for dental analgesia
- Causes megaloblastic anemia & bone marrow suppression
- Faster induction & recovery of anaesthesia
- Diffusion hypoxia occurs when supply of N_2O is stopped during recovery
- Laughing gas
- Poor muscle relaxant
- Patient maintained on 70% N_2O + 30% O_2 recalls events during anesthesia
- Odorless gas used as anaesthetic agent

Properties of Halothane

Trick - HALOTHANE CCC

- **H** – Hyperthermia
- **A** – Arrhythmias
- **L** – Liver toxicity
- **O** – Orthostatic hypotension
- **T** – Tocolytic
- **H** – Heart depression
- **A** – Asthma
- **Ne** – Non-explosive
- **C** – Childrens [safe in children]
- **C** – Chills
- **C** – Catecholamines [sensitizes heart to arrhythmogenic action]



Inhalational anaesthetics that can precipitate seizures

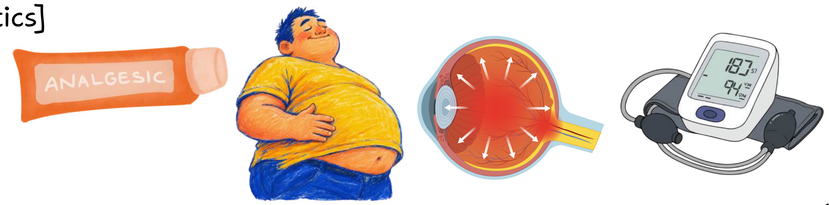
Trick - SEIzure

- **S** – Sevoflorane
- **E** – Enflurane (Maximum)
- **I** – Isoflurane

Ketamine

Trick - KETAMINE

- **K** - Kids (i.v. anaesthetic of choice in children)
- **E** - Emergence reaction [halluinations, illusions, vivid dreams etc. seen while recovery from anaesthesia]
- **T** - Thalamocortical junction [site of action, responsible for dissociative anaesthesia]
- **A** - Analgesic [maximum among anaesthetics]
- **M** - Meals [can be given in full stomach]
- **I** - Increases all pressures [BP, IOP, ICT]
- **N** - NMDA antagonist
- **E** - Excellent for asthmatics

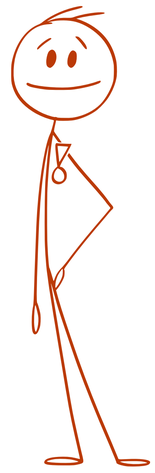


Drugs Useful for Day Care Surgery

Trick - Dr Manmohan Singh Is A PM

- **Dr** - Desflurane
- **M** - Midazolam (Benzodiazepine)
- **S** - Sevoflurane
- **I** - Isoflurane
- **A** - Alfentanil
- **P** - Propofol
- **M** - Mivacurium (Muscle relaxant)





SAMPLE

Mechanism of Action of BZD

Bind to specific site on GABA-A receptor (Different from GABA-binding site) → ↑ frequency of opening of Cl^- channels → ↑ GABA-mediated chloride current → Membrane hyperpolarization → CNS depression



Barbiturates

- Learning and memory impairment can occur
- Narrow therapeutic index
- Nonselective CNS depressants
- Contraindicated in acute intermittent porphyria
- Ascending reticular activating system (ARAS) being the main site
- Powerful enzyme inducing agents and are prone to several drug interactions
- GABA mimetic as well as GABA facilitatory action

Uses of Benzodiazepines

(Trick - Ben CAMPA DIA)



- **C** – Conscious sedation
- **A** – Anticonvulsant
- **M** – Muscle relaxant
- **P** – Preanaesthetic medication
- **A** – Anxiolytic
- **D** – Diagnostic & minor operative procedures
- **I** – Insomnia
- **A** – Alcohol withdrawal symptoms

Acute Barbiturate Poisoning

Causes coma, respiratory depression, hypotension, cardiovascular collapse, and barbiturate blisters

Treatment: Gastric lavage, supportive care, forced alkaline diuresis, and hemodialysis.



