Pharmacology Drugs for USMLE Step 1

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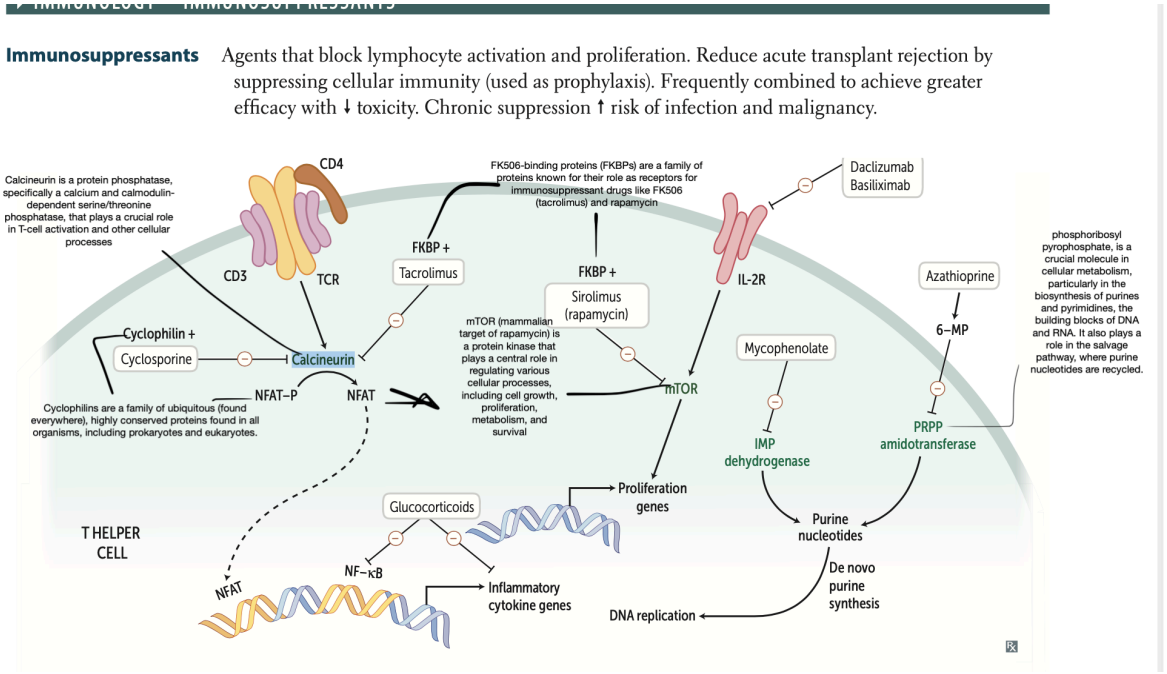
Pharm

- **Immunology**, **Autonomic**, **Antimicrobial = 3**
- **CVS, Endo, GIT**, ***MSK***, Hematology = 4
- CNS, Renal, ***Repro Resp,*** Psych = 5
-

Immunology

NFAT transcription factor, specifically, the p-isoform, Nuclear Factor of Activated T cells) is a family of transcription factors crucial for T cell activation, immune response, and other cellular processes. NFAT proteins regulate gene expression in response to various stimuli, including calcium signaling and other signaling pathways. These factors play a critical role in T cell development, activation, and differentiation, influencing various aspects of the immune system.



- Calcineurin is a calcium and calmodulin-dependent serine/threonine phosphatase enzyme found in many cell types, particularly in immune cells. It plays a crucial role in various cellular processes, especially in the activation of T-cells within the immune system.
- Key functions of calcineurin include:
- Dephosphorylating the nuclear factor of activated T-cells (NFAT), a transcription factor.
- Facilitating NFAT's movement into the nucleus, which promotes the expression of cytokine genes like IL-2, essential for T-cell activation and immune responses.

DRUG	MECHANISM	INDICATIONS
Cyclosporine	Calcineurin inhibitor; binds cyclophilin Blocks T-cell activation by **preventing IL-2 transcription**	Psoriasis, rheumatoid arthritis
Tacrolimus (FK506)	Calcineurin inhibitor; binds FK506 binding protein (FKBP) Blocks T-cell activation by **preventing IL-2 transcription**	Immunosuppression after solid organ transplant
Sirolimus (Rapamycin)	mTOR inhibitor; binds FKBP Blocks T-cell activation and B-cell differentiation by **preventing response to IL-2**	Kidney transplant rejection prophylaxis specifically Sir Basil's kidney transplant
Basiliximab	Monoclonal antibody; blocks IL-2R	

Cyclophilins are a family of ubiquitous(found everywhere) , highly conserved proteins found in all organisms, including prokaryotes and eukaryotes.
Cyclophilins are a family of ubiquitous (found everywhere), highly conserved proteins found in all organisms, including prokaryotes and eukaryotes.
They are present in many different organisms (from bacteria to humans).
Their core structure and function have changed very little
Cyclo = cyclosporin A
Philin = loving

FK506-binding proteins (FKBPs) are a family of proteins known for their role as receptors for immunosuppressant drugs like FK506 (tacrolimus) and rapamycin

mTOR (mammalian target of rapamycin) is a protein kinase that plays a central role in regulating various cellular processes, including cell growth, proliferation, metabolism, and survival

DRUG	MECHANISM	INDICATIONS
Azathioprine	Antimetabolite precursor of 6-mercaptopurine Inhibits lymphocyte proliferation by blocking nucleotide synthesis	Rheumatoid arthritis, Crohn disease, glomerulonephritis, other autoimmune conditions
Mycophenolate Mofetil	Reversibly inhibits IMP dehydrogenase, preventing purine synthesis of B and T cells	Glucocorticoid-sparing agent in rheumatic disease
Glucocorticoids	Inhibit NF-κB Suppress both B- and T-cell function by ↓ transcription of many cytokines Induce T cell apoptosis	Many autoimmune and inflammatory disorders, adrenal insufficiency, asthma, CLL, non-Hodgkin lymphoma

Cushing
Amenorrhea
Adrenaocortical Atrophy
Diabetes

Psychsois
Osteoperosis
PUD
AVN

Show Ami and BAba 4 things (1) PERSONAL state ent (2) Research (3) GOld vs Diamond (4)

IκB is an inhibitor of NF-κB, holding it inactive in the cytoplasm until it is activated. Yes, glucocorticoids are known to increase the levels of IκB, which contributes to their anti-inflammatory effects.

FK 506 binding protein

1.

- **F** = **Fujisawa**
- **K** = **Kanagawa** (the Japanese prefecture where the research facility was located)

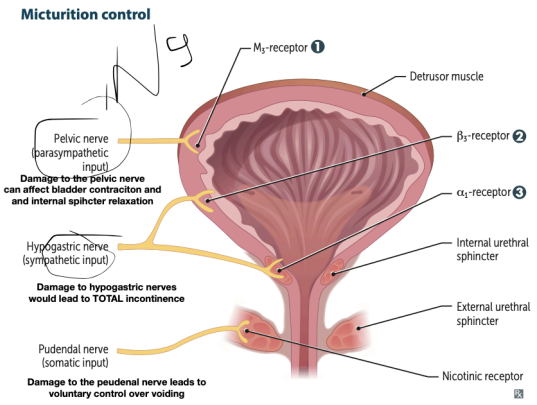
So, **FK506** is the discovery code:

- **"FK"** for the company and location
- **"506"** is just the compound number in their research series

Autonomic

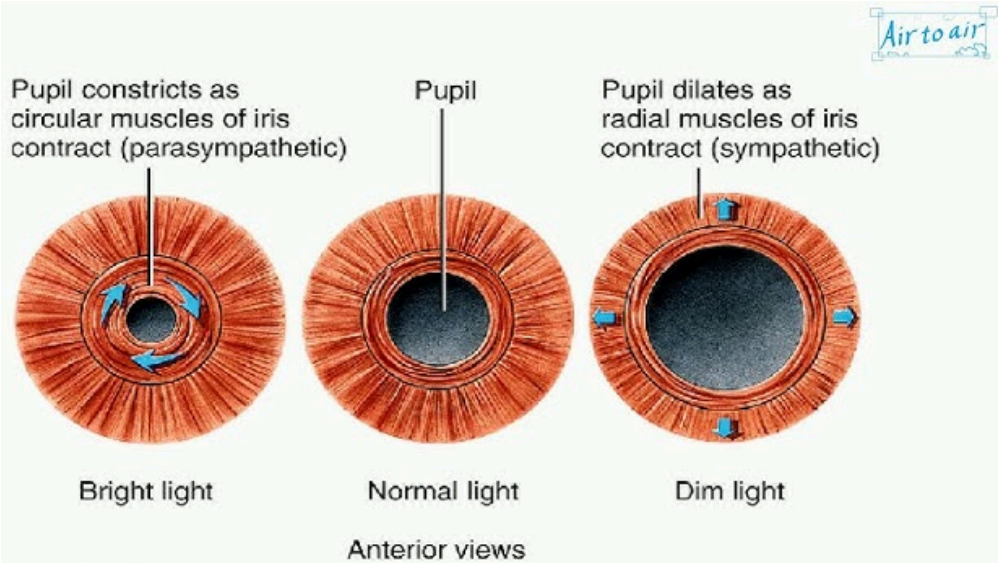
HY USMLE Q #679 – Pharm / Physio
What is the effect of Propranolol on SVR ?
{{c1::
Increase SVR}}

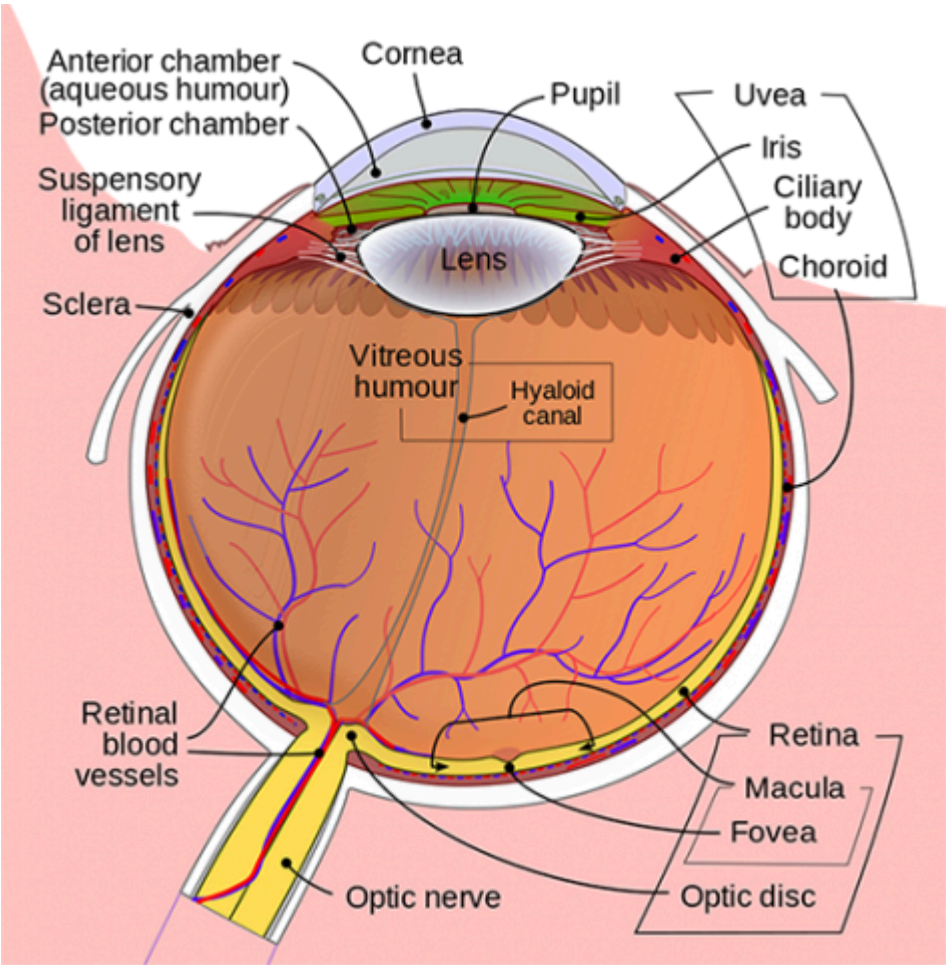
Propranolol --> blocks b1 and b2
What is the effect of labetalol on SVR ?
{{c2::decrease SVR}}
labetalol --> blocks b1 and b2 and blocks alpha 1



Micturition center in pons regulates involuntary bladder function via coordination of sympathetic and parasympathetic nervous systems.
⊕ sympathetic → ↑ urinary retention.
⊕ parasympathetic → ↑ urine voiding.
Some autonomic drugs act on smooth muscle receptors to treat bladder dysfunction.

DRUGS	MECHANISM	APPLICATIONS
❶ **Muscarinic antagonists** (eg, oxybutynin)	⊖ M_3 receptor → relaxation of detrusor smooth muscle → ↓ detrusor overactivity	Urgency incontinence
❶ **Muscarinic agonists** (eg, bethanechol)	⊕ M_3 receptor → contraction of detrusor smooth muscle → ↑ bladder emptying	Urinary retention
❷ **Sympathomimetics** (eg, mirabegron)	⊕ β_3 receptor → relaxation of detrusor smooth muscle → ↑ bladder capacity	Urgency incontinence
❸ **α_1-blockers** (eg, tamsulosin)	⊖ α_1-receptor → relaxation of smooth muscle (bladder neck, prostate) → ↓ urinary obstruction	BPH


Air to air
Pupil constricts as circular muscles of iris contract (parasympathetic)
Pupil
Pupil dilates as radial muscles of iris contract (sympathetic)
Bright light
Normal light
Dim light
Anterior views


Anterior chamber (aqueous humour)
Posterior chamber
Cornea
Pupil
Uvea
Iris
Ciliary body
Choroid
Suspensory ligament of lens
Lens
Sclera
Vitreous humour
Hyaloid canal
Retinal blood vessels
Retina
Macula
Fovea
Optic nerve
Optic disc

COPD = Activation of M3 muscarinic receptors causes bronchoconstriction
Ulcer = Cholinomimetics stimulate gastric acid secretion via M3 receptors in the stomach lining.

CAP
= COPD, asthma, Peptic Ulcer

Cholinomimetic agents

Watch for exacerbation of COPD, asthma, and peptic ulcers in susceptible patients.

DRUG	ACTION	APPLICATIONS
Direct agonists		
Bethanechol	Activates bladder smooth muscle; resistant to AChE. Acts on muscarinic receptors; no nicotinic activity. "Bethany, call me to activate your bladder."	Urinary retention.
Carbachol	Carbon copy of acetylcholine (but resistant to AChE).	Constricts pupil and relieves intraocular pressure in open-angle glaucoma.
Methacholine	Stimulates muscarinic receptors in airway when inhaled.	Challenge test for diagnosis of asthma.
Pilocarpine	Contracts ciliary muscle of eye (open-angle glaucoma), pupillary sphincter (closed-angle glaucoma); resistant to AChE, can cross blood-brain barrier. "You cry, drool, and sweat on your 'pilow.'"	Potent stimulator of sweat, tears, and saliva. Open-angle and closed-angle glaucoma; xerostomia (Sjögren syndrome).
Indirect agonists (anticholinesterases)		
Donepezil, rivastigmine, galantamine	↑ ACh.	1st line for Alzheimer disease (Don Riva forgot the gala).
Edrophonium	↑ ACh.	Historically used to diagnose myasthenia gravis; replaced by anti-AChR Ab (anti-acetylcholine receptor antibody) test.
Neostigmine	↑ ACh. Neo CNS = no CNS penetration due to positive charge.	Postoperative and neurogenic ileus and urinary retention, myasthenia gravis, reversal of neuromuscular junction blockade (postoperative).
Pyridostigmine	↑ ACh; ↑ muscle strength. Does not penetrate CNS. Pyridostigmine gets rid of myasthenia gravis.	Myasthenia gravis (long acting). Used with glycopyrrolate, hyoscyamine, or propantheline to control pyridostigmine adverse effects.
Physostigmine	↑ ACh. Phreely (freely) crosses blood-brain barrier as not charged → CNS.	Antidote for anticholinergic toxicity; physostigmine "phyxes" atropine overdose.
Anticholinesterase poisoning	Often due to organophosphates (eg, parathion) that irreversibly inhibit AChE. Organophosphates commonly used as insecticides; poisoning usually seen in farmers.	
Muscarinic effects	Diarrhea, Urination, Miosis, Bronchospasm, Bradycardia, Emesis, Lacrimation, Sweating, Salivation.	DUMBBELSS. Reversed by atropine, a competitive inhibitor. Atropine can cross BBB to relieve CNS symptoms.
Nicotinic effects	Neuromuscular blockade (mechanism similar to succinylcholine).	Reversed by pralidoxime, regenerates AChE via dephosphorylation if given early. Pralidoxime does not readily cross BBB.
CNS effects	Respiratory depression, lethargy, seizures, coma.	

Carbachol
Constricts the pupil

Ciliary Muscle --> Surrounds the lens in the ciliary body. Alters the shape of the lens for accommodation (near/far vision)

Pupillary Sphincter Muscle--> Located in the iris, encircling the pupil. Constricts the pupil to reduce light entry (miosis)

You're mostly correct! Mydriasis (especially mid-dilation) often precipitates the attack.
But during an actual acute angle-closure attack, using miotics like carbachol or pilocarpine is a double-edged sword:
May cause excessive pupillary constriction (miosis), which can make the iris bunch up even more in the narrow angle, worsening iris bombe and anterior chamber crowding.

Donepezil and Edrophonium is used for the diagnosis of the Myasthenia Gravis

Myasthetic Gravis
Urinary retention
Ileus
MUI=

Piers is old hence long acting

Glycopyrronium bromide is a medication of the muscarinic anticholinergic group. It does not cross the blood–brain barrier and consequently has few to no central effects.

medication works by decreasing acid production in the stomach, slowing down the natural movements of the gut, and relaxing muscles in many organs

Propantheline bromide is an antimuscarinic agent used for the treatment of excessive sweating, cramps or spasms of the stomach, intestines or bladder, and involuntary urination.

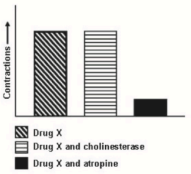
Neurogenic ileus = Neurogenic bowel is the loss of normal bowel function due to a nerve problem. It causes constipation and stool leakage or incontinence. Nerve damage may be due to a brain or spinal injury or a health condition, such as multiple sclerosis.
Nicotinic = nicotinic receptors are present at the neuromuscular junction

ACh binds to nicotinic acetylcholine receptors (nAChRs) on the motor end plate of the muscle cell.when ACh binds, the channel opens, allowing Na^+ in and K^+ out, leading to muscle depolarization and contraction.

Pralidoxime = reactivating acetylcholinesterase, an enzyme that is inhibited by organophosphates

22. The effects of drug X alone, drug X and cholinesterase, and drug X and atropine on an isolated gastrointestinal muscle are shown in the bar chart. Drug X is most likely which of the following?

A) Acetylcholine
B) Bethanechol
C) Nicotine
D) Succinylcholine
E) Trimethaphan



They are called nicotinic receptors because they are activated by nicotine.

Nicotinic ACh receptors = respond to nicotine (and ACh)

Muscarinic ACh receptors = respond to muscarine (and ACh)

Direct sympathomimetics

Albuterol, salmeterol, terbutaline	$\beta_2 > \beta_1$	↑ HR (little effect)	Albuterol for acute asthma/COPD. Salmeterol for serial (long-term) asthma/COPD. Terbutaline for acute bronchospasm in asthma and tocolysis.
Dobutamine	$\beta_1 > \beta_2, \alpha$	–/↓ BP, ↑ HR, ↑ CO	Cardiac stress testing, acute decompensated heart failure (HF) with cardiogenic shock (inotrope)
Dopamine	$D_1 = D_2 > \beta > \alpha$	↑ BP (high dose), ↑ HR, ↑ CO	Unstable bradycardia, shock; inotropic and chronotropic effects at lower doses via β effects; vasoconstriction at high doses via α effects.
Epinephrine	$\beta > \alpha$	↑ BP (high dose), ↑ HR, ↑ CO	Anaphylaxis, asthma, shock, open-angle glaucoma; α effects predominate at high doses. Stronger effect at β_2-receptor than norepinephrine.
Fenoldopam	D_1	↓ BP (vasodilation), ↑ HR, ↑ CO	Postoperative hypertension, hypertensive crisis. Vasodilator (coronary, peripheral, renal, and splanchnic). Promotes natriuresis. Can cause hypotension, tachycardia, flushing, headache.
Isoproterenol	$\beta_1 = \beta_2$	↓ BP (vasodilation), ↑ HR, ↑ CO	Electrophysiologic evaluation of tachyarrhythmias. Can worsen ischemia. Has negligible α effect.
Midodrine	α_1	↑ BP (vasoconstriction), ↓ HR, –/↓ CO	Autonomic insufficiency and postural hypotension. May exacerbate supine hypertension.
Mirabegron	β_3		Urinary urgency or incontinence or overactive bladder. Think "mirab3gron."
Norepinephrine	$\alpha_1 > \alpha_2 > \beta_1$	↑ BP, –/↓ HR (may have minor reflexive change in response to ↑ BP due to α_1 agonism outweighing direct β_1 chronotropic effect), –/↑ CO	Hypotension, septic shock.
Phenylephrine	$\alpha_1 > \alpha_2$	↑ BP (vasoconstriction), ↓ HR, –/↓ CO	Hypotension (vasoconstrictor), ocular procedures (mydriatic), rhinitis (decongestant), ischemic priapism.

D1 Increase renin and increase BP

Beta is more cuz more B1 receptor on the heart

Anaphylaxis
Ashtma
Angle glaucma

THHF
Tachycardia
Hypotension
Headache
Flushing

HR: Epinephrine acts on beta-1 adrenergic receptors in the heart, leading to an increase in HR (positive chronotropic effect). An increased HR leads to a greater volume of blood being pumped by the heart per minute.
Myocardial Contractility: Epinephrine also enhances the force of cardiac muscle contractions (positive inotropic effect). This means that each heartbeat is more powerful, contributing to a higher stroke volume.

D1 on the smooth muscle acts like B2

Epinephrine is a non-selective adrenergic agonist that stimulates alpha-adrenergic receptors in the eye. Activation of these receptors on the ciliary body reduces the production of aqueous humor, the fluid responsible for maintaining intraocular pressure.

Isoproterenol enhances sympathetic activity, leading to an increase in heart rate by stimulating β1 receptors in the sinoatrial (SA) node. This helps in assessing the responsiveness of the conduction system and the autonomic regulation of the heart.

HORI
Hypotension
Ocular procedure s
Rhinitis
Ischemia praipsim

Indirect sympathomimetics

Amphetamine	Indirect general agonist, reuptake inhibitor, also releases stored catecholamines.	Narcolepsy, obesity, ADHD.
Cocaine	Indirect general agonist, reuptake inhibitor. Causes vasoconstriction and local anesthesia. Caution when giving β-blockers if cocaine intoxication is suspected (unopposed α_1 activation → ↑↑↑ BP, coronary vasospasm).	Causes mydriasis in eyes with intact sympathetic innervation → used to confirm Horner syndrome.
Ephedrine	Indirect general agonist, releases stored catecholamines.	Nasal decongestion (pseudoephedrine), urinary incontinence, hypotension.

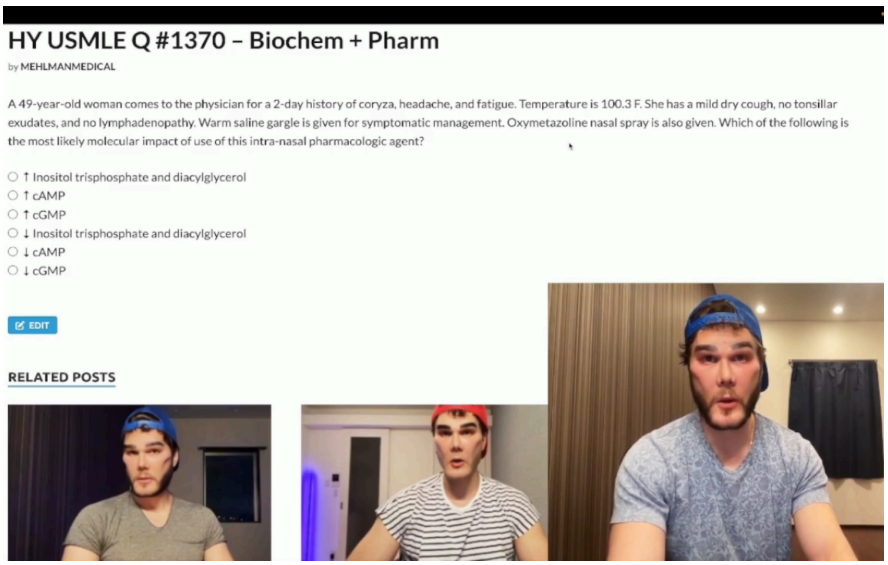
AON
ADHD
obesity
Narcolepsy

In Horner's syndrome, there's an interruption in the sympathetic pathway to the eye, leading to a lack of this vasoconstriction. Therefore, if cocaine is applied topically to the eye and there's no pupillary or conjunctival vasoconstriction, it strongly suggests the presence of Horner's syndrome. The lack of response to cocaine confirms the sympathetic denervation.

Decongestion
Urinary incontince
Hypotension

HUD

Stimulates the internal urethral sphincter (a smooth muscle at the bladder neck).
helps prevent leakage during increases in intra-abdominal pressure (e.g., coughing, sneezing, lifting).
NOT Used in urge incotinence doesn;t address involuntary bladder contraction
Overflow incontinence May worsen retention by tightening outlet



What is the other name of rebound congestion ?

The other name for **rebound congestion** is:

👉 **Rhinitis medicamentosa**

💡 **Key points:**

- It happens after prolonged use of topical nasal decongestants (like oxymetazoline or phenylephrine).

Correct A

Excess cholinergic stimulation leads to muscle spasms and abnormal movements, manifesting as acute dystonia (sudden sustained muscle contractions).

Muscarinic antagonists

DRUGS	ORGAN SYSTEMS	APPLICATIONS
Atropine, homatropine, tropicamide	Eye	Produce mydriasis and cycloplegia
Benztropine, trihexyphenidyl	CNS	Parkinson disease ("park my Benz") Acute dystonia
Glycopyrrolate	GI, respiratory	Parenteral: preoperative use to reduce airway secretions Oral: reduces drooling, peptic ulcer
Hyoscyamine, dicyclomine	GI	Antispasmodics for irritable bowel syndrome
Ipratropium, tiotropium	Respiratory	COPD, asthma Duration: tiotropium > ipratropium
Solifenacin, Oxybutynin, Flavoxate, Tolterodine	Genitourinary	Reduce bladder spasms and urge urinary incontinence (overactive bladder) Make bladder SOFT
Scopolamine	CNS	Motion sickness

HAT
Homatropine
Atropine
Tropicamide

mydriasis, or pupil dilation; whereas cycloplegics cause cycloplegia, or paralysis of the muscles that are responsible for accommodation to focus on nearby objects.

Dystonia is a movement disorder that causes the muscles to contract involuntarily. This can cause repetitive or twisting movements.

PUD —> decreases acid

SOLIFENACIN

Activation of cholinergic pathways in the brainstem and vestibular nuclei contributes to nausea and vomiting.

Atropine — Muscarinic antagonist. Used to treat bradycardia and for ophthalmic applications.

TIZANDINE !! MOA is ALpha 2 agonist

Sympatholytics (α_2-agonists)

Hypertension
ADHD
Tourette syndrome
HAT

MR BDDH
Miosis
Rebound Hypertension
Bradycardia
Depression CNS
Depression Resp
Hypotension

DRUG	APPLICATIONS	ADVERSE EFFECTS
Clonidine, guanfacine	Hypertensive urgency (limited situations), ADHD, Tourette syndrome, symptom control in opioid withdrawal	CNS depression, bradycardia, hypotension, respiratory depression, miosis, rebound hypertension with abrupt cessation
α-methyldopa	Hypertension in pregnancy	Direct Coombs ⊕ hemolysis, drug-induced lupus, hyperprolactinemia
Tizanidine	Relief of spasticity	Hypotension, weakness, xerostomia

Hemolysis
Hyperprolactinemia
Drug-Induced Lupus
Direct Coombs
HHDD

α-blockers

DRUG	APPLICATIONS	ADVERSE EFFECTS
Nonselective		HOT
Phenoxybenzamine	Irreversible. Pheochromocytoma (used preoperatively) to prevent catecholamine (hypertensive) crisis.	Hypotension Orthostatic Tachycardia (reflex)
Phentolamine	Reversible. Given to patients on MAO inhibitors who eat tyramine-containing foods and for severe cocaine-induced hypertension (2nd line). Also used to treat norepinephrine extravasation.	Orthostatic hypotension, reflex tachycardia.
α_1 selective (-osin ending)		
Prazosin, terazosin, doxazosin, tamsulosin	Urinary symptoms of BPH; PTSD (prazosin); hypertension (except tamsulosin).	1st-dose orthostatic hypotension, dizziness, headache.
α_2 selective		HOD
Mirtazapine	Depression.	Sedation, ↑ serum cholesterol, ↑ appetite.

Hypertension
Tyramine - Containing Food

PTTD
Prazosin
Tamsulosin
Terazosin
Doxazosin

Hedache
Orthostatic Hypotension
Dizziness

Relaxation the smooth muscle of the prostate

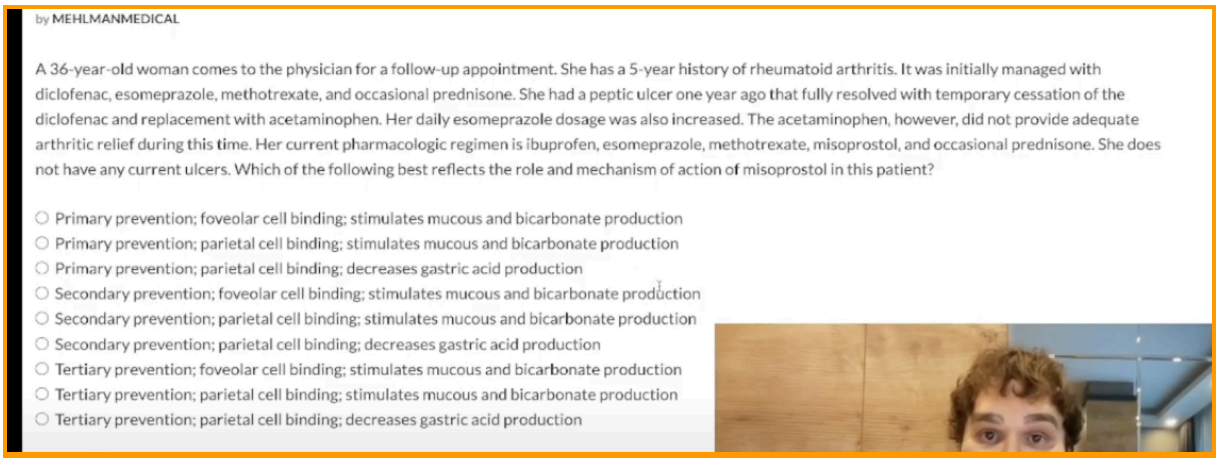
SSAD
Seduation
Serum Cholesterol
Appeitie
D

Blocking alpha-2 receptors prevents them from inhibiting norepinephrine release. As a result, there is an increase in synaptic norepinephrine levels in the brain.

Educational objective:

Health care value is increased by interventions that maximize quality (eg, reduced patient morbidity, mortality, adverse events) while minimizing total costs of care. The first step in determining the potential value of an intervention (eg, new device) involves conducting a needs assessment, which quantifies the baseline scope of the problem and its associated costs.
Primary = risk factor
Secondary = Risk factor or Disease, Early diagnosis or early management or management of recurrence "After an ulcer occurred, but healed"
Tietary

Active ulcer + managing complications



"fovea," meaning "pit" or "ditch**Foveolar cells**

- Also called **surface mucous cells**

Activation of α2 receptors on presynaptic nerve terminals reduces the release of norepinephrine (noradrenaline), serving as a negative feedback mechanism.

Phentoalmin vs Phenoxybenzamine

- **Phenoxybenzamine forms covalent bonds with receptors → irreversible blockade.**
- **Phentolamine binds non-covalently → reversible blockade.**

APPLICATION	ACTIONS	NOTES/EXAMPLES
Angina pectoris	↓ heart rate and contractility → ↓ O_2 consumption	
Glaucoma	↓ production of aqueous humor	Timolol
Heart failure	Blockade of neurohormonal stress → prevention of deleterious cardiac remodeling → ↓ mortality	Bisoprolol, carvedilol, metoprolol (β-blockers curb mortality)
Hypertension	↓ cardiac output, ↓ renin secretion (due to β_1-receptor blockade on JG cells)	
Hyperthyroidism/ thyroid storm	Symptom control (↓ heart rate, ↓ tremor)	Propranolol
Hypertrophic cardiomyopathy	↓ heart rate → ↑ filling time, relieving obstruction	
Myocardial infarction	↓ O_2 demand (short-term), ↓ mortality (long-term)	
Supraventricular tachycardia	↓ AV conduction velocity (class II antiarrhythmic)	Metoprolol, esmolol
Variceal bleeding	↓ hepatic venous pressure gradient and portal hypertension (prophylactic use)	Nadolol, propranolol, carvedilol
ADVERSE EFFECTS	~~Erectile dy~~sfunction, ~~cardiovascu~~lar (bradycardia, AV block, HF), ~~CN~~S (seizures, sleep alterations), dyslipidemia (metoprolol), masked hy~~poglycemia~~, asthma/COPD exacerbations	Use of β-blockers for acute cocaine-associated chest pain remains controversial due to unsubstantiated concern for unopposed α-adrenergic stimulation
SELECTIVITY	β_1-selective antagonists ($\beta_1 > \beta_2$)—acebutolol (partial agonist), atenolol, betaxolol, bisoprolol, esmolol, metoprolol	Selective antagonists mostly go from A to M (β_1 with 1st half of alphabet)
	Nonselective antagonists ($\beta_1 = \beta_2$)—nadolol, pindolol (partial agonist), propranolol, timolol	NonZelective antagonists mostly go from N to Z (β_2 with 2nd half of alphabet)
	~~Nonselective α- and β-antagonists—carvedi~~lol, labetalol	Nonselective α- and β-antagonists have modified suffixes (instead of "-olol")
	Nebivolol combines cardiac-selective β_1-adrenergic blockade with stimulation of β_3-receptors (activate NO synthase in the vasculature and ↓ SVR)	NebivOlol increases NO

HF
HYpertension
Hyperthyroidsm
HCM

causing harm or damage.

CNS
Carido
Erectile dysfucntion
Dyslipidemia
Hypoglycemia
Ashtma

Carvedilol and Labetalol Alpha-1, Beta-1, and Beta-2 Receptor Antagonist

Beta blockers are CI in WPW
Beta blockers slow conduction through the AV node but do not affect the accessory pathway.

Slight increases in triglycerides
Possible decreases in HDL cholesterol (the "good" cholesterol)

PHARMACOLOGY—TOXICITIES AND ADVERSE EFFECTS

Ingested seafood toxins Toxin actions include histamine release, total block of Na^+ channels, or opening of Na^+ channels to cause depolarization.

Mahi mahi is a rich source of protein as well as vitamins B3, B6, and B12.

TOXIN	SOURCE	ACTION	SYMPTOMS	TREATMENT
Histamine (scombroid poisoning)	Spoiled dark-meat fish such as tuna, mahi-mahi, mackerel, and bonito	Bacterial histidine decarboxylase converts histidine to histamine Frequently misdiagnosed as fish allergy	Mimics anaphylaxis: oral burning sensation, facial flushing, erythema, urticaria, itching; may progress to bronchospasm, angioedema, hypotension	Antihistamines Albuterol +/– epinephrine

MMB
mahi mahi
bonito

Burning sensation
Erythema
Flushing
Urtica
Iteching

Angiodeema
Hypotension

Phosphodiesterase inhibitors

Phosphodiesterase (PDE) inhibitors inhibit PDE, which catalyzes the hydrolysis of cAMP and/or cGMP, and thereby increase cAMP and/or cGMP. These inhibitors have varying specificity for PDE isoforms and thus have different clinical uses.

TYPE OF INHIBITOR	MECHANISM OF ACTION	CLINICAL USES	ADVERSE EFFECTS
Nonspecific PDE inhibitor Theophylline	↓ cAMP hydrolysis → ↑ cAMP → bronchial smooth muscle relaxation → bronchodilation	COPD/asthma (rarely used) **CAN** **Cardiotoxicity** **Abdominal Pain** **Neurotoxicity**	Cardiotoxicity (eg, tachycardia, arrhythmia), neurotoxicity (eg, seizures, headache), abdominal pain
PDE-5 inhibitors Sildenafil, vardenafil, tadalafil, avanafil	↓ hydrolysis of cGMP → ↑ cGMP → ↑ smooth muscle relaxation by enhancing NO activity → pulmonary vasodilation and ↑ blood flow in corpus cavernosum fills the penis **BPE** **Benign PH** **Pulm HyperT** **Erectile dysfunction**	Erectile dysfunction Pulmonary hypertension Benign prostatic hyperplasia (tadalafil only) **DIL** **Depreesion** **Insomnia** **Loss of weight**	Facial flushing, headache, dyspepsia, hypotension in patients taking nitrates; "hot and sweaty," then headache, heartburn, hypotension Sildenafil only: cyanopia (blue-tinted vision) via inhibition of PDE-6 (six) in retina
PDE-4 inhibitor Roflumilast **GBN** **Granulo** **Bronchial** **Neutrophi**	↑ cAMP in neutrophils, granulocytes, and bronchial epithelium	Severe COPD **Abdominal pain** **anxiety**	Abdominal pain, weight loss, depression, anxiety, insomnia
PDE-3 inhibitor Milrinone	In cardiomyocytes: ↑ cAMP → ↑ Ca^{2+} influx → ↑ ionotropy and chronotropy In vascular smooth muscle: ↑ cAMP → MLCK inhibition → vasodilation → ↓ preload and afterload	Acute decompensated HF with cardiogenic shock (inotrope)	Tachycardia, ventricular arrhythmias, hypotension **HAT** **Hypptension** **Arrthymia** **Tachycarida**
"Platelet inhibitors" Cilostazol[a] Dipyridamole[b] **SIC** **Stroke or TIA prevention with aspirin** **Intermittent claudicaiton** **Cardiac Stress test**	In platelets: ↑ cAMP → inhibition of platelet aggregation	Intermittent claudication Stroke or TIA prevention (with aspirin) Cardiac stress testing (dipyridamole only, due to coronary vasodilation) Prevention of coronary stent restenosis	Nausea, headache, facial flushing, hypotension, abdominal pain **FFANH** **Facial Flushing** **Abdominal PAin** **Nauea** **Headache**

[a]Cilostazol is a PDE-3 inhibitor, but due to its indications is categorized as a platelet inhibitor together with dipyridamole.
[b]Dipyridamole is a nonspecific PDE inhibitor, leading to inhibition of platelet aggregation. It also prevents adenosine reuptake by platelets → ↑ extracellular adenosine → ↑ vasodilation.

