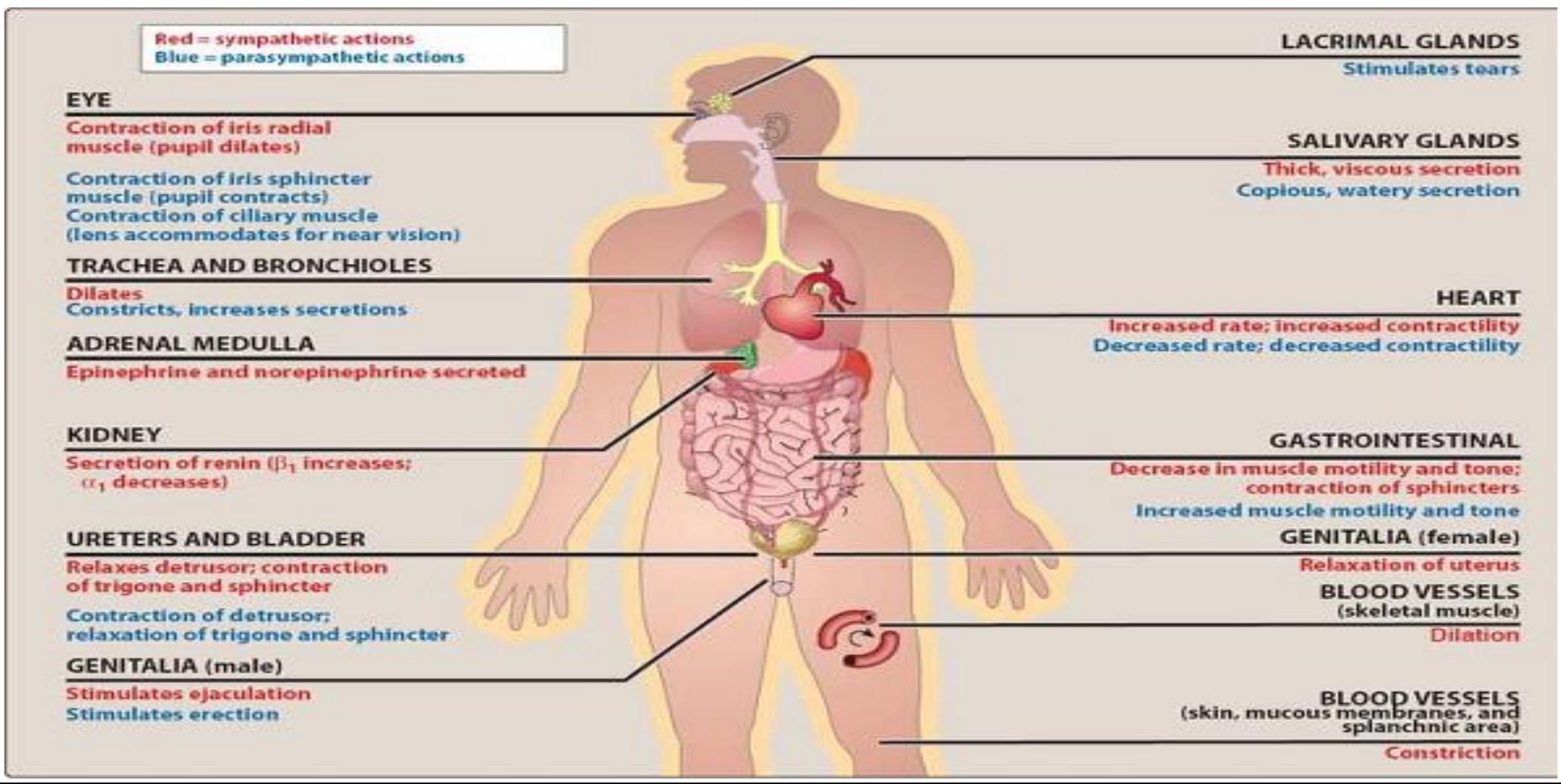
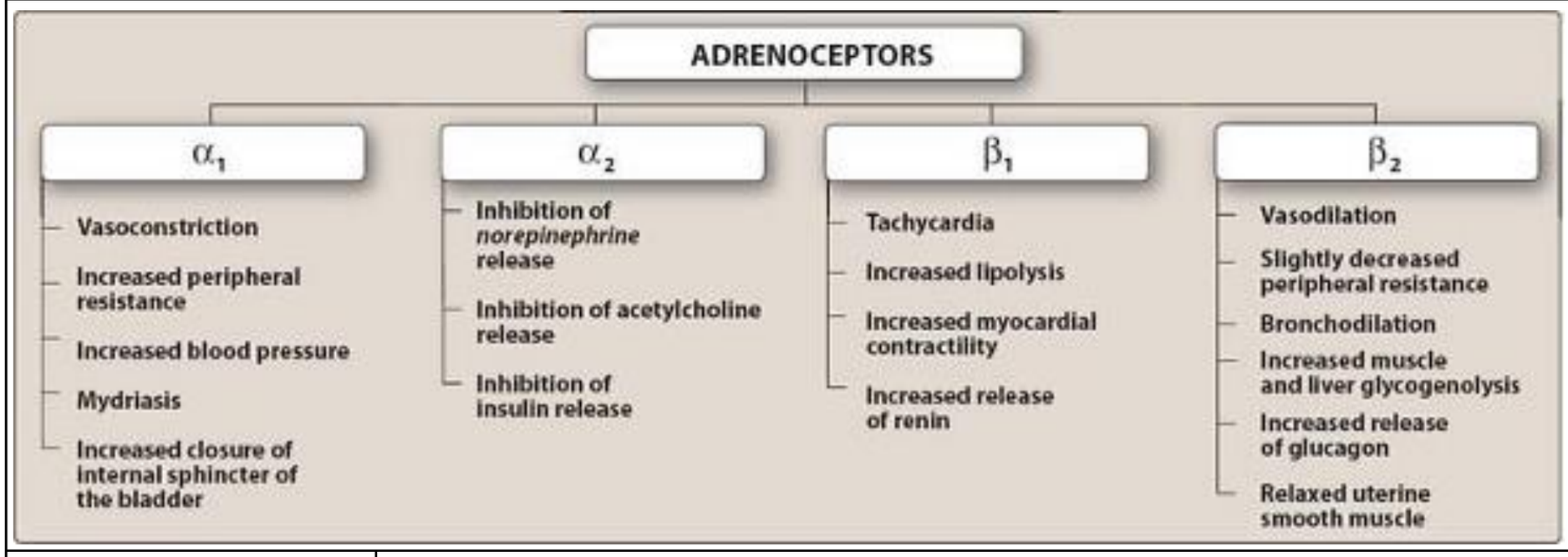
Pharmacokinetics			
Routes of Administration	Enteral : Oral, Sublingual	Parenteral : IV, IA, SC	Other: Inhalation, Intrathecal, rectal, Intraventricular, Topical, Transdermal
Absorption	Passive Diffusion, Fascilitated Diffusion, Active Transport, Exo & Endo Cytosis		
	Non Polar, Lipid Soluble, Non Ionised drugs easily cross membranes		
	Low pH favors acidic drugs, High pH favors basic drugs		
	factors : blood flow, surface area, contact time		
	Bioavailabilty: drug that reaches systemic circulation / Dose administered. Factors: 1st pass effect, solubility, chemical nature, formulation		
	Two drugs are bioequivalent if they show comparable bioavailability & times to achieve PPC		
	Two similar drugs are therapeutically equivalent if they have comparable efficacy and safety.		
	%age of Ionised drug = 100 / (1 + (10) $^{x(ph-pka)}$. (x= - 1 for acid & 1 for Basic)		
Distribution	Process by which a drug reversibly leaves the bloodstream and enters the interstitium (extracellular fluid) and/or the cells.		
	factors : blood flow, Capillary permiability, plasma protein binding, lipid soulubility.		
	Volume of Distribution(Vd)=D/C		
	Plasma Compartment, Extra cellular, Intracellular, Total body water 60% of adult body weight		
	Additional dosage needed = drug needed for PPC - drug initially in body		
	Additional dosage needed = (Vd x C2) - (Vd x C1)		
	Large Vd means Large Half Life		
	Class I: dose of drug is < the binding capacity of albumin, then the dose/capacity ratio is low. The binding sites are > the available drug, and the bound-drug fraction is high. This is the case for majority of clinically useful agents. Class II: doses that is > the number of albumin binding sites. The dose/capacity ratio is high, and a relatively high proportion of the drug exists in the free state, not bound to albumin. Importance of drug displacement: when a patient taking a Class I drug, such as warfarin, is given a Class II drug, such as a sulfonamide antibiotic. Warfarin is highly bound to albumin, and only a small fraction is free. This means that most of the drug is inert in terms of pharmacologic actions. If a sulfonamide is administered, it displaces warfarin from albumin, leading to a rapid increase in the concentration of free warfarin in plasma, because almost 100% is now free, compared with the initial small %age.		
	impact of protien binding is reduced with drugs with large Vd		
Metabolism	1st Order: the rate of drug metabolism is directly proportional to the concentration of free drug. V= {V(max) x C} / K(m)		
	0 Order: the rate of drug metabolism is independent of the concentration of free drug. V= V(max).		
	Phase I reactions convert lipophilic molecules into more polar ones by introducing or unmasking a polar functional group. i.e., Oxidation		
	Phase II: This phase consists of conjugation reactions. conjugation reaction with an endogenous substrate, such as glucuronic acid, sulfuric acid, acetic acid, or an amino acid, results in polar, usually more water-soluble compounds that are most often therapeutically inactive.		
Elimination	Removal of a drug from the body occurs via a number of routes, the most important being through the kidney into the urine. Other routes include the bile, intestine, lung, or milk in nursing mothers.		
	Extraction ratio: The drugs enter the kidneys at concentration C1 and exit the kidneys at concentration C2. The extraction ratio = C2/C1.		
	Excretion rate (mg/min): Clearnace (ml/min) x Plasma Conc. (mg/ml)		
	Elimination is usually 1st Order		
	$T_{1/2}$ = 0.693 Vd /CL		
	Total body clearance (CL_t)= Ke x Vd		
	rate of drug elimination from the body = CL_t x C		
	Css (steady-state concentration)= Ro (the infusion rate) / [ke (first-order elimination rate constant) x Vd (volume of distribution)]= Ro / CL_t. So **Css α Ro**		
	Because ke, CLt, and Vd are constant for most drugs showing first-order kinetics, Css is directly proportional to Ro; that is, the steady-state plasma concentration is directly proportional to the infusion rate.		
infusion	The rate constant for attainment of Css is the rate constant for total body elimination of the drug, ke. Thus, fifty percent of the final Css of drug is observed after the time t, is equal to $T_{1/2}$. i.e Rate of CSS achievemnt is dependant on $T_{1/2}$.		
	Infusion Rate affects the Css value not the Css atainment time		
	Oral Drugs	D=Dose F= Bioavailability T= Dosage Interval	$C_{ss} = \frac{1}{(k_e)(V_d)} \frac{(D)(F)}{T}$