Mechanism of Action of Barbiturates

Bind to specific site on GABA-A receptor (Different from GABA-binding site) → ↑ duration of opening of Cl^- channels → ↑ GABA-mediated chloride current → Membrane hyperpolarization → CNS depression



Non-Benzodiazepine Hypnotics

- Cause less REM sleep disturbance than benzodiazepines.
- Have lower abuse potential than benzodiazepines
- Produce less anxiolytic, anticonvulsant, and muscle-relaxant effects

Zolpidem, zopiclone, zaleplon, eszopiclone (Non-benzodiazepine hypnotics) → Bind selectively to BZD-binding site on GABA-A receptor → Facilitate GABA-mediated neuronal inhibition → CNS depression



Unsafe drugs in Porphyria

Trick - SEVERE PORPHyriA

- **S** - Sulfonamides
- **E** - Erythromycin
- **V** - Valproate
- **E** - Ergot Alkaloids
- **R** - Rifampicin
- **E** - Estrogens
- **P** - Phenobarbitone (and other barbiturates like thiopentone)
- **OR** - ORal contraceptives
- **P** - Phenytoin
- **H** - Hydralazine
- **A** - Alcohol



Ramelteon

Agonist of MT1 and MT2 receptors of melatonin in suprachiasmatic nucleus

Long term use in treatment of sleep onset insomnia

Triazolam

- Rapid; peak effect occurs within 1 hour.
- Anxiety due to a possible withdrawal phenomenon
- Effective for sleep induction
- Rebound insomnia
- Minimal morning residual effects at therapeutic doses.
- Used for short-term insomnia, including in travellers and shift workers
- **Adverse Effects** Anterograde amnesia, Paranoia and next-day anxiety.

SAMPLE

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INTRODUCTION TO CVS

Disorders of Heart

- **Tachycardia** — ↑sed rate of heart beat
- **Bradycardia** — ↓sed rate of heart beat
- **Arteriosclerosis** — Hardening or loss of elasticity of arteries
- **Coronary thrombosis** — Formation of clot in coronary artery
- **Myocardial Ischemia** — Inadequate flow of blood to a part of heart
- **Myocardial infarction** — Pain due to ischemic death of myocardium
- **Atherosclerosis** — Thickening of walls of blood vessels due to deposition of fat including cholesterol
- **Arrhythmia** — Irregular heartbeat / disorder of heart rate or rhythm

PLASMA KININS (BRADYKININ AND KALLIDIN)

Plasma Kinins polypeptides formed from plasma globulin Kininogen by the action of enzymes Kallikreins

Kallidin Decapeptide (10 amino acids)

Bradykinin Nonapeptide (9 amino acids)

Kinin Receptors

- B_1 receptors ↓ Induced during inflammation/tissue injury
- B_2 receptors ↓ Mediate most physiological actions of bradykinin

Agonists and Antagonists

- **Bradykinin and Kallidin** ↓ selective agonists of B2 receptors
- **Des Arg Kallidin** ↓ selective agonists of B1 receptor
- **Synthetic peptide HOE 140 (icatibant)** ↓ selective B2 antagonist

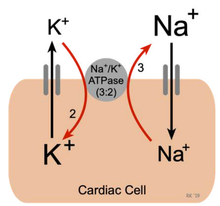
CARDIAC GLYCOSIDES

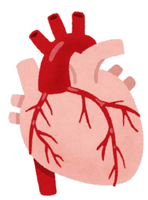
Digoxin

- Causes diuresis in CHF patients
- Produces cardiac arrhythmias due to disturbed impulse formation and conduction
- Hyperkalemia does not increase digoxin toxicity
- Preferable than digitoxin in the treatment of CHF because it has short half-life
- In renal patients ↓ risk of developing digoxin toxicity