HY USMLE Q#798 Pharm

What drug has vasodilatory and antiplatelets effects ?

- {{c4::cilostazol}}
- Yours Aspirin

Increased cAMP activates protein kinase A (PKA) PKA phosphorylates and inhibits platelet activation pathways, particularly those involved in:
Shape change
Granule release
Glycoprotein IIb/IIIa activation (needed for fibrinogen binding and aggregation)

TOXIN	TREATMENT
Acetaminophen	N-acetylcysteine (replenishes glutathione)
AChE inhibitors, organophosphates	Atropine > pralidoxime
Antimuscarinic, anticholinergic agents	Physostigmine (crosses BBB), control hyperthermia
Arsenic	Dimercaprol, succimer
Benzodiazepines	Flumazenil
β-blockers	Atropine, glucagon, saline
Carbon monoxide	100% O_2, hyperbaric O_2
Copper	"Penny"cillamine (penicillamine), trientine (3 copper pennies)
Cyanide	Hydroxocobalamin, nitrites + sodium thiosulfate
Dabigatran	Idarucizumab
Digoxin	Digoxin-specific antibody fragments
Direct factor Xa inhibitors (eg, apixaban)	Andexanet alfa
Heparin	Protamine sulfate
Iron (Fe)	Deferoxamine, deferasirox, deferiprone
Lead	Calcium disodium EDTA, dimercaprol, succimer, penicillamine
Mercury	Dimercaprol, succimer
Methanol, ethylene glycol (antifreeze)	Fomepizole > ethanol, dialysis
Methemoglobin	Methylene blue, vitamin C (reducing agent)
Methotrexate	Leucovorin
Opioids	Naloxone
Salicylates	$NaHCO_3$ (alkalinize urine), dialysis
TCAs	$NaHCO_3$ (stabilizes cardiac cell membrane)
Warfarin	Vitamin K (delayed effect), PCC (prothrombin complex concentrate)/FFP (immediate effect)

Contains two sulfhydryl (-SH) groups. Binds directly to heavy metals such as arsenic, mercury, and lead by forming stable chelate complexes.

Also contains two sulfhydryl groups. Binds to heavy metals such as lead, arsenic, and mercury, forming water-soluble chelate complexes.

antibody fragments bind to digoxin molecules in the blood.

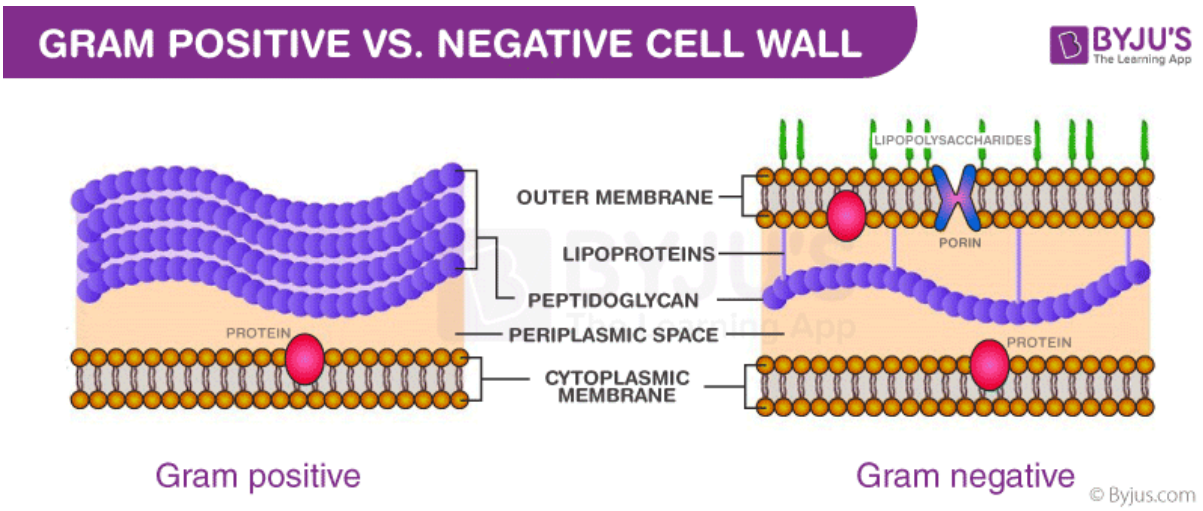
CDES P
Calcium Dimercaprol EDTA Succimer Peniclilamine

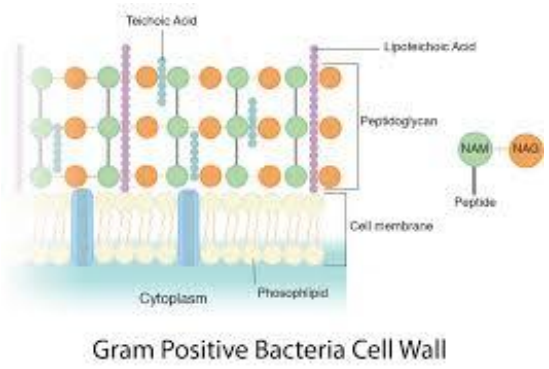
They are purified fragments obtained by enzymatic digestion of anti-digoxin antibodies (usually from animal sources like sheep or horses). These fragments contain the antigen-binding sites (Fab regions) that are specific for digoxin.

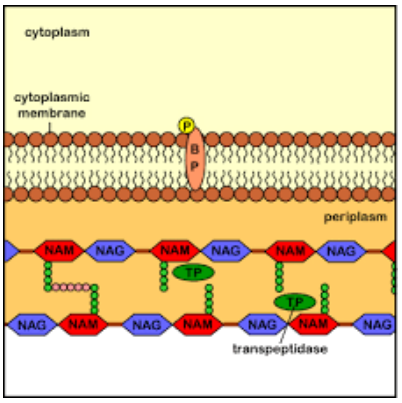
Antimicrobial

MOA Of ribavirin ?
Inhibits RNA synthesis

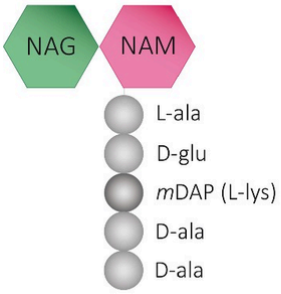
Bactericidal drugs





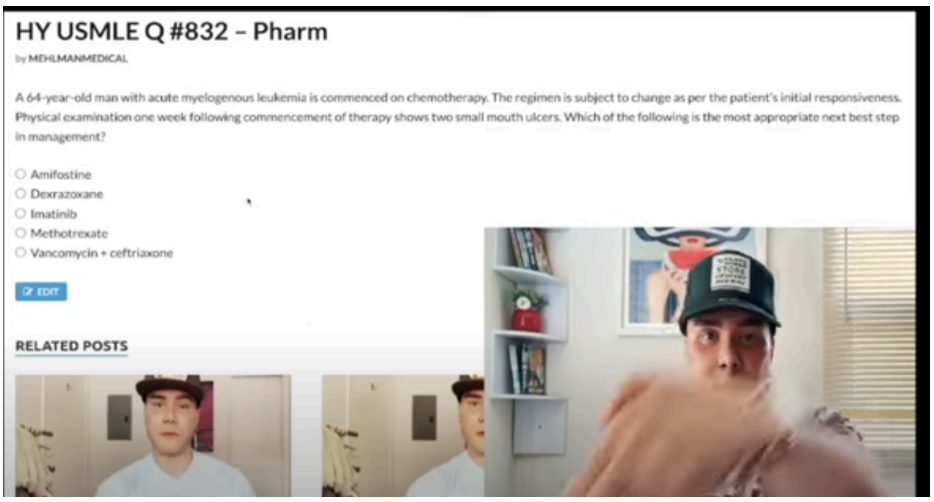


A



Drugs	MOA
Penicillin G, V → *S pneumoniae GAS, GBS, Pastrella, Acetinomyces Isreali, Niesseria Menigitis* Penicillinase-sensitive penicillin (amoxicillin ampicillin) → HHEELPSS Penicillinase-resistant penicillins	D-Ala-D-Ala structural analog. *(D-Ala-D-Ala is a dipeptide found at the end of the peptidoglycan precursors used by bacteria to build their cell wall.* *Penicillin mimics the shape of the D-Ala-D-Ala portion of the peptidoglycan.* *This allows penicillin to bind to the active site of bacterial transpeptidase enzymes (also called penicillin-binding proteins).*) Bind penicillin-binding proteins (transpeptidases). Block transpeptidase cross-linking of peptidoglycan in cell wall. Activate autolytic enzymes. *Bacteria naturally produce autolysins, enzymes that break down parts of their own cell wall. These help in remodeling or dividing the cell.* *When penicillin blocks cell wall synthesis, the balance between building and breaking down the cell wall is disrupted.* *Autolytic enzymes are still active (or become unregulated), but now the bacteria can't repair the damage because cross-linking is blocked.* *As a result, these enzymes cause the bacterial cell wall to degrade, leading to cell lysis (bursting).*

(Dicloxacillin, nafcillin, oxacillin) → Staph Aureus → bulky R group blocks access of β-lactamase to β-lactam ring. Piperacillin → gram neg rode and Pseudo monas Cephalosporins Carbapenems Gram ⊕ cocci, gram ⊖ rods, and anaerobes. Wide spectrum and significant adverse effects limit use to life-threatening infections or after other drugs have failed β-lactamase inhibitors	Organisms typically not covered by 1st–4th generation cephalosporins are LAME: Listeria, Atypicals (Chlamydia, Mycoplasma), MRSA, and Enterococci. β-lactam drugs that inhibit cell wall synthesis but are less susceptible to penicillinases. Yes, penicillinases are a type of β-lactamase. But not all β-lactamases are penicillinases. Bactericidal → The drug kills bacteria directly, rather than just stopping them from growing. Bactericidal by blocking cell wall synthesis --> Without proper cross-linking, the cell wall becomes weak and unstable. --> The pressure inside the bacteria causes it to rupture and die 1st gen → CeFAZolin, Cephalexin, gram ⊕ cocci, Proteus mirabilis, E coli, Klebsiella pneumoniae. Cefazolin used prior to surgery to prevent S aureus wound infections. 2nd gen → ceFAClor gram ⊕ cocci, H influenzae, Enterobacter aerogenes, Neisseria spp., Serratia marcescens, Proteus mirabilis, E coli, Klebsiella pneumoniae. HENS PEK 3rd gen Ceftriaxone—meningitis, gonorrhea, disseminated Lyme disease. Ceftazidime—Pseudomonas. 4th generation (cefepime)—gram ⊖ organisms, with increase activity against Pseudomonas and gram ⊕ organisms. 5th generation (ceftaroline)—broad gram ⊕ and gram ⊖ organism coverage; unlike 1st–4th generation cephalosporins, ceftaroline covers MRSA, and Enterococcus faecalis—does not cover Pseudomonas. Amoxicillin- Clavunate, Ampicillin - Subbactam, PT, ceftazidime-avibactam
Aztreonam	Less susceptible to β-lactamases. Prevents peptidoglycan cross-linking by binding to penicillin- binding protein 3. Synergistic with aminoglycosides (*Aztreonam enhances the entry and efficacy of aminoglycosides by disrupting the bacterial cell wall, leading to a synergistic bactericidal effect.)* No cross-allergenicity with penicillins.
Vancomycin	Inhibits cell wall peptidoglycan formation by binding D-Ala-D-Ala portion of cell wall precursors. Bactericidal against most bacteria (bacteriostatic against C difficile) *(The concentration of Vancomycin achieved in the colon may not always be high enough to exert a rapid bactericidal effect)*



Protein synthesis inhibitors

A-site (Aminoacyl site): Acceptor site

This is where incoming aminoacyl-tRNA molecules bind, bringing the next amino acid to be added to the growing polypeptide chain.

P-site (Peptidyl site):

This site binds the peptidyl-tRNA, which is the tRNA carrying the growing polypeptide chain.

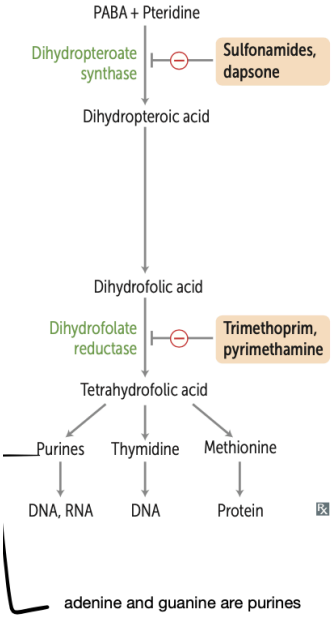
E-site (Exit site):

This is the site where the empty, deacylated tRNA leaves the ribosome after releasing its amino acid.

Aminoglycosides Gentamicin, Neomycin, Amikacin, Tobramycin, Streptomycin.	Bactericidal *(It causes the misreading of the genetic code, so the bacteria produce nonfunctional proteins. These faulty proteins get inserted into the cell membrane. This disrupts the membrane's integrity, causing leakage and cell damage. Most others (e.g., tetracyclines, macrolides) are bacteriostatic because they only block protein production without killing the bacteria directly)* ; irreversible inhibition of initiation complex *(Initiator tRNA: Carries the first amino acid (formylmethionine, fMet) to start the protein.) Initiation factors (IF-1, IF-2, IF-3): Help guide the proper assembly.* through binding of the 30S subunit. Can cause misreading of mRNA. Also block translocation. *(During protein synthesis, mRNA and tRNAs are moved through the ribosome by the dynamic process of translocation.)* Require O2 for uptake; therefore ineffective against anaerobes. Synergistic with β-lactam antibiotics. (*penicillin's disruption of the bacterial cell wall enhances aminoglycoside penetration and efficacy,)* Neomycin for bowel surgery.
Tetracycline	Bacteriostatic; bind to 30S and prevent attachment of aminoacyl-tRNA. Borrelia burgdorferi, M pneumoniae. Drugs' ability to accumulate intracellularly makes them very effective against Rickettsia and Chlamydia. Also used to treat acne. Doxycycline effective against community-acquired MRSA.
Tigecycline	Tetracycline derivative. Binds to 30S, inhibiting protein synthesis. Generally bacteriostatic.
Chloramphenicol	Blocks peptidyltransferase *(Peptidyl transferase is an enzyme that catalyzes the addition of an amino acid residue in order to grow the polypeptide chain in protein synthesis.)* at 50S ribosomal subunit. Bacteriostatic.
Clindamycin	Blocks peptide transfer (translocation) *(translocation is the step where the ribosome moves (or "shifts") along the mRNA, so the next codon can be read. ribosome shifts forward one codon. The tRNA with the growing peptide moves from the A site → P site. The empty tRNA moves from P site → E site and exits.)*

	at 50S ribosomal subunit. Bacteriostatic. Anaerobic infections (eg, Bacteroides spp., Clostridium perfringens) in aspiration pneumonia, lung abscesses, and oral infections. Also effective against invasive group A streptococcal infection. 
Linezolid	Inhibits protein synthesis by binding to 50S subunit and preventing formation of the initiation complex (*Initiator tRNA Carries the first amino acid (formylmethionine, fMet) to start the protein.* *Initiation factors (IF-1, IF-2, IF-3): Help guide the proper assembly.)*
Macrolides	inhibit protein synthesis by blocking translocation (*(translocation is the step where the ribosome moves (or "shifts") along the mRNA, so the next codon can be read.* *ribosome shifts forward one codon.* *The tRNA with the growing peptide moves from the A site → P site. The empty tRNA moves from P site → E site and exits.))* (“macroslides”); bind to the 23S rRNA of the 50S ribosomal subunit. Bacteriostatic. Atypical pneumonias (Mycoplasma, Chlamydia, Legionella), STIs (Chlamydia), gram ⊕ cocci (streptococcal infections in patients allergic to penicillin), and B pertussis.
Polymyxin	Cation polypeptides that bind to phospholipids on cell membrane of gram ⊖ bacteria. Disrupt cell membrane integrity → leakage of cellular components → cell death.

Other antimicrobial



Sulfonamides = Gram ⊕, gram ⊖, Nocardia. TMP-SMX for simple UTI.
Dapsone = Leprosy (lepromatous and tuberculoid), *Pneumocystis jirovecii* prophylaxis, or treatment when used in combination with TMP.
Trimethoprim = Combination used for UTIs, *Shigella, Salmonella, Pneumocystis jirovecii* pneumonia treatment and prophylaxis, toxoplasmosis prophylaxis.

Fluoroquinolones	Inhibit prokaryotic enzymes topoisomerase II (DNA gyrase) *(Topoisomerase 2 = Cuts both strands of DNA (double-strand break), passes another segment of DNA through, then reseals.)* and topoisomerase IV. *(Topoisomerase 4 = Similar mechanism, but specifically decatenates intertwined DNA molecules after replication. Decatenation refers to the unlinking or disentangling of connected components, particularly in the context of DNA, where it involves the separation of catenated DNA molecules. Catenation is the chemical bonding of atoms)* Bactericidal. Must not be taken with antacids. Gram ⊖ rods of urinary and GI tracts (including Pseudomonas), some gram ⊕ organisms, otitis externa.
Daptomycin	Lipopeptide that disrupts cell membranes of gram ⊕ cocci by creating transmembrane channels.
Metronidazole	Forms toxic free radical metabolites in the bacterial cell that damage DNA. Bactericidal, antiprotozoal. Anaerobs Baceriodes

Anti TB drugs

Rifampin is a specific rifamycin antibiotic used to treat tuberculosis

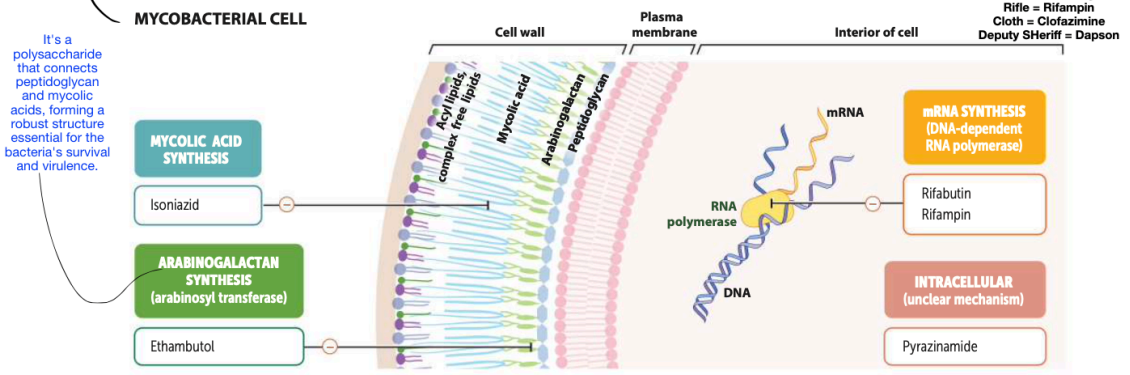
Antimycobacterial therapy

BACTERIUM	PROPHYLAXIS	TREATMENT
M tuberculosis	Rifamycin-based regimen for 3–4 months	Rifampin, Isoniazid, Pyrazinamide, Ethambutol (RIPE for treatment)
M avium–intracellulare	Azithromycin, rifabutin	Azithromycin or clarithromycin + ethambutol Can add rifabutin or ciprofloxacin
M leprae	N/A	Long-term treatment with dapsone and rifampin for tuberculoid form Add clofazimine for lepromatous form

Rifabutin and rifampin are both rifamycins

Think of the DNA as the blueprint, and RNA polymerase as the copier making working copies (RNA) so the cell can build things (proteins). all bacteria need DNA-dependent RNA polymerase to make RNA and live.

Lepromatous
Lion Facies Man = Symbol
Rifle = Rifampin
Cloth = Clofazimine
Deputy SHeriff = Dapson



Rifamycins

Rifampin, rifabutin, rifapentine.

MECHANISM
Inhibit DNA-dependent RNA polymerase.

CLINICAL USE
Mycobacterium tuberculosis; delay resistance to dapsone when used for leprosy. Used for meningococcal prophylaxis and chemoprophylaxis in contacts of children with *H influenzae* type b.

ADVERSE EFFECTS
Minor hepatotoxicity and drug interactions (↑ cytochrome P-450); orange body fluids (nonhazardous side effect). Rifabutin favored over rifampin in patients with HIV infection due to less cytochrome P-450 stimulation.

Rifamycin = Hepatotoxic

MECHANISM OF RESISTANCE
Mutations reduce drug binding to RNA polymerase. Monotherapy rapidly leads to resistance.

Rifampin's 4 R's:
- RNA polymerase inhibitor
- Ramps up microsomal cytochrome P-450
- Red/orange body fluids
- Rapid resistance if used alone

Rifampin ramps up cytochrome P-450, but rifabutin does not.

Mehlman
MOA of rifampin ?

{{c1::DNA dependent RNA polymerase
}}
Yours = RNA dependent DNA polymerase —> seen in HIV —> viral RNA as a template to synthesize complementary DNA (cDNA). Then it synthesizes the second DNA strand, forming double-stranded viral DNA. e viral enzyme integrase carries this DNA into the nucleus and inserts it into the host's genome.

Rifampin (or rifampicin) exhibits rapid development of resistance when used alone because it targets bacterial RNA polymerase, a crucial enzyme for transcription. Resistance arises quickly due to specific genetic mutations.

Isoniazid

Catalase activity:
It decomposes hydrogen peroxide (H_2O_2) into water and oxygen, protecting the bacteria from oxidative damage caused by reactive oxygen species.
Peroxidase activity:
It reduces peroxides (like H_2O_2) by transferring electrons from donor molecules, helping detoxify peroxides within the bacterial cell.

TIGER in the background = Kat G

MECHANISM
↓ synthesis of mycolic acids. Bacterial catalase-peroxidase (encoded by KatG) needed to convert INH to active metabolite.

KatG is an enzyme that functions as both catalase and peroxidase.

CLINICAL USE
Mycobacterium tuberculosis. Also used as monotherapy for latent TB.

Different INH half-lives in fast vs slow acetylators.

ADVERSE EFFECTS
Hepatotoxicity, cytochrome P-450 inhibition, drug-induced SLE, anion gap metabolic acidosis, vitamin B_6 deficiency (peripheral neuropathy, sideroblastic anemia), seizures (in high doses, refractory to benzodiazepines). Administer with pyridoxine (B_6).

yea tum nai ghalat keeya thah
HEPATOTOXIC

INH Injures Neurons and Hepatocytes.

Wolf = Drug indueced lupus

Man with seizures in the background

MECHANISM OF RESISTANCE
Mutations leading to underexpression of KatG.

Mudpiles

DICE = b6 defi

ethambutol is the inhibition of

MECHANISM OF RESISTANCE	Mutations leading to underexpression of KatG.

Mudpiles

DICE = b6 defi

Pyrazinamide

MECHANISM	Mechanism uncertain. Works best at acidic pH (eg, in host phagolysosomes).
CLINICAL USE	*Mycobacterium tuberculosis*.
ADVERSE EFFECTS HEPATOTOXIC	Hyperuricemia, hepatotoxicity.

ethambutol is the inhibition of arabinosyltransferase, which subsequently inhibits the synthesis of arabinogalactan, an important mycobacterial cell wall polysaccharide. Polysaccharides on the outer surface of bacteria are the principal antigens in most pathogenic bacteria, including M. tuberculosis.

Ethambutol

MECHANISM	↓ carbohydrate polymerization of mycobacterium cell wall by blocking arabinosyltransferase.
CLINICAL USE	*Mycobacterium tuberculosis*.
ADVERSE EFFECTS	Optic neuropathy (red-green color blindness, usually reversible). Pronounce "eyethambutol."

Streptomycin

MECHANISM	Interferes with 30S component of ribosome.
CLINICAL USE	*Mycobacterium tuberculosis* (2nd line).
ADVERSE EFFECTS	Tinnitus, vertigo, ataxia, nephrotoxicity.

Antimicrobial prophylaxis

Mefloquine

Atovaquone-proguanil

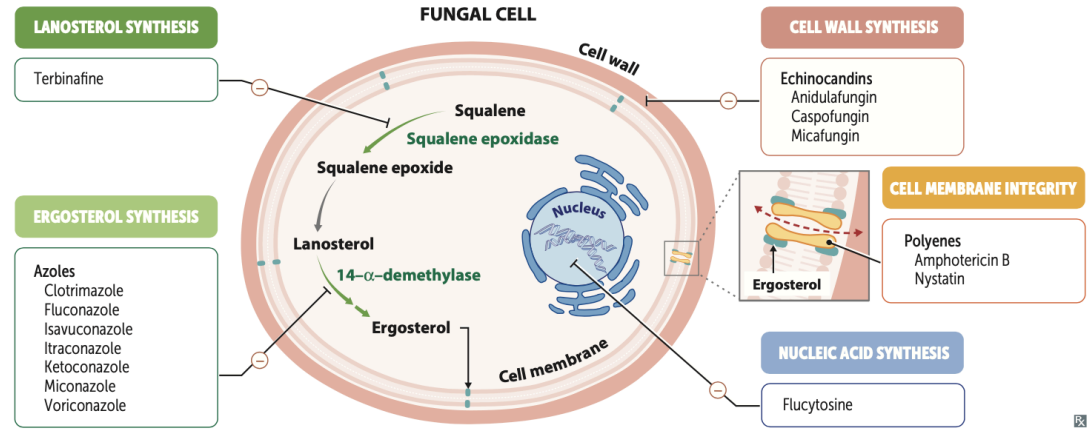
Doxycyline

Primaquitne or choloruqine

MAD PC

CLINICAL SCENARIO	MEDICATION
Exposure to meningococcal infection	Ceftriaxone, ciprofloxacin, or rifampin
High risk for infective endocarditis and undergoing surgical or dental procedures	Amoxicillin
History of recurrent UTIs	TMP-SMX
Malaria prophylaxis for travelers	Atovaquone-proguanil, mefloquine, doxycycline, primaquine, or chloroquine (for areas with sensitive species)
Pregnant patients carrying group B strep	Intrapartum penicillin G or ampicillin
Prevention of gonococcal conjunctivitis in newborn	Erythromycin ointment on eyes
Prevention of postsurgical infection due to *S aureus*	Cefazolin; vancomycin if ⊕ for MRSA
Prophylaxis of strep pharyngitis in child with prior rheumatic fever	Benzathine penicillin G or oral penicillin V

Antifungal therapy



16. A 5-year-old boy is brought to the office by his mother because of a 7-day history of worsening hair loss with an associated scaly patch on his scalp. The child says his scalp is itchy. Over-the-counter ointments have provided no improvement of the patient's symptoms. He has had no other symptoms and is otherwise healthy. Medical history is unremarkable and he takes no medications. Vital signs are temperature 37.1°C (98.7°F), pulse 80/min, respirations 20/min, and blood pressure 110/70 mm Hg. Physical examination shows no abnormalities except for the findings shown in the photograph. Which of the following is a potential complication of the oral pharmacotherapy used to treat this condition?

A) Anemia
B) Hepatotoxicity
C) Pancreatitis
D) Pulmonary fibrosis
E) Seizures

Amphotericin B		
MECHANISM	Binds ergosterol (unique to fungi); forms membrane pores that allow leakage of electrolytes.	Amphotericin "tears" holes in the fungal membrane by forming pores.
CLINICAL USE	Serious, systemic mycoses. *Cryptococcus* (amphotericin B +/– flucytosine for cryptococcal meningitis), *Blastomyces*, *Coccidioides*, *Histoplasma*, *Candida*, *Mucor*. Intrathecally for coccidioidal meningitis.	Supplement K^+ and Mg^{2+} because of altered renal tubule permeability.
ADVERSE EFFECTS	Fever/chills ("shake and bake"), hypotension, nephrotoxicity, arrhythmias, anemia, IV phlebitis ("amphoterrible").	Hydration ↓ nephrotoxicity. Liposomal amphotericin ↓ toxicity.
Nystatin		
MECHANISM	Same as amphotericin B. Topical use only as too toxic for systemic use.	
CLINICAL USE	"Swish and swallow" for oral candidiasis (thrush); topical for diaper rash or vaginal candidiasis.	
Flucytosine		
MECHANISM	Inhibits DNA and RNA biosynthesis by conversion to 5-fluorouracil by cytosine deaminase.	
CLINICAL USE	Systemic fungal infections (especially meningitis caused by *Cryptococcus*) in combination with amphotericin B.	
ADVERSE EFFECTS	Myelosuppression.	
Azoles	Clotrimazole, fluconazole, isavuconazole, itraconazole, ketoconazole, miconazole, voriconazole.	
MECHANISM	Inhibit fungal sterol (ergosterol) synthesis by inhibiting the cytochrome P-450 enzyme that converts lanosterol to ergosterol.	
CLINICAL USE	Local and less serious systemic mycoses. Fluconazole for chronic suppression of cryptococcal meningitis in people living with HIV and candidal infections of all types. Itraconazole may be used for *Blastomyces*, *Coccidioides*, *Histoplasma*, *Sporothrix schenckii*. Clotrimazole and miconazole for topical fungal infections. Voriconazole for *Aspergillus* and some *Candida*. Isavuconazole for serious *Aspergillus* and *Mucor* infections.	
ADVERSE EFFECTS	Testosterone synthesis inhibition (gynecomastia, especially with ketoconazole), liver dysfunction (inhibits cytochrome P-450), QT interval prolongation.	
Terbinafine		
MECHANISM	Inhibits the fungal enzyme squalene epoxidase.	
CLINICAL USE	Dermatophytoses (especially onychomycosis—fungal infection of finger or toe nails).	
ADVERSE EFFECTS	GI upset, headaches, hepatotoxicity, taste disturbance.	

BCCCHM
Blastomyces
Coccidiodis
Cryptoccus
Candida
Histoplasma
Mucor 6 fungi

PAAN
Phelbititis
Anemia
Arrthymia
Nephrotoxicty

NAAP
Nephro
Arrythemia
Anemia
Phelbitis

Shake and bake = Frog
Doctor Faiting = Hypotension
Emergency saline wash = IV normal saline

Cytosine deaminase =
Cytosine deaminase converts flucytosine into 5 FU

BCHS
Blastomyces
Coccidiodis
Histo
Sporothrinx schenicki

Azoles inhibit 11B-Hydroxylase, thus blocking cortisol synthesis and inhibit Desmolase and 17 alpha hydorxylase aka 17, 20 lyase

azoL e = Liver dysfucnion

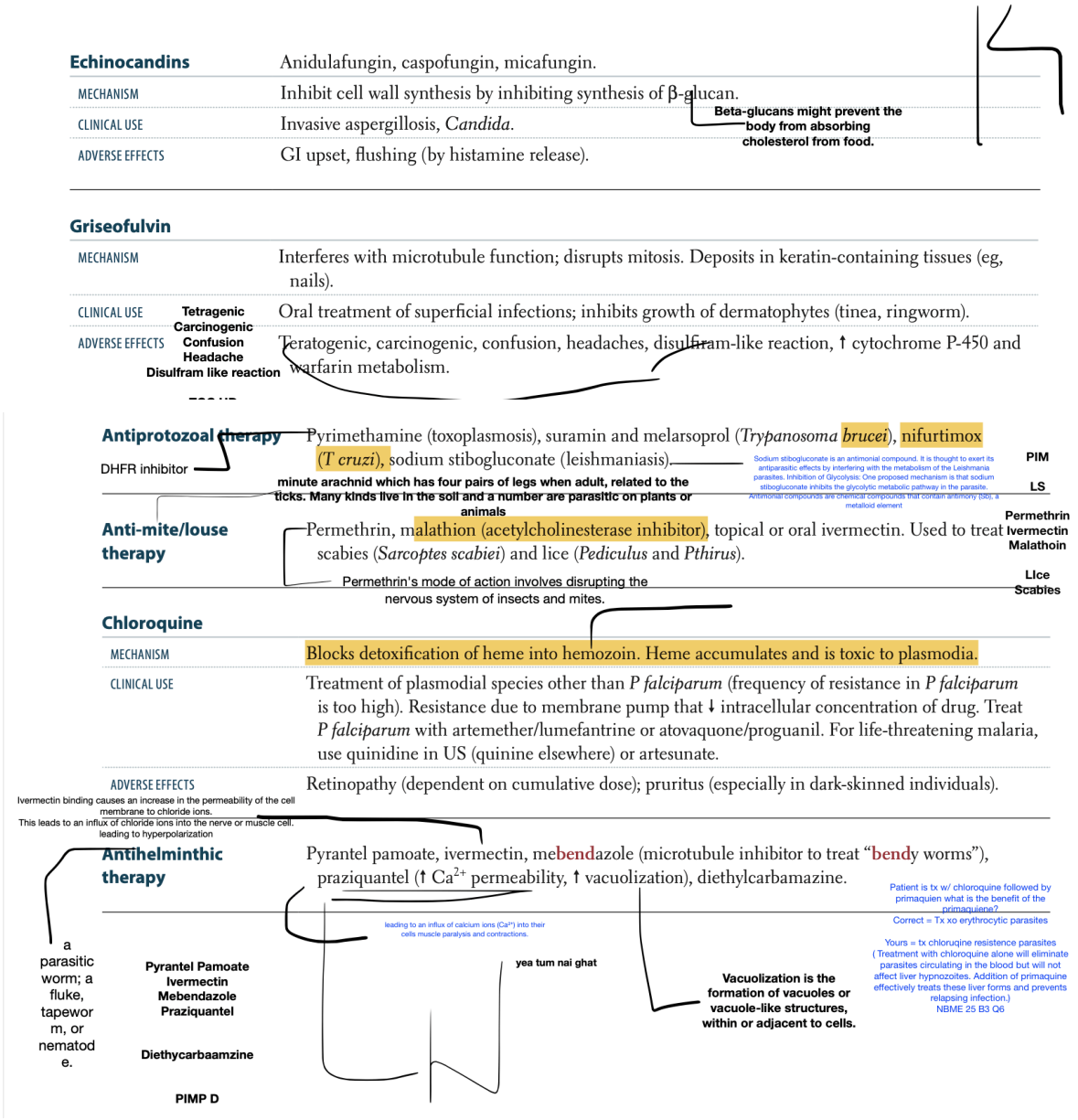
3 AE of Azoles
The LQ

Testesrone
Liver dysfucntion
QT prolongation

-Inhibit Cholesterol Desmolase, 17a-hydroxylase (aka 17,20-lyase), 11B-Hydroxylase

The clinical scenario and image show a child with a scaly, itchy scalp and patchy hair loss, which

is classic for tinea capitis, a superficial fungal infection of the scalp. It's common in children and often requires oral antifungal treatment because topical therapy is ineffective due to poor penetration into hair follicles.



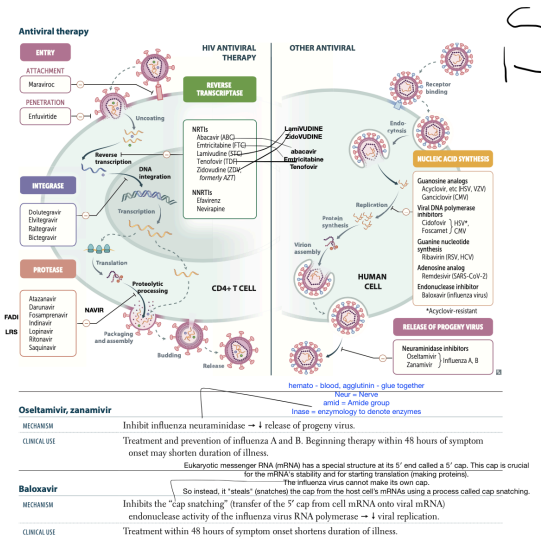
Hemozoin (HZ), also known as malaria pigment, is a crystalline, brown pigment formed by malaria parasites (Plasmodium) in the digestive vacuole of infected red blood cells. It's a byproduct of the parasite's digestion of hemoglobin, the protein that carries oxygen in red blood cells. Hemozoin is released into circulation during the parasite's life cycle and can accumulate in immune cells

Patient is tx w/ chloroquine followed by primaquine what is the benefit of the primaquine?

Correct = Tx exo erythrocytic parasites|| NBME 25 B3 Q6

Yours = tx chloruqine resistence parasites (Treatment with chloroquine alone will eliminate parasites circulating in the blood but will not affect liver hypnozoites. Addition of primaquine effectively treats these liver forms and prevents relapsing infection.)

Antivirals



Nucleosides are made up of a nitrogenous base and a sugar (ribose or deoxyribose), while nucleotides also contain one or more phosphate groups

Acyclovir, famciclovir, valacyclovir

MECHANISM	Guanosine analogs. Monophosphorylated by HSV/VZV thymidine kinase and not phosphorylated in uninfected cells → few adverse effects. Triphosphate formed by cellular enzymes. Preferentially inhibit viral DNA polymerase by chain termination.
CLINICAL USE	No activity against CMV because CMV lacks the thymidine kinase necessary to activate guanosine analogs. Used for HSV-induced mucocutaneous and genital lesions as well as for encephalitis. Prophylaxis in patients who are immunocompromised. Also used as prophylaxis for immunocompetent patients with severe or recurrent infection. No effect on latent forms of HSV and VZV. Valacyclovir, a prodrug of acyclovir, has better oral bioavailability. For herpes zoster, use famciclovir.
ADVERSE EFFECTS	Obstructive crystalline nephropathy and acute kidney injury if not adequately hydrated.
MECHANISM OF RESISTANCE	Mutated viral thymidine kinase.

Chain termination: Unlike natural nucleotides, acyclovir lacks a 3′-OH group necessary for forming a new phosphodiester bond. When incorporated, it prevents the addition of subsequent nucleotides, effectively halting DNA chain elongation.

short (7-10 days) course of oral acyclovir during primary genital HSV infection reduces the duration of viral shedding, time for lesion healing, and local pain; however, it does not appear to alter recurrence rates.
aily oral valacyclovir (preferred because of its once-daily dosing and good bioavailability), acyclovir, or famciclovir.
U world ghatal 2 baar

Ganciclovir

MECHANISM	Guanosine analog. 5′-monophosphate formed by a CMV viral kinase. Triphosphate formed by cellular kinases. Preferentially inhibits viral DNA polymerase.
CLINICAL USE	CMV, especially in patients who are immunocompromised. Valganciclovir, a prodrug of ganciclovir, has better oral bioavailability.
ADVERSE EFFECTS	Myelosuppression (leukopenia, neutropenia, thrombocytopenia), renal toxicity. More toxic to host enzymes than acyclovir.
MECHANISM OF RESISTANCE	Mutated viral kinase.