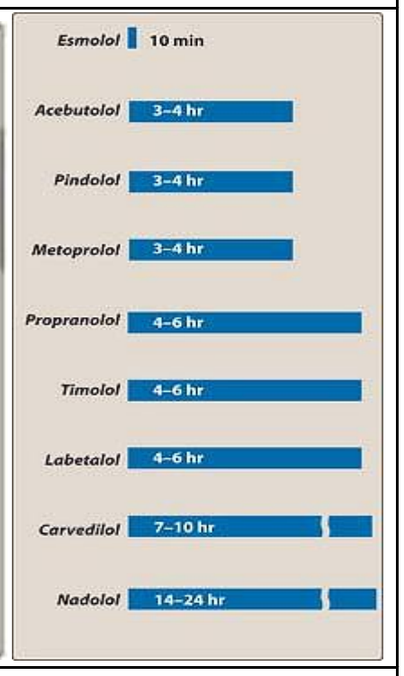
Autonomic Nervous System	
Choline --- > by Acetyle CoA Acetyle Choline --->Storage into viscles with ATP and Peptidoglycan --->Release --- >Degradation by (Acetylecholinestrase)--->Reuptake of Choline.	Areas with only sympathetic innervation : Adrenal Medula, Kidney, Pilomotor muscles, Sweat Glands. Areas with only parasympathetic innervation : lacrimal Glands.



Direct Acting Cholinergic Agonists	
Acetyle Choline	Actions:↓in heart rate and cardiac output, ↓ in blood pressure by production of NO, ↑ Salivation, ↑ GIT motility & Tone, ↑ Bronchial Secreations, Bronchospasm, Urinary expulsion, Miosis. Uses: In Eye for Miosis before surgery Side Effects: Urinary Urgency, Diaphoresis, Miosis, Hypotension, Bradycardia, Diarhea, Nausea, Bronchospasm, salivation

Bethenicol	Actions: same as Ach, but affects Muscarinic receptors only Uses: Atony of bladder Side Effects: same as Ach
Carbachol	Actions: same as Ach Uses: due to high Potency and Side effects only ophthalmic uses (Glaucoma) Side Effects: same as Ach
Pilocarpione	Actions: same as Ach, with CNS effects Uses: drug of choice in the emergency lowering of intraocular pressure in Glaucoma, xerostomia resulting from irradiation of the head and neck Side Effects: same as Ach
Cevimeline	used in Xerstomia
In-Direct Acting Cholinergic Agonists (Reversible)	
Physostigmine	Forms relatively stable carbamoylated intermediate with the AcHestrase, which then becomes reversibly inactivated. Naturally occuring compund. Can Enter CNS. Actions: Same as AcH Uses: Glaucome, Antidote for Atropine, phenothiazines, and tricyclic antidepressants. increases intestinal and bladder motility Side Effects: same as AcH with Convulsions.
Neostigmine	Actions: Same as Physostigmine, but no CNS and greater effect on Neuromuscular junctions Uses: ↑intestinal and bladder motility, Myasthinia Gravis. Side Effects: same as AcH
PyridoStigmine, Ambinomium	used in the chronic management of myasthenia gravis. Their durations of action are intermediate
Demicarium	glaucoma after irredectomy. Diagnosis and treatment of accommodative esotropia.
Edrophonium	Diagnosis of myasthenia gravis. IV edrophonium leads to a rapid increase in muscle strength
Tacrine, Donezipil, Rivastigmine, galantamine	Used in Alzhiemer's Desease. Tacrine is not used because of Hepato toxicity.
In-Direct Acting Cholinergic Agonists (IRReversible)	
Ecothiophate	organophosphate that covalently binds to acetylcholinesterase and permanantly deactivates it. Before aging pralidoxime can reverse its effects. Actions: generalized cholinergic stimulation, paralysis of motor function. Uses: Glaucoma Adverse effects: same as physostigmine
Cholinergic Antagonists (Muscarinic Blockers)	
Atropine	Actions: Mydriasis, Cycloplegia, ↓ GIT motility, ↓ Bladder motility, ↓Heart Rate at low doses while ↑HR at high doses, ↓ Secretions, Bronchodilation. Uses: Ophthalmic, Antispasmodic, antidote for cholinesterase inhibitor insecticides, anti secretory, Side effects: restlessness, confusion, hallucinations, and delirium, dry mouth, blurred vision, tachycardia.
Scopolamine	Actions: same as atropine, with CNS actions greater. Uses: anti motion sickness, blocking short term memory.
Ipratropium	Used as inhaler for Bronchospasm
Tropicamide & Cyclopentolate	Ophthalmic uses
Pirenzipine	M1 muscarinc blocker ↓GIT acid secretions
Cholinergic Antagonists (Ganglionic Blockers)	
Nicotine	1st stimulate than inhibts systems
Macamylamine	Used In emergency hypertension
Cholinergic Antagonists (Neuromuscular Blockers) Non depolarizing	
Tubocurarine, Atracurium, Pencuronium, Vecuronium	Actions:at low doses competetive blocking, at high doses blocks ion chennels. Musclar fucntions are blocked. Face & Eye--fingers--neck, limbs, Trunck--intercostal--respiratory. Tubo, miva, atra also release histamine causing ↓BP, bronchospasm. Uses: as adjuvants in aneasthesias. Side: Minimal. interact with Anticholinestrase Inhibitprs, aminoglycoside antibiotics, Ca chennel blockers
Cholinergic Antagonists (Neuromuscular Blockers) Depolarizing	
Succinyle choline	No histamine release, rapid onset, short duration. Used in endotracheal intubation hyperthermia with halothane, apnea, hyperkalemia.
Adrenergic Agonists (Direct Acting)	
Tyramine(Hydroxylation)-->DOPA(Decarboxylation)-->DOPAmine(Hydroxylation)--> Norepinephrine(20%)(Methylation)-->Epinephrine(80%)-->Storage-->Release(Exocytosis) ---------->Metabolism (COMT/MAO)-->Reuptake	