Mechanism of Action of Cardiac Glycosides

Act by inhibiting ↓ K^+ dependent Na^+-K^+ ATPase of myocardial fibres ↓ by binding to its extracellular surface → ↑ intracellular Na^+ → ↓ Ca^{2+} extrusion via Na^+/Ca^{2+} exchanger → ↑ intracellular Ca^{2+} → Entry of Ca^{2+} through L-type Ca^{2+} channels during the cardiac action potential → ↑ Ca^{2+} release during each action potential → ↑ Ca^{2+} uptake & storage in sarcoplasmic reticulum (SR) → More Ca^{2+} binds to troponin C → ↑ force of myocardial contraction → Positive inotropic effect





SAMPLE

β-adrenergic receptor antagonist

- Labetalol has alpha- & beta-adrenoceptor blocking action
- β-blockers act by blocking β1 receptors in heart, JG Cells and in CNS with the following mechanisms
  - Inhibition of central and peripheral sympathetic outflow
  - ↓se heart rate
  - ↓se force of contraction
  - ↓se cardiac output
  - ↓se Renin release

Reserpine

- Most likely to cause severe symptoms of depression → When used in trending hypertensive patients
- Acts by binding to adrenergic neurons and displaces noradrenaline & other catecholamines and also inhibits their uptake
- Contraindicated in patients with a history of mental depression

Minoxidil

- Potassium channel activator
- Produrg → Activated in liver to minoxidil sulphate
- Cause abnormal hair growth in females (hirsutism)
- Long-acting Arteriolar vasodilator
- Topically used for the treatment of alopecia
- Useful in patients with chronic renal failure

Thiazide

- Elevate plasma triglycerides
- Indapamide
  - Longer acting and more potent than hydrochlorothiazide
  - Has direct vasodilator action and fewer metabolic adverse effects
- Triamterene + Hydrochlorothiazide combination → treatment of hypertension
- First-line drugs for hypertension
- Useful class of drugs in the long-term treatment of hypertension

Mechanism of Action

Inhibit the Na^+–Cl^- symporter in the early part of the distal convoluted tubule (DCT) → ↑se excretion of sodium (Na^+) & water

- ↓se Na^+ concentration in vascular smooth muscle → ↓se PVR → ↓se BP
- ↓se blood volume & cardiac output (CO) → ↓se BP

Amiloride

- DOC in lithium-induced diabetes insipidus
- Inhibits renal epithelial and myocardial Na^+ channels

Mechanism of Action

Binds to Na^+ channel in DCT and CD → ↑ Na^+ excretion and retains K^+

Sodium Nitroprusside

Effects

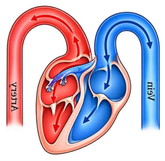
↓ BP, ↓ myocardial workload; improves cardiac output in heart failure

- Thiocyanate accumulation and the consequent toxicity is a possibility → When excess dose is administered
- Given during hypertensive emergencies as an IV infusion
- Contra-indicated in pregnancy

Mechanism of Action

Releases NO in vascular smooth muscle → vasodilation

- **Arteries** → ↓se PVR → ↓se After load
- **Veins** → Pooling of blood in veins → ↓se Venous Return → ↓se Preload → ↓se CO



→ ↓se BP

Moxonidine and Rilmenidine

Congeners of clonidine with longer half lives & are selective for imidazoline receptors

Phentolamine and Tolazoline

DOC for hypertensive emergencies in clonidine withdrawal and cheese reaction

Calcium Channel Blockers

(including amlodipine, diltiazem, and nifedipine) First-line therapy for idiopathic pulmonary hypertenstion

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DRUGS AFFECTING BLOOD AND BLOOD FORMATION

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Contraindications of Heparin

Trick - HCL BEST PLOT GRC

- **H** – **H**eparin-induced thrombocytopenia
- **C** – **C**hronic alcoholics
- **L** – **L**arge malignancies
- **B** – **B**leeding disorders
- **E** – **E**ndocarditis
- **S** – **S**evere hypertension
- **T** – **T**hreatened abortion
- **P** – **P**iles
- **L** – **L**umbar puncture
- **O** – **O**cular surgery
- **T** – **T**uberculosis
- **G** – **G**I ulcers
- **R** – **R**enal failure
- **C** – **C**irrhosis