Foscarnet

MECHANISM	Viral DNA/RNA polymerase inhibitor and HIV reverse transcriptase inhibitor. Binds to pyrophosphate-binding site of enzyme. Does not require any kinase activation.
CLINICAL USE	CMV retinitis in immunocompromised patients when ganciclovir fails; acyclovir-resistant HSV.
ADVERSE EFFECTS	Nephrotoxicity, multiple electrolyte abnormalities can lead to seizures.
MECHANISM OF RESISTANCE	Mutated DNA polymerase.

Foscarnet = pyrofosphate analog.

Foscarnet binds to the pyrophosphate-binding site of viral DNA polymerases and reverse transcriptases because it mimics the natural substrate—pyrophosphate—that is normally involved in the DNA synthesis process.

Cidofovir

MECHANISM	Preferentially inhibits viral DNA polymerase. Does not require phosphorylation by viral kinase.
CLINICAL USE	CMV retinitis in immunocompromised patients; acyclovir-resistant HSV. Long half-life.

HIV therapy

Antiretroviral therapy (ART): often initiated at the time of HIV diagnosis.

Strongest indication for use with patients presenting with AIDS-defining illness, low CD4+ cell counts (< 500 cells/mm^3), or high viral load. Regimen consists of 3 drugs to prevent resistance: 2 NRTIs and preferably an integrase inhibitor.

Most ARTs are active against both HIV-1 and HIV-2 (exceptions: NNRTIs and enfuvirtide not effective against HIV-2).

Nucleoside = a compound (e.g., adenosine or cytidine) commonly found in DNA or RNA, consisting of a purine or pyrimidine base linked to a sugar.

DRUG	MECHANISM	TOXICITY
NRTIs		
Abacavir (ABC) Emtricitabine (FTC) Lamivudine (3TC) Tenofovir (TDF) Zidovudine (ZDV, formerly AZT)	Competitively inhibit nucleotide binding to reverse transcriptase and terminate the DNA chain (lack a 3′ OH group). Tenofovir is a nucleoTide; the others are nucleosides. All need to be phosphorylated to be active. ZDV can be used for general prophylaxis and during pregnancy to ↓ risk of fetal transmission. Have you dined (vudine) with my nuclear (nucleosides) family?	Myelosuppression (can be reversed with granulocyte colony-stimulating factor [G-CSF] and erythropoietin), nephrotoxicity. Abacavir contraindicated if patient has HLA-B*5701 mutation due to ↑ risk of hypersensitivity.
NNRTIs		
Efavirenz Nevirapine **EFA VIR ENZ**	Bind to reverse transcriptase at site different from NRTIs. Do not require phosphorylation to be active or compete with nucleotides.	Rash and hepatotoxicity are common to all NNRTIs. Vivid dreams and CNS symptoms are common with efavirenz.
Integrase inhibitors		
Bictegravir Dolutegravir Elvitegravir Raltegravir	Inhibits HIV genome integration into host cell chromosome by reversibly inhibiting HIV integrase.	↑ creatine kinase, weight gain. **Musclar Guy = Myositis**
Protease inhibitors		
Atazanavir Darunavir Lopinavir Ritonavir	Assembly of virions depends on HIV-1 protease (*pol* gene), which cleaves the polypeptide products of HIV mRNA into their functional parts. Thus, protease inhibitors prevent maturation of new viruses. Navir (never) tease a protease.	Hyperglycemia, GI intolerance (nausea, diarrhea). Rifampin (potent CYP/UGT inducer) ↓ protease inhibitor concentrations; use rifabutin instead. Ritonavir (cytochrome P-450 inhibitor), ↑ other drug concentrations.
Entry inhibitors		
Enfuvirtide	Binds gp41, inhibiting viral entry.	Skin reaction at injection sites. Enfuvirtide inhibits fusion.
Maraviroc	Binds CCR-5 on surface of T cells/monocytes, inhibiting interaction with gp120.	Maraviroc inhibits docking.

These drugs work by interfering with the reverse transcriptase enzyme, specifically by binding to a different site than nucleoside inhibitors

Pre-exposure prophylaxis

Administered to patients with a negative HIV test, normal renal function, and any of the following indications:

- Men who have sex with men without protection
- Sexual activity with an HIV ⊕ partner or multiple partners of unknown HIV status
- Injection drug use with high-risk needle behavior

Treatment: tenofovir + emtricitabine.

Counsel on adherence and risk reduction with follow-up HIV testing every 3 months.

NS5A inhibitor stands for Nonstructural protein 5A inhibitor.

Hepatitis C therapy — Chronic HCV infection treated with multidrug therapy that targets specific steps within HCV replication cycle (HCV-encoded proteins). Examples of drugs are provided.

DRUG	MECHANISM	TOXICITY
NS5A inhibitors		
Ledipasvir Ombitasvir Velpatasvir	Inhibits NS5A, a viral phosphoprotein that plays a key role in RNA replication Exact mechanism unknown	Headache, diarrhea
NS5B inhibitors		
Sofosbuvir Dasabuvir	Inhibits NS5B, an RNA-dependent RNA polymerase acting as a chain terminator Prevents viral RNA replication	Fatigue, headache
NS3/4A inhibitors		
Grazoprevir Simeprevir	Inhibits NS3/4A, a viral protease, preventing viral replication	Grazoprevir: headache, fatigue Simeprevir: photosensitivity reactions, rash
Alternative drugs		
Ribavirin	Inhibits synthesis of guanine nucleotides by competitively inhibiting IMP dehydrogenase Used as adjunct in cases refractory to newer medications	Hemolytic anemia, severe teratogen

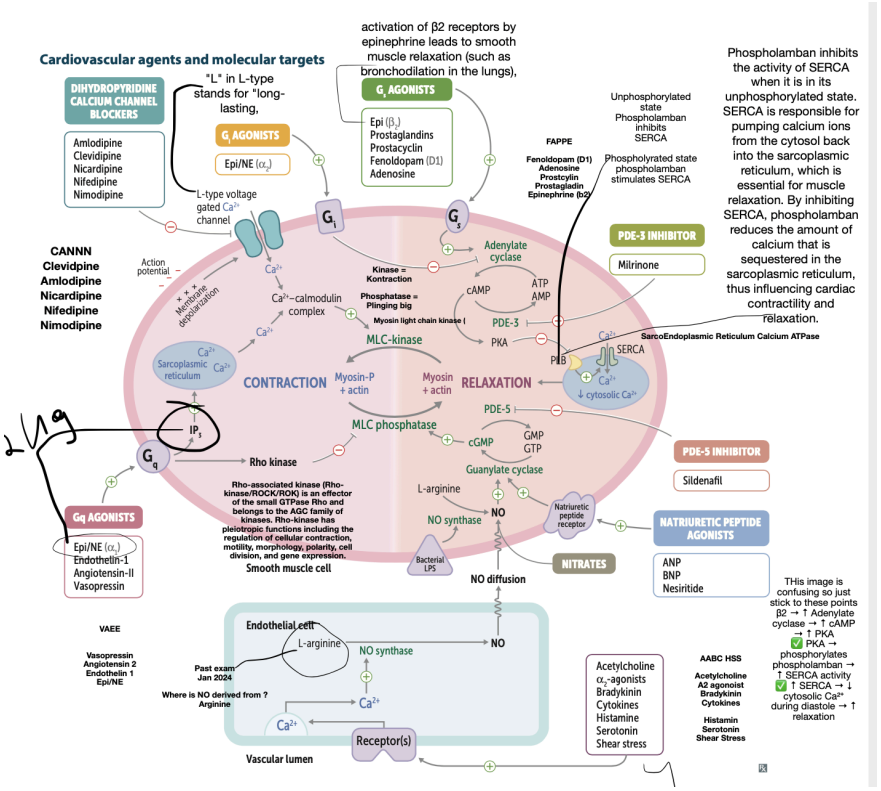
adenine and guanine are purines

By inhibiting inosine monophosphate (IMP) dehydrogenase, ribavirin depletes intracellular GTP pools. This limits the availability of guanosine nucleotides needed for both host and viral RNA synthesis.

Enzyme	Template	Product	Commonly Found In
DNA-dependent RNA polymerase	DNA	RNA	All living cells
DNA-dependent DNA polymerase	DNA	DNA	All living cells
RNA-dependent RNA polymerase	RNA	RNA	Many RNA viruses
RNA-dependent DNA polymerase	**RNA**	**DNA**	**Retroviruses, retrotransposons, telomerase**

Disinfection and Goals include the reduction of pathogenic organism counts to safe levels (disinfection) and the

CVS



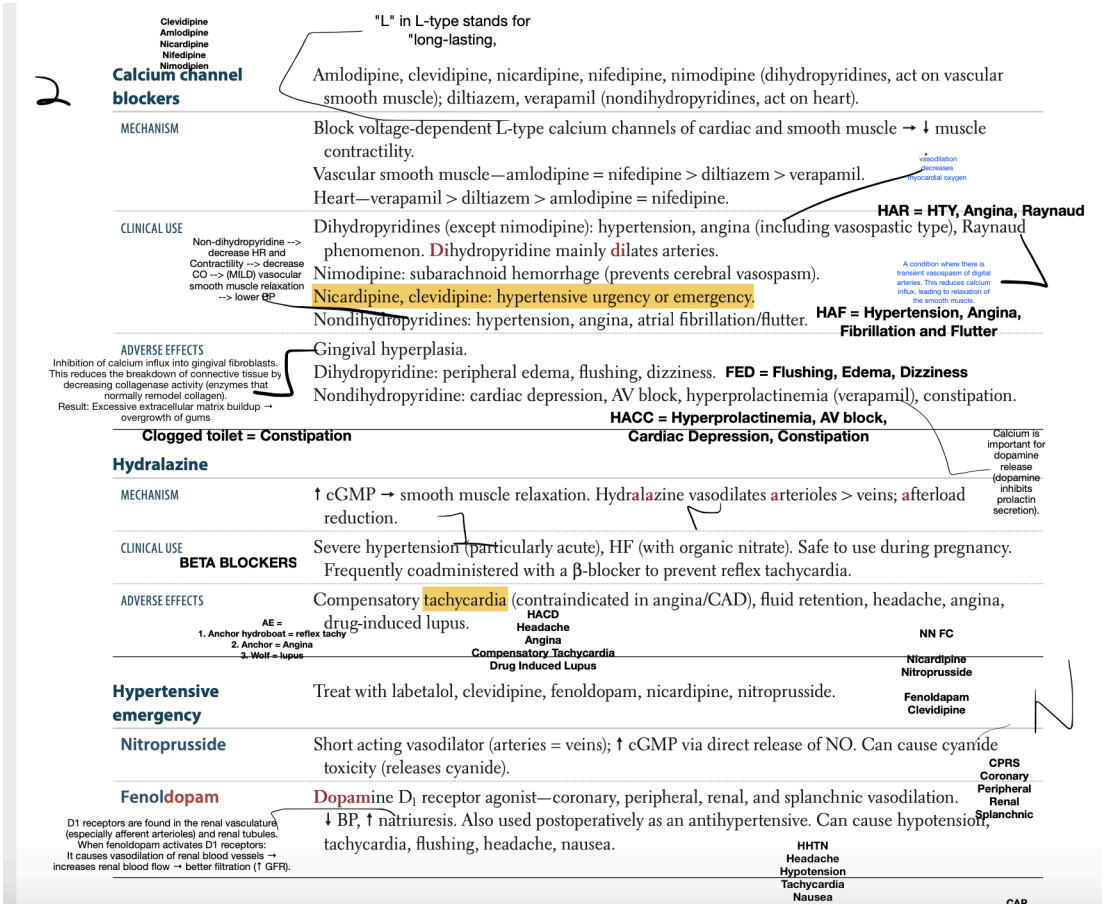
Drugs that increase cGMP is BNP Neseritide, Sildenfil and Nitrates

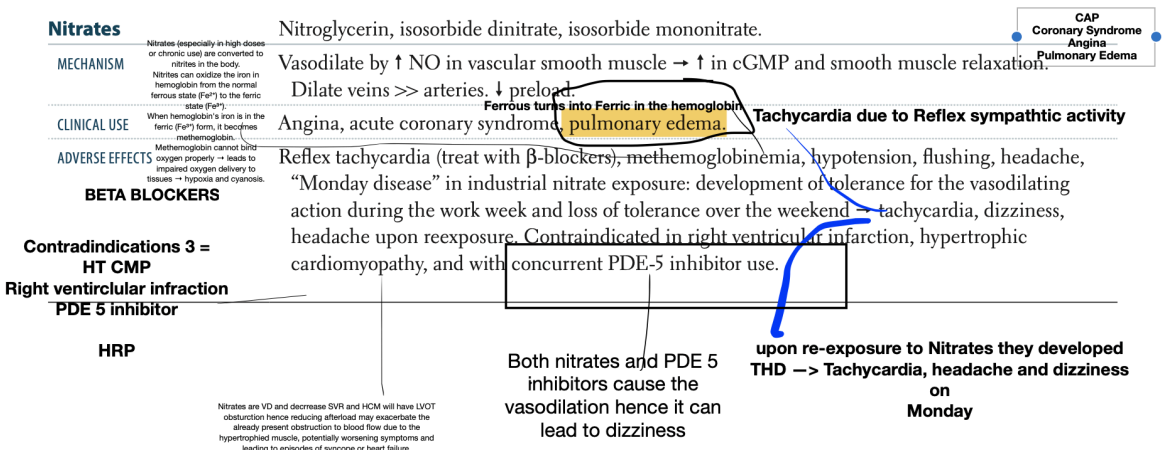
Hydralazine and Nitroprusside

HY USMLE Q #1044 – Cardio

3 days left !!!!

What increase coronary blood flow after NE adminsitration ?
{{c1::adenosine
}}
increase Blood flow adenosine is vasodialtor
more ATP use which will break down into adenosine
adensonine increase cardiac pain





But because pindolol and acebutolol have partial beta-agonist activity, they can prevent full slowing of the heart. They might even slightly stimulate the heart, especially during stress.
Result: They might not adequately decrease oxygen demand and can worsen angina symptoms.

beta blockers decrease HR and increase amount of filling time and increase EDV

Antianginal therapy

Goal is reduction of myocardial O_2 consumption (MVO_2) by ↓ 1 or more of the determinants of MVO_2: end-diastolic volume, BP, HR, contractility. ·

COMPONENT	NITRATES	β-BLOCKERS	NITRATES + β-BLOCKERS
End-diastolic volume	↓	No effect or ↑	No effect or ↓
Blood pressure	↓	↓	↓
Contractility	↑ (reflex response)	↓	Little/no effect
Heart rate	↑ (reflex response)	↓	No effect or ↓
Ejection time	↓	↑	Little/no effect
MVO_2	↓ vasodialiton of the coronary arteries may lead to decrease O2 consumption	↓ decrease HR decrease demand of O2	↓↓

Increase Ejection time --> decrease HR --> increase filling --> increase EDV --> improve the stroke volume --> enchance the ejection time

Verapamil is similar to β-blockers in effect.
Pindolol and acebutolol are partial β-agonists that should be used with caution in angina.

Ranolazine

By blocking this late Na^+ influx, it reduces intracellular sodium accumulation.
This indirectly reduces intracellular calcium (via the Na^+/Ca^{2+} exchanger working more efficiently).
Less intracellular calcium means less diastolic wall tension Less intracellular calcium results in decreased myocardial stiffness and improved relaxation

MECHANISM	Inhibits the late phase of inward sodium current thereby reducing diastolic wall tension and oxygen consumption. Does not affect heart rate or blood pressure.
CLINICAL USE	Refractory angina.
ADVERSE EFFECTS	Constipation, dizziness, headache, nausea.

Ranolazine —> decrease sodium in the cardiomyocyte —> reduce wall tension and o2 consumption

Sacubitril

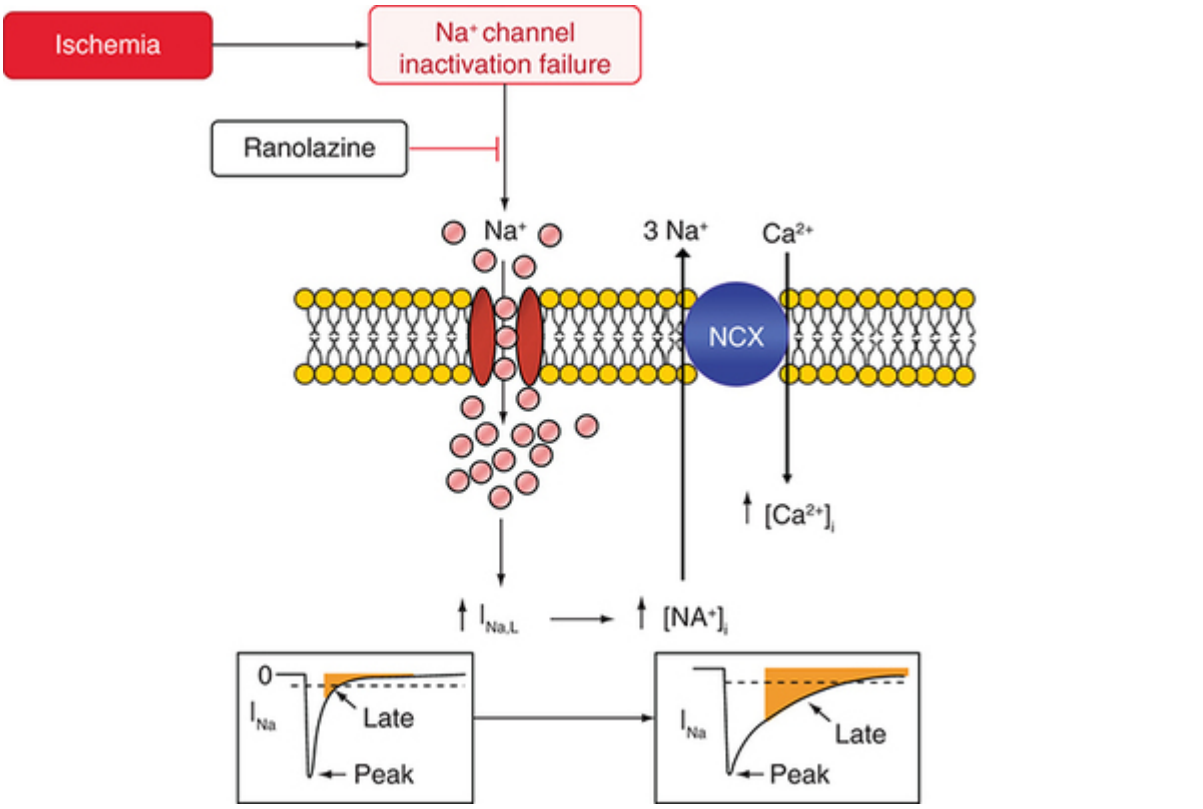
Natriutic peptides include ANP and BNP

Bradykinnin
Angiotensin 2
Natriuretic peptides
Substance P

BANS =

MECHANISM	A neprilysin inhibitor; prevents degradation of bradykinin, natriuretic peptides, angiotensin II, and substance P → ↑ vasodilation, ↓ ECF volume.
CLINICAL USE	Used in combination with valsartan (an ARB) to treat HFrEF.
ADVERSE EFFECTS	Hypotension, hyperkalemia, cough, dizziness; contraindicated with ACE inhibitors due to angioedema (both drugs ↑ bradykinin).

Low Neprilysin = MORE bradykinin = COUGH (Side ffect !!) Vasodilation



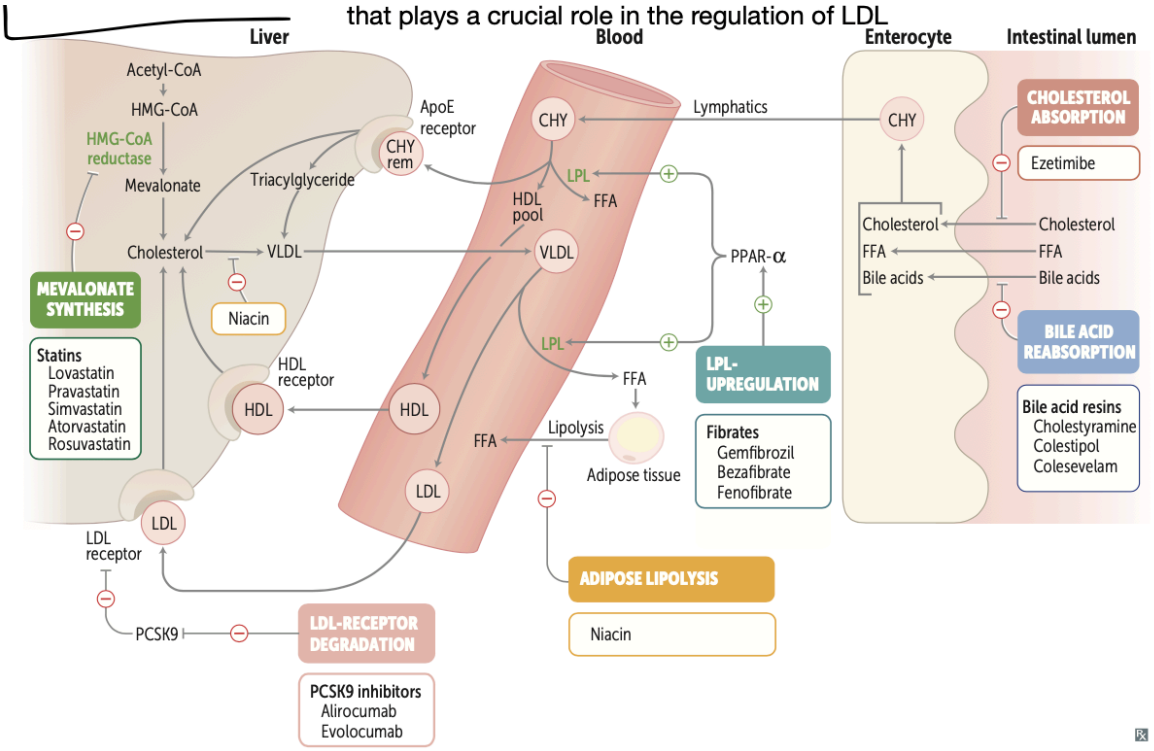
Lipid-lowering agents

DRUG	LDL	HDL	TRIGLYCERIDES	MECHANISM	ADVERSE EFFECTS/PROBLEMS
HMG-CoA reductase inhibitors Atorvastatin, simvastatin	↓↓↓	↑	↓	Inhibit conversion of HMG-CoA to mevalonate, a cholesterol precursor; → ↓ intrahepatic cholesterol → ↑ LDL receptor recycling → ↑ LDL catabolism → ↓ in mortality in patients with CAD	Hepatotoxicity (↑ LFTs), myopathy (especially when used with fibrates or niacin)
Bile acid resins Cholestyramine, colestipol, colesevelam	↓↓	↑ slightly	↑ slightly	Prevent intestinal reabsorption of bile acids; liver must use cholesterol to make more	GI upset, ↓ absorption of other drugs and fat-soluble vitamins
Ezetimibe	↓↓	↑/—	↓/—	Prevents cholesterol absorption at small intestine brush border	Rare ↑ LFTs, diarrhea

Bile acid resins increase triglycerides by stimulating hepatic VLDL production as a compensatory response to decreased bile acid reabsorption.

Resins serve various purposes, including: --> Adhesives: Used in glues and bonding agents.

that plays a crucial role in the regulation of LDL



NP BEFF
Naiacin
PCSK9 inhibitors

Bile Acid Resins
Ezetimibe
Fibrates
Fish oil

NigHt

FLighT

PPAR alpha stands for Peroxisome Proliferator-Activated Receptor Alpha. It is a type of nuclear receptor that is activated by certain fatty acids and other lipid molecules.

Ep

Lipid-lowering agents *(continued)*

DRUG	LDL	HDL	TRIGLYCERIDES	MECHANISM	ADVERSE EFFECTS/PROBLEMS
Fibrates Gemfibrozil, bezafibrate, fenofibrate	↓	↑	↓↓↓	Activate PPAR-α → upregulate LPL → ↑ TG clearance Activate PPAR-α → induce HDL synthesis	Myopathy (↑ risk with statins), cholesterol gallstones (via inhibition of cholesterol 7α-hydroxylase)
Niacin	↓↓	↑↑	↓	Inhibits lipolysis (hormone-sensitive lipase) in adipose tissue; reduces hepatic VLDL synthesis	Flushed face (prostaglandin mediated; ↓ by NSAIDs or long-term use) Hyperglycemia Hyperuricemia
PCSK9 inhibitors Alirocumab, evolocumab	↓↓↓	↑	↓	Inactivation of LDL-receptor degradation → ↑ removal of LDL from bloodstream	Myalgias, delirium, dementia, other neurocognitive effects
Fish oil and marine omega-3 fatty acids	↑ slightly	↑ slightly	↓ at high doses	Believed to decrease FFA delivery to liver and decrease activity of TG-synthesizing enzymes	Nausea, fishlike taste

FaT
Firbates
Triglycerides

Glucose –> DHAP –> Glycerol 3 Phosphate +FFA (LPL) –> TG

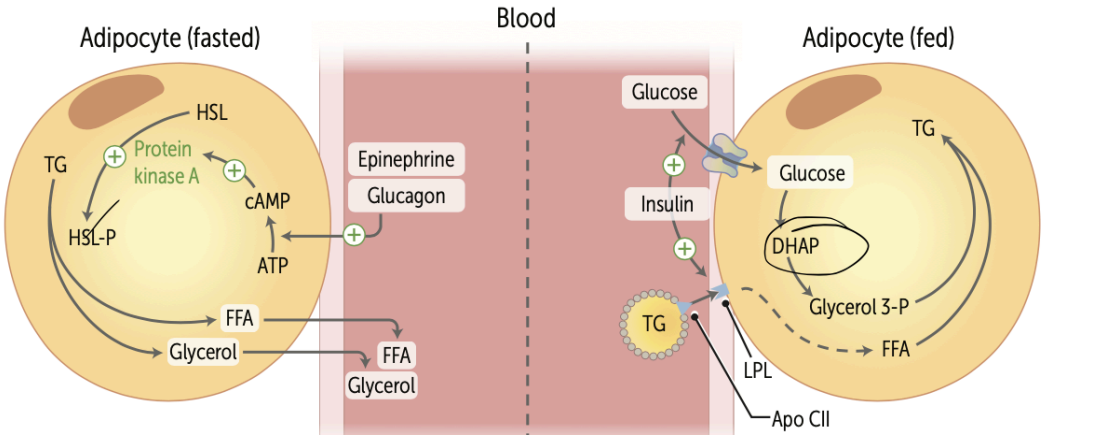
Niacin HDL
NigHT

Epinephrine
Glucagon
ATP –> cAMP –> Protein Kinase A
HSL –> prtoein kianse A break down TG into FFA and glycerol

ibrates inhibit cholesterol 7α-hydroxylase, the enzyme that converts cholesterol into bile acids.

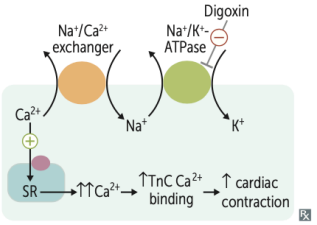
Cholesterol –> 7 alpha Hydroxy cholsterol –> Primary bile acid s

proprotein convertase subtilisin/kexin type 9 (PCSK9), a protein that plays a crucial role in the regulation of LDL



Cardiac glycosides — Digoxin

MECHANISM	Direct inhibition of Na^+/K^+-ATPase. → indirect inhibition of Na^+/Ca^{2+} exchanger. ↑ $[Ca^{2+}]_i$ → positive inotropy. Stimulates vagus nerve → ↓ HR.
CLINICAL USE	HF (↑ contractility); atrial fibrillation (↓ conduction at AV node and depression of SA node).
ADVERSE EFFECTS	Cholinergic effects (nausea, vomiting, diarrhea), blurry yellow vision ("van Glow"), arrhythmias, AV block. Can lead to hyperkalemia, which indicates poor prognosis. Factors predisposing to toxicity: renal failure (↓ excretion), hypokalemia (permissive for digoxin binding at K^+-binding site on Na^+/K^+-ATPase), drugs that displace digoxin from tissue-binding sites, and ↓ clearance (eg, verapamil, amiodarone, quinidine).
ANTIDOTE	Slowly normalize K^+, cardiac pacer, anti-digoxin Fab fragments, Mg^{2+}.



Digoxin is useful in the Increase the Parasympathetic during rest hence decrease HR but does NOT decrease HR during Exercise

U world Ghalat

Yellow Vision
Arrthymia
AV block
Kalemia
Cholinergic Effects

My KFC

Mg 2+

KCF
K+ normalzien
Fab Fragments
Cardiac Pacer

Antidigoxin Fab Fragments: antibody fragments (fab fragments) specifically designed to bind free digoxin molecules in the bloodstream.

Magnesium: Magnesium antagonizes the effects of digoxin on the myocardial cell membrane. It stabilizes cell membranes and helps correct hypomagnesemia (which can exacerbate digoxin toxicity).

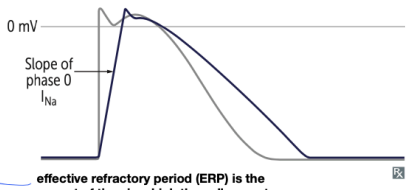
Antiarrhythmics—sodium channel blockers (class I)

Slow or block conduction (especially in depolarized cells). ↓ slope of phase 0 depolarization. ↑ action at faster HR. State dependent ↑ HR → shorter diastole, Na^+ channels spend less time in resting state (drugs dissociate during this state) → less time for drug to dissociate from receptor. Effect most pronounced in IC>IA>IB due to relative binding strength. Fast taxi CAB.

Class IA

Quinidine, procainamide, disopyramide.
"The queen proclaims Diso's pyramid."

MECHANISM	Moderate Na^+ channel blockade. ↑ AP duration, ↑ effective refractory period (ERP) in ventricular action potential, ↑ QT interval, some K^+ channel blocking effects.
CLINICAL USE	Both atrial and ventricular arrhythmias, especially reentrant and ectopic SVT and VT.
ADVERSE EFFECTS	Cinchonism (headache, tinnitus with quinidine), reversible SLE-like syndrome (procainamide), HF (disopyramide), thrombocytopenia, torsades de pointes due to ↑ QT interval.



effective refractory period (ERP) is the amount of time in which the cell cannot respond to a new conducted stimulus.

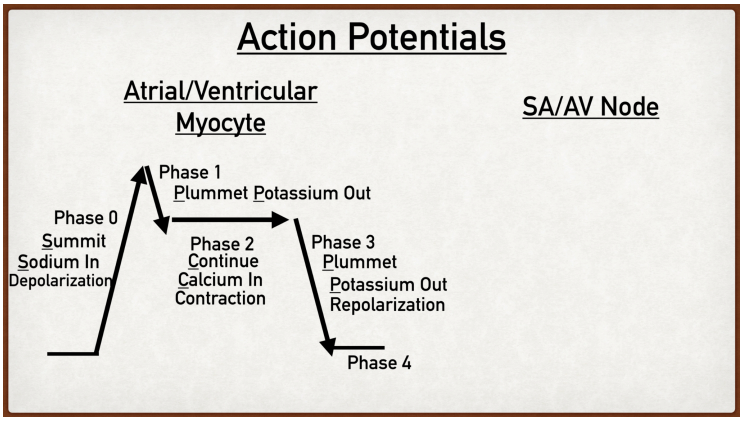
Quinine causes cinchonism (nausea, vomiting and tinnitus) in overdose but also blindness which is delayed and sometimes not noticed until the morning after the acute toxicity has resolved.

Tin = Tinnitus headache and dizziness

Broken plates TCP

T CFS

TCP, TDP
Cinchonism
Failrue of Halirue
SLE syndrome

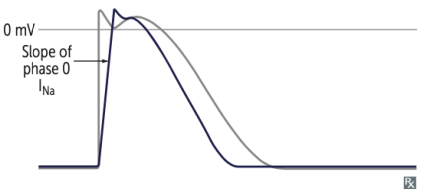


↑ QT interval.

Class IB

Lidocaine, phenytoin, mexiletine.
"I'd Buy Liddy's phine Mexican tacos."

MECHANISM	Weak Na^+ channel blockade. ↓ AP duration. Preferentially affect ischemic or depolarized Purkinje and ventricular tissue.
CLINICAL USE	Acute ventricular arrhythmias (especially post-MI), digitalis-induced arrhythmias. IB is Best post-MI.



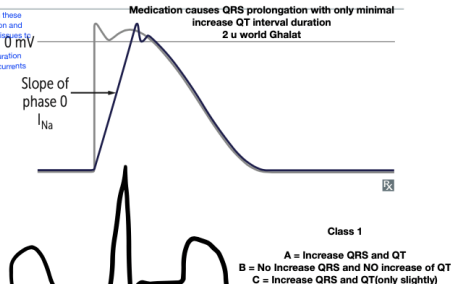
Antiarrhythmics—sodium channel blockers (class I) *(continued)*

Class IC	Flecainide, propafenone. "Can I have fries, please?"
MECHANISM	Strong Na^+ channel blockade. Significantly prolongs ERP in AV node and accessory bypass tracts. No effect on ERP in Purkinje and ventricular tissue. Minimal effect on AP duration.
CLINICAL USE	SVTs, including atrial fibrillation. Only as a last resort in refractory VT.
ADVERSE EFFECTS	Proarrhythmic, especially post-MI

The prolongation of ERP (effective refractory period) in these pathways occurs because the drugs delay repolarization and recovery of sodium channels, making it harder for these tissues to conduct subsequent impulses immediately. In normal, healthy myocardium, the action potential duration (APD) and ERP are primarily determined by potassium currents rather than sodium channels.

Class Ic can cause QRS prolongation because it blocks Sodium Channels reponsible for ventricular depolirzation but minimal increase in QT duration

They increase ERP in AV node



Class 1

A = Increase QRS and QT
B = No Increase QRS and NO increase of QT
C = Increase QRS and QT(only slightly)

repolarization are common.

Antiarrhythmics—β-blockers (class II)

Metoprolol, propranolol, esmolol, atenolol, timolol, carvedilol.

Esmolol is SHORT acting drug

MECHANISM	Decrease SA and AV nodal activity by ↓ cAMP, ↓ Ca^{2+} currents. Suppress abnormal pacemakers by ↓ slope of phase 4.
	AV node particularly sensitive—↑ PR interval. Esmolol very short acting.
CLINICAL USE	SVT, ventricular rate control for atrial fibrillation and atrial flutter.

s a result, the time it takes for electrical impulses to pass from the atria to the ventricles increases, which manifests as a lengthening of the PR interval on the ECG.

A 38-year-old woman is brought to the emergency department because of a 4-hour history of confusion and lethargy. Medical history is remarkable for major depressive disorder and a 6-month history of moderate low back pain that began after she lifted heavy boxes during a move. Her medications are fluoxetine daily and acetaminophen with codeine as needed. Family history is remarkable for hypertension and congestive heart failure in her mother. The patient lives with her husband and her mother. The patient drinks two glasses of wine on weekends. On arrival, she is somnolent but arousable to sternal rub. Temperature is 36.4°C (97.5°F), pulse is 32/min, respirations are 16/min, and blood pressure is 74/36 mm Hg. Oxygen saturation is 100% on room air. Pupils measure 6 mm in diameter. Examination shows no other abnormalities. Results of laboratory studies are shown:

Serum		Blood	
ALT	180 U/L	Hemoglobin	12 g/dL
AST	150 U/L	WBC	12,000/mm^3
Creatinine	2.5 mg/dL	Platelet count	400,000/mm^3
Acetaminophen	negative		
Urine toxicology			
Opiates	positive		

Urine toxicology
Opiates positive

An overdose of a drug with which of the following mechanisms of action is the most likely cause of this patient's condition?

Free 137 B2 Q15

A. Agonism of μ-opioid receptors
B. Inhibition of aldosterone
C. Inhibition of angiotensin-converting enzyme
D. Inhibition of β_1-adrenergic receptors
E. Inhibition of central nervous system neuron serotonin reuptake
F. Inhibition of prostaglandin synthesis
G. Inhibition of renal sodium and chloride resorption

Show Answer

Proceed to Next Item

Correct is D yours A

Antiarrhythmics—potassium channel blockers (class III)

Amiodarone, Ibutilide, Dofetilide, Sotalol. AIDS.

MECHANISM	↑ AP duration, ↑ ERP, ↑ QT interval.
CLINICAL USE	Atrial fibrillation, atrial flutter; ventricular tachycardia (amiodarone, sotalol).
ADVERSE EFFECTS	Sotalol—torsades de pointes, excessive β blockade. Ibutilide—torsades de pointes. Amiodarone—~~pulmonary fibrosis~~, he~~patotoxicity~~, ~~hypothyroidism~~ or ~~hyperthyroidism (amiodarone is 40% iodine by weight), acts as hapten (corneal deposits, blue/gray skin deposits resulting~~ in ~~photodermatitis),~~ neurologic effects, constipation, cardiovascular effects (bradycardia, heart block, HF).

Blocks the potassium channel and prolong phase 3 repolarization increase AP duration increase QT interval predisposes to TdP

Remember to check PFTs, LFTs, and TFTs when using amiodarone.

Amiodarone is lipophilic and has class I, II, III, and IV effects.

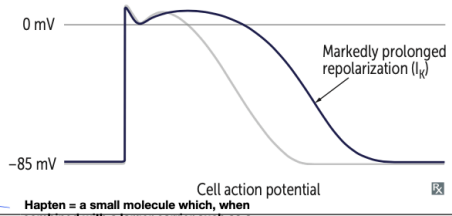
EL PETS mnemonic

Electrolyte
Liver function test

Pulmonary
Eye
Thryoid
Skin deposits that can be blue/ gray

CNC

Consitpaiton
Neuro
Cardiova



Hapten = a small molecule which, when combined with a larger carrier such as a protein, can elicit the production of antibodies which bind specifically to it (in the free or combined state).

Antiarrhythmics—calcium channel blockers (class IV)

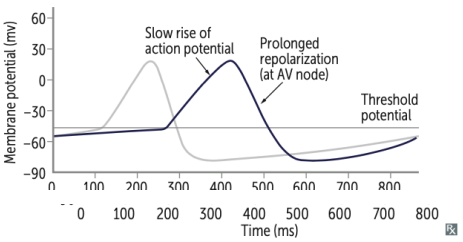
Diltiazem, verapamil.

MECHANISM	Decrease conduction velocity, ↑ ERP, ↑ PR interval.
CLINICAL USE	Prevention of nodal arrhythmias (eg, SVT), rate control in atrial fibrillation.
ADVERSE EFFECTS	Constipation, flushing, edema, cardiovascular effects (HF, AV block, sinus node depression).

fecc

Flushing
edema
constipaiton
Cardiovascular (HF AV block SInus node depression)

CCBs increase the PR interval by inhibiting calcium-dependent conduction in the AV node, thereby slowing atrioventricular conduction and prolonging the time between atrial and ventricular depolarizations.