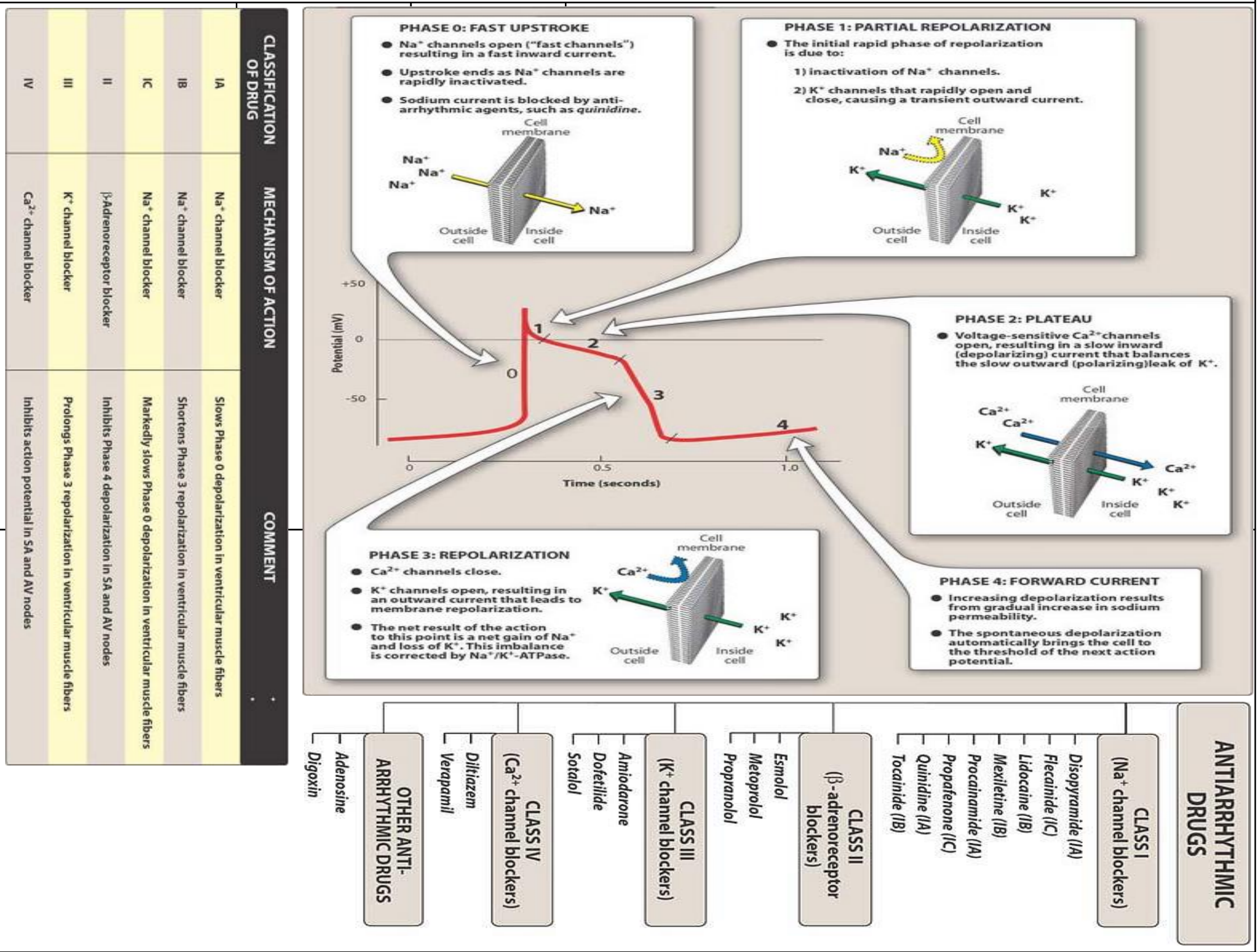


Catecholamines	3, 4-dyhroxy benzine structure, Natural (Epi, Norepi, Dopamine), Synthetic (Isopro, dobutamine). Rapid action & Inctivation, no CNS penetration
Epinephrine (α, β)	Actions: ↑HR, ↑HT, ↑BP(Sys), ↓BP(Dias)-β effect, Bronchodilation, hyperglycemia, lypolisis, Mydriasis. Uses: Bronchodiation, Ophthalmic, Anaphylactic shcok, cardiac arrest, with Local aneasthetics. Adverse: anxiety, fear, tension, headache, and tremor, arrhythmias, heamorrhage, pulmonary oedema.
Nor epinephrine (α, β1)	Actions: ↓HR-reflex action of marked vasoconstriction , ↑BP(Sys) (Dias) Uses: Shock, but Metaraminol is prefferd b/c it does not inhibit renel flow. Adverse: same as epinephrine
Dopamine (α, β, D)	Same as Epi, but renel flow is ↑ due to action on Dopa receptors. Drug of Chioce for shock Adverse:same as Epi