FIBRINOLYTICS/THROMBOLYTICS

Drugs
(Trick → AUSTRiA)
- **A**lteplase
- **U**rokinase
- **S**treptokinase
- **T**enecteplase
- **R**eteplase
- **A**nistreplase

Fibrinogen and thrombin ↓ most important constituents of Fibrin sealant kit

Agents that dissolve formed blood clots by activating plasminogen into plasmin which breaks down fibrin

Tenecteplase, Reteplase ↓ Obtained from recombinant DNA technology, known as bolus fibrinolytics

Fibrin clot is produced when thrombin is mixed with fibrinogen

Not used in hypertensive crisis

Plasminogen activator Activates the conversion of plasminogen to plasmin

Urokinase

Isolated from human urine

Nonantigenic

Activates plasminogen directly and has a plasma $t_{1/2}$ of 10–15 min

Streptokinase

Obtained from β hemolytic streptococci

Antigenic ↓ can cause hypersensitivity reactions

Adverse effect ↓ bleeding

Alteplase

Recombinant tissue plasminogen activator

Also Used in during myocardial infarction

Used to prevent embolism in lungs

ANTIFIBRINOLYTICS

Drugs Used
- **A**protinin
- **T**ranexamic acid
- **E**psilon aminocaproic acid (EACA)

(Trick → ATE)

They inhibit plasmin activity, reducing fibrin breakdown

Agents that prevent or reduce fibrin breakdown by inhibiting plasminogen activation

Epsilon Aminocaproic Acid (EACA)

Lysine analogue

Binds to the lysine-binding sites of plasminogen and plasmin ↓ Prevents plasmin from binding to fibrin → Inhibiting fibrin breakdown (fibrinolysis)

Used as an adjunct in Haemophilia to control bleeding after tooth extraction, prostatectomy, and trauma

Tranexamic Acid

Approximately 7 times more potent than EACA

Uses
- Fibrinolytic drug-induced bleeding
- Cardiopulmonary bypass surgery
- Menorrhagia
- Recurrent epistaxis
- Hyphema

Adverse Effects
- Diarrhoea
- Disturbed colour vision
- Thromboembolic events
- Allergic reactions

Contraindications
- History of intracranial haemorrhage
- Ischaemic stroke within the past 3 months
- Head injury within the past 3 months
- Intracranial tumour, vascular abnormality, or aneurysm
- Peptic ulcer or oesophageal varices
- Recent wound, fracture, or tooth extraction

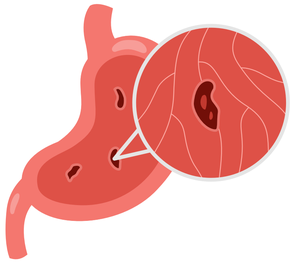
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PEPTIC ULCER AND GERD DRUGS

Peptic Ulcer

A localized sore or erosion in the mucosal lining of the stomach, duodenum & lower esophagus

caused by damage from gastric acid and digestive enzymes



Imbalance between

- Aggressive factors (acid, pepsin, H. pylori)
- Defensive factors (mucus, bicarbonate, mucosal blood flow).

Loss of mucosal protection allows acid and pepsin to erode the lining, leading to ulcer formation

Characteristics of Duodenal ulcer

- Hypersecretion of acid-pepsin
- H. pylori infection
- Night pain is common

Anti-Ulcer Drugs

Reduction of Gastric Acid Secretion

H_2 Antihistamines

- Nizatidine
- Loxatidine
- Roxatidine
- Famotidine
- Ranitidine
- Cimetidine

(Trick → NiLoR FaRCi)

(Suffix → tidine)

Proton pump inhibitors

- Pantoprazole
- Esomeprazole
- Rabeprazole
- Lansoprazole
- Dexrabeprazole
- Omeprazole

(Trick → PERL DeO)

(Suffix → prazole)

Anticholinergic drugs

- Telenzepine
- Oxyphenonium
- Propantheline
- Pirenzepine

(Trick → TOP Pi)

Prostaglandin analogue

- Rioprostil
- Enprostil
- Misoprostol

(Trick → REM)