Adenosine is a neuromodulator in the brain that promotes sleep and relaxation by binding to its receptors (primarily A1 and A2A receptors). When adenosine binds, it generally has inhibitory effects on neural activity, leading to feelings of drowsiness and decreased arousal.

Caffeine and Theophylline as Antagonists: Both caffeine and theophylline are structurally similar to adenosine. They bind competitively to adenosine receptors without activating them, effectively blocking adenosine from exerting its inhibitory effects.

Other antiarrhythmics

Adenosine

Brochospasm
Chest Pain
Doom
e
Flusing
Hypotension

↑ K^+ out of cells → hyperpolarizing the cell and ↓ I_{Ca}, decreasing AV node conduction. Drug of choice in diagnosing/terminating certain forms of SVT. Very short acting (~ 15 sec). Effects blunted by theophylline and caffeine (both are adenosine receptor antagonists). Adverse effects include flushing, hypotension, chest pain, sense of impending doom, bronchospasm.

Magnesium

Effective in torsades de pointes and digoxin toxicity.

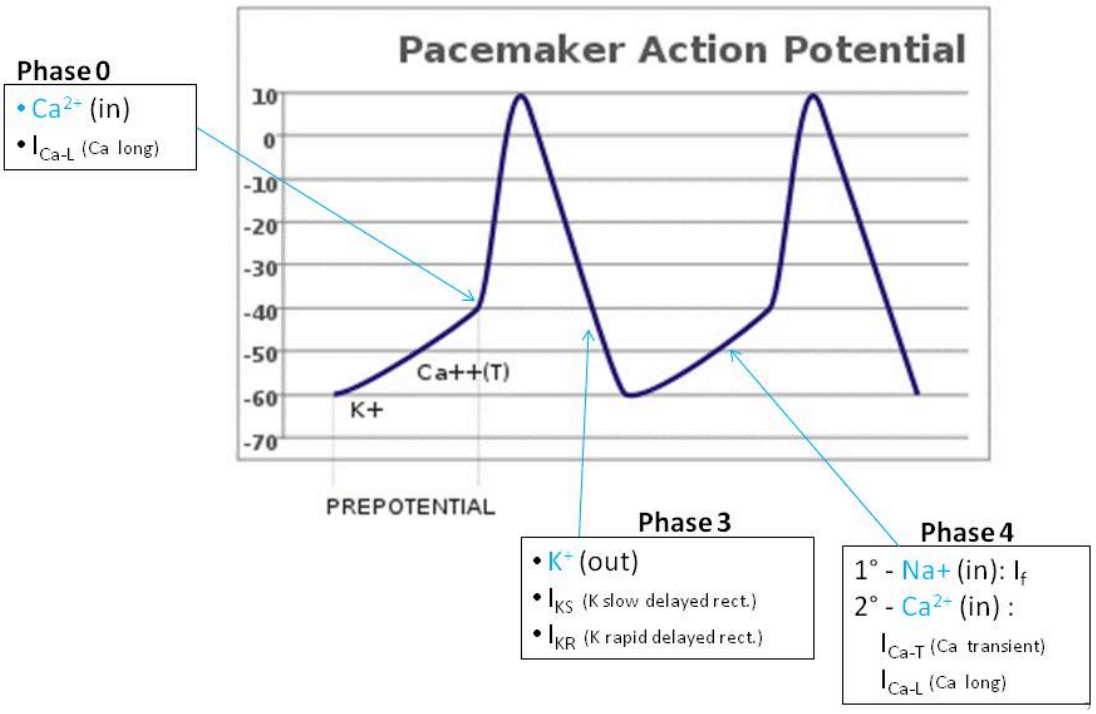
something life threatening or tragic is about to occur, despite no apparent danger

hey were named "funny" due to their distinctive activation behavior. hese channels contribute to the spontaneous depolarization during the pacemaker potential in the sinoatrial (SA) node of the heart, helping generate rhythmic heartbeat. They conduct both sodium (Na^+) and potassium (K^+) ions (though primarily sodium influx).

They are found in the SA node

Ivabradine

MECHANISM	IVabradine prolongs slow depolarization (phase "IV") by selectively inhibiting "funny" sodium channels (I_f).
CLINICAL USE	Chronic stable angina in patients who cannot take β-blockers. Chronic HFrEF.



Ivabradine: IVabradine prolongs slow depolarization (phase “IV”) by selectively inhibiting “funny” sodium channels (If).
They were named "funny" due to their distinctive activation behavior. These channels contribute to the spontaneous depolarization during the pacemaker potential in the sinoatrial (SA) node of the heart, helping generate rhythmic heartbeat. They conduct both sodium (Na^+) and potassium (K^+) ions (though primarily sodium influx).
They are found in the SA node
ENdo

Diabetes mellitus therapy

All patients with diabetes mellitus should receive education on diet, exercise, blood glucose monitoring, and complication management. Treatment differs based on the type of diabetes and glycemic control:

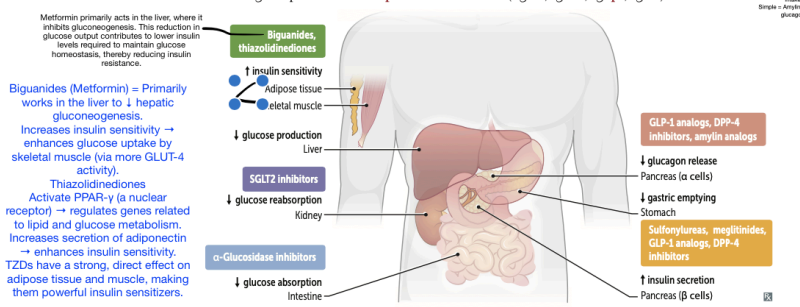
- Type 1 DM—insulin replacement
- Type 2 DM—oral agents (metformin is first line), non-insulin injectables, insulin replacement; weight loss particularly helpful in lowering blood glucose
- Gestational DM—insulin replacement if nutrition therapy and exercise alone fail

Regular (short-acting) insulin is preferred for DKA (IV), hyperkalemia (+ glucose), stress hyperglycemia.

These drugs help To normalize pancreatic function (-glits, -glins, -glips, -glifs).

Glucagon-like peptide-1 receptor agonists.
Amylin Analog
Dipeptidyl peptidase-4 (DPP-4) inhibitors
Sodium Glucose co-transporter 2 inhibitor

Amylin = Amylin and Pancreatic β-cells, alongside insulin. Slows gastric emptying, which delays the absorption of glucose from the gut. Suppresses postprandial (after-meal) glucagon secretion from α-cells. Promotes satiety, reducing food intake. Simple = Amylin decreases glucagon.

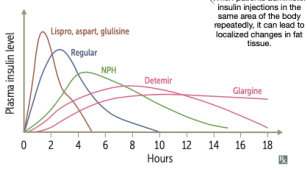


Biguanides (Metformin) = Primarily works in the liver to ↓ hepatic gluconeogenesis.
Increases insulin sensitivity → enhances glucose uptake by skeletal muscle (via more GLUT-4 activity).
Thiazolidinediones
Activate PPAR-γ (a nuclear receptor) → regulates genes related to lipid and glucose metabolism.
Increases secretion of adiponectin → enhances insulin sensitivity.
TZDs have a strong, direct effect on adipose tissue and muscle, making them powerful insulin sensitizers.

DRUG CLASS	MECHANISM	ADVERSE EFFECTS
Insulin preparations		
Rapid acting (1-hr peak): Lispro, Aspart, Glulisine (no LAG) Short acting (2–3 hr peak): regular Intermediate acting (4–10 hr peak): NPH Long acting (no real peak): detemir, glargine	Bind insulin receptor (tyrosine kinase activity) Liver: ↑ glucose storage as glycogen Muscle: ↑ glycogen, protein synthesis Fat: ↑ TG storage Cell membrane: ↑ K^+ uptake	Hypoglycemia, lipodystrophy, hypersensitivity reactions (rare), weight gain

lose fat from some parts of the body, while gaining it in others, including on organs like the liver.

Repetitive Injection Sites: When patients administer insulin injections in the same area of the body repeatedly, it can lead to localized changes in fat tissue.



neural protamine hagedorn

Insulin activates the sodium-potassium ATPase pump (Na+/K+ ATPase) in cell membranes. This pump moves sodium (Na+) out of the cell and potassium (K+) into the cell against their concentration gradients.

transmembrane protein that consists of two alpha (α) subunits and two beta (β) subunits, forming a heterotetramer. alpha subunits are responsible for insulin binding, while the beta subunits contain the intrinsic tyrosine kinase activity. When insulin binds to the alpha subunits, it triggers autophosphorylation of tyrosine residues on the beta subunits.

Insulin promotes the process of lipogenesis, which involves converting excess glucose and other energy substrates (like amino acids) into fatty acids.

Insulin decrease activity of HSL. By reducing the activity of enzymes like hormone-sensitive lipase (HSL), insulin decreases the release of fatty acids from adipose tissue into the bloodstream

Vit B12 defiency = mechanism is currently thought to be multifactorial, comprising altered intestinal motility, bacterial overgrowth, and reduced uptake of vitamin B12 within the small intestine (or a combination of these factors).

Diabetes mellitus therapy *(continued)*

DRUG CLASS	MECHANISM	ADVERSE EFFECTS
Increase insulin sensitivity		
Biguanides Metformin	Inhibit mitochondrial glycerol-3-phosphate dehydrogenase (mGPD) → inhibition of hepatic gluconeogenesis and the action of glucagon. ↑ glycolysis, peripheral glucose uptake (↑ insulin sensitivity).	GI upset, lactic acidosis (use with caution in renal insufficiency), vitamin B_{12} deficiency. Weight loss (often desired).
Thiazolidinediones "-glits" Pioglitazone, rosiglitazone	Activate PPAR-γ (a nuclear receptor) → ↑ insulin sensitivity and levels of adiponectin → regulation of glucose metabolism and fatty acid storage.	Weight gain, edema, HF, ↑ risk of fractures. Delayed onset of action (several weeks). Rosiglitazone: ↑ risk of MI, cardiovascular death.
Increase insulin secretion		
Sulfonylureas (1st gen) Chlorpropamide, tolbutamide **Sulfonylureas (2nd gen)** Glipizide, glyburide	Close K^+ channels in pancreatic B cell membrane → cell depolarizes → insulin release via ↑ Ca^{2+} influx.	Disulfiram-like reaction with first-generation sulfonylureas only (rarely used). Hypoglycemia (↑ risk in renal insufficiency), weight gain.
Meglitinides "-glins" Nateglinide, repaglinide		
Increase glucose-induced insulin secretion		

N 27

Glucose --> Glc 6 P --> F6P --> F1,6 bisphosphate --> G3P --> 1,2 BPG

Glyceraldehyde 3 Phosphate —> 1,2 Bisphosphoglycerate by the enzyme mitochondrial glycerol-3-phosphate dehydrogenase (mGPD)
Opposite of the above is glucoeogensis

Impaired renal function (as metformin is renally cleared)
Liver dysfunction (e.g., cirrhosis) The liver plays a crucial role in metabolizing lactic acid.
Conditions with increased anaerobic metabolism (e.g., sepsis, hypoperfusion/shock)

Peroxisome proliferator- activated receptor gamma

Adiponectin contributes to the control of glucose uptake by reducing gluconeogenesis and enhancing glycolysis. Adipo = Fat nectin = bind or adhere or connecting
It's a cytokine/hormone secreted by adipocytes.

Adiponectin, an adipokine secreted by adipocytes, is a well-known homeostatic factor for regulating glucose levels, lipid metabolism, and insulin sensitivity through its anti-inflammatory, anti-fibrotic, and antioxidant effects.

PPAR-γ is essential for the differentiation of preadipocytes into adipocytes. Well-differentiated adipocytes play a role in insulin sensitivity through the storage of excess fatty acids

When K^+ channels are closed, K^+ can't leave, so the inside of the cell becomes less negative. This depolarizes the β cell membrane. Depolarization triggers voltage-gated calcium channels to open. Ca^{2+} floods into the cell from outside.

Insulin Release via Calcium influx along with C peptide
U world Ghalat

Inhibition of DPP-4 results in increased levels of these peptides, which may have indirect effects on immune function, potentially leading to increased susceptibility to infections.

WEFF
Weight gain
Edema
Failure
Fractures

For SU it you thought they cause WL but they cause weight gain, For Canagliflozins you forgot orthostatic hypotension, you forgot amylin and its effect in causing decrease gastric emptying, and amylin sdeeffect, also, amylin"Amyo = starch" and In means polypeptide

Increase glucose-induced insulin secretion		
GLP-1 analogs Exenatide, liraglutide, semaglutide	↓ glucagon release, ↓ gastric emptying, ↑ glucose-dependent insulin release.	Nausea, vomiting, pancreatitis. Weight loss (often desired). ↑ satiety (often desired).
DPP-4 inhibitors "-glips" Linagliptin, saxagliptin, sitagliptin	Inhibit DPP-4 enzyme that deactivates GLP-1 → ↓ glucagon release, ↓ gastric emptying. ↑ glucose-dependent insulin release.	Respiratory and urinary infections, weight neutral. ↑ satiety (often desired).
Decrease glucose absorption		
Sodium-glucose co-transporter 2 inhibitors "-glifs" Canagliflozin, dapagliflozin, empagliflozin	Block reabsorption of glucose in proximal convoluted tubule.	Glucosuria (UTIs, vulvovaginal candidiasis), dehydration (orthostatic hypotension), weight loss. Use with caution in renal insufficiency (↓ efficacy with ↓ GFR).
α-glucosidase inhibitors Acarbose, miglitol	Inhibit intestinal brush-border α-glucosidases → delayed carbohydrate hydrolysis and glucose absorption → ↓ postprandial hyperglycemia.	GI upset, bloating. Not recommended in renal insufficiency.
Others		
Amylin analogs Pramlintide	↓ glucagon release, ↓ gastric emptying.	Hypoglycemia, nausea. ↑ satiety (often desired).

susceptibility to infections.

Glucagon-like peptide-1 analogues:

Increase glucose due to increase GLP 1 analog

In T1DM, the primary treatment is insulin therapy, since the body does not produce insulin.

Ghalat

Amylin is a peptide hormone produced by the pancreatic beta-cells and co-secreted with insulin. It plays a role in regulating blood sugar levels

Amylin acts on the central nervous system and specifically targets the brain areas involved in the regulation of food intake and gastric emptying. It inhibits gastric motility, which leads to delayed emptying of the stomach contents into the small intestine.

Increased Satiety: By promoting a feeling of fullness or satiety, amylin reduces the urge to eat, which indirectly can affect gastric emptying.

U world ghlata x 2
PTU can cross placenta and cause Hypothyroidsm in the baby

$I^- \rightarrow I_2$
I^- = 54 electrons
I_2 = 53 electrons
oxidation is loss of electrons

Organificaiton = incorporation of iodine into thyroglobulin for the production of thyroid hormone

Thionamides	Propylthiouracil, methimazole.
MECHANISM	Block thyroid peroxidase, inhibiting the oxidation of iodide as well as the organification and coupling of iodine → inhibition of thyroid hormone synthesis. PTU also blocks 5′-deiodinase → ↓ Peripheral conversion of T_4 to T_3.
CLINICAL USE	Hyperthyroidism. PTU used in Primary (first) trimester of pregnancy (due to methimazole teratogenicity); methimazole used in second and third trimesters of pregnancy (due to risk of PTU-induced hepatotoxicity). Not used to treat Graves ophthalmopathy (treated with glucocorticoids).
ADVERSE EFFECTS	Skin rash, agranulocytosis (rare), aplastic anemia, hepatotoxicity. PTU use has been associated with ANCA-positive vasculitis. Methimazole is a possible teratogen (can cause aplasia cutis).
Levothyroxine, liothyronine	
MECHANISM	Hormone replacement for T_4 (levothyroxine) or T_3 (liothyronine).
CLINICAL USE	Hypothyroidism, myxedema. May be misused for weight loss. Distinguish exogenous hyperthyroidism from endogenous hyperthyroidism by using a combination of TSH receptor antibodies, radioactive iodine uptake, and/or measurement of thyroid blood flow on ultrasound.
ADVERSE EFFECTS	Tachycardia, heat intolerance, tremors, arrhythmias. Avoid levothyroxine with antacids, bile acid resins, or ferrous sulfate (decrease absorption).
Hypothalamic/pituitary drugs	

TPO catalyzes the coupling of one MIT with one DIT to form T3, or two DITs to form T4.

Even though T4 levels may remain relatively higher, blocking the conversion to T3 results in:
Less active hormone (T3) in circulation
Reduced symptoms of hyperthyroidism (like tachycardia, tremor, anxiety, etc.)
Slower onset of clinical effects, but very useful especially in thyroid storm (where rapid reduction of T3 is urgent)
T3 is more active than t4 so we wont
less of that

Agranulocytosis is a condition in which the absolute neutrophil count (ANC) is less than 100 neutrophils per microlitre of the blood.

Hepatoxicty
Aplastic anemia
Agranulocytosis
Skin rash

HAAS

U world ghalat X2

Fever and phyrangitis shortly after initation of anthyroidmedication is suggestive of drug induced nuetropenia

Aplasia cutis congenita (ACC) is a rare malformation characterized by localized absence of the skin, mostly on the scalp, but also on any part of the body.

RAB
Radioactive iodine uptake
Antibodies
Blood flow

HATT
Heat intolerance
Arrhythmias
Yachycardia
tremor

Antacids: Medications that neutralize stomach acid can decrease the absorption of levothyroxine. Drugs such as cholestyramine and colestipol that are used to lower cholesterol levels can also impact levothyroxine absorption

V1 Receptors
Location: Primarily found in vascular smooth muscle, the liver, and some areas of the brain.
Function: V1 receptors are involved in vasoconstriction, which increases BP. When vasopressin binds to V1 receptors, it can lead to an increase in intracellular calcium levels.

You for got about liothyronine

2 time liothyronine wrong

ADVERSE EFFECTS	Tachycardia, heat intolerance, tremors, arrhythmias. Avoid levothyroxine with antacids, bile acid resins, or ferrous sulfate (decrease absorption).

Heat intolerance
Arrhythmias
Yachycardia
tremor

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Function: V1 receptors are involved in vasoconstriction, which increases BP. When vasopressin binds to V1 receptors, it can lead to an increase in intracellular calcium levels.

V2 Receptors
Location: Primarily located in the kidneys, specifically in the collecting ducts.
Function: V2 receptors are crucial for water reabsorption. When vasopressin binds to V2 receptors, it stimulates the insertion of aquaporin-2 water channels into the apical membrane of kidney collecting duct cells, leading to increased water reabsorption.

Hypothalamic/pituitary drugs

DRUG	CLINICAL USE
Conivaptan, tolvaptan	ADH antagonists SIADH (block action of ADH at V_2-receptor)
Demeclocycline	ADH antagonist, a tetracycline SIADH (interferes with ADH signaling)
Desmopressin	ADH analog Central DI, von Willebrand disease, sleep enuresis, hemophilia A
GH	GH deficiency, Turner syndrome
Oxytocin	Induction of labor (stimulates uterine contractions), control uterine hemorrhage
Somatostatin (octreotide)	Acromegaly, carcinoid syndrome, gastrinoma, glucagonoma, esophageal varices

CS VA

Central DI
Sleep enuresis

Von Willibrand disease
A Hemophili A

VAGG C

Varices
Acromegaly
Gastrinoma
Glucogagoma

Carcinoid

Fludrocortisone

MECHANISM	Synthetic analog of aldosterone with glucocorticoid effects. Fluidrocortisone retains fluid.
CLINICAL USE	Mineralocorticoid replacement in 1° adrenal insufficiency.
ADVERSE EFFECTS	Similar to glucocorticoids; also edema, exacerbation of heart failure, hyperpigmentation.

Heart Failure
Hyperpigmentation
Edema

HHE

Increased Melanocyte Activity: Corticosteroids can stimulate melanocytes, the cells responsible for producing melanin (the pigment in skin). Increased activity of these cells can lead to hyperpigmentation.

Desmopressin (DDAVP) is a synthetic analog of vasopressin (antidiuretic hormone, ADH) with selective activity on V2 receptors.
Central DI --> Acts on renal V2 receptors → increases water reabsorption in the collecting ducts → reduces polyuria and polydipsia.
VWD --> Desmopressin stimulates release of von Willebrand factor (vWF) and factor VIII from endothelial cells.
Enuresis --> : Reduces nocturnal urine production by enhancing water reabsorption.
HemophiliA: Increases factor VIII levels by stimulating its release from endothelial stores.

Cinacalcet

It works as a calcimimetic agent, which means it increases the sensitivity of the calcium-sensing receptors on the parathyroid glands to extracellular calcium, thereby reducing the secretion of parathyroid hormone (PTH).

MECHANISM	Sensitizes calcium-sensing receptor (CaSR) in parathyroid gland to circulating Ca^{2+} → ↓ PTH. Pronounce "Senacalcet."
CLINICAL USE	2° hyperparathyroidism in patients with CKD receiving hemodialysis, hypercalcemia in 1° hyperparathyroidism (if parathyroidectomy fails), or in parathyroid carcinoma.
ADVERSE EFFECTS	Hypocalcemia.

By controlling PTH levels, cinacalcet can help mitigate complications related to secondary hyperparathyroidism, such as bone disease (renal osteodystrophy) and cardiovascular problems associated with hypercalcemia and hyperphosphatemia.

Sevelamer

MECHANISM	Nonabsorbable phosphate binder that prevents phosphate absorption from the GI tract.
CLINICAL USE	Hyperphosphatemia in CKD.
ADVERSE EFFECTS	Hypophosphatemia, GI upset.

Patrimore
Sodium Polystryene sulfonate
Zirconimum Cyclosiclicate

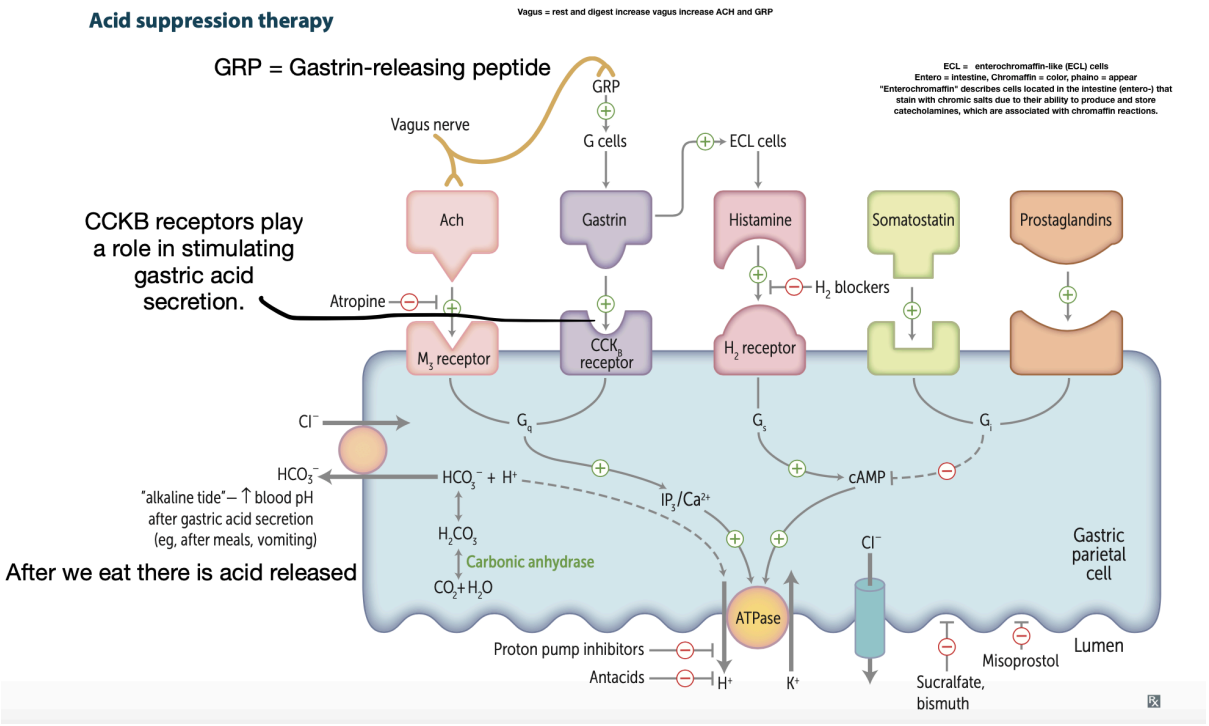
PSZ

Cation exchange resins

Patiromer, sodium polystyrene sulfonate, zirconium cyclosilicate.

MECHANISM	Bind K^+ in colon in exchange for other cations (eg, Na^+, Ca^{2+}) → K^+ excreted in feces.
CLINICAL USE	Hyperkalemia.
ADVERSE EFFECTS	Hypokalemia, GI upset.

GIT



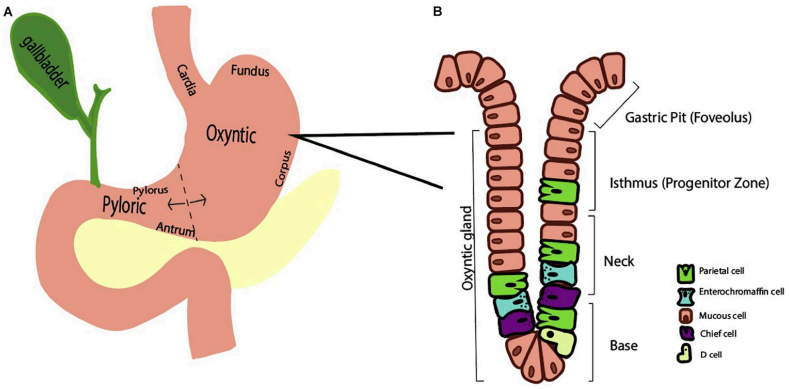
H2 Blockers u forgot gastritis, PPI you forgot AIN, Ca Carbonate (milkaliki)

H_2-blockers	Cimetidine, famotidine, nizatidine.	Take H_2 blockers before you dine. Think "table for 2" to remember H_2.
MECHANISM	Reversible block of histamine H_2-receptors → ↓ H^+ secretion by parietal cells.	RUG Reflux Ulcer Gastritis
CLINICAL USE	Peptic ulcer, gastritis, mild esophageal reflux.	PIG = Prolactin release Impotanec Gynecomastia
ADVERSE EFFECTS	Cimetidine is a potent inhibitor of cytochrome P-450 (multiple drug interactions); it also has antiandrogenic effects (prolactin release, gynecomastia, impotence, ↓ libido in males); can cross blood-brain barrier (confusion, dizziness, headaches) and placenta. Cimetidine ↓ renal excretion of creatinine. Other H_2 blockers are relatively free of these effects.	Cimetidine can produce antiandrogenic effects by binding to the androgen receptors and blocking the function of androgen receptors. Renal exercise is decreation inhibitor of Cytochrome p-450 BBB (confusion, dizziness, headache) and placenta
		Antiandrogenic (prolactin release, gynecomastia, impotence, decrease libido in males)
Proton pump inhibitors	Omeprazole, lansoprazole, esomeprazole, pantoprazole, dexlansoprazole.	A RIB RUGZ HU Reflux Ulcer Gastritis ZE
MECHANISM	Irreversibly inhibit H^+/K^+-ATPase in stomach parietal cells.	
CLINICAL USE	Peptic ulcer, gastritis, esophageal reflux, Zollinger-Ellison syndrome, component of therapy for *H pylori*, stress ulcer prophylaxis.	Stress, in combination with other factors such as mechanical ventilation, coagulopathy, or major surgery, can increase the risk of gastric mucosal injury. Reducing gastric acidity can help prevent the formation of stress ulcers. H Pylori Ulcer prophylaxis
ADVERSE EFFECTS	↑ risk of *C difficile* infection, pneumonia, acute interstitial nephritis, Vitamin B_{12} malabsorption; ↓ serum Mg^{2+}/Ca^{2+} absorption (potentially leading to increased fracture risk in older adults).	Metallic tast in the MBE sawall ghalt ABCC AIN B12 malabsorption C Diff
Antacids	Can affect absorption, bioavailability, or urinary excretion of other drugs by altering gastric and urinary pH or by delaying gastric emptying. All can cause hypokalemia.	Ca absorption decrease
Aluminum hydroxide	Constipation, Hypophosphatemia, Osteodystrophy, Proximal muscle weakness, Seizures	Aluminimum amount of feces CHOPS
Calcium carbonate	Hypercalcemia (milk-alkali syndrome), rebound acid ↑	Can chelate and ↓ effectiveness of other drugs (eg, tetracycline)

When aluminum levels become elevated, it can lead to aluminum toxicity, which affects several systems, including the nervous and muscular systems.

Parietal cells are 80% of them are found in the stomach, mainly in the stomach body and fundus.

Magnesium = Diarrhea, Bismuth compounds, such as bismuth oxychloride or bismuth salts, tend to be more soluble in acidic solutions.



Magnesium hydroxide	Diarrhea, hyporeflexia, hypotension, cardiac arrest	Mg^{2+} = Must go 2 the bathroom

Magnesium hydroxide is an osmotic laxative (e.g., in Milk of Magnesia). It draws water into the intestinal lumen, softening stool and stimulating bowel movements.

Hypermagnesemia depresses neuromuscular and cardiac function:

Diaahrea
Hypotesion
Hyporeflexion

DiarHHea

Bismuth, sucralfate	
MECHANISM	Bind to ulcer base, providing physical protection and allowing HCO_3^- secretion to reestablish pH gradient in the mucous layer. Sucralfate requires acidic environment, not given with PPIs/H_2 blockers.
CLINICAL USE	↑ ulcer healing, travelers' diarrhea (bismuth). Bismuth also used in quadruple therapy for *H pylori*.

Bismuth has some antimicrobial properties that can help inhibit the growth of certain gastrointestinal pathogens, such as bacteria and viruses that are commonly associated with traveler's diarrhea.

Healing of the ulcer
Traveler's diarrhea

Decrease Acid
Lemon in the trash
Increase Mucus =Mucus like seeweed

Misoprostol	
MECHANISM	PGE_1 analog. ↑ production and secretion of gastric mucous barrier, ↓ acid production.
CLINICAL USE	Prevention of NSAID-induced peptic ulcers (NSAIDs block PGE_1 production). Also used off-label for induction of labor (ripens cervix).
ADVERSE EFFECTS	Diarrhea. Contraindicated in patients of childbearing potential (abortifacient).

By stimulating uterine contractions, misoprostol can help facilitate cervical ripening and promote the progression of labor.

Octreotide	
MECHANISM	Long-acting somatostatin analog; inhibits secretion of various splanchnic vasodilatory hormones.
CLINICAL USE	Acute variceal bleeds, acromegaly, VIPoma, carcinoid tumors.
ADVERSE EFFECTS	Nausea, cramps, steatorrhea. ↑ risk of cholelithiasis due to CCK inhibition.

VIPOMA
Acromegaly
Acute Varicela Bleeds
Carcinoids tumors

VAAC

Inhibition of Cholecystokinin (CCK): CCK stimulates the contraction of the gallbladder and promotes the release of bile from the gallbladder into the intestines. When octreotide is administered, it inhibits the secretion of CCK, leading to reduced gallbladder contraction. This decreased contraction means that bile is not expelled as effectively from the gallbladder.

I cells (duodenum, jejunum)
pancreatic secretion
gallbladder contraction
gastric emptying sphincter of Oddi relaxation

Sulfasalazine	
MECHANISM	A combination of sulfapyridine (antibacterial) and 5-aminosalicylic acid (anti-inflammatory). Activated by colonic bacteria.
CLINICAL USE	Ulcerative colitis, Crohn disease (colitis component).
ADVERSE EFFECTS	Malaise, nausea, sulfonamide toxicity, reversible oligospermia.

MONS

Malasia
Oligospermia
nausea
Sulfanomide toxicity

Diphenoxylate is Mu Opiod Agonist that dose cross the

While ondansetron mainly blocks 5-HT3 receptors, it influences serotonergic pathways. Serotonin syndrome occurs due to excessive serotonergic activity in the central nervous system, often from combined or excessive serotonergic agents.
Octeroride → carcinoid tumors

Loperamide

Diphenoxylate is Mu Opiod Agonist that dose cross the BBB is combined with atropine to prevent abuse.

MECHANISM	Agonist at μ-opioid receptors; slows gut motility. Poor CNS penetration (low addictive potential).
CLINICAL USE	Diarrhea.
ADVERSE EFFECTS	Constipation, nausea.

Antiemetics

All act centrally in chemoreceptor trigger zone of area postrema.

The area postrema is a small region of the brain located in the medulla oblongata, part of the brainstem.

HCQS
HeadQuaterS
~~Headchae~~
Constirpation
QT prolongation
Serotonin syndrome

DRUG	MECHANISM	CLINICAL USE	ADVERSE EFFECTS
Ondansetron, granisetron	5-HT_3-receptor antagonists Also act peripherally (↓ vagal stimulation)	Nausea and vomiting after chemotherapy, radiotherapy, or surgery	Headache, constipation, QT interval prolongation, serotonin syndrome
Prochlorperazine, metoclopramide	D_2-receptor antagonists Metoclopramide also causes ↑ gastric emptying and ↑ LES tone	Nausea and vomiting Metoclopramide is also used in gastroparesis (eg, diabetic), persistent GERD	Extrapyramidal symptoms, hyperprolactinemia, anxiety, drowsiness, restlessness, depression, GI distress
Aprepitant, fosaprepitant	NK_1 (neurokinin-1) receptor antagonists NK_1 receptor = substance P receptor	Chemotherapy-induced nausea and vomiting	Fatigue, GI distress

Antipsychotics block D_2 receptors (they don't stimulate them). So even though D_2 receptors are inhibitory, blocking them prevents dopamine from exerting its effect.

HARDDD

Hyperprolactinemia
Anxiety
Restlessness
Drowsiness
Depression
Distress

Neuro = Nerve and Kinin = Bioactive peptide

neurokinin A (NKA) and substance P, which are neuropeptides involved in various physiological processes, including pain modulation, stress response, and inflammation.

Orlistat

MECHANISM	Inhibits gastric and pancreatic lipase → ↓ breakdown and absorption of dietary fats. Taken with fat-containing meals.
CLINICAL USE	Weight loss.
ADVERSE EFFECTS	Abdominal pain, flatulence, bowel urgency/frequent bowel movements, steatorrhea; ↓ absorption of fat-soluble vitamins.

Flatulence

BASS F

Bowel urgency/ freq bowemoments
Abdominal pain
Absorption of Fat Soluble vitamin
Steatorhea

Both the stomach and pancreas produce lipase, but they play different roles.
Gastric Lipase
Produced by: Chief cells of the stomach (same ones that make pepsinogen).
Function: Begins digestion of fats in the stomach.
Pancreatic Lipase
Produced by: Acinar cells of the pancreas
Function: Does the majority of fat digestion in the small intestine

Anticonstipation drugs

They contain soluble or insoluble fiber that absorbs water, swelling and forming a bulky mass.

having a thick, sticky consistency between solid and liquid; having a high viscosity.

DRUG	MECHANISM	ADVERSE EFFECTS
Bulk-forming laxatives Methylcellulose, psyllium	Soluble fibers that draw water into gut lumen, forming viscous liquid that promotes peristalsis	Bloating
Osmotic laxatives Lactulose, magnesium citrate, magnesium hydroxide, polyethylene glycol	Provide osmotic load to draw water into GI lumen Lactulose also treats hepatic encephalopathy: gut microbiota degrades lactulose into metabolites (lactic acid, acetic acid) that promote nitrogen excretion as NH_4^+ by trapping it in colon	Diarrhea, dehydration; may be misused by patients with bulimia
Stimulant laxatives Bisacodyl, senna	Enteric nerve stimulation → colonic contraction	Diarrhea
Emollient laxatives Docusate	Surfactants that ↓ stool surface tension, promoting water entry into stool	Diarrhea
Lubiprostone	Chloride channel activator → ↑ intestinal fluid secretion	Diarrhea, nausea

MMPL

Lactulose increase lactic acid increase amount of NH_4^+
NH_4^+ is a positively charged, hydrophilic ion. Charged molecules generally have difficulty crossing the lipid bilayer of intestinal epithelial cell membranes, which favor the passive diffusion of non-polar, uncharged molecules.

Melanosis coli = brown pigmentation of the colon

having the quality of softening or soothing the skin.

Blease

LOSE

Emollient = having the quality of softening or soothing the skin.

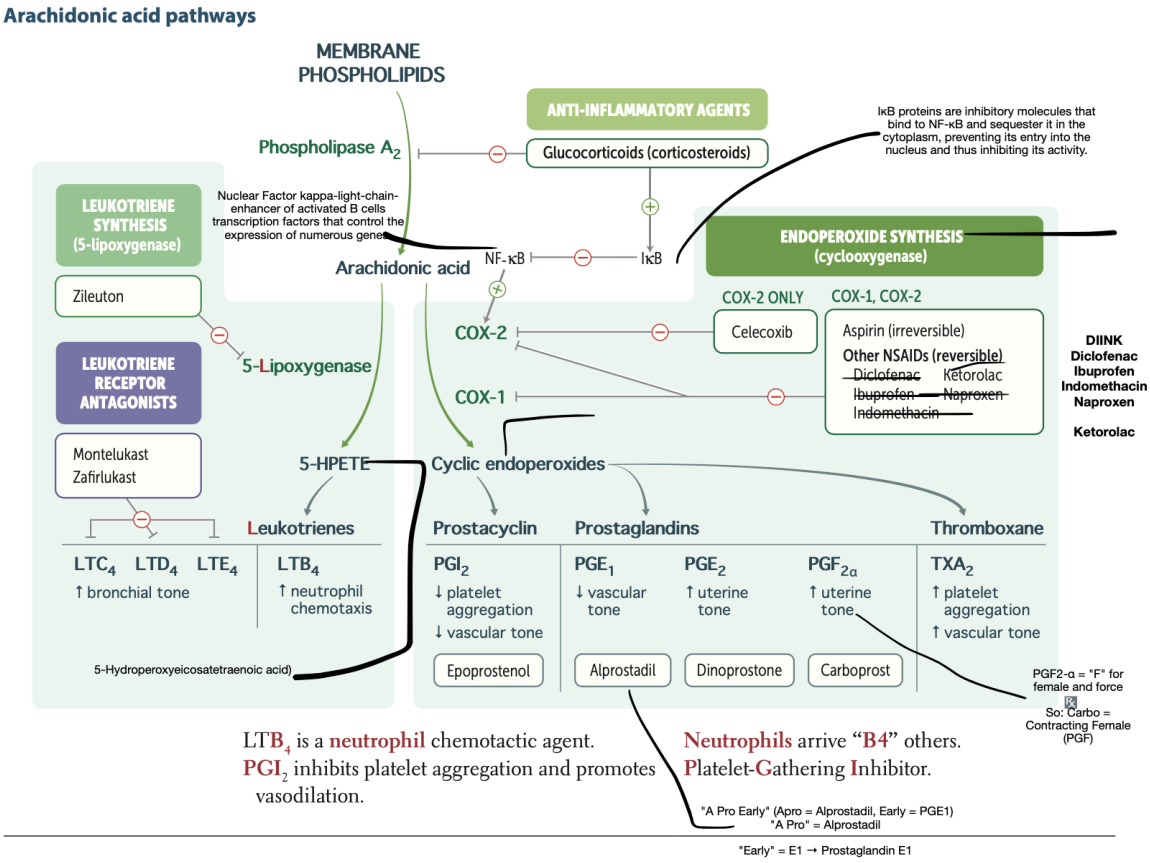
methylnaltroxone = peripherally acting mu opiod recptor

Mehlman
What is the MOA of lactulose ?