Oxymetaxoline (α 1, 2)	used locally in the eye or the nose as a vasoconstrictor, causing Nasal Decongestion.
Phenylephrine (α1)	vasoconstrictor that ↑BP(Sys) (Dias), reflex bradycardia. Used as Nasal Decongestant, supraventricular tachydardia.
Methoxamine (α1)	used in supraventricular tachycardia & to overcome hypotension during surgery. Adverse: Hypertensive headache, vomiting
Clonidine , α-Methyldopa (α2)	Used in Hypertension, ADHD, alleviate Opiate withdrawal symptoms, Migraine
Isopreterinol (β 1, 2)	Actions: ↑HR, ↑HT, ↑BP(Sys), ↓BP(Dias), bronchodilation, ↑Sugar Levels. Uses: Arterioventricular Shock Adverse: same as epinephrine
Dobutamine (β 1)	Used to ↑cardiac output in congestive heart failure, inotropic support after cardiac surgery. The does not ↑HR & O2 demands. Adverse: Tolerance, same as epi
Metaproterinol (β 2 > 1)	Bronchodilation, with some cardiac stimulation
Albuterol, Pirbuterol, Terbutaline (β 2)	Short acting bronchodilators
Salmetrol, Formetrol, (β 2)	Long acting bronchodilators
Adrenergic Agonists (INDirect Acting)	
Amphetamine (α, β)-CNS	See CNS stimulants
Adrenergic Agonists (Direct Acting)	
Ephiderine Psuedo Ephiderine (α, β)	Release stored norepinephrine from nerve endings, & directly stimulate both α, β receptors. Ephedrine and pseudoephedrine have excellent absorption orally and penetrate into the CNS; however, pseudoephedrine has fewer CNS effects used as Nasal Decongestant, ↑BP, Bronchodilation
Adrenergic Antagonists	
Phenoxybenzamine (α)	Vasodilation, ↓peripheral Resistance, Reflex tachycardia, ↓BP, Epinephrine Reversal. Used in Pheochromocytoma, Ranaud's Desease Adverse:postural hypotension, nasal stuffiness, nausea, and vomiting, Sexual dysfunction
Phentolamine (α)	Vasodilation, ↓peripheral Resistance, Reflex tachycardia, ↓BP, Epinephrine Reversal. Used in Pheochromocytoma, Impotense, Ranaud's Desease Adverse:Postural hypotension, nasal stuffiness, nausea, and vomiting, Sexual dysfunction, arythmias, anginal pain
Doxazocin, Prazocin, Trazocin, Alfuzocin, Tamsulosin (α1)	Vasodilation, ↓peripheral Resistance, ↓BP 1st three are used in Hypertension, 1st dose effect. other 2 are used in benign prostatic hyperplasia or BPH Adverse: dizziness, a lack of energy, nasal congestion, headache, drowsiness, and orthostatic hypotension
Yohimbine (α2)	Yohimbine works at the level of the CNS to increase sympathetic outflow to the periphery. It directly blocks Î±2 receptors and has been used to relieve vasoconstriction associated with Raynaud's disease. Yohimbine is contraindicated in CNS and cardiovascular conditions because it is a CNS and cardiovascular stimulant.
Propranolol (β)	Actions: ↓HR, ↓HT, ↓Heart O2 Demand, ↓BP, no Postural Hypotensin due to Peripheral Vasoconstriction, Bronchoconstriction, ↓Renel Flow due to ↓BP results in Na Retention, disturbances in glucose metabolism, blocks action of Isoproterinol. Uses: Hypertension, glaucoma, angina, hyperthyroidism, Myocardial Infarction, Migrain prophylaxis Adverse: Bronchoconstriction, Arrhythmias, Sexual impairment, Disturbances in metabolism.
Timolol, Nadolol (β)	more potent than propranolol, with longer duration of action. Used in Glaucoma, & occasionally, for systemic treatment of hypertension
Acebutolol, Atenolol, Esmolol, Metoprolol (β1)	antagonize β1 receptors at doses 50- to 100-fold less than those required to block β2 receptors. ↓BP in hypertension and increase exercise tolerance in angina. Esmolol has a very short lifetime. little effect on pulmonary function, peripheral resistance, and carbohydrate metabolism useful in hypertensive patients with impaired pulmonary function, & Diabetes. Atenolol (Glaucoma) Adverse:dizziness, drowsiness, fatigue, bradycardia
Acebutolol, Pindolol (β1-ISA)	intrinsic sympathomimetic activity, i.e, stimulate β1,2. effective in hypertensive patients with moderate bradycardia
Labetolol, Carvedilol (α, β)	Peripheral vasodilation, ↓BP, useful in treating hypertensive patients for whom increased peripheral vascular resistance is undesirable. Labetalol may be employed as an alternative to methyldopa in the treatment of pregnancy-induced hypertension. Adverse:Orthostatic hypotension and dizziness
Anti-Inflammatory drugs	
Inflamation initiation-->WBC Activation-->T-Lymphocytes Activation-->Monocytes & Macrophages Activation-->secretion of proinflammatory cytokines (TNF-α, IL-1) in Synovium-->1)↑ cellular infiltration into endothelium by release of histamines, kinins, & prostaglandins. 2)↑C-reactive protein by hepatocytes.3)↑release of proteolytic enzymes (collagenases and metalloproteinases) by chondrocytes (cells that maintain cartilage), leading to degradation of cartilage & joint space narrowing.4)↑osteoclast activity (osteoclasts regulate bone breakdown), resulting in focal bone erosions and bone demineralization around joints; 5) systemic manifestations in which organs such as the heart, lungs, and liver are adversely affected. B lymphocytes are also involved and will produce rheumatoid factor (inflammatory marker) and other autoantibodies with the purpose of maintaining inflammation.	
Arachidonic acid, a 20-carbon fatty acid, is the primary precursor of the prostaglandins and related compounds. All eicosanoids with ring structures, i.e, prostaglandins, thromboxanes, and prostacyclins are synthesized via the cyclooxygenase pathway. Cyclooxygenase-1 (COX-1, Housekeeping enz) is responsible for the physiologic production of prostanoids. (COX-2) causes the elevated production of prostanoids that occurs in sites of disease and inflammation.	
PG-E2	causes Pain, pyrexia, ↑GIT mucosal Secretions, oppose vasoconstrition of renel vessels
PG-F2	↑GIT mucosal Secretions, oppose vasoconstrition of renel vessels
PG-I2	↓GIT acid secretion
Salicylates (Asprin, Salicylic acid, Methyl SA)	Asprin ireversibly acetylates Cox. Others are reversible. Actions: Anti-inflammatory, Analgesic action (Musculoskeletal, not visceral), Antipyretic, at therapeutic doses ↑alveolar ventilation, hyperventilation & Repiratory alkalosis at higher doses & Resp. paralysis & resp. acidosis with toxic doses. ↑GI secretion ↓mucus protection causing epigastric distress, ulceration, hemorrhage, & Fe-deficiency anemia. Low doses (60-81 mg/day) can irreversibly inhibit TXA production in platelets via acetylation of cox. B/c platelets lack nuclei, they cannot synthesize new enzyme, and the lack of TXA persists for the lifetime of the platelet (3-7 days). As a result platelet aggregation is reduced, producing prolonged bleeding time. Finally, aspirin also inhibits cox in endothelial cells, resulting in reduced PGI2 formation; however, endothelial cells are able to re-synthesize new cox. Therefore, PGI2 is available for antiplatelet action. Na & water retention(inhibition of synthesis of PGE2 and PGI2). Uses:Anti-inflammatory, antipyretic, and analgesic uses, External Products, ↓Platelet aggregation in heart conditons that are benifited by it (Ischemia, Myo. Infarction.) Adverse:ulceration, epigastric distress, nausea, and vomiting, microscopic GI bleeding, prolonged bleeding time, Hypersensitivity, Reye's syndrome, pregnancy category C in Trimesters 1 & 2 & D in Trimester 3
Propionic Acids (Ibuprofen, Ketoprofen, Naproxen, Flurbiprofen, fenoprofen, Oxaprozin)	All possess anti-inflammatory, analgesic, and antipyretic activity; additionally, they can can alter platelet function and prolong bleeding time. uses: chronic treatment of RA and osteoarthritis, because their GI effects are generally less intense than those of aspirin. adverse effects are GI, ranging from dyspepsia to bleeding. Heafaches, tinnitus, dizziness

Acetic acids, indomethacin, sulindac, etodolac	All have anti-inflammatory, analgesic, and antipyretic activity. toxicity of indomethacin limits its use to the treatment of acute gouty arthritis, ankylosing spondylitis, and osteoarthritis of the hip.
Fenamates (Mefenamic Acid)	have no advantages over other NSAIDs as anti-inflammatory agents. Their side effects, such as diarrhea, can be severe, and they are associated with inflammation of the bowel. Cases of hemolytic anemia have been reported.
Oxicams (Piroxicam, Meloxicam)	used to treat RA, ankylosing spondylitis, and osteoarthritis. They have long half-lives, which permit once-daily administration. Meloxicam inhibits both COX-1 and COX-2, with preferential binding for COX-2, and at low to moderate doses shows less GI irritation than piroxicam. However, at high doses, meloxicam is a nonselective NSAID, inhibiting both COX-1 and COX-2
Hetero Arylacids (Diclofenac, Ketorolac, Tolmetin)	Used in long-term use in the treatment of RA, osteoarthritis, and ankylosing spondylitis. Ketorolacis a potent analgesic but has moderate anti-inflammatory effects, can cause fatal peptic ulcers as well as GI bleeding and/or perforation of the stomach or intestines
Cox-2 Inhibitor (Celecoxib)	selective for inhibition of COX-2. approved for treatment of RA, osteoarthritis, and pain. celecoxib does not inhibit platelet aggregation and does not increase bleeding time. Celecoxib has similar efficacy to NSAIDs in the treatment of pain and the risk for cardiovascular events. Adverse: Headache, dyspepsia, diarrhea, and abdominal pain
Nebumetone	Nabumetone [na-BYOO-meh-tone] is indicated for the treatment of RA and osteoarthritis and is associated with a low incidence of adverse effects. dose should be adjusted in those with creatinine clearance of less than 50 mL/min.
Others (Acetaminophen)	inhibits prostaglandin synthesis in the CNS. This explains its antipyretic and analgesic properties. does not affect platelet function or increase blood clotting time. Acetaminophen is the analgesic/antipyretic of choice for children with viral infections or chickenpox (recall that aspirin increases the risk of Reye's syndrome). Acetaminophen does not antagonize the uricosuric agents probenecid or sulfinpyrazone and, therefore, may be used in patients with gout who are taking these drugs. Adverse:virtually free of any significant adverse effects, hepatotoxicity with ↑doses.
Desease Modifying AntiInflamatory Drugs (DMARDs)	
Methotrixate	Immunosupresant, slows the appearance of new erosions within involved joints on radiographs, Response time 3-6 weeks, lower doses are required as compared to for cancer treatment. Adverse: ulceration and nausea, Cytopenias. Cirrhosis of the liver, & an acute pneumonia-like syndrome with prolonged usage. leucovorin (Folinic acid) once daily after methotrexate reduces the severity of the adverse effects.
Hydroxy Chloroquine	also used in the treatment of malaria. It is used for early, mild RA and has relatively few side effects, including Renel Toxicity. Used with MTX.
Leflunomide	immunomodulatory agent that preferentially causes cell arrest of the autoimmune lymphocytes through its action on dihydroorotate dehydrogenase. approved for RA. It not only ↓pain and inflammation but also ↓progression of structural damage. headache, diarrhea, and nausea, weight loss, allergies.
Salfasalzine	used for early, mild RA in combination with hydroxycholoroquine and methotrexate
D-Penicillamine	slows the progression of bone destruction and RA, Heavy metal poisoning.
Gold salts	Gold compounds are being used infrequently by rheumatologists because of the need for meticulous monitoring for serious toxicity
eternacept	Genetically engineered fusion protein that binds to TNF-α & block its interaction with TNF receptors. use in patients with polyarticular-course juvenile RA, psoriatic arthritis, ankylosing spondylitis, and psoriasis. With MTX more effective. Adverse:local inflammation at the site of injection
infliximab	Chimeric IgG monoclonal antibody. binds specifically to human TNF-α. used with MTX in patients with RA. Not used alone. also in plaque psoriasis, psoriatic arthritis, ulcerative colitis, ankylosing spondylitis, and Crohn's disease. Adverse: Infusion reactions,as fever, chills, pruritus, or urticaria.
Adalimumab	Recombinant monoclonal antibody that binds to human TNF-α. Used in moderate to severe RA, either as monotherapy or in combination. Adverse:headache, nausea, rash, reaction at the injection site or increased risk of infection.
Anakinra	Anakinra is an IL-1 receptor antagonist. Administered subcutaneously once a day if renal function is normal, and every other day in those with moderate to severe renal impairment.
Abatacept	Abatacept soluble recombinant fusion protein that prevents full T-cell activation. Used in moderate to severe RA. Adverse: Headache, upper respiratory infections, nasopharyngitis, and nausea
Rituximab	Chimeric murine/human monoclonal antibody against CD20 antigen on normal and malignant B lymphocytes, resulting in B-cell depletion. Used in moderate to severe RA. Adverse: Infusion reactions (i.e, urticaria, hypotension, or angioedema)
Anti-Gout Drugs	
Colchicine	plant alkaloid, has been used for the treatment of acute gouty attacks as well as chronic gout. Colchicine inhits the fuctino of tubulin, disrupting cellular functions, such as the mobility of granulocytes, thus ↓their migration into the affected area. Furthermore, blocks cell division by binding to mitotic spindles. Colchicine also inhibits the synthesis and release of the leukotrienes. Colchicine must be administered within 24 to 48 hours of onset of attack to be effective. Adverse: nausea, vomiting, abdominal pain, and diarrhea. Chronic administration may lead to myopathy, neutropenia, aplastic anemia, and alopecia.
Allopurinol	purine analog that the ↓production of uric acid by competitively inhibiting the last two steps in uric acid biosynthesis that are catalyzed by xanthine oxidase. Used in reatment of primary hyperuricemia of gout and hyperuricemia secondary to other conditions. Adverse: Hypersensitivity reactions, especially skin rashes
Uricosuric agents Probenecid & sulfinpyrazone	Uricosuric drugs are weak organic acids that promote renal clearance of uric acid by inhibiting the urate-anion exchanger in the proximal tubule that mediates urate reabsorption. Adverse: gastric distress
Heart Failure (Arteriosclerotic HD, myocardial infarction, Hypertensive HD, Valvular HD, Dilated cardiomyopathy, Congenital HD)	
Heart failure (HF) is a complex, progressive disorder in which the heart is unable to pump sufficient blood to meet the needs of the body. Its cardinal symptoms are dyspnea, fatigue, and fluid retention. Often accompanied by abnormal ↑in blood volume & interstitial fluid, hence the term Congestive HF b/c symptoms include dyspnea from pulmonary congestion in left HF, and peripheral edema in right HF.	