Anti-H. pylori drugs

- Amoxicillin
- Tinidazole
- Metronidazole
- Clarithromycin
- Tetracycline

(Trick → ATM CT)

Ulcer protectives

- Sucralfate
- Colloidal Bismuth Subcitrate (CBS)

(Trick → SuC BiS)

Neutralization of Gastric Acid (Antacids)

Nonsystemic

- Magnesium hydroxide
- Mag. trisilicate
- Aluminium hydroxide gel
- Magaldrate
- Calcium carbonate

Systemic

- Sodium bicarbonate
- Sod. citrate

Proton Pump Inhibitor

Mechanism of Action
Inhibit H^+/K^+ ATPase in parietal cells of the stomach
↓
reduces stomach acid

Prolonged use of proton pump inhibitors inhibits absorption of vitamin B_{12}

Lansoprazole
Most potent and safest PPI in pregnancy

Lansoprazole, Esomeprazole, pantoprazole
↓
shows maximum bioavailability

Uses
Peptic ulcer disease (PUD), including NSAID-induced ulcers, GERD, Zollinger–Ellison syndrome (ZES)

Proton pump inhibitors (PPI) markedly reduce bioavailability of ketoconazole because PPI ↑ses gastric pH

PPIs have short $t_{1/2}$ but can inhibit acid secretion for more than 24 hours due to irreversible inhibition of proton pump.

Adverse Effects
Long-term use
↓ Vitamin B_{12} absorption,
↓ Ca^{2+} absorption
↑ hip-fracture risk

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ANTIMICROBIAL DRUGS

Indications of Cotrimoxazole

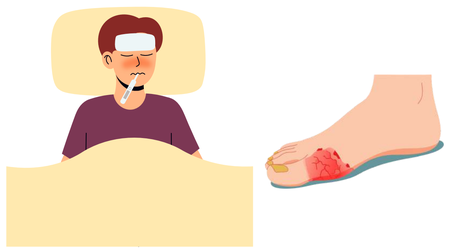
Trick - SEPTRAN

- **S – S**TD's (Chancroid, LGV)
- **E – E**nteritis (E.coli, Shigella)
- **P – P**neumocystis pneumonia
- **T – T**yphoid
- **R – R**espiratory Tract Infection
- **A – A**cute uncomplicated UTI
- **N – N**ocardia

Indications of Fluoroquinolones

Trick - UGC BoWS CoMe Bat TuG Reg

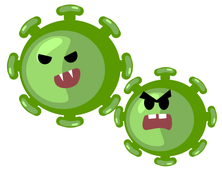
- **U - U**TI
- **G - G**onorrhoea
- **C - C**hancroid
- **B - B**one
- **W - W**ound infections
- **S - S**oft tissue
- **C - C**onjunctivitis
- **M - M**eningitis
- **B - B**acterial gastroenteritis
- **T - T**yphoid
- **T - T**uberculosis
- **G - G**ram-negative septicaemias
- **R - R**espiratory infections
- **G - G**ynaecological infections



Quinolones

Nalidixic acid

- First quinolone; mainly used as a urinary antiseptic
- Active mainly against Gram-negative bacteria
- **Especially coliforms** E. coli, Proteus, Klebsiella, Enterobacter, Shigella
- Not active against Pseudomonas
- Contraindicated in infants



Fluoroquinolones

- Synthetic, fluorinated analogues of nalidixic acid

Mechanism of Action

- Bacterial DNA gyrase (Topoisomerase II) (primarily active in gram negative bacteria) → Nicks dsDNA, introduces negative supercoils and then reseals the nicked ends
- Topoisomerase IV (primarily active in gram-positive bacteria) → Nicks and separates daughter DNA strands after DNA replication

Classification of Fluoroquinolones

(Suffix - floxacin)

2nd Generation
- Ciprofloxacin
- Ofloxacin

(Trick - CiOf)

1st Generation
- Norfloxacin
- Lomefloxacin

(Trick - NorLo)