Lactulose increase {{c1::lactic acid}} increase amount of {{c2::NH4+}}
NH_4^+ is a positively charged, hydrophilic ion. Charged molecules generally have difficulty crossing the lipid bilayer of intestinal epithelial cell membranes, which favor the passive diffusion of non-polar, uncharged molecules.

Yours = Lactulose --> decrease conversion of NH3 into NH4+

Docusate MOA of decrease surface tension
MSK

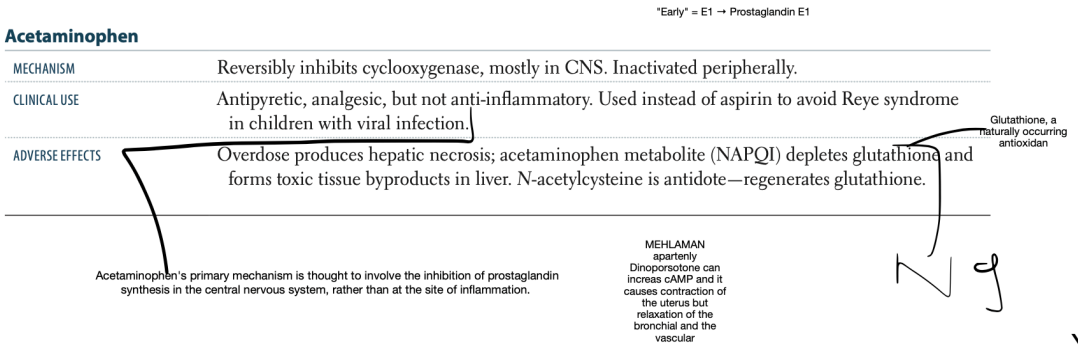


"leuko-" meaning white, referring to leukocytes, and "triene" meaning three conjugated double bonds.
Function. Lipase is an enzyme that breaks down triglycerides into free fatty acids and glycerol by catalyzing the hydrolysis of the ester bonds in triglycerides.
YOU FORGOT ABOUT TBXA2 ONLY produced by COX 1 !!!!!!

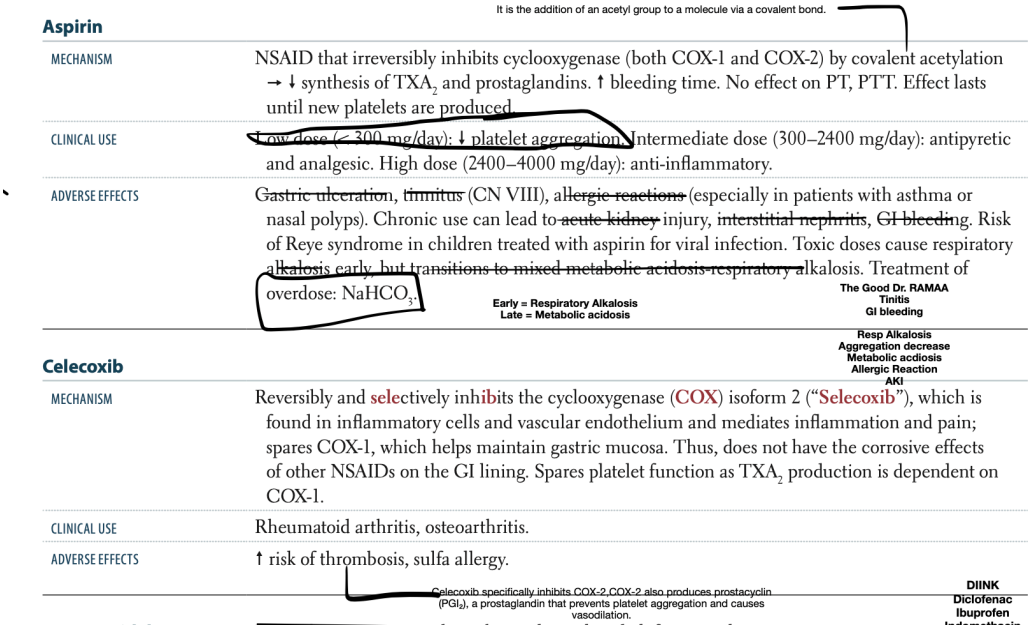
PGE1 (and PGE2) & PGI2 (prostacyclin) → vasodilation

Gs protein-coupled → ↑ adenylate cyclase → ↑ cAMP → smooth muscle relaxation → vasodilation

PGF2α s Gq protein-coupled → activates phospholipase C → ↑ IP3/DAG → ↑ intracellular Ca^{2+} → smooth muscle contraction → uterine contraction



YOU FORGOT AOUT THEadverse effects of aspriinthat at i**ntermediate dose they cause antipyretic and analgesic**



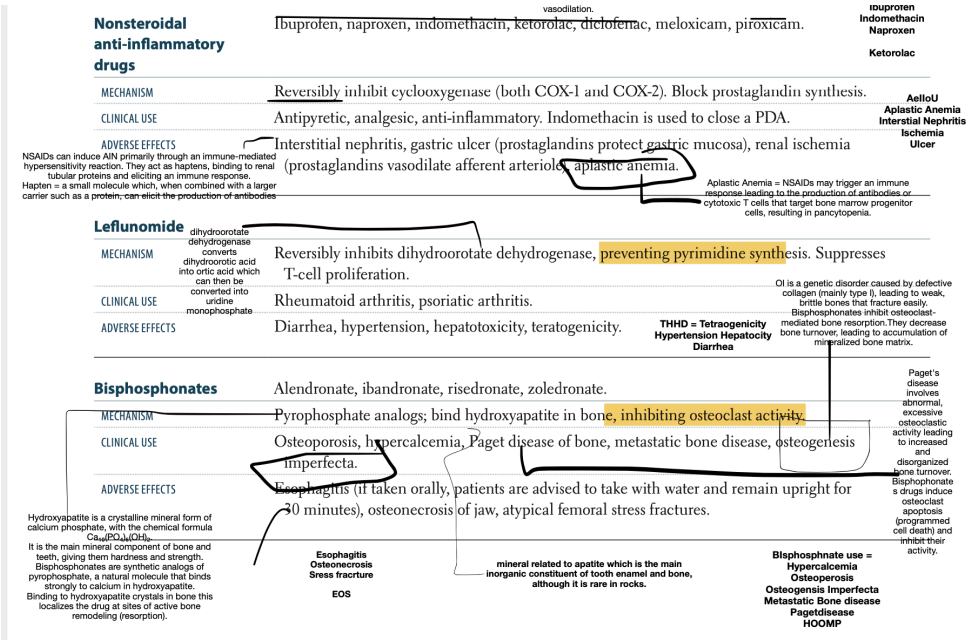
Aspirin

MECHANISM	NSAID that irreversibly inhibits cyclooxygenase (both COX-1 and COX-2) by covalent acetylation → ↓ synthesis of TXA_2 and prostaglandins. ↑ bleeding time. No effect on PT, PTT. Effect lasts until new platelets are produced.
CLINICAL USE	Low dose (< 300 mg/day): ↓ platelet aggregation. Intermediate dose (300–2400 mg/day): antipyretic and analgesic. High dose (2400–4000 mg/day): anti-inflammatory.
ADVERSE EFFECTS	Gastric ulceration, tinnitus (CN VIII), allergic reactions (especially in patients with asthma or nasal polyps). Chronic use can lead to acute kidney injury, interstitial nephritis, GI bleeding. Risk of Reye syndrome in children treated with aspirin for viral infection. Toxic doses cause respiratory alkalosis early, but transitions to mixed metabolic acidosis-respiratory alkalosis. Treatment of overdose: $NaHCO_3$.

Celecoxib

MECHANISM	Reversibly and selectively inhibits the cyclooxygenase (COX) isoform 2 ("Selecoxib"), which is found in inflammatory cells and vascular endothelium and mediates inflammation and pain; spares COX-1, which helps maintain gastric mucosa. Thus, does not have the corrosive effects of other NSAIDs on the GI lining. Spares platelet function as TXA_2 production is dependent on COX-1.
CLINICAL USE	Rheumatoid arthritis, osteoarthritis.
ADVERSE EFFECTS	↑ risk of thrombosis, sulfa allergy.

You forgot the other adverse effects of NSAID like AIN and renal ischemia and aplstic anemia and you for gor the enzyme that inhibits dihydroorate dehydrogenease For Bipshophate you forgot metstatic bone disease.



Nonsteroidal anti-inflammatory drugs

Ibuprofen, naproxen, indomethacin, ketorolac, diclofenac, meloxicam, piroxicam.

MECHANISM	Reversibly inhibit cyclooxygenase (both COX-1 and COX-2). Block prostaglandin synthesis.
CLINICAL USE	Antipyretic, analgesic, anti-inflammatory. Indomethacin is used to close a PDA.
ADVERSE EFFECTS	Interstitial nephritis, gastric ulcer (prostaglandins protect gastric mucosa), renal ischemia (prostaglandins vasodilate afferent arteriole), aplastic anemia.

Leflunomide

MECHANISM	Reversibly inhibits dihydroorotate dehydrogenase, preventing pyrimidine synthesis. Suppresses T-cell proliferation.
CLINICAL USE	Rheumatoid arthritis, psoriatic arthritis.
ADVERSE EFFECTS	Diarrhea, hypertension, hepatotoxicity, teratogenicity.

Bisphosphonates

Alendronate, ibandronate, risedronate, zoledronate.

MECHANISM	Pyrophosphate analogs; bind hydroxyapatite in bone, inhibiting osteoclast activity.
CLINICAL USE	Osteoporosis, hypercalcemia, Paget disease of bone, metastatic bone disease, osteogenesis imperfecta.
ADVERSE EFFECTS	Esophagitis (if taken orally, patients are advised to take with water and remain upright for 30 minutes), osteonecrosis of jaw, atypical femoral stress fractures.

Forgot metastatic bone disease

g), tumor cells in the bone microenvironment release factors (e.g., PTHrP, cytokines) that:

➡ Stimulate osteoclast activity → increase bone resorptio

Which agen prevents the releases of autacoid?

cromolyn sodium

hormones, are biologically active substances produced locally in the body that have short-lived, localized effects.

Yours = Inhaled ipratropium --> No use for asthma

These drugs block muscarinic (M3) receptors → cause bronchodilation by inhibiting vagally mediated bronchoconstriction.

asthma, the primary problem is airway inflammation and bronchial hyperresponsiveness — not just bronchospasm due to cholinergic tone.

✅ The mainstay of asthma therapy focuses on:

Reducing inflammation → inhaled corticosteroids (ICS)

Relaxing airway smooth muscle → β2 agonists (SABA/LABA)

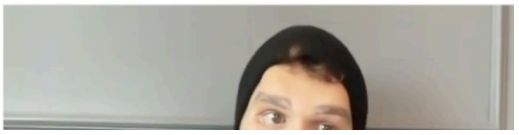
HY USMLE Q #1008 – Pulmonary

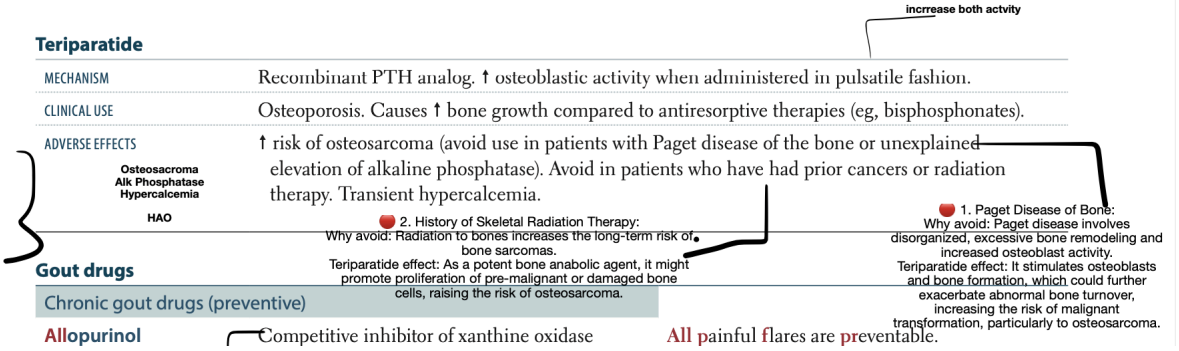
by MEHLMANMEDICAL

A 21-year-old man with history of asthma comes to emergency 2 hours after acute-onset wheezing that did not respond to albuterol. One hour following administration of nebulized albuterol and intravenous methylprednisolone, his lungs are clear to auscultation and FEV1 has increased from 30% to 95% of predicted. Which of the following is the most effective pharmacologic agent to prevent asthma recurrence?

- ○ Inhaled cromolyn sodium
- ○ Inhaled ipratropium
- ○ Oral prednisone
- ○ Oral theophylline
- ○ Oral zileuton

EDIT





TUBULAR SECRETION → Diuretics or low dose salicylates or tubular reabsorption probenecid or high dose salicylates Pleboticuase is a uricase

Gout drugs

Teriparatide effect: As a potent bone anabolic agent, it might promote proliferation of pre-malignant or damaged bone cells, raising the risk of osteosarcoma.

Teriparatide effect: It stimulates osteoblasts and bone formation, which could further exacerbate abnormal bone turnover, increasing the risk of malignant transformation, particularly to osteosarcoma.

All painful flares are preventable.

Chronic gout drugs (preventive)

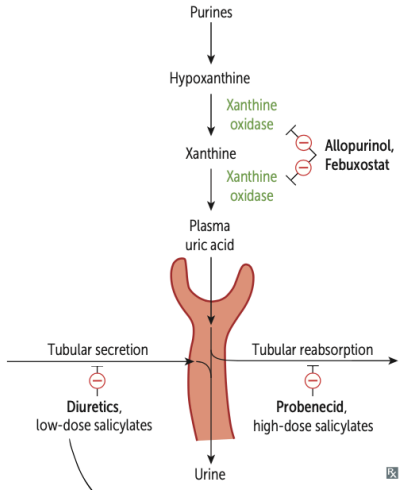
Allopurinol	Competitive inhibitor of xanthine oxidase → ↓ conversion of hypoxanthine and xanthine to urate. Also used in lymphoma and leukemia to prevent tumor lysis–associated urate nephropathy. ↑ concentrations of xanthine oxidase active metabolites, azathioprine, and 6-MP.
Pegloticase	Recombinant uricase catalyzing uric acid to allantoin (a more water-soluble product).
Febuxostat	Inhibits xanthine oxidase. Think, "febu-xo-stat makes Xanthine Oxidase static."
Probenecid	Inhibits reabsorption of uric acid in proximal convoluted tubule (also inhibits secretion of penicillin). Can precipitate uric acid calculi or lead to sulfa allergy.

Competitive inhibition occurs when a substance (here, allopurinol) competes with the substrate (xanthine) for binding to the active site of the enzyme.

Azathioprine
6 MP
A6

Pegloticase
Probeniceid
Allopurinol
Fedboxtstate
PPAF

Probenecid inhibits the reabsorption of uric acid in the proximal tubules of the kidneys, increasing uric acid excretion in urine.



Acute gout drugs

NSAIDs	Any NSAID. Use salicylates with caution (may decrease uric acid excretion, particularly at low doses).
Glucocorticoids	Oral, intra-articular, or parenteral.
Colchicine	Binds and stabilizes tubulin to inhibit microtubule polymerization, impairing neutrophil chemotaxis and degranulation. Acute and prophylactic value. GI, neuromyopathic adverse effects. Can also cause myelosuppression, nephrotoxicity.

IPO = IA, Parental Oral

Low dose salicytase prevent secretion of urice acid

GI = Abdominal pain and nausea with colchiene

Did not mention the microtubule they mentioed the cytoskeleton teek hai

Colchicine = Microtuble polymerization Neutrophil Chemotaxis degranulaiton

MND

GI
Neuromyopathic
Nephrotoxicty
Myelosuppresion

GNNM

Chemotaxis
Degranulation
Microtubule polymerization

CDM

TNF-α inhibitors

DRUG	MECHANISM	CLINICAL USE	ADVERSE EFFECTS
Etanercept	Fusion protein (decoy receptor for TNF-α + IgG_1 Fc), produced by recombinant DNA. Etanercept intercepts TNF.	Rheumatoid arthritis, psoriasis, ankylosing spondylitis.	Predisposition to infection, including reactivation of latent TB, since TNF is important in granuloma formation and stabilization. Can also lead to drug-induced lupus.
Infliximab, adalimumab, certolizumab, golimumab	Anti-TNF-α monoclonal antibody.	Inflammatory bowel disease, rheumatoid arthritis, ankylosing spondylitis, psoriasis.	

RAP
Rheumatoid Arthtitis
Ankylosing Spondylitis
Psoarisis

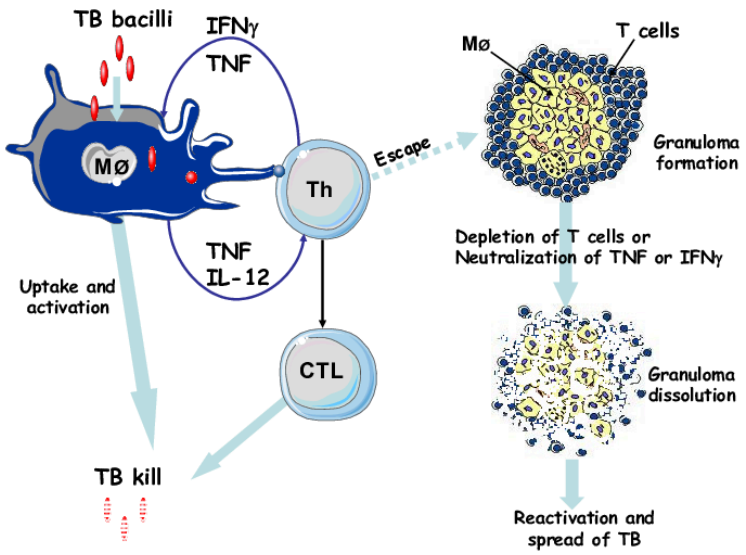
RAP I
Rheumatoid Arthtitis
Ankylosing Spondylitis
Psoarisis

IBD

Imiquimod

MECHANISM	Binds toll-like receptor 7 (TLR-7) of macrophages, monocytes, and dendritic cells to activate them → topical antitumor immune response modifier.
CLINICAL USE	Anogenital warts, actinic keratosis.
ADVERSE EFFECTS	Itching, burning pain at site of application, rashes.

RIB
Rashies
Itching
Burning pain



TNF-alpha is a key mediator in the inflammatory cascade, activating cells, recruiting other immune cells, and triggering the release of other inflammatory molecules.

Hematology

Hydroxyurea → 2 times wrong mehlman DoC 1

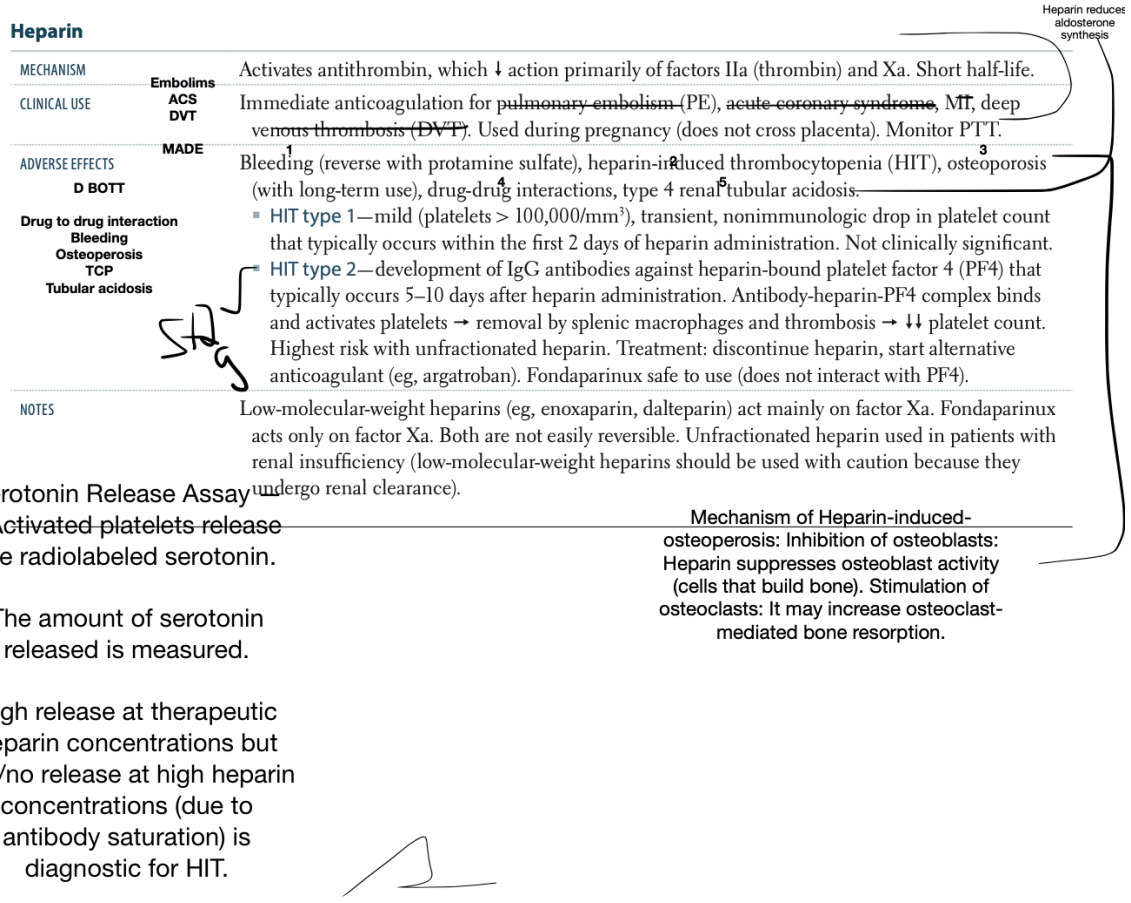
Bortezomib = Presentation of antigens to CD8+ T lymphocytes

All nucleated cells present intracellular peptides (including viral or tumor antigens) on MHC Class I molecules. These peptides are degraded by proteasome --> peptides are transported to the ER by TAP loaded onto MHC I --> transported to cell surfaces --> recognized by CD8+ T cells via TCR

Bortezomib = proteasome inhibitor --> Inhibiting the proteasome → decreased generation of peptides for MHC I presentation --> reduced activation of CD8+ T cell --> less MHC I presentation -->MORE apoptosis

In the human body, mature red blood cells and blood platelets are not nucleated, meaning they lack a nucleus. Prokaryotic cells, such as bacteria, also lack a nucleus. Additionally, cornified cells in the skin, hair, and nails are not nucleated.

HIT type 1 > 100, 000 platelets



Heparin

MECHANISM	Activates antithrombin, which ↓ action primarily of factors IIa (thrombin) and Xa. Short half-life.
CLINICAL USE	Immediate anticoagulation for ~~pulmonary embolism~~ (PE), ~~acute coronary syndrome~~, ~~MI~~, deep ~~venous thrombosis (DVT)~~. Used during pregnancy (does not cross placenta). Monitor PTT.
ADVERSE EFFECTS	Bleeding (reverse with protamine sulfate), heparin-induced thrombocytopenia (HIT), osteoporosis (with long-term use), drug-drug interactions, type 4 renal tubular acidosis. ▪ HIT type 1—mild (platelets > 100,000/mm³), transient, nonimmunologic drop in platelet count that typically occurs within the first 2 days of heparin administration. Not clinically significant. ▪ HIT type 2—development of IgG antibodies against heparin-bound platelet factor 4 (PF4) that typically occurs 5–10 days after heparin administration. Antibody-heparin-PF4 complex binds and activates platelets → removal by splenic macrophages and thrombosis → ↓↓ platelet count. Highest risk with unfractionated heparin. Treatment: discontinue heparin, start alternative anticoagulant (eg, argatroban). Fondaparinux safe to use (does not interact with PF4).
NOTES	Low-molecular-weight heparins (eg, enoxaparin, dalteparin) act mainly on factor Xa. Fondaparinux acts only on factor Xa. Both are not easily reversible. Unfractionated heparin used in patients with renal insufficiency (low-molecular-weight heparins should be used with caution because they undergo renal clearance).

Embolims
ACS
DVT

MADE

D BOTT

Drug to drug interaction
Bleeding
Osteoperosis
TCP
Tubular acidosis

1 2 3 4 5

Heparin reduces aldosterone synthesis

Mechanism of Heparin-induced-osteoperosis: Inhibition of osteoblasts: Heparin suppresses osteoblast activity (cells that build bone). Stimulation of osteoclasts: It may increase osteoclast-mediated bone resorption.

Serotonin Release Assay
>~~Activated platelets release~~ the radiolabeled serotonin.

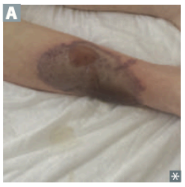
The amount of serotonin released is measured.

High release at therapeutic heparin concentrations but low/no release at high heparin concentrations (due to antibody saturation) is diagnostic for HIT.

Vitamin K epoxide reductase (VKOR) converts vitamin K epoxide back into vitamin K (quinone), which is then reduced to vitamin K hydroquinone — the active, reduced form required for γ-glutamyl carboxylase to function.

Warfarin

MECHANISM	Inhibits vitamin K epoxide reductase by competing with vitamin K → inhibition of vitamin K–dependent γ-carboxylation of clotting factors II, VII, IX, and X and proteins C and S. Metabolism affected by polymorphisms in the gene for vitamin K epoxide reductase complex (*VKORC1*). In laboratory assay, has effect on extrinsic pathway and ↑ PT. Long half-life. "The ex-PresidenT went to war(farin)."
CLINICAL USE	Chronic anticoagulation (eg, venous thromboembolism prophylaxis and prevention of stroke in atrial fibrillation). Not used in pregnant patients (because warfarin, unlike heparin, crosses placenta). Monitor PT/INR.
ADVERSE EFFECTS	Bleeding, teratogenic effects, skin/tissue necrosis A, drug-drug interactions (metabolized by cytochrome P-450 [CYP2C9]). Initial risk of hypercoagulation: protein C has shorter half-life than factors II and X. Existing protein C depletes before existing factors II and X deplete, and before warfarin can reduce factors II and X production → hypercoagulation. Skin/tissue necrosis within first few days of large doses believed to be due to small vessel microthrombosis. Heparin "bridging": heparin frequently used when starting warfarin. Heparin's activation of antithrombin enables anticoagulation during initial, transient hypercoagulable state caused by warfarin. Initial heparin therapy reduces risk of recurrent venous thromboembolism and skin/tissue necrosis. For reversal of warfarin, give vitamin K. For rapid reversal, give FFP or PCC.



Heparin vs warfarin

	Heparin	Warfarin
ROUTE OF ADMINISTRATION	Parenteral (IV, SC)	Oral
SITE OF ACTION	Blood	Liver
ONSET OF ACTION	Rapid (seconds)	Slow, limited by half-lives of normal clotting factors
DURATION OF ACTION	Hours	Days
MONITORING	PTT (intrinsic pathway)	PT/INR (extrinsic pathway)
CROSSES PLACENTA	No	Yes (teratogenic)

Direct coagulation factor inhibitors

DRUG	MECHANISM	CLINICAL USE	ADVERSE EFFECTS
Bivalirudin, argatroban, dabigatran	Directly inhibit thrombin (factor IIa)	Venous thromboembolism, atrial fibrillation. Can be used in HIT, when heparin is BAD for the patient	Bleeding (reverse dabigatran with idarucizumab) Dabigatran is the only oral agent in class Do not require lab monitoring
Apixaban, edoxaban, rivaroxaban	Directly inhibit factor Xa	Treatment and prophylaxis for DVT and PE; stroke prophylaxis in patients with atrial fibrillation	Bleeding (reverse with andexanet alfa) Oral agents that do not usually require lab monitoring

Embolism
AFIB
HIT
EAH

Embolism
AFIB
DVT
EA D

Anticoagulation reversal

ANTICOAGULANT	REVERSAL AGENT	NOTES
Heparin	Protamine sulfate	⊕ charged peptide that binds ⊖ charged heparin
Warfarin	Vitamin K (slow) +/– FFP or PCC (rapid)	
Dabigatran	Idarucizumab	Monoclonal antibody Fab fragments
Direct factor Xa inhibitors	Andexanet alfa	Recombinant modified factor Xa (inactive)

Humanized monoclonal antibody fragment (Fab)
Target: Binds specifically to dabigatran and its active metabolites

Tinnitus
Allergy
Renal Injury
Ulcer
U RAT

Stroke
ACS
COronary stenting
SAC =

Antiplatelets

All work by ↓ platelet aggregation.

DRUG	MECHANISM	CLINICAL USE	ADVERSE EFFECTS
Aspirin	Irreversibly blocks COX → ↓ TXA_2 release	Acute coronary syndrome; coronary stenting. ↓ incidence or recurrence of thrombotic stroke	Gastric ulcers, tinnitus, allergic reactions, renal injury
Clopidogrel, prasugrel, ticagrelor, ticlopidine	Block ADP ($P2Y_{12}$) receptor → ↓ ADP-induced expression of GpIIb/IIIa	Same as aspirin; dual antiplatelet therapy	Neutropenia (ticlopidine); TTP may be seen
Abciximab, eptifibatide, tirofiban	Block GpIIb/IIIa (fibrinogen receptor) on activated platelets. Abciximab is made from monoclonal antibody Fab fragments	Unstable angina, percutaneous coronary intervention	Bleeding, thrombocytopenia
Cilostazol, dipyridamole	Block phosphodiesterase → ↓ cAMP hydrolysis → ↑ cAMP in platelets	Intermittent claudication, stroke prevention, cardiac stress testing, prevention of coronary stent restenosis	Nausea, headache, facial flushing, hypotension, abdominal pain
Thrombolytics	Alteplase (tPA), reteplase (rPA), streptokinase, tenecteplase (TNK-tPA).		

Aspirin and other salicylates affect the outer hair cells in the cochlea, which are essential for sound amplification and sensitivity.

adenosine diphosphate (ADP)
$P2Y_{12}$ receptor is a G-protein-coupled receptor (GPCR) that is activated by ADP (adenosine diphosphate).ADP binds to $P2Y_{12}$ on the platelet surface, it amplifies platelet activation, promoting Shape change, granule release and, fibrinogen binding and platelet aggregation.

Unstable Angina
PCI

UP

TB

Thrombocytopenia
Bleeding

Elevated cAMP activates protein kinase A (PKA), which phosphorylates various target proteins involved in platelet activation pathways. This phosphorylation results in decreased intracellular calcium levels, reduced shape change, secretion of granules, and aggregation responses.

They induce coronary vasodilation, simulating the effects of exercise by increasing blood flow in healthy coronary arteries more than in diseased ones, revealing perfusion abnormalities.

✅ Antiplatelet – via ↑ cAMP in platelets
✅ Vasodilator – via ↑ cAMP in vascular smooth muscle

TB

Thrombocytopenia
Bleeding

MI

HY USMLE Q#798 Pharm

What drug has vasodilatory and antiplatelets effects ?

- {{c4::cilostazol}}
- Yours Aspirin

Increased cAMP activates protein kinase A (PKA) PKA phosphorylates and inhibits platelet activation pathways, particularly those involved in:

Shape change

Granule release

Glycoprotein IIb/IIIa activation (needed for fibrinogen binding and aggregation)

in decreased intracellular calcium levels, reduced shape change, secretion of granules, and aggregation responses.

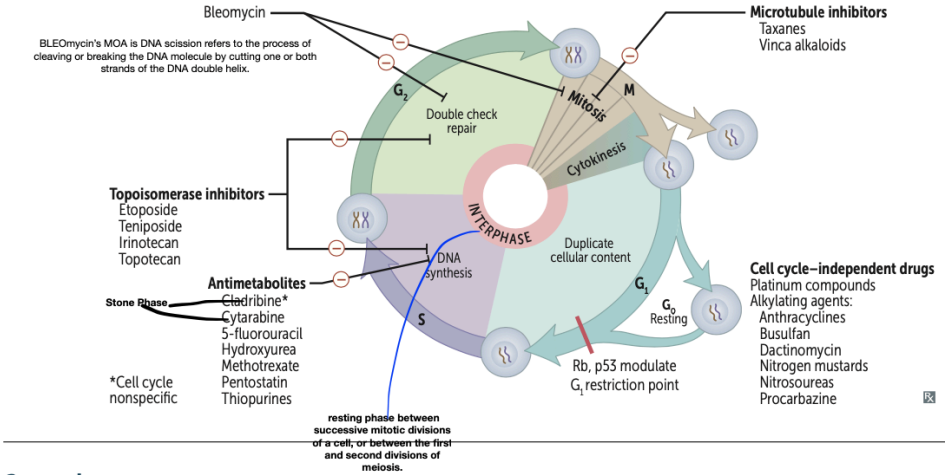
✅ Antiplatelet – via ↑ cAMP in platelets
✅ Vasodilator – via ↑ cAMP in vascular smooth muscle

Thrombocytopenia
Bleeding

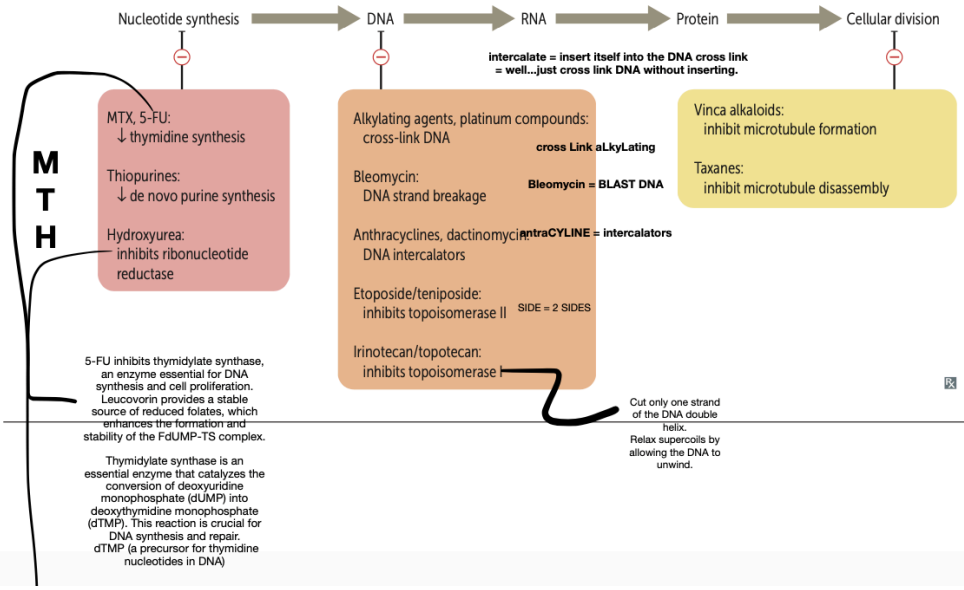
Thrombolytics	Alteplase (tPA), reteplase (rPA), streptokinase, tenecteplase (TNK-tPA).
MECHANISM	Directly or indirectly aid conversion of plasminogen to plasmin, which cleaves thrombin and fibrin clots. ↑ PT, ↑ PTT, no change in platelet count.
CLINICAL USE	Early MI, early ischemic stroke, direct thrombolysis of severe PE.
ADVERSE EFFECTS	Bleeding. Contraindicated in patients with active bleeding, history of intracranial bleeding, recent surgery, known bleeding diatheses, or severe hypertension. Nonspecific reversal with antifibrinolytics (eg, aminocaproic acid, tranexamic acid), platelet transfusions, and factor corrections (eg, cryoprecipitate, FFP, PCC).

MI
Stroke
Emb
MES

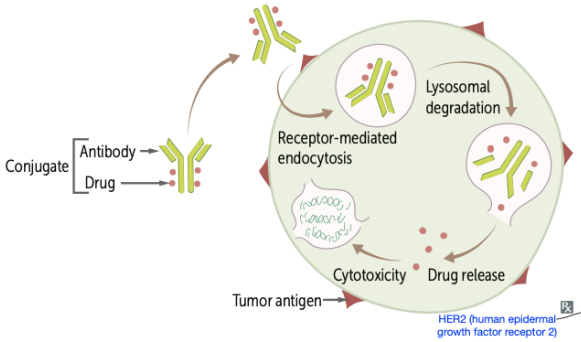
Cancer therapy—cell cycle



Cancer therapy—targets



Antibody-drug conjugates



Formed by linking monoclonal antibodies with cytotoxic chemotherapeutic drugs. Antibody selectivity against tumor antigens allows targeted drug delivery to tumor cells while sparing healthy cells → ↑ efficacy and ↓ toxicity.

Example: ado-trastuzumab emtansine (T-DM1) for HER2 ⊕ breast cancer.

Trastuzumab, sold under the brand name Herceptin among others, is a monoclonal antibody used to treat breast cancer and stomach cancer. It is specifically used for cancer that is HER2 receptor positive. It may be used by itself or together with other chemotherapy medication.

Antitumor antibiotics

All are cell cycle nonspecific, except bleomycin which is G_2/M phase specific.

DRUG	MECHANISM	CLINICAL USE	ADVERSE EFFECTS
Bleomycin	Induces free radical formation → breaks in DNA strands	Testicular cancer, Hodgkin lymphoma	Pulmonary fibrosis, skin hyperpigmentation
Dactinomycin (actinomycin D)	Intercalates into DNA, preventing RNA synthesis	Wilms tumor, Ewing sarcoma, rhabdomyosarcoma	Myelosuppression
Anthracyclines Doxorubicin, daunorubicin	Generate free radicals Intercalate in DNA → breaks in DNA → ↓ replication Inhibit topoisomerase II	Solid tumors, leukemias, lymphomas	Dilated cardiomyopathy (often irreversible; prevent with dexrazoxane), myelosuppression

Fan = Fibrosis

Test = Orange in the bag
Hodgkin = Lympho node like veg

Wilms Tumor = Wholring stair case

DNA strand breaks by inducing free radical formation (donkey breaking inbetween dock)

A solid tumor is an abnormal mass of tissue that usually does not contain cysts or liquid areas. Solid tumors may be cancerous, or non-cancerous. Diverse types of solid tumors are named for the type of cells that form them. Examples of solid tumors are sarcomas and carcinomas.