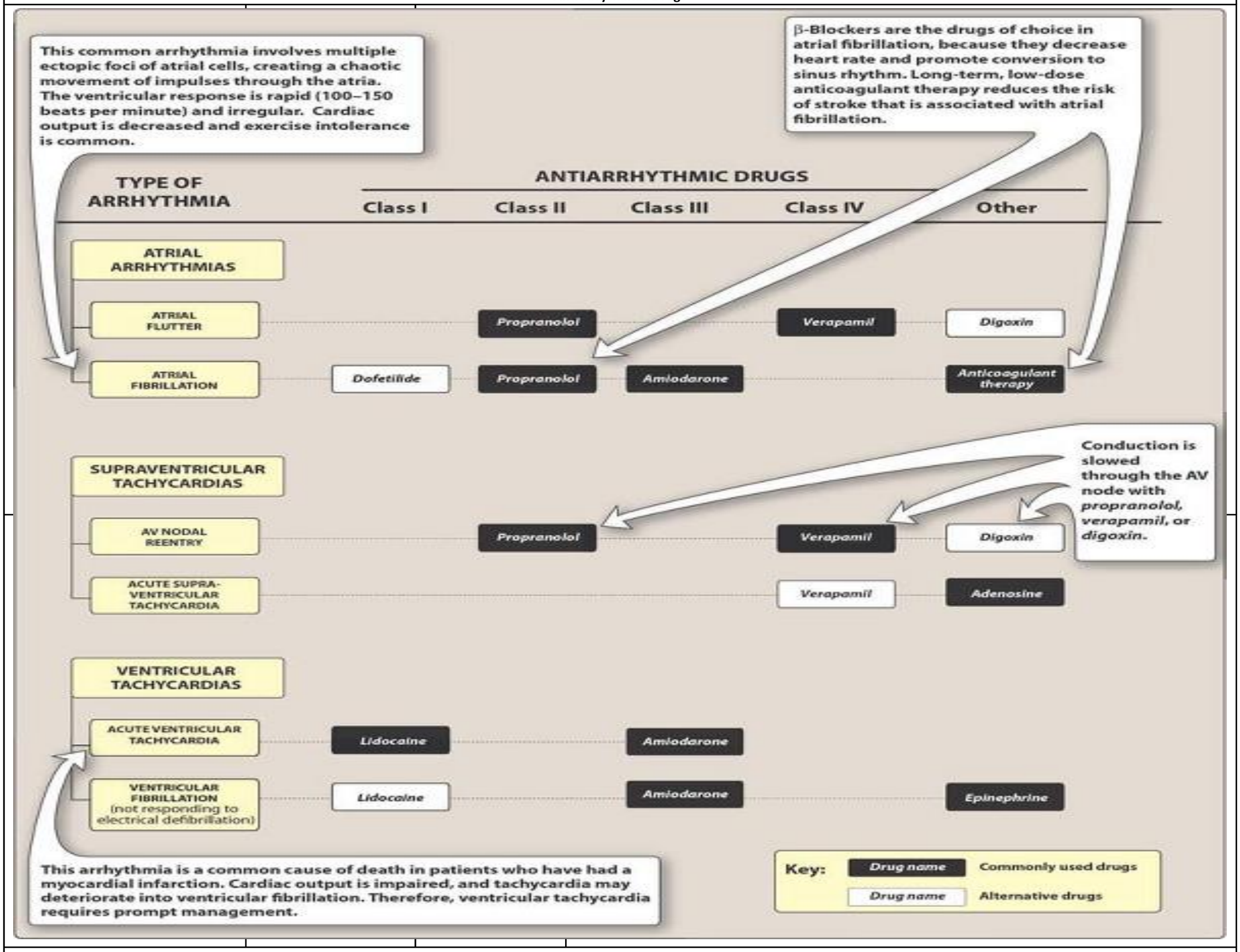
Compensatory physiological responses in HF:
↑ sympathetic activity: Baroreceptors sense a ↓ in BP and activate the sympathetic nervous system, which stimulates β-adrenergic receptors in the heart. This results in an ↑HR & HT. In addition, vasoconstriction (α1-mediated) ↑venous return & ↑cardiac preload. These responses ↑the work of the heart &, therefore, contribute to further decline in cardiac function.
Activation of the renin-angiotensin system: results in ↑peripheral resistance & retention of sodium and water. Blood volume ↑, & more blood is returned to the heart.
Myocardial hypertrophy: The heart increases in size, and the chambers dilate and become more globular. Initially, stretching of the heart muscle leads to a stronger contraction of the heart. However, excessive elongation of the fibers results in weaker contractions, and the geometry diminishes the ability to eject blood.