3rd Generation
- Levofloxacin
- Gatifloxacin
- Pefloxacin
- Sparfloxacin

(Trick - LeG Pe Spa)

4th Generation
- Gemifloxacin
- Trovafloxacin
- Fleroxacin
- Garenoxacin
- Moxifloxacin

(Trick - GeT FleGarM)

Adverse Reactions

- Hypersensitivity Reactions
- Tenosynovitis & tendon rupture
- **Moxifloxacin** Cause QT prolongation
- Contraindicated in Pregnancy

- Ciprofloxacin ↑ses the plasma concentration of Warfarin, Theophylline by inhibiting their metabolism
- NSAIDs potentiates CNS side effects of fluoroquinolones

BETA LACTAM ANTIBIOTICS

Contains ß-lactam ring as a part of their biological interactions

Classification

- Penicillin
- Cephalosporin
- Beta lactamase inhibitors
- Carbapenems

Mechanism of Action

ß-Lactam antibiotic → Binds to Penicillin-Binding Proteins (PBPs) → Inhibits transpeptidase → No peptidoglycan cross-linking → Weak & unstable cell wallng → Cell lysis → Bactericidal effect

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Nenleoside reverse transcriptase inhibitors (NRTIs)

Mechanism of Action

Transported into cells → in presence of host-cell kinase → activated to respective triphosphate forms

Inhibit HIV reverse transcriptase → DNA chain termination

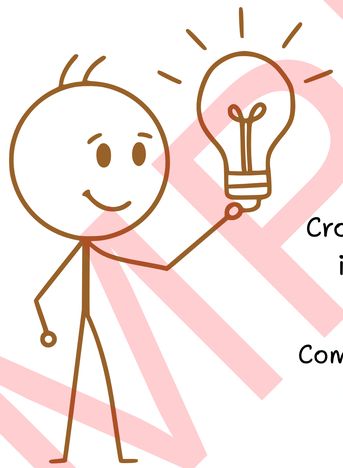
Zidovudine

- Standard choice for post-exposure prophylaxis of HIV, as well as for mother to offspring transmission
- Thymidine analogue
- Effective against HIV-1 and HIV-2
- Causes bone marrow suppression, anaemia, neutropenia
- Protects uninfected cells from HIV but has no effect on already infected cells
- Crosses the placenta and blood–brain barrier and is secreted in breast milk

Nonnucleoside Reverse Transcriptase Inhibitors (NNRTIs)

Mechanism of Action

Bind directly to reverse transcriptase enzyme → inhibit (non-competitively) their function (Donot require intracellular phosphorylation)



Protease inhibitors

- Cross-resistance is common
- Competitively inhibit HIV protease
- Administered orally in combination with reverse transcriptase inhibitors

Causes (Trick - Muscle IDLi)

- **Muscle** wasting
- **I**nsulin resistance
- **D**iabetes mellitus
- **Li**podystrophy





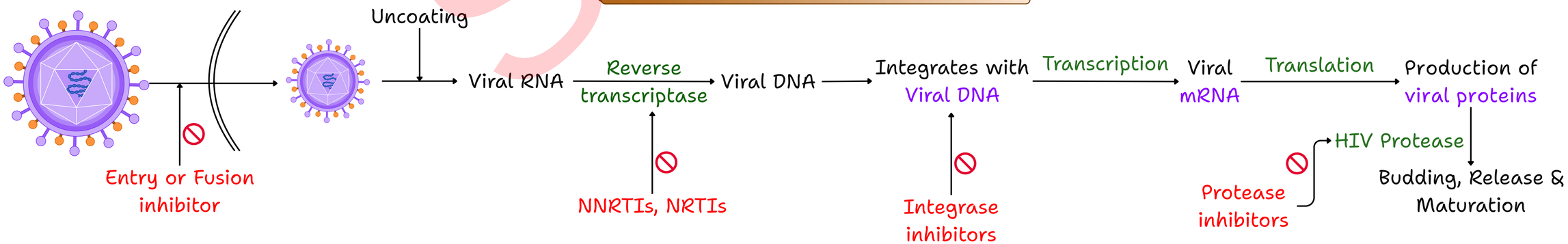
Oseltamivir and Zanamivir

- Effective against both influenza A including H1N1 and influenza B
- Oseltamivir is a prodrug