Dexrazoxane = Deck of cards

Cardio tox = Heart cards

Inserts between between base pair of the DNA

A thiol analog is a compound that resembles a thiol, which is a compound containing a sulfhydryl group (-SH). Thiols are structurally similar to alcohols, but with oxygen replaced by sulfur.

S phase, or synthesis phase, of the cell cycle is where DNA replication occurs, ensuring each daughter cell receives an identical copy of the genome. It's a crucial step before cell division, happening between G1 phase and G2 phase.

I RAS IBD

RA ALL SLE

Antimetabolites

All are S-phase specific except cladribine, which is cell cycle nonspecific.

DRUG	MECHANISM	CLINICAL USE	ADVERSE EFFECTS
Thiopurines Azathioprine, 6-mercaptopurine	Purine (thiol) analogs → ↓ de novo purine synthesis AZA is converted to 6-MP, which is then activated by HGPRT	Rheumatoid arthritis, IBD, SLE, ALL; steroid-refractory disease Prevention of organ rejection Weaning from glucocorticoids	Myelosuppression; GI, liver toxicity 6-MP is inactivated by xanthine oxidase (↑ toxicity with allopurinol or febuxostat)
Cladribine, pentostatin	Purine analogs → multiple mechanisms (eg, inhibition of ADA, DNA strand breaks)	Hairy cell leukemia	Myelosuppression
Cytarabine (arabinofuranosyl cytidine)	Pyrimidine analog → DNA chain termination Inhibits DNA polymerase	Leukemias (AML), lymphomas	Myelosuppression
5-Fluorouracil	Pyrimidine analog bioactivated to 5-FdUMP → thymidylate synthase inhibition → ↓ dTMP → ↓ DNA synthesis Capecitabine is a prodrug	Colon cancer, pancreatic cancer, actinic keratosis, basal cell carcinoma (topical) Effects enhanced with the addition of leucovorin	Myelosuppression, palmar-plantar erythrodysesthesia (hand-foot syndrome)
Hydroxyurea	Inhibits ribonucleotide reductase → ↓ DNA synthesis	Myeloproliferative disorders (eg, CML, polycythemia vera), sickle cell disease (↑ HbF)	Severe myelosuppression, megaloblastic anemia
Methotrexate	Folic acid analog that competitively inhibits dihydrofolate reductase → ↓ dTMP → ↓ DNA synthesis	Cancers: leukemias (ALL), lymphomas, choriocarcinoma, sarcomas Nonneoplastic: ectopic pregnancy, medical abortion (with misoprostol), rheumatoid arthritis, psoriasis, IBD, vasculitis	Myelosuppression (reversible with leucovorin "rescue"), hepatotoxicity, mucositis (eg, mouth ulcers), pulmonary fibrosis, folate deficiency (teratogenic), nephrotoxicity

Cladribine resembles deoxyadenosine but contains a chlorine atom at the 2-position, which makes it resistant to ADA.
It's a purine analog designed to be ADA-resistant, allowing it to accumulate in cells and exert cytotoxic effects, especially in lymphocytes where ADA activity is normally high.

6 MP
Military Police

HGPRT
HOG

Broken DNA cloud
Hair of the women

CLAdRA has hairy PANTS

Cytarabine = scythe
pipkin = pyrimdine analog
DNA light pole = DNA polymerase

dTMP stands for deoxythymidine monophosphate

Leucovorin, a reduced folate, is converted in the body to 5,10-methylenetetrahydrofolate (5,10-methylene-THF), a cofactor essential for the binding of the active metabolite of 5-FU, FdUMP, to TS.

SCD
PCV
CML

PCS
Leukemia
Lymphomas
Choriocarcinoma
Sarcomas

Ectopic pregnancy
Rheumatoid Arthritis
IBD
Misoprostol
Vascitilitis

PREMIV

Leucovorin is a reduced form of folic acid that does not require DHFR for activation.

It directly replenishes THF stores, allowing DNA/RNA synthesis to resume in healthy cells.

DHF —(DHF Red) > THF —> CH3
THF —> allow for the methylation of purine and pyrimidine

Mehlman Medical Pharma
What is the MOA of Hydorxyurea ?

Correct = Inhibits conversion of ribonucleotides to acetylated nucleotides (catalyzed by ribonucleotide reductase)
Ribonucleotide reductase acts by removing a hydroxyl group from the ribose ring of nucleotide diphosphates (NTPs) in order to make deoxynucleotide diphosphates (dNTPs)

Yours – Thymylate synthase

Blood cells are Blue in color

Patient is the has CML + Fibrosis Wha tis the likley cause ?
Correct = Busulfan
Yours = Bleomycin

Bleeding from Bladder = Hemoragheic Cystitis
Fanconi Syndrome = Falcon

Alkylating agents

All are cell cycle nonspecific.

DRUG	MECHANISM	CLINICAL USE	ADVERSE EFFECTS
Busulfan	Cross-links DNA	Used to ablate patient's bone marrow before bone marrow transplantation	Severe myelosuppression (in almost all cases), pulmonary fibrosis, hyperpigmentation
Nitrogen mustards Cyclophosphamide, ifosfamide	Cross-link DNA Require bioactivation by liver	Solid tumors, leukemia, lymphomas, rheumatic disease (eg, SLE, granulomatosis with polyangiitis)	Myelosuppression, SIADH, Fanconi syndrome (ifosfamide), hemorrhagic cystitis and bladder cancer (prevent with mesna)
Nitrosoureas Carmustine, lomustine	Cross-link DNA Require bioactivation by liver Cross blood-brain barrier → CNS entry	Brain tumors (including glioblastoma multiforme) Put nitro in your Mustang and travel the globe	CNS toxicity (convulsions, dizziness, ataxia)
Procarbazine	Mechanism unknown Weak MAO inhibitor	Hodgkin lymphoma, brain tumors	Myelosuppression, pulmonary toxicity, leukemia, disulfiram-like reaction
Temozolomide	DNA methylation	Glioblastoma multiforme	Myelosuppression

Busulfan =Business Man
Cross links = crosslinks legs
Fan = Pulm Fibrosis
Dish ablated = BM ablation

Cyclops = Cyclophosphomides
Fossil = Ifosfamide
Ankle Cuff = Cross Links
Messenger Bag = MESNA

Mesna acts as a "scavenger" for acrolein in the bladder. By binding to acrolein and inactivating it before it can damage the bladder lining,

Chained Down Car = Cross links DNA
Lumpy Helment = Brain tumor
SHaking from Hydraulics = CNS toxicity

Post Card = Procarbazine
Chains = Alkalyating agent
Hodge Hog = Hodgelymphoma
Alcohol = Disulfram reaction

Platinum compounds

Cisplatin, carboplatin, oxaliplatin.

Frayed wire = Peirpheral Neuropathy
Amesthyst (jewel) = Amifosfatine
Covering ear because of the alarm = ototoxicty
Wire = Peripheral NP
Falcon = Fanconi syndrome
Kidney shaped geode (valcano rocks) = Nephrotox

MECHANISM	Cross-link DNA. Cell cycle nonspecific.
CLINICAL USE	Solid tumors (eg, testicular, bladder, ovarian, GI, lung), lymphomas.
ADVERSE EFFECTS	Nephrotoxicity (eg, Fanconi syndrome; prevent with amifostine), peripheral neuropathy, ototoxicity.

Scavenging of Reactive Oxygen Species (ROS) in the Kidneys: Carboplatin, like cisplatin, can induce oxidative stress in kidney cells by generating reactive oxygen species. Amifostine is a free radical scavenger

Microtubule inhibitors

All are M-phase specific.

Packing
Wire = Peripheral Neuropathy
taxanes = tax returns
Inner tube = Blocks Microtuble breakdown

DRUG	MECHANISM	CLINICAL USE	ADVERSE EFFECTS
Taxanes Docetaxel, paclitaxel	Hyperstabilize polymerized microtubules → prevent mitotic spindle breakdown	Various tumors (eg, ovarian and breast carcinomas)	Myelosuppression, neuropathy, hypersensitivity Taxes stabilize society
Vinca alkaloids Vincristine, vinblastine	Bind β-tubulin and inhibit its polymerization into microtubules → prevent mitotic spindle formation	Solid tumors, leukemias, Hodgkin and non-Hodgkin lymphomas	Vincristine (crisps the nerves): neurotoxicity (axonal neuropathy), constipation (including ileus) Vinblastine (blasts the marrow): myelosuppression

Vinca Alkaloid (Vincristine and Vinblastine)
Unable to correct irrigation tubing = Block MT formation

ABDV

Adriamycin (doxorubicin), Bleomycin, Vinblastine, and Dacarbazine.

alpha tubulin and beta tubulin --> The alpha and beta tubulin dimers are the units that assemble head-to-tail to form long, hollow tubes called microtubule. Beta-tubulin is a GTPase. This means it can bind and hydrolyze Guanosine Triphosphate (GTP). The binding and hydrolysis of GTP by beta-tubulin are critical for the dynamic behavior of microtubules, including their assembly (polymerization) and disassembly (depolymerization).

Microtubules are dynamic structures made of α- and β-tubulin dimers. They constantly grow (polymerize) and shrink (depolymerize) — a process called dynamic instability. Taxane-stabilized microtubules freeze the spindle, blocking cells in metaphase.

Topoisomerase 1 relieves supercoiling by making a single stranded break in DNA hence cuts 1 strand. Topoisomerase 2 Relieves supercoiling and untangles DNA by making double-stranded breaks, hence cuts both strands.

S phase, or Synthesis phase, is the part of the cell cycle where DNA replication takes place. G1 phase – Cell grows and prepares for DNA replication. S phase – DNA is replicated. G2 phase – Cell prepares for division by checking DNA for errors. M phase – Mitosis (cell division) occurs. Growth means the cell increase in size, organellese (like mitochondria, ribosomes are duplicated). Protein and RNA synthesis, the cell produces proteins and mRNA needed for DNA synthesis.

IT EaT
Irinotecan
Topotecan
Etoposide
Teniposide

Topoisomerase inhibitors

All cause ↑ DNA degradation resulting in cell cycle arrest in S and G_2 phases.

bird dropping = Diarrhea

DRUG	MECHANISM	CLINICAL USE	ADVERSE EFFECTS
Irinotecan, topotecan	Inhibit topoisomerase I "-tecone"	Colon, ovarian, small cell lung cancer	Severe myelosuppression, diarrhea
Etoposide, teniposide	Inhibit topoisomerase II "-bothside"	Testicular, small cell lung cancer, leukemia, lymphoma	Myelosuppression, alopecia

Topoisomerase II preventing DNA strand breaks from being repaired and increase the rate of DNA degradation.

Tamoxifen

MECHANISM	Selective estrogen receptor modulator with complex mode of action: antagonist in breast tissue, partial agonist in endometrium and bone. Blocks the binding of estrogen to ER in ER ⊕ cells.
CLINICAL USE	Prevention and treatment of breast cancer, prevention of gynecomastia in patients undergoing prostate cancer therapy.
ADVERSE EFFECTS	Hot flashes, ↑ risk of thromboembolic events (eg, DVT, PE) and endometrial cancer.

Ghalat

Antibody-Dependent Cell-mediated Cytotoxicity (ADCC) mediated by Natural Killer (NK) cells.NK cells are a type of cytotoxic lymphocyte that are part of the innate immune system, but they can also participate in adaptive immunity through ADCC.

Cotton inthe nose = Thrombvosis

In the hypothalamus, tamoxifen acts as an estrogen receptor agonist. While it seems counterintuitive that an "anti-estrogen" would cause hot flashes, in the hypothalamus, tamoxifen's estrogen-like activity actually disrupts the normal regulation of the thermoneutral zone.

Anticancer monoclonal antibodies

Work against extracellular targets to neutralize them or to promote immune system recognition (eg, ADCC by NK cells). Eliminated by macrophages (not cleared by kidneys or liver).

Olaparib

Poly(ADP-ribose) polymerase (↓ DNA repair) — Breast, ovarian, pancreatic, and prostate cancers — Myelosuppression, edema, diarrhea

primary function is to catalyze the synthesis of poly(ADP-ribose) (PAR) chains on target proteins. This process, called PARylation or ADP-ribosylation, involves transferring ADP-ribose units from NAD$^+$ (nicotinamide adenine dinucleotide) to specific amino acid residues (like glutamate, aspartate, lysine, or arginine) on acceptor proteins.

the act of making something better; improvement.

Phosphorylation of Target Proteins: CDKs phosphorylate a wide variety of proteins involved in DNA replication, chromosome condensation, spindle formation, and nuclear envelope breakdown.

Platinum can interact with molecular oxygen, leading to the formation of superoxide radicals

Chemotoxicity amelioration

DRUG	MECHANISM	CLINICAL USE
Amifostine	Free radical scavenger	Nephrotoxicity from platinum compounds
Dexrazoxane	Iron chelator	Cardiotoxicity from anthracyclines
Leucovorin (folinic acid)	Tetrahydrofolate precursor	Myelosuppression from methotrexate (leucovorin "rescue"); also enhances the effects of 5-FU
Mesna	Sulfhydryl compound that binds acrolein (toxic metabolite of cyclophosphamide/ifosfamide)	Hemorrhagic cystitis from cyclophosphamide/ifosfamide
Rasburicase	Recombinant uricase that catalyzes metabolism of uric acid to allantoin	Tumor lysis syndrome
Ondansetron, granisetron	5-HT_3 receptor antagonists	Acute nausea and vomiting (usually within 1-2 hr after chemotherapy)
Prochlorperazine, metoclopramide	D_2 receptor antagonists	
Aprepitant, fosaprepitant	NK_1 receptor antagonists	Delayed nausea and vomiting (>24 hr after chemotherapy)
Filgrastim, sargramostim	Recombinant G(M)-CSF	Neutropenia
Epoetin alfa	Recombinant erythropoietin	Anemia

5-FU is metabolized into 5-fluoro-2'-deoxyuridine monophosphate (FdUMP). FdUMP inhibits thymidylate synthase. Leucovorin is a reduced form of folic acid that gets converted to 5,10-methylenetetrahydrofolate in cells.

By supplying more of this cofactor, leucovorin enhances and stabilizes the FdUMP–TS–folate complex, making the inhibition of thymidylate synthase more prolonged

immune system, but they can also participate in adaptive immunity through ADCC.

tamoxifen's estrogen-like activity actually disrupts the normal regulation of the thermoneutral zone.

Anticancer monoclonal antibodies

Work against extracellular targets to neutralize them or to promote immune system recognition (eg, ADCC by NK cells). Eliminated by macrophages (not cleared by kidneys or liver).

AGENT	TARGET	CLINICAL USE	ADVERSE EFFECTS
Alemtuzumab	CD52	Chronic lymphocytic leukemia (CLL), multiple sclerosis.	↑ risk of infections and autoimmunity (eg, ITP)
Bevacizumab	VEGF (inhibits blood vessel formation)	Colorectal cancer (CRC), renal cell carcinoma (RCC), non–small cell lung cancer (NSCLC), angioproliferative retinopathy	Hemorrhage, blood clots, impaired wound healing
Cetuximab, panitumumab	EGFR	Metastatic CRC (wild-type RAS), head and neck cancer	Rash, elevated LFTs, diarrhea
Rituximab	CD20	Non-Hodgkin lymphoma, CLL, rheumatoid arthritis, ITP, TTP, AIHA, multiple sclerosis	Infusion reaction due to cytokine release following interaction of rituximab with its target on B cells
Trastuzumab	HER2 ("trust HER")	Breast cancer, gastric cancer	Dilated cardiomyopathy (often reversible)
Pembrolizumab, nivolumab, cemiplimab	PD-1	Various tumors (eg, NSCLC, RCC, melanoma, urothelial carcinoma)	↑ risk of autoimmunity (eg, dermatitis, enterocolitis, hepatitis, pneumonitis, endocrinopathies)
Atezolizumab, durvalumab, avelumab	PD-L1		
Ipilimumab	CTLA-4		

Cetuximab = Seduction
Panitumumab = Panni
Egg Fruit = EGFR
Liver = LFT
Rash on neck = Rash
Dripping sauce = Dairrhea

Rituxmiab = Red Tux
B cell Bow = B cells
20 centurary box offic = 20
Beverage = Bevaciczumab
Vegetables = VEGF

No Flashcards

Cytotoxic T lymphocyte-associated antigen (CTLA-4)

What is the impact of rutiximab on B cells ?

~~Depletion of {{c1::B cells }}~~

Yours - interruption of cytokine function

step 3 wrong
Rituximab is a monoclonal antibody directed against CD20, a cell surface receptor on developing and mature B cells. Binding of rituximab to CD20 results in B-cell cytotoxicity and phagocytosis, which reduces the B-cell population. This reduces inflammatory symptoms in a wide range of rheumatologic diseases.

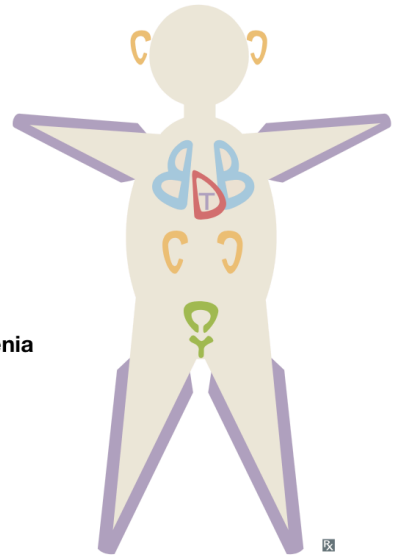
PD-L1 is the primary ligand for PD-1. When PD-L1 on one cell binds to PD-1 on a T cell, it triggers the inhibitory signal in the T cell.PD-L1 and PD-1 helps to control immune responses and prevent autoimmunity.

Primarily found on activated T cells, particularly on regulatory T cells (Tregs), which are a type of T cell that helps to suppress immune responses. CTLA-4 plays a critical role in the initial activation of T cells in lymphoid organs. It helps to set the threshold for T cell activation and prevent excessive or inappropriate immune responses.

PD-1 (Programmed Cell Death Protein 1)

Location: Primarily found on activated T cells (a type of immune cell that is critical for recognizing and destroying infected or cancerous cells), B cells, and NK cells.

Key chemotoxicities



Cisplatin, Carboplatin → ototoxicity

Vincristine → peripheral neuropathy
Bleomycin, Busulfan → pulmonary fibrosis
Doxorubicin, Daunorubicin → cardiotoxicity
Trastuzumab → cardiotoxicity
Cisplatin, Carboplatin → nephrotoxicity

CYclophosphamide → hemorrhagic cystitis

Nonspecific common toxicities of nearly all cytotoxic chemotherapies include myelosuppression (neutropenia, anemia, thrombocytopenia), GI toxicity (nausea, vomiting, mucositis), alopecia.

TAN

My VAN

Thrombocytopenia
Anemia
Nuetropenia

Mucositis
Vomiting
Alopcea
Nausea

Mucositis is when your mouth or gut is sore and inflamed.

Direct coagulation factor inhibitors

DRUG	MECHANISM
Bivalirudin, argatroban, dabigatran	Directly inhibit thrombin (factor IIa)
Apixaban, edoxaban, rivaroxaban	Directly inhibit factor Xa

Embolism

AFIB
HIT

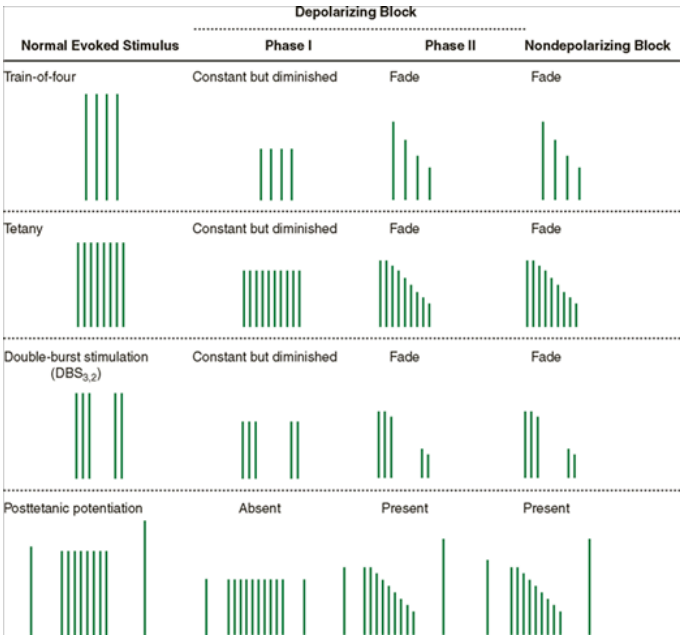
EAH

Embolism

AFIB
DVT

EA D

CNS



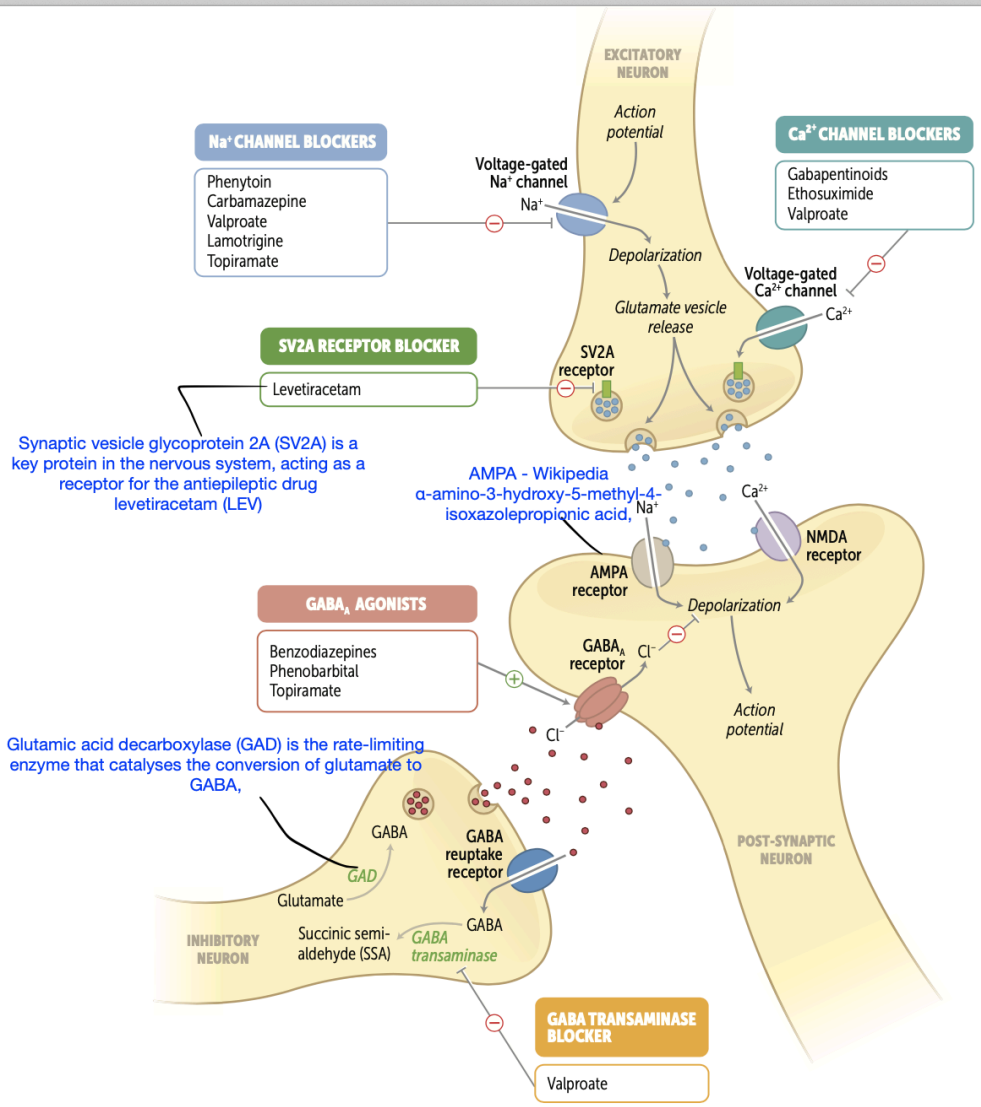
Phase 2: After initial depolarization, the receptor channels become desensitized or inactivated, leading to a reduction in muscle response over time, resembling non-depolarizing blockade.

Anticonvulsants

(Drug Reaction with Eosinophilia and Systemic Symptoms)

	MECHANISM	COMMON ADVERSE EFFECTS	RARE BUT SERIOUS ADVERSE EFFECTS
Narrow spectrum (focal seizures)			
Phenytoin	Block Na^+ channel	Sedation, dizziness, diplopia, gingival hypertrophy (preventable with folate supplementation), rash, hirsutism, drug interactions (CYP450 induction)	SJS, DRESS, hepatotoxicity, neuropathy, osteoporosis, folate depletion, teratogenicity
Carbamazepine		Sedation, dizziness, diplopia, vomiting, diarrhea, SIADH, rash, drug interactions (CYP450 induction)	SJS, DRESS, hepatotoxicity, agranulocytosis, aplastic anemia, folate depletion, teratogenicity
Gabapentinoids Gabapentin, pregabalin	Block Ca^{2+} channel	Sedation, dizziness, ataxia, weight gain	
Narrow spectrum (absence seizures only)			
Ethosuximide	Blocks Ca^{2+} channel	Sedation, dizziness, vomiting	
Broad spectrum (focal and generalized seizures)			
Valproate	Blocks Na^+ channel Blocks Ca^{2+} channel Blocks GABA transaminase	Sedation, dizziness, vomiting, weight gain, hair loss, easy bruising, drug interactions (CYP450 inhibition)	Hepatotoxicity, pancreatitis, teratogenicity (highest risk of all anticonvulsants)
Lamotrigine	Blocks Na^+ channel	Sedation, dizziness, rash	SJS, DRESS
Levetiracetam	Blocks Synaptic Vesicle protein 2A (SV2A)	Sedation, dizziness, fatigue	Neuropsychiatric (eg, psychosis)
Topiramate	Blocks Na^+ channel Potentiates $GABA_A$ receptor	Sedation, dizziness, mood disturbance (eg, depression), weight loss, paresthesia	Kidney stones, angle-closure glaucoma

Specifically, it degrades GABA by converting it into succinic semialdehyde, a process essential for maintaining appropriate GABA levels in the brain.


EXCITATORY NEURON
Action potential
Na+ CHANNEL BLOCKERS
Phenytoin
Carbamazepine
Valproate
Lamotrigine
Topiramate
Voltage-gated Na+ channel
Na+
Depolarization
Ca2+ CHANNEL BLOCKERS
Gabapentinoids
Ethosuximide
Valproate
Voltage-gated Ca2+ channel
Ca2+
Glutamate vesicle release
SV2A RECEPTOR BLOCKER
Levetiracetam
SV2A receptor
Synaptic vesicle glycoprotein 2A (SV2A) is a key protein in the nervous system, acting as a receptor for the antiepileptic drug levetiracetam (LEV)
AMPA - Wikipedia α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid,
Na+
Ca2+
NMDA receptor
AMPA receptor
Depolarization
GABAA AGONISTS
Benzodiazepines
Phenobarbital
Topiramate
GABAA receptor
Cl−
Action potential
Glutamic acid decarboxylase (GAD) is the rate-limiting enzyme that catalyses the conversion of glutamate to GABA,
GABA
GAD
Glutamate
GABA reuptake receptor
GABA
INHIBITORY NEURON
Succinic semi-aldehyde (SSA)
GABA transaminase
POST-SYNAPTIC NEURON
GABA TRANSAMINASE BLOCKER
Valproate

Seizures in neonates can result from hypoxic-ischemic encephalopathy (HIE), intracranial hemorrhage, infections, metabolic disturbances, or congenital brain malformations. Barbiturates have a long history of use in neonatology, so dosing, safety profile, and monitoring are well understood.

Barbiturates	Phenobarbital, pentobarbital, thiopental, secobarbital.
MECHANISM	Facilitate $GABA_A$ action by ↑ **duration** of Cl^- channel opening, thus ↓ neuron firing (barbidurates ↑ duration).
CLINICAL USE	Sedative for anxiety, seizures, insomnia, induction of anesthesia (thiopental).
ADVERSE EFFECTS	Respiratory and cardiovascular depression (can be fatal); CNS depression (can be exacerbated by alcohol use); dependence; drug interactions (induces cytochrome P-450). Overdose treatment is supportive (assist respiration and maintain BP). Contraindicated in porphyria.

ISAA
- Insomnia
Seizures
Anxiety
Anethesia

ADdictive sign is dependence

Barbiturates induce other enzymes, notably δ-aminolevulinic acid (ALA) synthetase.

Benzodiazepines	Diazepam, lorazepam, triazolam, temazepam, oxazepam, midazolam, chlordiazepoxide, alprazolam.
MECHANISM	Facilitate $GABA_A$ action by ↑ **frequency** of Cl^- channel opening ("frenzodiazepines" ↑ frequency). ↓ REM sleep. Most have long half-lives and active metabolites (exceptions [ATOM]: Alprazolam, Triazolam, Oxazepam, and Midazolam are short acting → higher addictive potential).
CLINICAL USE	Anxiety, panic disorder, spasticity, status epilepticus (lorazepam, diazepam, midazolam), eclampsia, detoxification (eg, alcohol withdrawal/DTs; long-acting chlordiazepoxide and diazepam are preferred), night terrors, sleepwalking, general anesthetic (amnesia, muscle relaxation), hypnotic (insomnia). Lorazepam, Oxazepam, and Temazepam can be used for those with liver disease who drink a LOT due to minimal first-pass metabolism.
ADVERSE EFFECTS	Dependence, additive CNS depression effects with alcohol and barbiturates (all bind the $GABA_A$ receptor). Less risk of respiratory depression and coma than with barbiturates. Treat overdose with flumazenil (competitive antagonist at GABA benzodiazepine receptor). Can precipitate seizures by causing acute benzodiazepine withdrawal.

Spasticity
Night terrror
Sleep Walking

SNS

First-pass metabolism, also known as the first-pass effect or presystemic metabolism, is a phenomenon of drug metabolism that occurs before a drug reaches systemic circulation.

GABA A receptor are pentameric chloride ion channels activated by the neurotransmitter GABA, the primary inhibitory neurotransmitter in the brain. These receptors are made up of various combinations of subunits (α, β, γ, δ, etc.). The most common configuration includes two α subunits, two β subunits, and one γ subunit. BZ1 is specifically on GABA A receptors that contain the α1 subunit (usually in an α1βxγ2 configuration).

Insomnia therapy

HAC = Headache Ataxia Confusion

AGENT	MECHANISM	ADVERSE EFFECTS	NOTES
Nonbenzodiazepine hypnotics	Examples: Zolpidem, Zaleplon, esZopiclone Act via the BZ_1 subtype of GABA receptor	Ataxia, headaches, confusion Cause only modest day-after psychomotor depression and few amnestic effects (vs older sedative-hypnotics)	These ZZZs put you to sleep Short duration due to rapid metabolism by liver enzymes; effects reversed by flumazenil ↓ dependency risk and ↓ sleep cycle disturbance (vs benzodiazepine hypnotics)
Suvorexant ANTAGONIST	Orexin (hypocretin) receptor antagonist	CNS depression (somnolence), headache, abnormal sleep-related activities	Contraindications: narcolepsy, combination with strong CYP3A4 inhibitors Not recommended in patients with liver disease Limited risk of dependency
Ramelteon AGONIST	Melatonin receptor agonist: binds MT1 and MT2 in suprachiasmatic nucleus	Dizziness, nausea, fatigue, headache	No known risk of dependency

"Psychomotor agitation" is also common. This means not being able to relax or sit still, and constantly fidgeting. At the other extreme, a person with psychotic depression may have "psychomotor retardation", where both their thoughts and physical movements slow down.

Nacrolepsy is TOO Much sleeping, Suvorexant --> causes too much sleep

LL N I
Liver
Limited Risk of dependcy
Inhibitors
Narcolepsy

MT1 and MT2 receptors are two types of melatonin receptors that are G protein-coupled receptors (GPCRs) in the body.

Trigmental Nerve Activation
Vasoactive peptide release
Vasoconstriction

TVV

Triptans	Sumatriptan
MECHANISM AGONIST	$5\text{-}HT_{1B/1D}$ agonists. Inhibit trigeminal nerve activation, prevent vasoactive peptide release, induce vasoconstriction.
CLINICAL USE	Acute migraine, cluster headache attacks. A sumo wrestler trips and falls on their head.
ADVERSE EFFECTS	Coronary vasospasm (contraindicated in patients with CAD or vasospastic angina), mild paresthesia, serotonin syndrome (in combination with other 5-HT agonists).

Paresthesia, Conornary Vasospasm, Serotonin Syndrome
PCS

Impulse control disorders (ICDs) are a group of behavioral conditions that make it difficult to control your actions or reactions.

Parkinson disease therapy

The most effective treatments are non-ergot dopamine agonists which are usually started in younger patients, and levodopa (with carbidopa) which is usually started in older patients. Deep brain stimulation of the STN or GPi may be helpful in advanced disease.

GPI = globus pallidus internus

STRATEGY	AGENTS
Dopamine agonists	Non-ergot (preferred)—pramipexole, ropinirole; toxicity includes nausea, impulse control disorder (eg, gambling), postural hypotension, hallucinations, confusion, sleepiness, edema. Ergot—bromocriptine; rarely used due to toxicity.
↑ dopamine availability	Amantadine (↑ dopamine release and ↓ dopamine reuptake); mainly used to reduce levodopa-induced dyskinesias; toxicity = peripheral edema, livedo reticularis, ataxia.
↑ L-DOPA availability	Agents prevent peripheral (pre-BBB) L-DOPA degradation → ↑ L-DOPA entering CNS → ↑ central L-DOPA available for conversion to dopamine. ▨ Levodopa (L-DOPA)/carbidopa—carbidopa blocks peripheral conversion of L-DOPA to dopamine by inhibiting DOPA decarboxylase. Also reduces adverse effects of peripheral L-DOPA conversion into dopamine (eg, nausea, vomiting). ▨ Entacapone and tolcapone prevent peripheral L-DOPA degradation to 3-O-methyldopa (3-OMD) by inhibiting COMT. Used in conjunction with levodopa.
Prevent dopamine breakdown	Agents act centrally (post-BBB) to inhibit breakdown of dopamine. ▨ Selegiline, rasagiline—block conversion of dopamine into DOPAC by selectively inhibiting MAO-B, which is more commonly found in the Brain than in the periphery. ▨ Tolcapone—crosses BBB and blocks conversion of dopamine to 3-methoxytyramine (3-MT) in the brain by inhibiting central COMT.
Curb excess cholinergic activity	Benztropine, trihexyphenidyl (Antimuscarinic; improves tremor and rigidity but has little effect on bradykinesia in Parkinson disease). Tri Parking my Mercedes-Benz.

HHENS C
Hallucination
Hypotension
Edema
Nausea
Confusion
Sleepiness

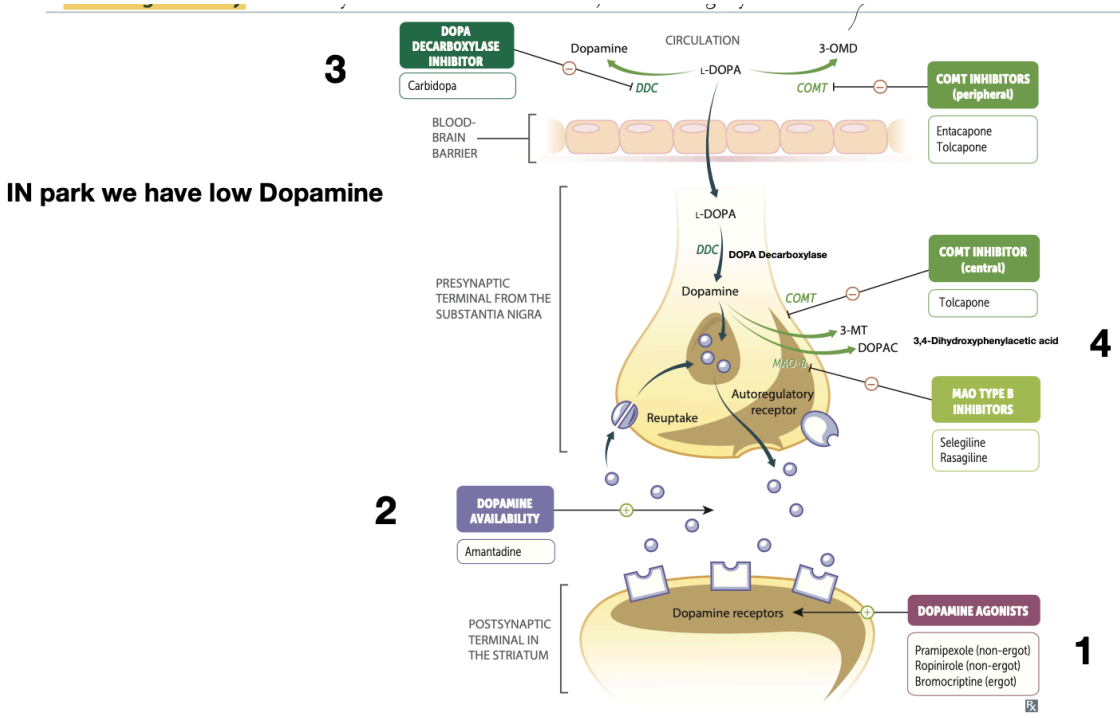
LAP
Livdeo reticularis
Ataxia
Peripheral edeam

Livedo reticularis = Livedo reticularis (LR) is a cutaneous physical sign characterized by transient or persistent, blotchy, reddish-blue to purple, net-like cyanotic pattern.

Dyskinesia = Dyskinesias are involuntary, erratic, writhing movements of the face, arms, legs or trunk.

3,4-Dihydroxyphenylacetic acid

IN park we have low Dopamine



Leva Dopa is LOOSE and can Cross BBB

Carbidopa/levodopa

MECHANISM	↑ dopamine in brain. Unlike dopamine, L-DOPA can cross BBB and is converted by DOPA decarboxylase in the CNS to dopamine. Carbidopa, a peripheral DOPA decarboxylase inhibitor that cannot cross BBB, is given with L-DOPA to ↑ bioavailability of L-DOPA in the brain and to limit peripheral adverse effects.
CLINICAL USE	Parkinson disease.
ADVERSE EFFECTS	Nausea, hallucinations, postural hypotension. With progressive disease, L-DOPA can lead to "on-off" phenomenon with improved mobility during "on" periods, then impaired motor function during "off" periods when patient responds poorly to L-DOPA or medication wears off.