ACE-Inhibitors (Captopril, Enalapril, Lisinopril, Fosinopril, Ramipril, Quinapril)	Actions:Angiotensin-converting enzyme (ACE) inhibitors cause Vasodilation as a result of the combined effects of lower vasoconstriction caused by ↓angiotensin II & the potent vasodilating effect of ↑ bradykinin. ACE inhibitors decrease vascular resistance, venous tone, and blood pressure, resulting in an increased cardiac output. Also↓ secretion of aldosterone, resulting in ↓ Na & water retention & ↑ K. Uses: Agents of choice in HF. Presence of food may decrease absorption. Adverse: Postural hypotension, renal insufficiency, hyperkalemia, angioedema, and a persistent dry cough
Angiotensin-receptor blockers (Candesartan, Losartan, Telmisartan, Valsartan)	Actions:Nonpeptide, orally active extremely potent compounds that have more complete blockade of angiotensin action, but no effect on Bardykinin. Also↓ secretion of aldosterone, resulting in ↓ Na & water retention & ↑ K. Uses: Hypertension, in HF as substitute for ACE inhibitors. Once daily dosage Adverse:Same as Ace-Inhi. But not Cough
β-Blockers (Atenoloo, Carvedilol, Metoprolol)	Actions:benefit of β-blockers is due to their ability to prevent the changes that occur b/c of the chronic activation of the sympathetic nervous system, including ↓ HR & inhibiting the release of renin. In addition, β-blockers also prevent the direct deleterious effects of norepinephrine on the cardiac muscle fibers, ↓remodeling, hypertrophy & cell death. Uses: β-Blockade is recommended for all patients with heart disease except those who are at high risk but no symptoms or those who are in acute HF. Adverse: dizziness, drowsiness, fatigue, bradycardia

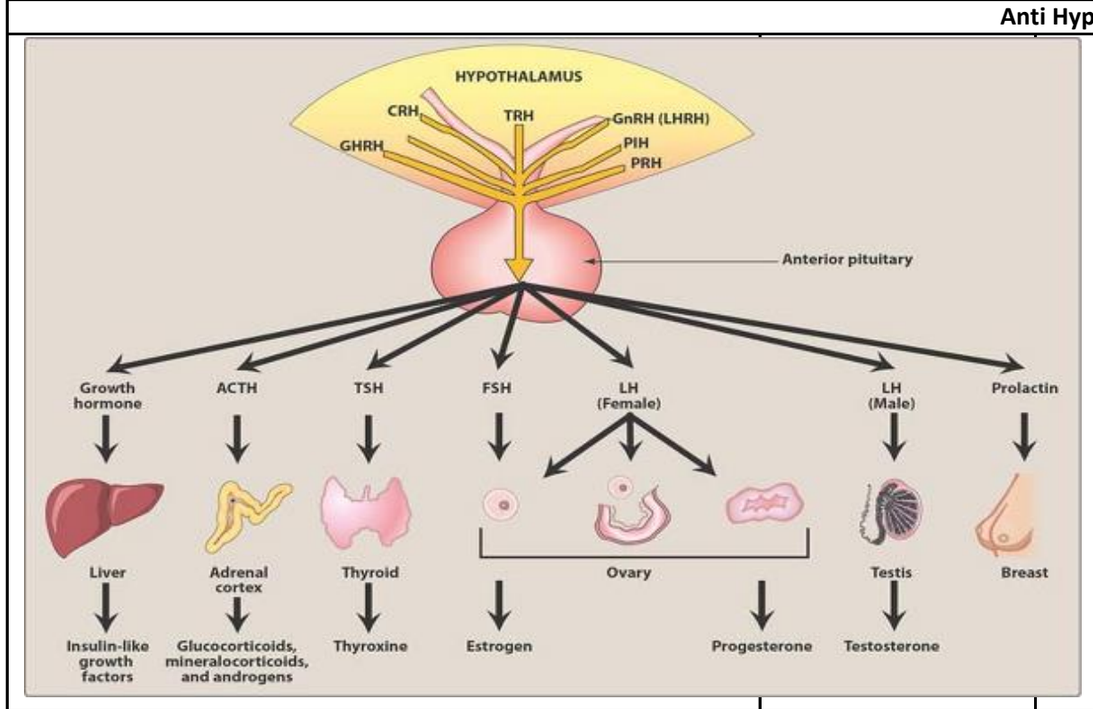
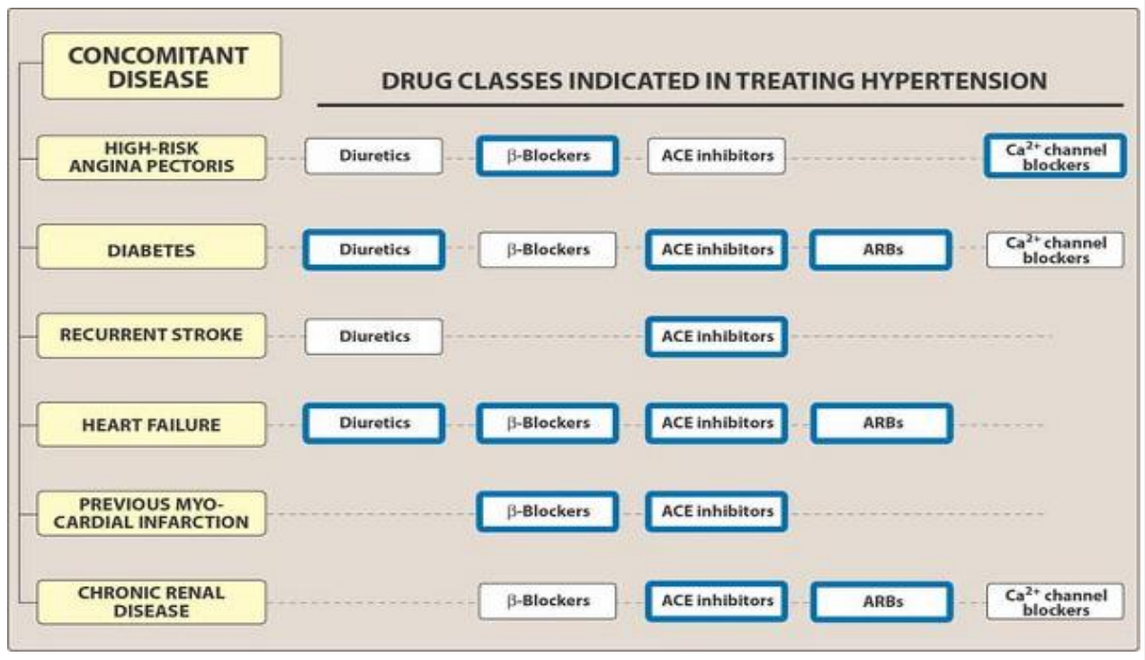
Diuretics (Furosimide, loop , Bumetnide, loop Matolazone, Thiazide Hydrochlorthiazide)	Diuretics relieve pulmonary congestion & peripheral edema. Also useful in ↓the symptoms of volume overload, including orthopnea & paroxysmal nocturnal dyspnea. Also ↓ plasma volume &, subsequently, ↓ venous return (preload). This ↓ cardiac workload & oxygen demand. May also ↓afterload by ↓ plasma volume, thus ↓BP. Thiazide diuretics are relatively mild diuretics & lose efficacy if patient creatinine clearance is less than 50 mL/min. Loop diuretics are used for patients who require extensive diuresis & those with renal insufficiency.
Direct Vasodilators (Hydralazine , Isosorbide DiNo3 Na Nitropruside)	Dilation of venous blood vessels leads to a ↓in cardiac preload by ↑the venous capacitance; arterial dilators ↓ systemic arteriolar resistance & ↓ afterload. If the patient is intolerant of ACE inhibitors or β-blockers, the combination of hydralazine & isosorbide dinitrate is most commonly used. [Note: Calcium-channel blockers should be avoided in patients with HF.]
Inotropic Drugs Digitalis Glycosides-Foxglove Plant (Digoxin, Digitoxin)	Cardiac glycosides are a group of chemically similar compounds that can ↑the contractility of the heart muscle &, are widely used in treating HF. Very low therapeutic index. They influence the Na & Ca ion flows in the cardiac muscle, thereby ↑contraction of the atrial & ventricular myocardium. ↓Na (out)-K (in) exchange, & leads to ↓Ca extrusion in exchange for Na. thus inracellular Ca is ↑. Uses: Atrial Fibrilation, Left Ventricular systolic dysfunction. only used in Left sided HF. Adverse: Toxicity, Hypokalemia, arrhythmia, Anorexia, nausea, and vomiting.
Inotropic Drugs β-Adrenergic agonists (Dobutamine)	Dobutamine leads to ↑ in intracellular cAMP, resulting in the activation of protein kinase. Slow Ca channels are one important site of phosphorylation by protein kinase. When phosphorylated, the entry of Ca into the myocardial cells ↑, thus ↑ contraction. obutamine must be given by intravenous infusion and is primarily used in the treatment of acute HF in a hospital setting.
Phosphodiestrase Inhibitors (Amrinone, Milrinone)	↑intracellular cAMP, resulting in ↑intracellular Ca &, therefore, cardiac contractility. Used in Acute HF
Aldosterone Antagonist (Spironolactone)	Patients with ↑heart disease have ↑levels of aldosterone due to angiotensin II stimulation & ↓hepatic clearance of the hormone. Spironolactione prevents salt retention, myocardial hypertrophy, & hypokalemia. Pottasim should not be given with it. Adverse:Gastric disturbances, as gastritis & peptic ulcer; lethargy & confusion; endocrine abnormalities, as gynecomastia, decreased libido, and menstrual irregularities.