Mechanism of Action

Inhibit the viral neuraminidase → Inhibit release of daughter virions → Inhibit viral replication

Sites of Actions of Anti-Retroviral Drugs



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ANTICANCER DRUGS

Targeted Drugs

- **Tyrosine Protein-Kinase Inhibitors**
  - Nilotinib
  - Imatinib
  - (Trick – NilIma)
  - (Suffix – tinib)
- **Proteasome Inhibitor**
  - Bortezomib
- **Angiogenesis Inhibitor**
  - Bavacizumab
  - Sunitinib
  - (Trick – BaSu)
- **Unarmed Monoclonal Antibody**
  - Rituximab
  - Trastuzumab
  - (Trick – RiTras)
- **EGF Receptor Inhibitors**
  - Erlotinib
  - Cetuximab
  - Gefitinib
  - (Trick – ECG)

Hormonal Drugs

- **Glucocorticoids**
  - Prednisolone
- **Estrogen**
  - Fosfestrol
  - Ethinylestradiol
  - (Trick – FoE)
- **Progestins**
  - Hydroxyproges terone acetate
- **Antiandrogen**
  - Bicalutamide
  - Flutamide
  - (Trick – Bica Flu)
- **GnRH analogues**
  - Leuprorelin
  - Nafarelin
  - (Trick – LeNa)
  - (Suffix – relin)
- **Aromatase inhibitors**
  - Letrozole
  - Exemestane
  - Anastrozole
  - (Trick – LExA)
- **Selective estrogen receptor down regulators**
  - Fulvestrant
- **5-α reductase Inhibitor**
  - Finasteride
  - Dutasteride
  - (Trick – FinaDu)
  - (Suffix – steride)
- **Selective Estrogen Receptor Modulators**
  - Toremifene
  - Tamoxifen
  - (Trick – ToTa)

Toxicities of Anti-cancer Drugs

- **Anthracycline (Doxorubicin, Daunorubicin)**
  - Cardiotoxicity
- **Busulphan, Bleomycin (G-16)**
  - Pulmonary fibrosis
- **Vincristine, Vinblastine, Vinorelbine**
  - Peripheral neuropathy
- **Cyclophosphamide, Ifosfamide**
  - Haemorrhagic cystitis
  - Alopecia
- **Doxifluridine**
  - Bone marrow depression
  - Hearing loss
  - Neuritis
- **Paclitaxel, Vincristine**
  - Peripheral neuropathy
  - Hypersensitivity
- **Cisplatin (G-16)**
  - Emesis
  - Nephrotoxicity
  - Neuropathy
  - Ototoxicity
- **Methotrexate (G-17)**
  - Megaloblastic anaemia
  - Hepatotoxicity
  - Obstructive nephropathy
- **Docetaxel**
  - Peripheral neuropathy
  - Fluid retention
- **Cytarabine**
  - Cerebral ataxia (neurotoxicity)
- **6-Mercaptopurine, 6-Thioguanine**
  - Hepatotoxicity
- **Irinotecan, Gemcitabine**
  - Diarrhea
- **5-Fluorouracil, Capecitabine, Fludarabine, Cytarabine**
  - Hand and foot syndrome
  - Neurotoxicity

Cyclophosphamide

- Powerful vesicant
- DOC for Wegener's granulomatosis
- Ifosfamide is congener of Cyclophosphamide
  - Used in testicular cancer and sarcomas
- Prodrug
- **Mechanism of Action**
  - Activated by hepatic biotransformation to aldophosphamide
    - Phosphoramide mustard (Cytotoxic Effects)
    - Acrolein (Toxic Effects)
      - Hemorrhagic cystitis
        - Reduced by the use of mercapto ethane sulfonic acid **(Mesna)**
- **Powerful Immunosupressant**
  - Useful in Rheumatoid arthritis, Nephrotic synfrome

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