NBME sawaal yea tum nai ghalat keeya thah

Agitation and anxiety can NOT be prevented as it central other peipheral side effects can be prevented like hypotension or N/V

PNH

Postural Hypotension
Nausea
Hallucinations

Neurodegenerative disease therapy

DISEASE	AGENT	MECHANISM	NOTES
Alzheimer disease	Donepezil, rivastigmine, galantamine	AChE inhibitor	1st-line treatment Adverse effects: nausea, dizziness, insomnia; contraindicated in patients with cardiac conduction abnormalities Dona Riva dances at the gala
	Memantine	NMDA receptor antagonist; helps prevent excitotoxicity (mediated by Ca^{2+})	Used for moderate to advanced dementia Adverse effects: dizziness, confusion, hallucinations
Amyotrophic lateral sclerosis	Riluzole	↓ neuron glutamate excitotoxicity	↑ survival Treat Lou Gehrig disease with riLouzole
Huntington disease	Tetrabenazine	Inhibit vesicular monoamine transporter (VMAT) → ↓ dopamine vesicle packaging and release	May be used for Huntington chorea and tardive dyskinesia

تم نے یہ کلت کیا

DIN
Dizzine
Insomnia
Nausea

DIN
Dizzine
Confusion
Hullcinaiton

In Alzheimer's disease, abnormal glutamate activity can lead to excessive stimulation of NMDA receptors, causing calcium overload in neurons. This excitotoxicity contributes to neuronal damage and death. NMDA antagonists block these receptors, preventing calcium influx and thereby reducing excitotoxicity.

By blocking VMAT2, it prevents the packaging of dopamine into synaptic vesicles,s results in decreased release of dopamine into the synaptic cleft, leading to reduced dopaminergic activity. Chorea and Huntingon disease are characterized by involuntary movement due to excessive dopamine activity. Lowering dopamine levels will lower the activity.

Tardive dyskinesia (TD) is a movement disorder characterized by uncontrollable, abnormal, and repetitive movements of the face, torso, and/or other body parts.

Low blood solubility decrease CO and high minute ventilation will increase speed of induction

Anesthetics—general principles

CNS drugs must be lipid soluble (cross the blood-brain barrier) or be actively transported.
Drugs with ↓ solubility in blood = rapid induction and recovery times.
Drugs with ↑ solubility in lipids = ↑ potency.
MAC = Minimum Alveolar Concentration (of inhaled anesthetic) required to prevent 50% of subjects from moving in response to noxious stimulus (eg, skin incision). Potency = 1/MAC.
Examples: nitrous oxide (N_2O) has ↓ blood and lipid solubility, and thus fast induction and low potency. Halothane has ↑ lipid and blood solubility, and thus high potency and slow induction.

Anesthetics with high tissue solubility are characterized by large arteriovenous concentration gradients and slower onsets of action.

Inhaled anesthetics

Desflurane, halothane, enflurane, isoflurane, sevoflurane, methoxyflurane, N_2O.

Metabolic Demand decrease
Myocardial depression
VOmiting
Cerebral Flow Increase
Resp depression

MECHANISM	Mechanism unknown.
EFFECTS	Myocardial depression, respiratory depression, ~~postoperative nausea/vomiting~~, ↑ cerebral blood flow and ICP, ↓ cerebral metabolic demand.
ADVERSE EFFECTS	Hepatotoxicity (halothane), nephrotoxicity (methoxyflurane), proconvulsant (enflurane, epileptogenic), expansion of trapped gas in a body cavity (N_2O). Malignant hyperthermia—rare, life-threatening condition in which inhaled anesthetics or succinylcholine induce severe muscle contractions and hyperthermia. Susceptibility is often inherited as autosomal dominant with variable penetrance. Mutations in ryanodine receptor (*RYR1*) cause ↑ Ca^{2+} release from sarcoplasmic reticulum. Treatment: dantrolene (a ryanodine receptor antagonist).

Intravenous anesthetics

AGENT	MECHANISM	ANESTHESIA USE	NOTES
Thiopental	Facilitates $GABA_A$ (barbiturate)	Anesthesia induction, short surgical procedures	↓ cerebral blood flow. High lipid solubility Effect terminated by rapid redistribution into tissue, fat
Midazolam	Facilitates $GABA_A$ (benzodiazepine)	Procedural sedation (eg, endoscopy), anesthesia induction	May cause severe postoperative respiratory depression, ↓ BP, anterograde amnesia
Propofol	Potentiates $GABA_A$	Rapid anesthesia induction, short procedures, ICU sedation	May cause respiratory depression, ↓ BP
Ketamine	NMDA receptor antagonist	Dissociative anesthesia Sympathomimetic	↑ cerebral blood flow Emergence reaction possible with disorientation, hallucination, vivid dreams

Short, Anesthesia
SA

Sedation, Anesthesia
SA

ICU sedation, Short, Anesthesia
ISA

Resp depression
Amnesai
BP

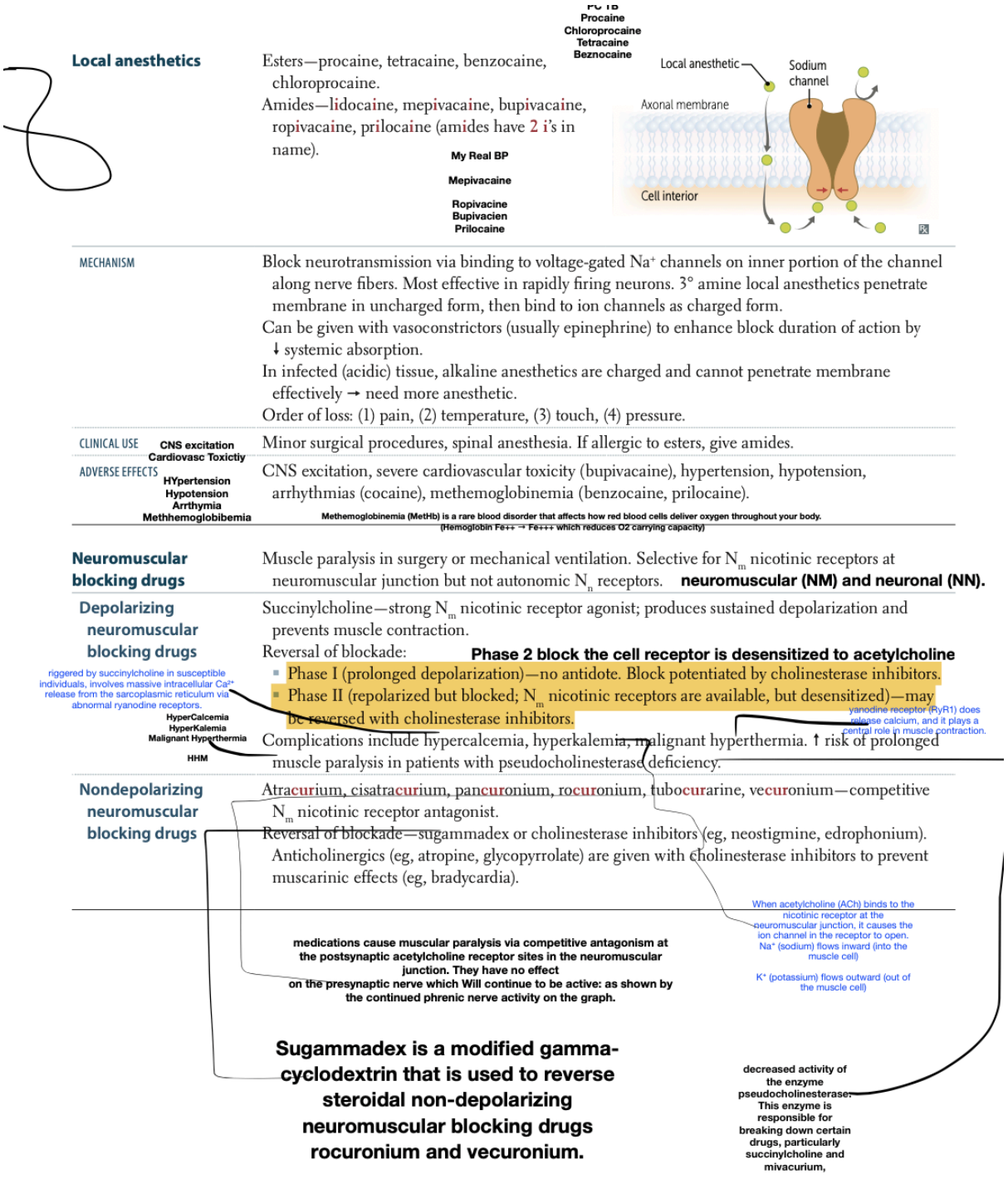
BAR

Dissociatives (also referred to as 'dissociative anaesthetics') are a class of psychedelic drug. This class of drug causes people to feel separated or detached from their body or physical environment.

Vivid dreams are intense dreams that linger in your mind and feel similar to real-life memories. T

Dissociative anesthetics are a class of drugs that produce a state of altered consciousness characterized by:
Sensory dissociation: A feeling of detachment from one's body and surroundings.
Analgesia: Loss of pain sensation.
Amnesia: Inability to recall events during anesthesia.
Catalepsy: A state of rigidity or immobility.

The hippocampus and medial temporal lobes—key areas involved in converting short-term memories into long-term storage—are rich in GABA-A receptors. When midazolam enhances GABAergic inhibition here, it disrupts the neural activity necessary for encoding new memories.



NBME 137 Q 9

What is an adverse effect of opioids ?

{{c2::pruritus }}

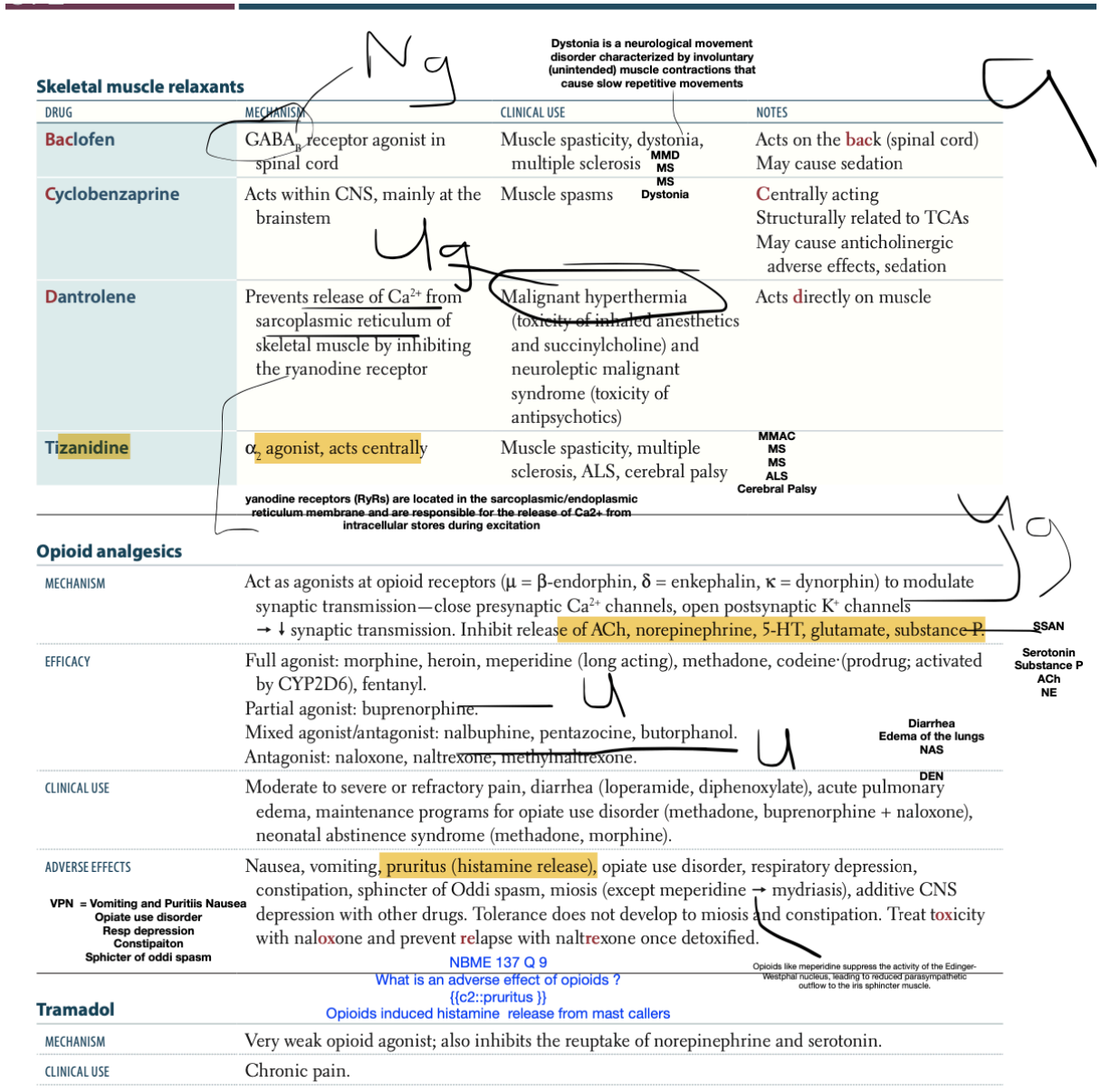
Opioids induced histamine release from mast callers

Free 137 Q 29 B4

62M
(1) postop pain in the knee
What is the NBS ?

Femoral nerve block w/ {{c8::bupivacine }}

Yours = Oxygen



Skeletal muscle relaxants

DRUG	MECHANISM	CLINICAL USE	NOTES
Baclofen	$GABA_B$ receptor agonist in spinal cord	Muscle spasticity, dystonia, multiple sclerosis	Acts on the back (spinal cord) May cause sedation
Cyclobenzaprine	Acts within CNS, mainly at the brainstem	Muscle spasms	Centrally acting Structurally related to TCAs May cause anticholinergic adverse effects, sedation
Dantrolene	Prevents release of Ca^{2+} from sarcoplasmic reticulum of skeletal muscle by inhibiting the ryanodine receptor	Malignant hyperthermia (toxicity of inhaled anesthetics and succinylcholine) and neuroleptic malignant syndrome (toxicity of antipsychotics)	Acts directly on muscle
Tizanidine	α_2 agonist, acts centrally	Muscle spasticity, multiple sclerosis, ALS, cerebral palsy	

Dystonia is a neurological movement disorder characterized by involuntary (unintended) muscle contractions that cause slow repetitive movements

MMD
MS
MS
Dystonia

MMAC
MS
MS
ALS
Cerebral Palsy

yanodine receptors (RyRs) are located in the sarcoplasmic/endoplasmic reticulum membrane and are responsible for the release of Ca2+ from intracellular stores during excitation

Opioid analgesics

MECHANISM	Act as agonists at opioid receptors (μ = β-endorphin, δ = enkephalin, κ = dynorphin) to modulate synaptic transmission—close presynaptic Ca^{2+} channels, open postsynaptic K^+ channels → ↓ synaptic transmission. Inhibit release of ACh, norepinephrine, 5-HT, glutamate, substance P.
EFFICACY	Full agonist: morphine, heroin, meperidine (long acting), methadone, codeine (prodrug; activated by CYP2D6), fentanyl. Partial agonist: buprenorphine. Mixed agonist/antagonist: nalbuphine, pentazocine, butorphanol. Antagonist: naloxone, naltrexone, methylnaltrexone.
CLINICAL USE	Moderate to severe or refractory pain, diarrhea (loperamide, diphenoxylate), acute pulmonary edema, maintenance programs for opiate use disorder (methadone, buprenorphine + naloxone), neonatal abstinence syndrome (methadone, morphine).
ADVERSE EFFECTS	Nausea, vomiting, pruritus (histamine release), opiate use disorder, respiratory depression, constipation, sphincter of Oddi spasm, miosis (except meperidine → mydriasis), additive CNS depression with other drugs. Tolerance does not develop to miosis and constipation. Treat toxicity with naloxone and prevent relapse with naltrexone once detoxified.

SSAN
Serotonin
Substance P
ACh
NE

Diarrhea
Edema of the lungs
NAS

DEN

VPN = Vomiting and Puritiis Nausea
Opiate use disorder
Resp depression
Constipaiton
Sphicter of oddi spasm

NBME 137 Q 9
What is an adverse effect of opioids ?
{{c2::pruritus }}
Opioids induced histamine release from mast callers

Opioids like meperidine suppress the activity of the Edinger-Westphal nucleus, leading to reduced parasympathetic outflow to the iris sphincter muscle.

Tramadol

MECHANISM	Very weak opioid agonist; also inhibits the reuptake of norepinephrine and serotonin.
CLINICAL USE	Chronic pain.

Mixed agonist and antagonist opioid analgesics

DRUG	MECHANISM	CLINICAL USE	NOTES
Pentazocine	κ-opioid receptor agonist and μ-opioid receptor weak antagonist or partial agonist.	Analgesia for moderate to severe pain.	Can cause opioid withdrawal symptoms if patient is also taking full opioid agonist (due to competition for opioid receptors).
Butorphanol	κ-opioid receptor agonist and μ-opioid receptor partial agonist.	Severe pain (eg, migraine, labor).	Causes less respiratory depression than full opioid agonists. Use with full opioid agonist can precipitate withdrawal. Not easily reversed with naloxone.

Partial agonists have a lower intrinsic activity at receptors than full agonists, allowing them to act either as a functional agonist or a functional antagonist, depending on the surrounding levels of naturally occurring neurotransmitter (full agonist).

Capsaicin	Naturally found in hot peppers.
MECHANISM	Excessive stimulation and desensitization of nociceptive fibers → ↓ substance P release → ↓ pain.
CLINICAL USE	Musculoskeletal and neuropathic pain.

Nerve pain, also called neuralgia or neuropathic pain, occurs when a health condition affects the nerves that carry sensations to your brain. Nerve pain can feel different from other kinds of pain.

Glaucoma therapy ↓ IOP via ↓ amount of aqueous humor (inhibit synthesis/secretion or ↑ drainage).

Beta blockers is on the ciliar epithelium u world ghalat

"βαD humor may not be politically correct."

Alpha-1 activation causes vasoconstriction of the blood vessels supplying the ciliary body,

DRUG CLASS	EXAMPLES	MECHANISM	ADVERSE EFFECTS
β-blockers	Timolol, betaxolol, carteolol	↓ aqueous humor synthesis	No pupillary or vision changes
α-agonists	Epinephrine (α_1), apraclonidine, brimonidine (α_2)	↓ aqueous humor synthesis via vasoconstriction (epinephrine) ↓ aqueous humor synthesis (apraclonidine, brimonidine) ↑ outflow of aqueous humor via uveoscleral pathway	Mydriasis (α_1); do not use in closed-angle glaucoma Blurry vision, ocular hyperemia, foreign body sensation, ocular allergic reactions, ocular pruritus
Diuretics	Acetazolamide	↓ aqueous humor synthesis via inhibition of carbonic anhydrase	No pupillary or vision changes
Prostaglandins	Bimatoprost, latanoprost ($PGF_{2\alpha}$)	↑ outflow of aqueous humor via ↓ resistance of flow through uveoscleral pathway	Darkens color of iris (browning), eyelash growth
Cholinomimetics (M_3)	Direct: pilocarpine, carbachol Indirect: physostigmine, echothiophate	↑ outflow of aqueous humor via contraction of ciliary muscle and opening of trabecular meshwork Use pilocarpine in acute angle closure glaucoma—very effective at opening meshwork into canal of Schlemm	Miosis (contraction of pupillary sphincter muscles) and cyclospasm (contraction of ciliary muscle)

The ciliary epithelium (which secretes aqueous humor) contains beta-1 and beta-2 adrenergic receptors. Activation of these receptors by catecholamines (like norepinephrine and epinephrine) stimulates adenylate cyclase, increasing cyclic AMP (cAMP) levels.Beta blockers (e.g., timolol, betaxolol) competitively inhibit these beta-adrenergic receptors.

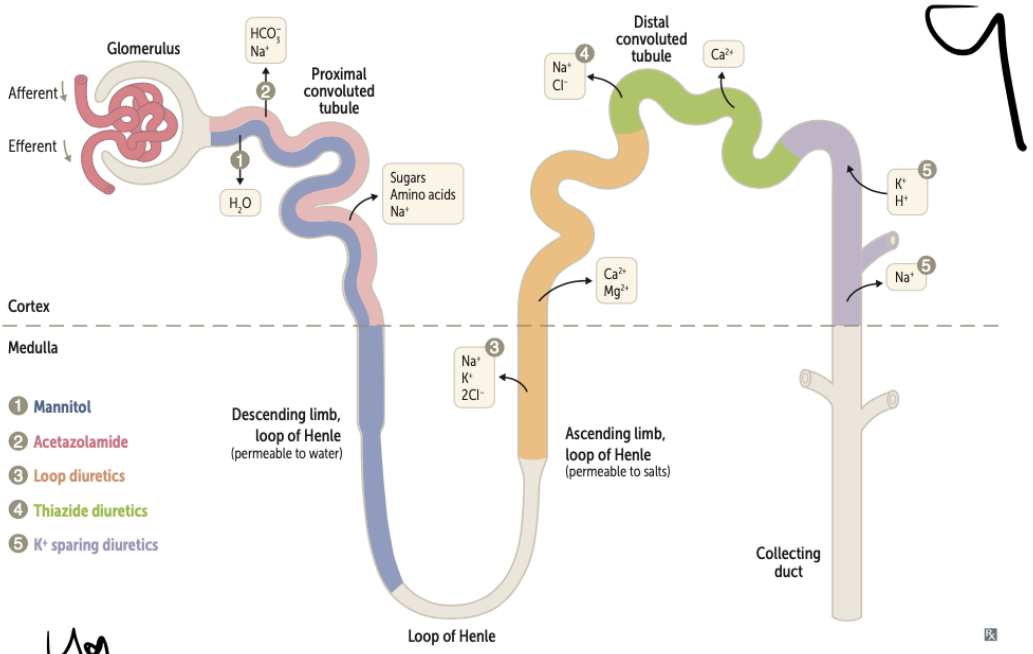
Vision
Ocular Hyperemia
Occular allergic reaction
Ocular pruritis
Foreign Body Sensation

VOOOF

Inhibit CA, reducing the formation of bicarbonate ions. This leads to decreased availability of bicarbonate, which diminishes the ionic gradient necessary for aqueous humor secretion.Less ion transport results in reduced osmotic gradient and less water movement into the posterior chamber.

Renal

Diuretics site of action



Mannitol

MECHANISM	Osmotic diuretic. ↑ serum osmolality → fluid shift from interstitium to intravascular space → ↑ urine flow, ↓ intracranial/intraocular pressure.
CLINICAL USE	Drug overdose, elevated intracranial/intraocular pressure.
ADVERSE EFFECTS	Dehydration, hypo- or hypernatremia, pulmonary edema. Contraindicated in anuria, HF.

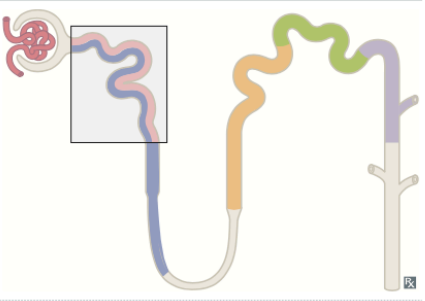
initially may cause hyponatremia due to increased ECF volume (mannitol is in the tubular lumen and due to isotonic movement in the PT salt will follow); may later cause hypernatremia due to diuresis (due to loss of blood volume)

It increases the osmolality of plasma, drawing water out of cells into the extracellular (including intravascular) space. Increased hydrostatic pressure in pulmonary capillaries. The heart (especially if weak) can't handle the extra volume. Pressure backs up into the pulmonary circulation. This leads to fluid leaking into the lungs → pulmonary edema.

Mannitol is an osmotic diuretic that is primarily eliminated via the kidneys. In anuric patients (who produce little to no urine), mannitol cannot be effectively excreted. This leads to accumulation in the plasma.

Acetazolamide

MECHANISM	Carbonic anhydrase inhibitor. Causes self-limited $NaHCO_3$ diuresis and ↓ total body HCO_3^- stores. Alkalinizes urine.
CLINICAL USE	Glaucoma, metabolic alkalosis, altitude sickness (by offsetting respiratory alkalosis), idiopathic intracranial hypertension.
ADVERSE EFFECTS	Proximal renal tubular acidosis (type 2 RTA), paresthesias, NH_3 toxicity, sulfa allergy, hypokalemia. Promotes calcium phosphate stone formation (insoluble at high pH).



Glucoma
Altitude Sickness
IIH

Acetazolamide decreases the CSF produciton in the choriod plexus and decrease ICP

Caused by metabolic acidosis and electrolyte disturbances (especially low potassium and calcium shifts).
Peripheral nerves become more excitable or impaired, leading to tingling or pins-and-needles sensation, especially in the fingers and toes.

"Acid"azolamide causes acidosis.

AE of the Acetazolamide =
RTA
PS
NH3 Toxicity
Hypokalemia
Ca Po3

In the proximal tubule, carbonic anhydrase is also involved in handling NH_3/NH_4^+ (ammonia/ammonium) balance.

Inhibiting carbonic anhydrase causes:
↓ H^+ secretion
↑ Urinary pH (more alkaline)
More alkaline urine favors conversion of NH_4^+ (trapped form) to NH_3 (diffusible form).

RPNH C

RiPiNinH Calcium

Loop diuretics

Furosemide, bumetanide, torsemide

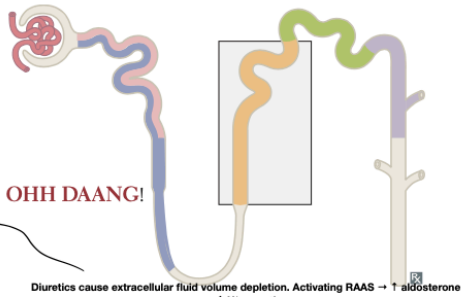
MECHANISM	Sulfonamide loop diuretics. Inhibit cotransport system ($Na^+/K^+/2Cl^-$) of thick ascending limb of loop of Henle. Abolish hypertonicity of medulla, preventing concentration of urine. Associated with ↑ PGE (vasodilatory effect on afferent arteriole); inhibited by NSAIDs. ↑ Ca^{2+} excretion. Loops lose Ca^{2+}.
CLINICAL USE	Edematous states (HF, cirrhosis, nephrotic syndrome, pulmonary edema), hypertension, hypercalcemia.
ADVERSE EFFECTS	Ototoxicity, Hypokalemia, Hypomagnesemia, Dehydration, Allergy (sulfa), metabolic Alkalosis, Nephritis (interstitial), Gout.

TAL contains numerous mitochondria, giving it a thick epithelial appearance.

Why? It needs ATP to power the Na^+/K^+ ATPase pumps on the basolateral membrane.

HF
Cirrhosis
Nephrotic syn
Hypertension
HyperCa

OHH DAANG!



Diuretics cause extracellular fluid volume depletion. Activating RAAS → ↑ aldosterone → ↑ H^+ secretion
Diuretics cause K^+ loss in the urine. Cells to exchange intracellular K^+ for extracellular H^+ → drives H^+ into cells → ↑ blood pH

Ethacrynic acid

MECHANISM	Nonsulfonamide inhibitor of cotransport system ($Na^+/K^+/2Cl^-$) of thick ascending limb of loop of Henle.
CLINICAL USE	Diuresis in patients allergic to sulfa drugs.
ADVERSE EFFECTS	Similar to furosemide, but more ototoxic.

diuretic-induced volume depletion activates the renin-angiotensin system and increases proximal tubular reabsorption of uric acid.

Loop earrings hurt your ears.

Do Na CL is reabsorbed then the urine is diluted and the the urine is left with more water and more Na CL so the no urine NOT diluted because there is alot of Na CL

Thiazide diuretics

Hydrochlorothiazide, chlorthalidone, metolazone.

MECHANISM

Inhibit NaCl reabsorption in early DCT → ↓ diluting capacity of nephron. ↓ Ca^{2+} excretion.

HF
Hypertenson
Hypercalciuria
NDI
Osteperosis

CLINICAL USE

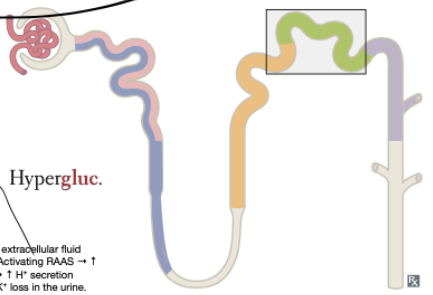
Hypertension, HF, idiopathic hypercalciuria, nephrogenic diabetes insipidus, osteoporosis.

HypoKal
HypoNat
GLUCS

ADVERSE EFFECTS

Hypokalemic metabolic alkalosis, hyponatremia, hyperglycemia, hyperlipidemia, hyperuricemia, hypercalcemia. Sulfa allergy.

Hypergluc.



Thiazides reduce urine volume in nephrogenic DI by causing mild volume depletion, which stimulates proximal tubule reabsorption of sodium and water — diverting fluid away from the defective collecting ducts.

via hypovolemic reabsorptive mechanisms in the PCT and via enhanced Na+-Ca2+ exchange in the DCT
Na goes into the urine
Ca goes into the body at the DCT

Diuretics cause extracellular fluid volume depletion. Activating RAAS → ↑ aldosterone → ↑ H^+ secretion
Diuretics cause K^+ loss in the urine.
Cells to exchange intracellular K^+ for extracellular H^+ → drives H^+ into cells → ↑ blood pH

Potassium-sparing diuretics

Spironolactone, Eplerenone, Amiloride, Triamterene.

Keep your SEAT.

MECHANISM

Spironolactone and eplerenone are competitive aldosterone receptor antagonists in cortical collecting tubule. Triamterene and amiloride block Na^+ channels at the same part of the tubule.

ENAC located at the Principal cells of the colelcting tubules

HyperAldo
HF
AScites
Antiandrogen
Nephrogenic DI

HHAAN

CLINICAL USE

Hyperaldosteronism, K^+ depletion, HF, hepatic ascites (spironolactone), nephrogenic DI (amiloride), ~~antiandrogen (spironolactone)~~.

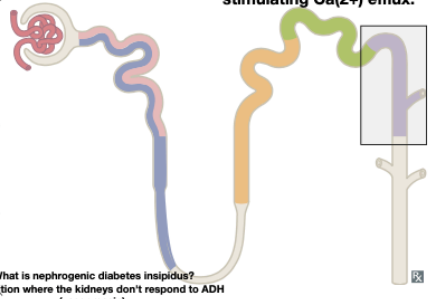
ADVERSE EFFECTS

Hyperkalemia (can lead to arrhythmias), endocrine effects with spironolactone (eg, gynecomastia, antiandrogen effects), metabolic acidosis.

Gynecomastia
Antiandorgenic effects
metabolic Acidosis
Hyperkalemia

GAMH

amiloride enhances Ca(2+) reabsorption in the DCT2-CNT predominantly by increasing the driving force across NCX1, thereby stimulating Ca(2+) efflux.



What is nephrogenic diabetes insipidus?
A condition where the kidneys don't respond to ADH (vasopressin).
Amiloride blocks ENAC in the cortical collecting duct. This prevents lithium from entering principal cells.By stopping lithium accumulation in principal cells, amiloride preserves aquaporin-2 expression and restores partial water reabsorption in response to ADH.

Diuretics: electrolyte changes

Urine NaCl

↑ with all diuretics (concentration varies based on potency of diuretic effect). Serum NaCl may decrease as a result.

Urine K^+

↑ especially with loop and thiazide diuretics, excluding K^+-sparing diuretics.

Blood pH

↓ (**acidemia**): carbonic anhydrase inhibitors: ↓ HCO_3^- reabsorption. K^+ sparing: aldosterone blockade prevents K^+ secretion and H^+ secretion. Additionally, hyperkalemia leads to K^+ entering all cells (via H^+/K^+ exchanger) in exchange for H^+ exiting cells.

↑ (**alkalemia**): loop diuretics and thiazides cause alkalemia through several mechanisms:

- Volume contraction → ↑ AT II → ↑ Na^+/H^+ exchange in PCT → ↑ HCO_3^- reabsorption ("contraction alkalosis")
- K^+ loss leads to K^+ exiting all cells (via H^+/K^+ exchanger) in exchange for H^+ entering cells
- In low K^+ state, H^+ (rather than K^+) is exchanged for Na^+ in cortical collecting tubule → alkalosis and "paradoxical aciduria"

Angiotensin II stimulates the Na^+/H^+ exchanger (NHE3) in the proximal convoluted tubule (PCT). This transporter does the following: Reabsorbs Na^+ from the tubular fluid into the blood Secretes H^+ into the tubular fluid
The secreted H+ combines w/ filtered HCO3- in the tubule to form H2CO3 Carbonic anhydrase then converts H_2CO_3 into CO_2 and H_2O, which are reabsorbed into the cell.
Inside the cell, CO_2 is converted back to HCO_3^-, which is then transported into the blood.

Urine Ca^{2+}

↑ with loop diuretics: ↓ paracellular Ca^{2+} reabsorption → hypocalcemia.

↓ with thiazides: enhanced Ca^{2+} reabsorption.

Normal state = Normal Na^+ is reabsorbed (via ENaC). K^+ is secreted into the urine (to maintain K^+ balance). H^+ is also secreted by alpha-intercalated cells when needed to regulate acid-base balance.
When K+ is low --> The kidney decreases K^+ loss by minimizing K^+ secretion in the collecting tubule. and H+ is being secreted into the urine, the blood become more alkaline

Paradoxical aciduria*** — why it's paradoxical: In alkalosis, you would expect the urine to be alkaline (more bicarbonate, fewer H^+ ions).

But in hypokalemia, the kidneys still secrete H^+ into the urine

MECHANISM		Inhibit ACE → ↓ AT II → ↓ GFR by preventing constriction of efferent arterioles. ↑ renin due to loss of negative feedback. Inhibition of ACE also prevents inactivation of bradykinin, a potent vasodilator.	
CLINICAL USE	HTN HF DN HHD	Hypertension, HF (↓ mortality), proteinuria, diabetic nephropathy. Prevent unfavorable heart remodeling as a result of chronic hypertension.	In chronic kidney disease (eg, diabetic nephropathy), ↓ intraglomerular pressure, slowing GBM thickening.
ADVERSE EFFECTS		Cough, Angioedema (both due to ↑ bradykinin; contraindicated in C1 esterase inhibitor deficiency), Teratogen (fetal renal malformations), ↑ Creatinine (↓ GFR), Hyperkalemia, and Hypotension. Used with caution in bilateral renal artery stenosis because ACE inhibitors will further ↓ GFR → renal failure.	Captopril's CATCHH.

Both renal arteries are narrowed → ↓ renal perfusion.

The body senses low kidney perfusion as low blood pressure → activates RAAS → ↑ angiotensin II → constricts efferent arteriole to preserve GFR.

This is a compensatory mechanism to maintain filtration despite reduced blood flow.

Angiotensin II receptor blockers		Losartan, candesartan, valsartan.
MECHANISM		Selectively block binding of angiotensin II to AT_1 receptor. Effects similar to ACE inhibitors, but ARBs do not increase bradykinin.
CLINICAL USE	HTN HF Proteinuria CKD	Hypertension, HF, proteinuria, or chronic kidney disease (eg, diabetic nephropathy) with intolerance to ACE inhibitors (eg, cough, angioedema).
ADVERSE EFFECTS	HHPC	Hyperkalemia, ↓ GFR, hypotension; teratogen.

ARBs lower intraglomerular pressure by dilating th efferent arteriole, reducing damage to the glomeru This leads to reduced protein loss in urine—a key marker and cause of CKD progression and lowers

Aliskiren	
MECHANISM	Direct renin inhibitor, blocks conversion of angiotensinogen to angiotensin I. Aliskiren kills renin.
CLINICAL USE	Hypertension.
ADVERSE EFFECTS	Hyperkalemia, ↓ GFR, hypotension, angioedema. Relatively contraindicated in patients already taking ACE inhibitors or ARBs and contraindicated in pregnancy.

Psych

What is the MoA of trazodone?

primarily blocks 5-HT2, alpha1-adrenergic, and H1 receptors and inhibits 5HT reuptake

FTT CHP

partial agonist

Antipsychotics

CAAP

Clonzapine = Claw
Arpirpazole = airpit
Olanzapine = Oil
Quetiapine = Quiet
Risperidone = Risperidone
Ziprosidone = Zlpper

Typical (1st-generation) antipsychotics—haloperidol, pimozide, trifluoperazine, fluphenazine, thioridazine, chlorpromazine.

Atypical (2nd-generation) antipsychotics—aripiprazole, asenapine, ~~clozapine~~, ~~olanzapine~~, ~~quetiapine~~, iloperidone, paliperidone, ~~risperidone~~, lurasidone, ~~ziprasidone~~.

MECHANISM

Block dopamine D_2 receptor (↑ cAMP). Atypical antipsychotics also block serotonin 5-HT_2 receptor. Aripiprazole is a D_2 partial agonist.

CLINICAL USE

HOTS
Huntingon
OCD
Toureete
Schzioprhenia

Schizophrenia (typical antipsychotics primarily treat positive symptoms; atypical antipsychotics treat both positive and negative symptoms), disorders with concomitant psychosis (eg, bipolar disorder), Tourette syndrome, OCD, Huntington disease. Clozapine is used for treatment-resistant psychotic disorders or those with persistent suicidality (cloze to the edge).

Blocking 5-HT2A receptors in the prefrontal cortex increases dopamine release in that region.

This is beneficial because low dopamine in the prefrontal cortex is associated with negative symptoms and cognitive deficits in schizophrenia (e.g., flat affect, poor executive function).

ADVERSE EFFECTS

Antihistaminic (sedation), anti-α_1-adrenergic (orthostatic hypotension), antimuscarinic (dry mouth, constipation) (anti-HAM). Use with caution in dementia.

Metabolic: weight gain, hyperglycemia, dyslipidemia. Highest risk with clozapine and olanzapine (obesity).

Endocrine: hyperprolactinemia → galactorrhea, oligomenorrhea, gynecomastia.

Cardiac: QT prolongation.

Neurologic: neuroleptic malignant syndrome.

Ophthalmologic: chlorpromazine—corneal deposits; thioridazine—retinal deposits.

Clozapine—agranulocytosis (monitor WBCs clozely), seizures (dose related), myocarditis.

Extrapyramidal symptoms—ADAPT:

- Hours to days: Acute Dystonia (muscle spasm, stiffness, oculogyric crisis). Treatment: benztropine, diphenhydramine.
- Days to months:
  - Akathisia (restlessness). Treatment: β-blockers, benztropine, benzodiazepines.
  - Parkinsonism (bradykinesia). Treatment: benztropine, amantadine.
- Months to years: Tardive dyskinesia (chorea, especially orofacial). Treatment: benzodiazepines, botulinum toxin injections, valbenazine, deutetrabenazine.

Oculogyric Crisis (OGC) is a rare, acute dystonic reaction involving the extraocular muscles.