Anti Arrythamic Drugs



Inhibition of K channels (Class III activity) widens the action potential, leading to a prolonged QT interval on the electrocardiogram. Such an effect is associated with ↑risk of developing life-threatening ventricular tachyarrhythmias (**torsades de pointes**). The most common cause of QT prolongation is drug-induced, although it may also be genetic. QT prolongation is not only seen with Class III antiarrhythmics. Drugs such as cisapride, grepafloxacin, terfenadine, and astemizole were withdrawn from the market because of severe and fatal arrhythmias. Erythromycin, clarithromycin, pentamidine, moxifloxacin, levofloxacin, imipramine, desipramine, amitriptyline, doxepin, thioridazine, mesoridazine, haloperidol, risperidone, ziprasidone, and quetiapine are some of the drugs known to prolong the QT interval.

Class I-A Quinidine	Actions: Binds to open & inactivated Na channels & prevents Na influx, thus ↓ rapid upstroke during Phase 0. Also Has Class III activity (K channel Blocking). Alos has mild anticholinergic effects. Uses: In wide variety of arrhythmias, including atrial, AV-junctional, & ventricular tachyarrhythmias. Adverse: Torsades de pointes, SA & AV block or asystole, Ventricular Tachicardia, Nausea, Vomiting, Diarhea
Class I-A Procainamide	Same as Quinidine Adverse:Lupus erythematosus, SA & AV block or asystole, depression, hallucination, and psychosis, low GIT problems

Class I-A Disopyramide.	Same as Quinidine, plus greater -ve inotropic effect & also peripheral vasocinstriction. Adverse:anticholinergic activity (for eg, dry mouth, urinary retention, blurred vision, & constipation)
Class I-B Lidocaine, Mixelitine, Tocainide	Class IB agents rapidly associate and dissociate from sodium channels. Thus, the actions of Class IB agents are manifested when the cardiac cell is depolarized or firing rapidly. Lidocaine is used in ventricular arrhythmias during myocardial infarction. Also Local Aneasthetic. Only CNS effects i.e, drowsiness, slurred speech, paresthesia, agitation, confusion, & convulsions. Mexiletine is used in chronic ventricular arrhythmias with previous myocardial infarction. Tocainide is used in ventricular tachyarrhythmias. Has pulmonary toxicity, which may lead to pulmonary fibrosis.
Class I-C Flecainide, Propefenone	They suppresses Phase 0 upstroke marked slowing of conduction in all cardiac tissue, even at normal heart rates. Used in ventricular arrhythmias. Adverse: dizziness, blurred vision, headache, & nausea, aggravate preexisting arrhythmias, Induce life-threatening ventricular tachycardia.
Class II Propranolol, Metoprolol, Esmolol	Class II agents are useful in treating tachyarrhythmias caused by increased sympathetic activity. Propranolol ↓ sudden arrhythmic death after myocardial infarction. Has ability to prevent ventricular arrhythmias. Metoprolol is most widely used in arrhythmias. Compared to propranolol, it reduces the risk of bronchospasm.
Class III Amiodarone	Class III agents block K-channels &, thus, ↓ K current during repolarization of cardiac cells. All Class III drugs have the potential to induce arrhythmias. Amiodarone is most commonly used drug .it contains iodine & is related to thyroxine. Has complex effects, showing Class I, II, III, & IV actions. It has antianginal effect as well. used in the treatment of severe refractory supraventricular & ventricular tachyarrhythmias.nterstitial pulmonary fibrosis, gastrointestinal tract intolerance, tremor, ataxia, dizziness, hyper- or hypothyroidism, liver toxicity, photosensitivity, neuropathy, muscle weakness, and blue skin discoloration
Class III Sotalol	A class III antiarrhythmic agent, with potent nonselective β-blocker activity. lowest rate of acute or long-term adverse effects, Torsades de Pointes
Class III-Dofetilide	first-line antiarrhythmic agent in patients with persistent atrial fibrillation and heart failure or in those with coronary artery disease with impaired left ventricular function
Class IV Verapamil, Diltiazem	Block open, depolarized Voltage-Sensitive channels causing a ↓in slow inward current that triggers cardiac contraction. use-dependent; i.e, they block most effectively when the heart is beating rapidly. Uses: More effective against atrial than ventricular arrhythmias, Hypertension, Angina. Adverse: Bradycardia, Hypotension
Other Digoxin	Digoxin shortens the refractory period in atrial & ventricular cells while prolong effective refractory period & diminishing conduction velocity in the AV node. Used to control the ventricular response rate in atrial fibrillation & flutter.
Other Adenosine	Naturally occurring nucleoside. At ↑doses, ↓conduction velocity, ↑refractory period, & ↓automaticity in AV node. given IV is drug of choice for acute supraventricular tachycardia. Has low toxicity but causes flushing, chest pain, and hypotension.
Anti Angina Drugs	
Angina pectoris is a characteristic sudden, severe, pressing chest pain radiating to the neck, jaw, back, and arms. It is caused by coronary blood flow that is insufficient to meet the oxygen demands of the myocardium, leading to ischemia.	
Stable Angina	characterized by a burning, heavy, or squeezing feeling in the chest. Caused by the ↓ of coronary perfusion due to a fixed obstruction produced by coronary atherosclerosis.
Unstable Angina	Unstable angina lies between stable angina on the one hand and myocardial infarction on the other.
Prinzmetal's angina	Prinzmetal's angina is an uncommon pattern of episodic angina that occurs at rest and is due to coronary artery spasm
Organic Nitrates (Nitroglycerin, Isosorbide DiNO3 Isosorbide MonoNo3, Amyl Nitrile)	Organic nitrates (& nitrites) are simple nitric & nitrous acid esters of glycerol. Nitares-->Nitrites-->NO-->↑cAMP-->Vasodilation. Nitrates ↓ coronary vasoconstriction & ↑perfusion of the myocardium by relaxing coronary arteries. In addition, they relax veins, ↓preload & myocardial oxygen consumption. Adverse: headache. ↑doses cause Postural Hypotension, tachycardia & Flushing. Tolerance (NItrate free Interval 10-12hrs requird)
β-Blockers Acebutolol, Atenolol, Metoprolol, Esmolol	The β-blockers ↓the oxygen demands of the myocardium by lowering both the rate and the force of contraction of the heart. Propranolol is the prototype for this class of compounds, but it is not cardioselective. Thus, other Î²-blockers, such as metoprolol or atenolol, are preferred. It is important not to discontinue Î²-blocker therapy abruptly. The dose should be gradually tapered off over 5 to 10 days to avoid rebound angina or hypertension.
Ca-Channel Blockers Verapamil, Diltiazem, Amlodipine, Nifedipine	The calcium-channel blockers protect the tissue by inhibiting the entrance of calcium into cardiac and smooth muscle cells of the coronary and systemic arterial beds. All calcium-channel blockers are therefore arteriolar vasodilators that cause a decrease in smooth muscle tone and vascular resistance. Verapamil mainly affects the myocardium, whereas nifedipine exerts a greater effect on smooth muscle in the peripheral vasculature. Diltiazem is intermediate in its actions.
Anti Hypertension Drugs	
	
Diuretics (Thiazide) Hydrchorlthiazide, chorlthiazide	Diuretics can be used as first-line drug therapy for hypertension unless there are compelling reasons to choose another agent. They ↓bp initially by ↑ Na & water excretion. This causes a ↓in extracellular volume, resulting in a ↓in cardiac output & renal blood flow. Thiazide diuretics ↓ blood pressure in both the supine & standing positions, & postural hypotension is rarely observed except in elderly, volume-depleted patients. They counteract the Na & water retention observed with other agents used in the treatment of hypertension (for example, hydralazine).Thiazides are useful in combination therapy with β-blockers, ACE inhibitors, ARBs, and K-sparing diuretics. They are particularly useful in black or elderly patients. Not effective in Patients with inadequate kidney function (creatinine clearance, <50 mL/min). Adverse: Hypokalenmia, Hypomagnesemia, Hyperurecimia, Hyperglycemia
Diuretics (Loop) Furosemide, Bumetanide	The loop diuretics act promptly, even in patients with poor renal function or who have not responded to thiazides or other diuretics. Loop diuretics cause↓renal vascular resistance &↑renal blood flow. Loop diuretics ↑Ca2+ content of urine, whereas thiazide diuretics ↓it. Adverse: Ototoxicity, Hyperuricemia, Hypomagnicemia, Hypokalemia
Diuretics (K-Sparing) Furosemide, Bumetanide, Hydrcholthiazide, Spironolactone, Eplirinone, Triametrene	Amiloride [a-MIL-oh-ride] and triamterene [tri-AM-ter-een] (inhibitors of epithelial sodium transport at the late distal and collecting ducts) as well as spironolactone [speer-on-oh-LAK-tone] and eplerenone [eh-PLEH-reh-none](aldosterone-receptor antagonists) reduce potassium loss in the urine. Spironolactone has the additional benefit of diminishing the cardiac remodeling that occurs in heart failure.