Akathisia is defined as an inability to remain still Rock back and forth

Valbenazine is a selective vesicular monoamine transporter 2 (VMAT2) inhibitor. It works by inhibiting VMAT2, which is responsible for packaging monoamines (such as dopamine) into synaptic vesicles.

NOTES

Lipid soluble → stored in body fat → slow to be removed from body.

Typical antipsychotics have greater affinity for D_2 receptor than atypical antipsychotics → ↑ risk for hyperprolactinemia, extrapyramidal symptoms, neuroleptic malignant syndrome.

High-potency typical antipsychotics: haloperidol, trifluoperazine, pimozide, fluphenazine (Hal tries pie to fly high)—more neurologic adverse effects (eg, extrapyramidal symptoms).

Low-potency typical antipsychotics: chlorpromazine, thioridazine (cheating thieves are low)—more antihistaminic, anti-α_1-adrenergic, antimuscarinic effects.

Tricyclic antidepressants

Amitriptyline, nortriptyline, imipramine, desipramine, clomipramine, doxepin, amoxapine.

AND
Amitryptilien
Nortyrptyline
Desipermine

MECHANISM

TCAs inhibit 5-HT and NE reuptake.

CLINICAL USE

MDD, peripheral neuropathy, chronic neuropathic pain, migraine prophylaxis, OCD (clomipramine), nocturnal enuresis (imipramine).

Nocturnal enuresis
OCD
Chronic Neuropathic pain

ADVERSE EFFECTS

Sedation, α_1-blocking effects including postural hypotension, and atropine-like (anticholinergic) adverse effects (tachycardia, urinary retention, dry mouth). 3° TCAs (amitriptyline) have more anticholinergic effects than 2° TCAs (nortriptyline). Can prolong QT interval.

Tri-CyCliC's: Convulsions, Coma, Cardiotoxicity (arrhythmia due to Na^+ channel inhibition); also respiratory depression, hyperpyrexia. Confusion and hallucinations are more common in older adults due to anticholinergic adverse effects (2° amines [eg, nortriptyline] better tolerated). Treatment: $NaHCO_3$ to prevent arrhythmia.

TSS
MDL P

TCA
SSRI
St John wort

Merperidine
Dextromethrophan
Linzezolid Psudeoephrine

Monoamine oxidase inhibitors

Tranylcypromine, phenelzine, isocarboxazid, selegiline (selective MAO-B inhibitor). (MAO takes pride in Shanghai).

MECHANISM

Nonselective MAO inhibition → ↑ levels of amine neurotransmitters (norepinephrine, 5-HT, dopamine).

Monoamine oxidase degrades biogenic amine neurotransmitters (eg, serotonin, dopamine, norepinephrine, epinephrine).

CLINICAL USE

Atypical depression, anxiety. Parkinson disease (selegiline).

Anxiety
Atypical depresion
Parinsion

ADVERSE EFFECTS

CNS stimulation; hypertensive crisis, most notably with ingestion of tyramine. Contraindicated with SSRIs, TCAs, St. John's wort, meperidine, dextromethorphan, pseudoephedrine, linezolid (to avoid precipitating serotonin syndrome).

NBME ghalat

Opioid analgesic
Meperidine inhibits serotonin reuptake in the CNS.

dextro = Cough suppressant (NMDA antagonist)it also has serotonin reuptake inhibition properties

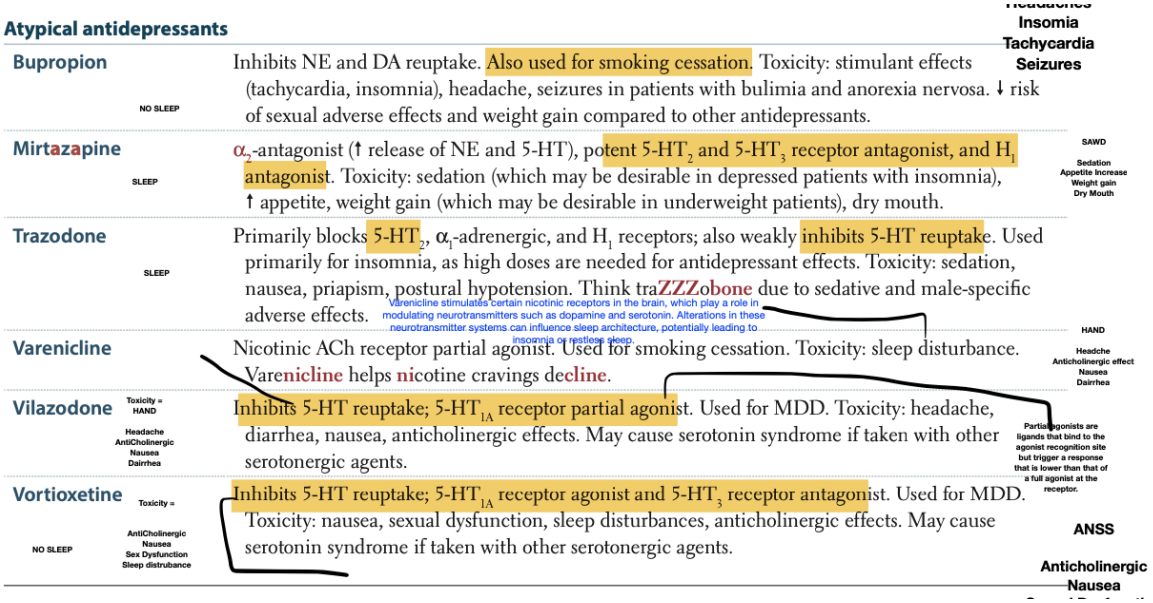
Wait 2 weeks after stopping MAO inhibitors before starting serotonergic drugs or stopping dietary restrictions.

Atypical Depression = atypical depression. Increased appetite. Increased sleep. Leaden paralysis (i.e., heavy, leaden feelings in arms or legs)

TCA
The MDSS PLease
Mepredine
Dextromethropahn
SSRI
St John Wort
Pseudopherdrine

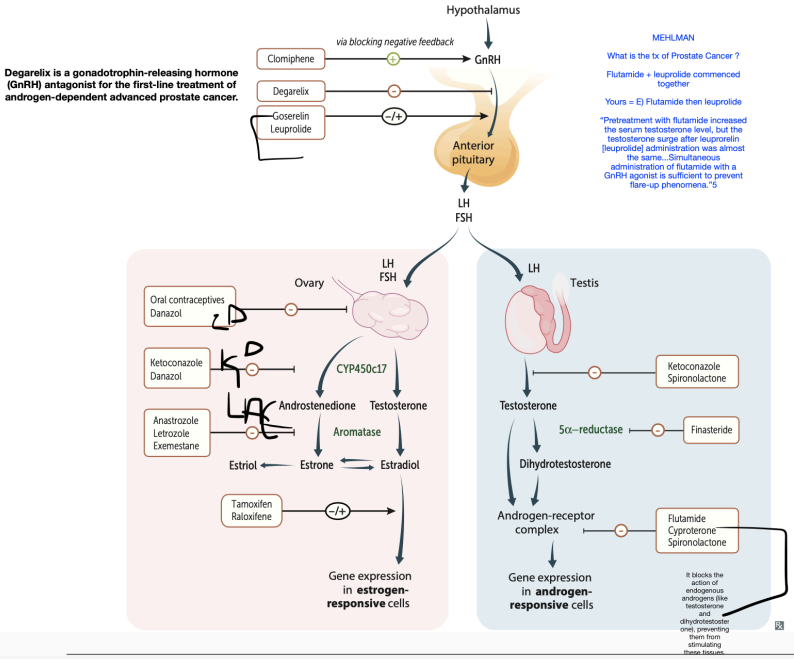
St. John's Wort is a herbal antidepressant supplement. Serotonin reuptake inhibition

Pseudoephedrine releases norepinephrine and has weak action on dopamine and serotonin.


Atypical antidepressants
Bupropion
Inhibits NE and DA reuptake. Also used for smoking cessation. Toxicity: stimulant effects (tachycardia, insomnia), headache, seizures in patients with bulimia and anorexia nervosa. ↓ risk of sexual adverse effects and weight gain compared to other antidepressants.
NO SLEEP
Insomia
Tachycardia
Seizures
Mirtazapine
α2-antagonist (↑ release of NE and 5-HT), potent 5-HT2 and 5-HT3 receptor antagonist, and H1 antagonist. Toxicity: sedation (which may be desirable in depressed patients with insomnia), ↑ appetite, weight gain (which may be desirable in underweight patients), dry mouth.
SLEEP
SAWD
Sedation
Appetite Increase
Weight gain
Dry Mouth
Trazodone
Primarily blocks 5-HT2, α1-adrenergic, and H1 receptors; also weakly inhibits 5-HT reuptake. Used primarily for insomnia, as high doses are needed for antidepressant effects. Toxicity: sedation, nausea, priapism, postural hypotension. Think traZZZobone due to sedative and male-specific adverse effects.
SLEEP
Varenicline stimulates certain nicotinic receptors in the brain, which play a role in modulating neurotransmitters such as dopamine and serotonin. Alterations in these neurotransmitter systems can influence sleep architecture, potentially leading to insomnia or restless sleep.
Varenicline
Nicotinic ACh receptor partial agonist. Used for smoking cessation. Toxicity: sleep disturbance. Varenicline helps nicotine cravings decline.
HAND
Headche
Anticholinergic effect
Nausea
Dairrhea
Vilazodone
Inhibits 5-HT reuptake; 5-HT1A receptor partial agonist. Used for MDD. Toxicity: headache, diarrhea, nausea, anticholinergic effects. May cause serotonin syndrome if taken with other serotonergic agents.
Toxicity = HAND
Headache
AntiCholinergic
Nausea
Dairrhea
Partial agonists are ligands that bind to the agonist recognition site but trigger a response that is lower than that of a full agonist at the receptor.
Vortioxetine
Inhibits 5-HT reuptake; 5-HT1A receptor agonist and 5-HT3 receptor antagonist. Used for MDD. Toxicity: nausea, sexual dysfunction, sleep disturbances, anticholinergic effects. May cause serotonin syndrome if taken with other serotonergic agents.
Toxicity =
NO SLEEP
AntiCholinergic
Nausea
Sex Dysfunction
Sleep distrubance
ANSS
Anticholinergic
Nausea

Repro

Control of reproductive hormones



Degarelix is a gonadotrophin-releasing hormone (GnRH) antagonist for the first-line treatment of androgen-dependent advanced prostate cancer.

MEHLMAN

What is the tx of Prostate Cancer ?

Flutamide + leuprolide commenced together

Yours = E) Flutamide then leuprolide

"Pretreatment with flutamide increased the serum testosterone level, but the testosterone surge after leuprorelin [leuprolide] administration was almost the same...Simultaneous administration of flutamide with a GnRH agonist is sufficient to prevent flare-up phenomena."5

Gonadotropin-releasing hormone analogs	Leuprolide, goserelin, nafarelin, histrelin. GNrH
MECHANISM	Act as GnRH agonists when used in pulsatile fashion. In pulses happend when the menstural cycle needs to activated When used in continuous fashion, first transiently act as GnRH agonists (tumor flare), but subsequently act as GnRH antagonists (downregulate GnRH receptor in pituitary → ↓ FSH and ↓ LH → ↓ estrogen in females and ↓ testosterone in males). Can be used in lieu of GnRH.
CLINICAL USE	Uterine fibroids, endometriosis, precocious puberty, prostate cancer, infertility. Pulsatile for pregnancy, continuous for cancer. PEUI = puberty, Endometriosis, Uterione fibriods and infertigity HEL
ADVERSE EFFECTS	Hypogonadism, ↓ libido, erectile dysfunction, nausea, vomiting. Hypogonadism ED Libido decrease
Degarelix	Flare = until the amount becomes stable amount.
MECHANISM	GnRH antagonist. No start-up flare.
CLINICAL USE	Prostate cancer.
ADVERSE EFFECTS	Hot flashes, liver toxicity.
Estrogens	Ethinyl estradiol, DES, mestranol.
MECHANISM	Bind estrogen receptors.
CLINICAL USE	Hypogonadism or ovarian failure, menstrual abnormalities (combined OCPs), hormone replacement therapy in postmenopausal females.
ADVERSE EFFECTS	↑ risk of endometrial cancer (when given without progesterone), bleeding in postmenopausal patients, clear cell adenocarcinoma of vagina in females exposed to DES in utero, ↑ risk of thrombi. Contraindications—ER ⊕ breast cancer, history of DVTs, tobacco use in females > 35 years old.

Fibroids = Fibroids are benign tumors of the uterine smooth muscle that grow in response to estrogen and progesterone.
Effect of leuprolide: By lowering estrogen levels.
Endometriosis: Hormonal dependence: Endometrial tissue outside the uterus (endometriosis) responds to estrogen, leading to proliferation, inflammation, and pain.
Effect of leuprolide: Suppressing estrogen:

diethylstilbestrol

Hypogondiasm
HRT
Ovarian failure
Menstural abnormalties

CI of Estrogen =
Tobacco use in females > 35 years old
ER Breast
DVT history

AE of Estrogen =
Bleeding in postmenopausal patient
Endometrial Cancer
Thrombi
Clear Cell Adenocarcinoma

AE of Clomiphene =
Hot flasshes, Ovarian enlargement,
Multiple simultaneous Preg
Visual distrubances

Selective estrogen receptor modulators

HOM V

Clomiphene	Antagonist at estrogen receptors in hypothalamus. Prevents normal feedback inhibition and ↑ release of LH and FSH from pituitary, which stimulates ovulation. Used to treat infertility due to anovulation (eg, PCOS). May cause hot flashes, ovarian enlargement, multiple simultaneous pregnancies, visual disturbances.
Tamoxifen AE of Tamoxifen = HET Hot Flushes Endoomedical carcinoma Thromboembolism	Antagonist at breast, partial agonist at uterus, bone. Hot flashes, ↑ risk of thromboembolic events (especially with tobacco smoking), and endometrial cancer. Used to treat and prevent recurrence of ER/PR ⊕ breast cancer and to prevent gynecomastia in patients undergoing prostate cancer therapy.
Raloxifene AE and use Raloxifene = HOT Hot Flushes Osteopoerisis Thromboembolism	Antagonist at breast, uterus; agonist at bone; hot flashes, ↑ risk of thromboembolic events (especially with tobacco smoking), but no increased risk of endometrial cancer (vs tamoxifen, so you can "relax"); used primarily to treat osteoporosis.
Aromatase inhibitors	Anastrozole, letrozole, exemestane.
MECHANISM	Inhibit peripheral conversion of androgens to estrogen.
CLINICAL USE	ER ⊕ breast cancer in postmenopausal females.

Ovarian enlargment = When the hypothalamus senses low estrogen levels, it signals the pituitary gland to release more follicle-stimulating hormone (FSH) and luteinizing hormone (LH). FSH stimulates the growth of follicles in the ovaries.

multiple simultaneous pregnancies = clomiphene stimulates the development of multiple follicles

visual disburtances = Estrogen receptors are present in the retina, the light-sensitive tissue at the back of the eye. Clomiphene's anti-estrogenic action might affect the function of these receptors, leading to visual changes.

Unlike tamoxifen, raloxifene does not stimulate the endometrium, reducing the risk of endometrial hyperplasia and cancer.

Hormone replacement therapy	Used for relief or prevention of menopausal symptoms (eg, hot flashes, vaginal atrophy), osteoporosis (↑ estrogen, ↓ osteoclast activity). Unopposed estrogen replacement therapy ↑ risk of endometrial cancer, progesterone/progestin is added. Possible increased cardiovascular risk.

Hot Flash
Osteoperosis
Vaginal atrophy

Progestins are synthetic progestogens and are used in medicine.

MELt

Progestins	Levonorgestrel, medroxyprogesterone, etonogestrel, norethindrone, megestrol.
MECHANISM	Bind progesterone receptors, ↓ growth and ↑ vascularization of endometrium, thicken cervical mucus.
CLINICAL USE	Contraception (forms include pill, intrauterine device, implant, depot injection), endometrial cancer, abnormal uterine bleeding. Progestin challenge: presence of bleeding upon withdrawal of progestins excludes anatomic defects (eg, Asherman syndrome) and chronic anovulation without estrogen.

If the Progestin Challenge does induce bleeding, the patient does have adequate estrogen levels; anovulation is the problem

positive response is any bleeding more than light spotting that occurs within 2 weeks after the progestin is given. This bleeding will usually occur 2-7 days after the progestin is finished. Withdrawal bleeding will usually be seen if the patient's estradiol level has been over about 40 pg/ml.

Contraception =
Endometrial cancer
AUB
Progestin Challenge: presence of bleeding upon withdrawal of progestins and anovulaiton without estrogen

Estrogen --> means build up endometrium and there will be withdrawal bleeding
anovulation without estrogen --> means NO build up, there will be withdrawal bleeding

Asherman syndrome (intrauterine adhesions or intrauterine synechiae) occurs when scar tissue forms inside the uterus and/or the cervix.

EAP

Antiprogestins	Mifepristone, ulipristal.
MECHANISM	Competitive inhibitors of progestins at progesterone receptors.
CLINICAL USE	Termination of pregnancy (mifepristone with misoprostol); emergency contraception (ulipristal).

Ulipristal acetate exerts its pharmacological activity by binding to the body's progesterone receptors to produce an anti-progesterone contraceptive effect on the ovary (by suppressing or delaying ovulation) and on the endometrium (by decreasing endometrial thickness).

Ulipristal's action: By blocking progesterone receptors in the hypothalamus and pituitary, ulipristal delays or suppresses the LH surge.

Combined contraception Progesterone is the natural hormone involved in female reproductive physiology. Function of Progesterone: —> Preparing the endometrium for implantation. —> Maintaining pregnancy. —> Regulating the menstrual cycle. Progestins are synthetic compounds designed to mimic progesterone's effects. —> Suppressing ovulation. —> Thinning the endometrial lining. —> Thickening cervical mucus. CI = Smoking Cardiovascular events Migraine Cancer Liver disease	Progestins and ethinyl estradiol; forms include pill, patch, vaginal ring. Estrogen and progestins inhibit LH/FSH and thus prevent estrogen surge. No estrogen surge → no LH surge → no ovulation. Progestins cause thickening of cervical mucus, thereby limiting access of sperm to uterus. Progestins also inhibit endometrial proliferation → endometrium is less suitable to the implantation of an embryo. Adverse effects: breakthrough menstrual bleeding, breast tenderness, VTE, hepatic adenomas. Contraindications: people > 35 years old who smoke tobacco (↑ risk of cardiovascular events), patients with ↑ risk of cardiovascular disease (including history of venous thromboembolism, coronary artery disease, stroke), migraine (especially with aura), breast cancer, liver disease. Hepatic Adenoma Embolism Bleeding Breat tenderness HEBB = AE Estrogens can impair bile flow by affecting bile salt transporters in hepatocytes. This leads to cholestasis, a condition where bile cannot flow properly from the liver, causing accumulation of bile acids and bilirubin.
Copper intrauterine device	
MECHANISM	Produces local inflammatory reaction toxic to sperm and ova, preventing fertilization and implantation; hormone free.
CLINICAL USE	Long-acting reversible contraception. Most effective emergency contraception.
ADVERSE EFFECTS	Heavier or longer menses, dysmenorrhea. Insertion contraindicated in active PID (IUD may impede PID resolution).
Tocolytics TIN Terbutaline (B2 Agonist) Indomethacin (NSAID)	Medications that relax the uterus; include terbutaline (β_2-agonist action), nifedipine (Ca^{2+} channel blocker), indomethacin (NSAID). Used to ↓ contraction frequency in preterm labor and allow time for administration of glucocorticoids (to promote fetal lung maturity) or transfer to appropriate medical center with obstetrical care.

Danazol

MECHANISM	Synthetic androgen that acts as partial agonist at androgen receptors.
CLINICAL USE	Endometriosis, hereditary angioedema.
ADVERSE EFFECTS	Weight gain, edema, acne, hirsutism, masculinization, ↓ HDL levels, hepatotoxicity, idiopathic intracranial hypertension.

Danazol is a weak androgen that exerts a negative feedback effect on the hypothalamus and pituitary gland.
It decreases the secretion of gonadotropins (LH and FSH).Since endometriosis is estrogen-dependent (the ectopic endometrial tissue proliferates under estrogen stimulation)

it activates the receptor, but not to the same extent as a full agonist, resulting in a weaker effect.

HHHH
A
G
E
decrease HDL
Hirtusium
Hepatotoxicity
Hypertension
Acne
Gain
Edema

Danazol stimulates the liver to produce more C1-INH, a key regulator of the complement system and bradykinin pathway.With more C1-INH available, the overproduction of bradykinin is controlled, decreasing vascular permeability and swelling episodes.

They reduce HDL (good cholesterol) levels by decreasing HDL synthesis and increasing HDL catabolism.

Danazol increases androgen levels, which can affect cerebrospinal fluid (CSF) dynamics. Elevated androgens may lead to increased venous pressure or impaired CSF absorption, resulting in increased intracranial pressure.

Testosterone, methyltestosterone

MECHANISM	Agonists at androgen receptors.
CLINICAL USE	Treat hypogonadism and promote development of 2° sex characteristics.
ADVERSE EFFECTS	Virilization in females; testicular atrophy in males. Premature closure of epiphyseal plates. ↑ LDL, ↓ HDL.

↓ HDL.

Adds a hydroxyl group at the 17th carbon of pregnenolone and progesterone.
17 alpha hydroxylase = Pregnenolone → 17α-hydroxypregnenolone
Progesterone → 17α-hydroxyprogesterone

Antiandrogens

DRUG	MECHANISM	CLINICAL USE	ADVERSE EFFECTS
Abiraterone	17α-hydroxylase/17,20-lyase inhibitor (↓ steroid synthesis)	Prostate cancer	Hypertension, hypokalemia (↑ mineralocorticoids)
Finasteride	5α-reductase inhibitor (↓ conversion of testosterone to DHT)	BPH, male-pattern baldness	Gynecomastia, sexual dysfunction
Flutamide, bicalutamide	Nonsteroidal competitive inhibitors at androgen receptor (↓ steroid binding)	Prostate cancer	Gynecomastia, sexual dysfunction
Ketoconazole	17α-hydroxylase/17,20-lyase inhibitor	Prostate cancer	Gynecomastia
Spironolactone	Androgen receptor and 17α-hydroxylase/17,20-lyase inhibitor	PCOS	Amenorrhea

u world ghalat 2 baar
5 alpha reductase inhibitors leads to more testerone
which leads to more estrogen leading to gynecomastia by aromatase

Cleaves the bond between carbons 17 and 20 of 17α-hydroxylated steroids.

Converts:

~~17α-hydroxypregnenolone →~~ Dehydroepiandrosterone (DHEA)

17α-hydroxyprogesterone → Androstenedione (less efficiently)

Lower DHT levels reduce androgenic stimulation of tissues. This relative increase in estrogen activity (or decrease in androgenic suppression) in breast tissue can stimulate glandular growth, causing breast enlargement.
DHT is critical for:

Libido (sex drive)

Erectile function

Penile sensitivity

Tamsulosin

MECHANISM	α_1-antagonist selective for $\alpha_{1A/D}$ receptors in prostate (vs vascular α_{1B} receptors) → ↓ smooth muscle tone → ↑ urine flow.
CLINICAL USE	BPH.

Minoxidil

MECHANISM	Direct arteriolar vasodilator.
CLINICAL USE	Androgenetic alopecia (pattern baldness), severe refractory hypertension.

Resp

H_1-blockers	Also called antihistamines. Reversible inhibitors of H_1 histamine receptors. May function as neutral antagonists or inverse agonists.	
First generation	Diphenhydramine, dimenhydrinate, chlorpheniramine, doxylamine.	Names usually contain "-en/-ine" or "-en/-ate."
CLINICAL USE	Allergy, motion sickness, vomiting in pregnancy, sleep aid.	
ADVERSE EFFECTS	Sedation, antimuscarinic, anti-α-adrenergic.	
Second generation	Loratadine, fexofenadine, desloratadine, cetirizine.	Names usually end in "-adine." Setirizine (cetirizine) is second-generation agent.
CLINICAL USE	Allergy.	
ADVERSE EFFECTS	Far less sedating than 1st generation because of ↓ entry into CNS.	

VAMS
Vomiting
Allergy
Motion sicknes
Sleep Aid

inhibit the action of histamine on these receptors, resulting in decreased neuronal activity related to arousal.

Dextromethorphan is chemically related to opioids like codeine and morphine, allowing it to bind to opioid receptors. Dextromethorphan itself does not bind with high affinity to mu-opioid receptors (MORs). It's structurally related to opioids.

Dextromethorphan Antitussive (antagonizes NMDA glutamate receptors). Synthetic codeine analog. Has mild opioid effect when used in excess. Naloxone can be given for overdose. Mild abuse potential. May cause serotonin syndrome if combined with other serotonergic agents.

Dextromethorphan is primarily an antitussive agent, but it also acts as a weak non-selective serotonin reuptake inhibitor (SRI) and a sigma-1 receptor agonist. By inhibiting serotonin reuptake, it increases the levels of serotonin (5-HT) in the synaptic cleft.
DXM is also an agonist at the sigma-1 receptor, a protein that modulates neurotransmitter systems including serotonin.
Activation of this receptor may indirectly enhance serotonin signaling.
Dextromethorphan works by blocking NMDA receptors can affect overall neurotransmitter balance, including serotonin, through complex feedback mechanisms.

U got this wrong in the u world
یہ تم کو غلت ہوا تھا

Pseudoephedrine, phenylephrine	
MECHANISM	Activation of α-adrenergic receptors in nasal mucosa → local vasoconstriction.
CLINICAL USE	Reduce hyperemia, edema (used as nasal decongestants); open obstructed eustachian tubes.
ADVERSE EFFECTS	Hypertension. Rebound congestion (rhinitis medicamentosa) if used more than 4–6 days. Associated with tachyphylaxis. Can also cause CNS stimulation/anxiety (pseudoephedrine).

tachyphylaxis
= rapidly diminishing response to successive doses of a drug, rendering it less effective. The effect is common with drugs acting on the nervous system.

Hypertension
Congestion
Tachyphylaxis
CNS stimulation/anxieity

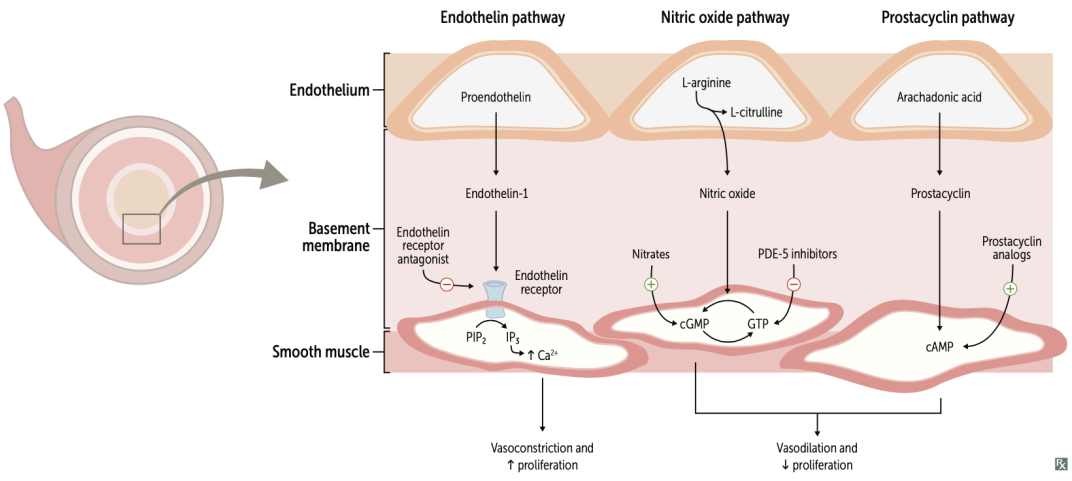
If u use for more than 4 to 6 days you can get the nasal congestion

Pulmonary hypertension drugs

DRUG	MECHANISM	CLINICAL NOTES
Endothelin receptor antagonists	Competitively antagonizes endothelin-1 receptors → ↓ pulmonary vascular resistance.	Hepatotoxic (monitor LFTs). Example: bosentan.
PDE-5 inhibitors	Inhibits PDE-5 → ↑ cGMP → prolonged vasodilatory effect of NO.	Also used to treat erectile dysfunction. Contraindicated when taking nitroglycerin or other nitrates (due to risk of severe hypotension). Example: sildenafil.
Prostacyclin analogs	PGI_2 (prostacyclin) with direct vasodilatory effects on pulmonary and systemic arterial vascular beds. Inhibits platelet aggregation.	Adverse effects: flushing, jaw pain. Examples: epoprostenol, iloprost.

NBME asked your study partner

They cause dilation of blood vessels in various tissues, including the oral and facial regions.



Asthma drugs	Bronchoconstriction is mediated by (1) inflammatory processes and (2) parasympathetic tone; therapy is directed at these 2 pathways.
Inhaled β_2-agonists	**Albuterol, salmeterol, formoterol**—relax bronchial smooth muscle. Can cause tremor, arrhythmia. Albuterol is short-acting, used for acute symptoms. Salmeterol and formoterol are long-acting.
Inhaled glucocorticoids	**Fluticasone, budesonide**—inhibit the synthesis of virtually all cytokines. Inactivate NF-κB, the transcription factor that induces production of TNF-α and other inflammatory agents. 1st-line therapy for chronic asthma. Use a spacer or rinse mouth after use to prevent oral thrush.
Muscarinic antagonists	**Tiotropium, ipratropium**—competitively block muscarinic receptors, preventing bronchoconstriction. Also used for COPD. Tiotropium is long acting.
Antileukotrienes	**Montelukast, zafirlukast**—block leukotriene receptors (CysLT1). Especially good for aspirin-induced and exercise-induced asthma. **Zileuton**—5-lipoxygenase inhibitor. ↓ conversion of arachidonic acid to leukotrienes. Hepatotoxic.
Anti-IgE monoclonal therapy	**Omalizumab**—binds mostly unbound serum IgE and blocks binding to FcεRI. Used in allergic asthma with ↑ IgE levels resistant to inhaled glucocorticoids and long-acting β_2-agonists.
Methylxanthines	**Theophylline**—likely causes bronchodilation by inhibiting phosphodiesterase → ↑ cAMP levels due to ↓ cAMP hydrolysis. Limited use due to narrow therapeutic index (cardiotoxicity, neurotoxicity); metabolized by cytochrome P-450. Blocks actions of adenosine.
PDE-4 Inhibitors	**Roflumilast**—inhibits phosphodiesterase → ↑ cAMP → bronchodilation, ↓ airway inflammation. Used in COPD to reduce exacerbations.
Chromones	**Cromolyn**—prevents mast cell degranulation. Prevents acute asthma symptoms. Rarely used.
Anti-IL-5 monoclonal therapy	Prevents eosinophil differentiation, maturation, activation, and survival mediated by IL-5 stimulation. For maintenance therapy in severe eosinophilic asthma. **Mepolizumab, reslizumab**—against IL-5. **Benralizumab**—against IL-5 receptor α.

Cysteinyl leukotriene receptor 1, also termed CYSLTR1, is a receptor for cysteinyl leukotrienes (LT)

Beta-2 stimulation in skeletal muscles increases muscle excitability and tremor. arrhythmia --> at higher doses it can stimulate beta-1

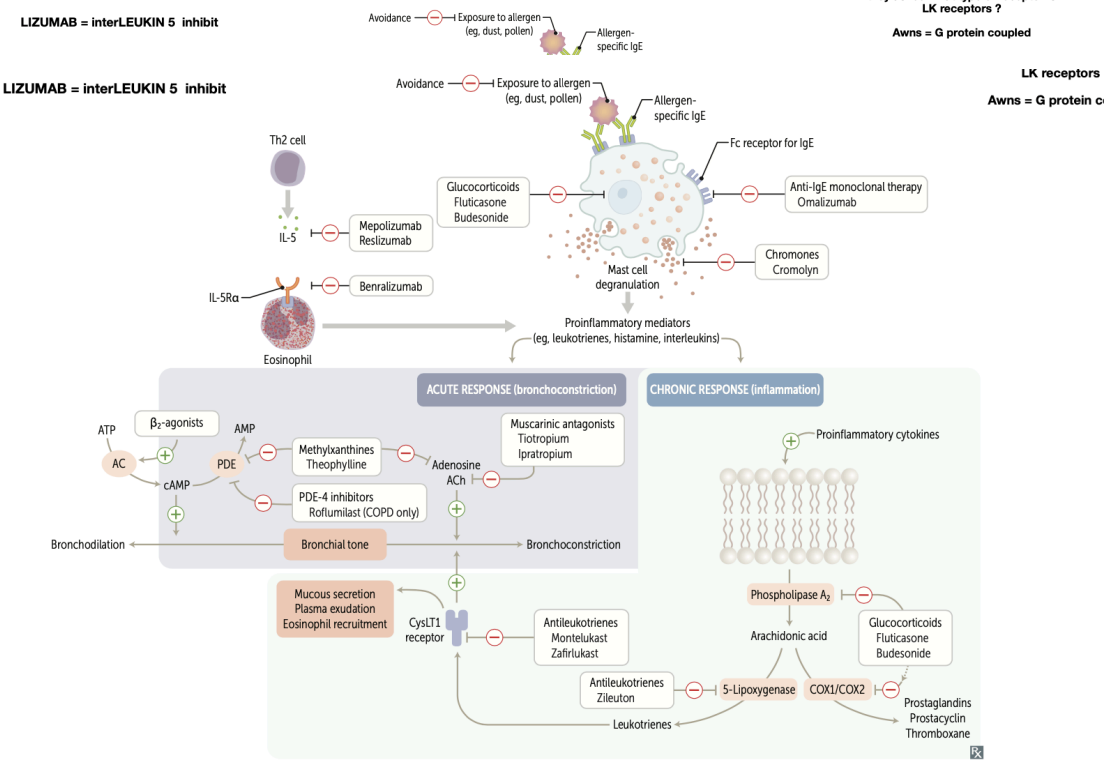
NF-κB (Nuclear Factor kappa-light-chain-enhancer of activated B cells) is a protein complex that functions as a transcription factor in cells. It plays a crucial role in regulating the immune response, inflammation, cell survival, and proliferation.

Exercise-induced asthma presents with dyspnea, cough: and/or wheezing that begins during or shortly after exercise. It is usually treated with SABAs although montelukast is an alternative therapy.

Fc Epsilon R1
Epsilon is a heavy chain of IgE

NBME 31 ghalat
they asked what type of receptor is LK receptors ?
Awns = G protein coupled

LIZUMAB = interLEUKIN 5 inhibit



Gram positive
4 rods

9 Cocci

2 filamentous rods

Gram negative

Fungus
10
B, C, H, P (4)
C, A (2)
Mucormycosis, Cryptococcus (2)
Sporothrix and PCP (2)
Virus DNA and RNA

NBME 25 B2 Q24 2 times

The test for Bartonella henselae is positive. A biopsy specimen of this lymph node is most likely to show which of the following histologic patterns?

- Yours = Neutrophili nonspecific, Correct = **Granulomas containing stellate microabsce**sses, Histologic examination typically demonstrates necrotizing granulomas with stellate (star-shaped) microabscesses. Multinucleated giant cells may or may not be present.

Free 137 B4 Q 10

31F

(1) 1 day of fever and

(2) sore throat

(3) musle aches

(4) vesicles on both tonsils

(5) Strep Neg

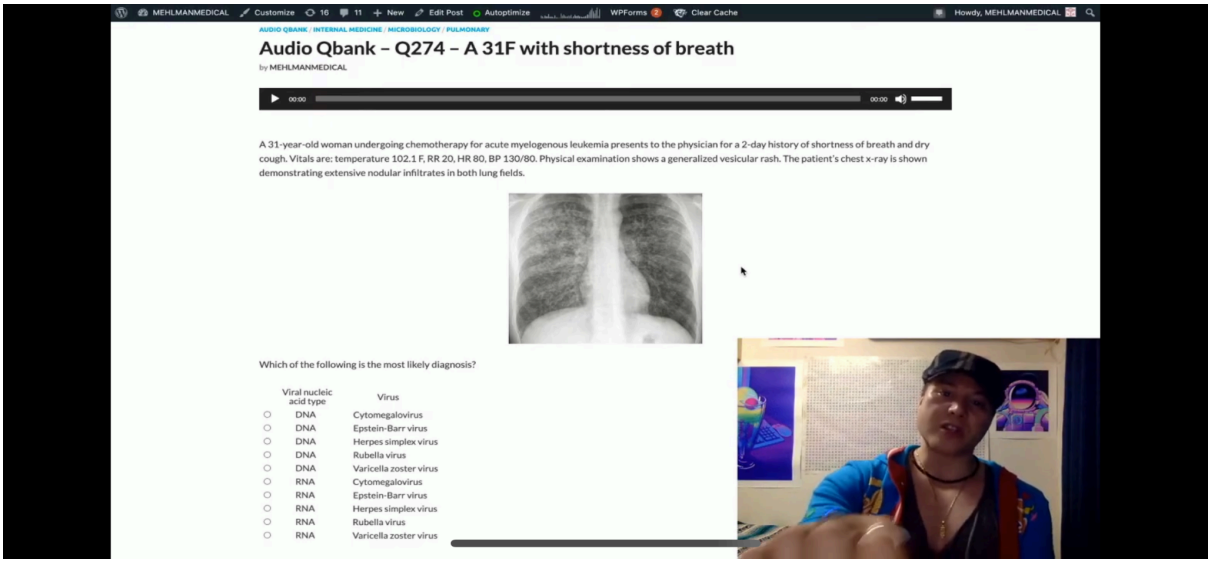
What is the tx ?

{{c2::Ibuprofen }}

Your= Amox

Cox = Vesicles on tonsils

HSV pharyngitis = Vesi on anterior mouth, gingiva, lips and tongue


MEHLMANMEDICAL Customize 16 11 New Edit Post Autoptimize WPForms Clear Cache Howdy, MEHLMANMEDICAL
AUDIO QBANK / INTERNAL MEDICINE / MICROBIOLOGY / PULMONARY
Audio Qbank – Q274 – A 31F with shortness of breath
by MEHLMANMEDICAL
00:00 00:00
A 31-year-old woman undergoing chemotherapy for acute myelogenous leukemia presents to the physician for a 2-day history of shortness of breath and dry cough. Vitals are: temperature 102.1 F, RR 20, HR 80, BP 130/80. Physical examination shows a generalized vesicular rash. The patient's chest x-ray is shown demonstrating extensive nodular infiltrates in both lung fields.
Which of the following is the most likely diagnosis?
Viral nucleic acid type
Virus
DNA Cytomegalovirus
DNA Epstein-Barr virus
DNA Herpes simplex virus
DNA Rubella virus
DNA Varicella zoster virus
RNA Cytomegalovirus
RNA Epstein-Barr virus
RNA Herpes simplex virus
RNA Rubella virus
RNA Varicella zoster virus

Correct= E