β-Blockers Propranolol, Atenolol, Metoprolol, Esmolol	β-Blockers are currently recommended as first-line drug therapy for hypertension when when concomitant disease is present. They ↓ BP by ↓ cardiac output. More effective for treating hypertension in white than in black patients and in young compared to elderly patients. Adverse: Sexual Dysfunction, Exercise Intolerance
ACE-Inhibitors (Captopril, Enalapril, Lisinopril, Fosinopril, Ramipril, Quinapril)	ACE inhibitors ↓BP by ↓ peripheral vascular resistance without reflexively ↑cardiac output, rate, or contractility. ACE inhibitors are most effective in hypertensive patients who are white and young. However, when used in combination with a diuretic, the effectiveness of ACE inhibitors is similar in white and black patients with hypertension.ACE inhibitors slow the progression of diabetic nephropathy and decrease albuminuria.
Angiotensin-receptor blockers (Candesartan, Losartan, Telmisartan, Valsartan)	ARBs are alternatives to the ACE inhibitors. ARBs do not increase bradykinin levels. ARBs decrease the nephrotoxicity of diabetes, making them an attractive therapy in hypertensive diabetics.
Renin Inhibitor-Aliskerin	Aliskiren directly inhibits renin and, thus, acts earlier in the renin-angiotensin-aldosterone system than ACE inhibitors or ARBs. Aliskiren can also cause cough and angioedema
Ca-Channel Blockers Verapamil, Diltiazem, Amlodipine, Nifedipine	Calcium-channel blockers are recommended when the preferred first-line agents are contraindicated or ineffective. Diphenylalkylamines: Verapamil-----Benzothiazepines: Diltiazem-----Dihydropyridines: 1st Gen Nifedipine 2nd Gen: Amlodipine, Felodipine, Isradipine, Nicardipine, & Nisoldipine. Adverse:Constipation, Dizziness, headache, & a feeling of fatigue due to Low BP.
α-Blockers Doxazocin, Prazoson, Trazocin	They ↓peripheral vascular resistance & ↓arterial bp by causing relaxation of both arterial & venous smooth muscle. These drugs cause only minimal changes in cardiac output, renal blood flow, &glomerular filtration rate. Therefore, long-term tachycardia does not occur, but salt & water retention does. Adverse: Postural Hypotension, Reflex tachycardia and first-dose syncope.
α, β-Blockers--Carvedilol, Labeltolol	They although are effective antihypertensive, are mainly used in the treatment of heart failure.
Other-Clonidine	α2 Agonist. Used primarily for the hypertension not responding adequately to two or more drugs, and with Renel desease.
Other-α-Methyl DOPA	α2-agonist that is converted to methylnorepinephrine centrally. especially valuable in treating hypertensive patients with renal insufficiency. Adverse: sedation & drowsiness.
Other Hydralazine	Causes direct vasodilation of arteries & arterioles. Results in a ↓peripheral resistance, which in turn prompts a reflex ↑in HR & output. almost always used in combination with β-blockers & Diuretic to balance reflex Tachycardia. Together, the three drugs ↓cardiac output, plasma volume, & peripheral vascular resistance. Monotherapy used in pregnancy-induced hypertension. Adverse: headache, tachycardia, nausea, sweating, arrhythmia, & precipitation of angina. A lupus-like syndrome high dosage.
Other Minoxidil	Causes dilation of arterioles but not of venules. administered orally for treatment of severe to malignant hypertension that is refractory to other drugs. Reflex tachycardia & fluid retention require the concomitant use of a loop diuretic & β-blocker. Adverse: Na & water Retention
In Emergencies Na-Niropruside, Labetalol, Fenoldopam, Nicardipine	Used in Hypertensive Emergencies
Drugs affecting blood	
Pletilet Aggregation Inhibitor Asprin	Arachidonic acid-->PgH2 by COX-1-->TXA2, which is released into plasma which promotes the clumping process that is essential to the rapid formation of a hemostatic plug. Aspirin inhibits TXA2 synthesis from arachidonic acid. Used in transient cerebral ischemia, to ↓recurrence myocardial infarction, & to ↓ mortality in pre & post myocardial infarct patients. Adverse: Git, ↑bleeding time
Pletilet Aggregation Inhibitor Ticlopidine, Clopidogril	Irreversibly inhibit the binding of ADP to its receptors on platelets &, thus, inhibit the activation of the GP IIb/IIIa receptors. Adverse:Neutropenia/agranulocytosis, thrombotic thrombocytopenic purpura (TTP), and aplastic anemia
Pletilet Aggregation Inhibitor Absiximab	Chimeric monoclonal antibody directed against the GP IIb/IIIa complex. The major adverse effect of abciximab therapy is the potential for bleeding.
Pletilet Aggregation Inhibitor Eptifibatide, Tirofeban	Block the GP IIb/IIIa receptors. Only intravenous formulations are available, because oral preparations of GP IIb/IIIa blockers are too toxic. The major adverse effect of both drugs is bleeding.
Pletilet Aggregation Inhibitor Dipyridamol	a coronary vasodilator, used prophylactically to treat angina pectoris. Usually given in combination with aspirin or warfarin as ineffective when used alone. ↑ intracellular levels of cAMP by inhibiting cyclic nucleotide phosphodiesterase, resulting in decreased thromboxane A2 synthesis.
Anticoagulants Thrombin inhibitors: heparin & (LMWHs dalteparin, enoxaparin)	Binds to antithrombin III, resulting in inactivation if thrombin (Factor IIa) and Factor Xa. treatment of acute deep-vein thrombosis and pulmonary embolism. Adverse: Bleeding complications, Hypersensitivity reactions, Thrombocytopenia
Lepirudin	direct thrombin antagonist, lepirudin is a polypeptide that is closely related to hirudin a thrombin inhibitor derived from medicinal leech saliva. Lepirudin is produced in yeast cells by recombinant DNA technology. Bleeding is the major adverse effect
Argatroban	direct inhibits thrombin. major side effect is bleeding.
Fondaparinux	Binds to antithrombin III. Bleeding is the major side effect. Thrombocytopenia is not a problem,
Vitamin K inhibitors Warfrin, Dicoumarol	they antagonize the cofactor functions of vitamin K in synthesis of Factors II, VII, IX, and X. Bleeding disorders, never be used during pregnancy, because it is teratogenic
Thrombolytic Drugs Alteplase, Streptokinase, Anistreplase	Convert plasminogen to plasmin, which in turn cleaves fibrin, thus lysing thrombi. Alteplase specificly binds to non free plasminogen, streptokinase is non specific. Anistreplase is a preformed complex of streptokinase and plasminogen and it is considered to be a prodrug. Streptokinase must be released, and only plasminogen to which it was associated will get converted to plasmin. Adverse: Blleding, GIT problems, hypersensitivity
Drugs Used to Treat Bleeding Aminocaproic acid, Tranexamic acid, Protamine SO4, Vitamin K, Aprotinin	Aminocaproic acid, Tranexamic acid, Both agents are synthetic, inhibit plasminogen activation, Protamine sulfate antagonizes the anticoagulant effects of heparin. vitamin K1 (phytonadione) administration can stem bleeding problems. response to vitamin K is slow, requiring about 24 hours. Aprotinin is a serine protease inhibitor that stops bleeding by blocking plasmin. It can inhibit streptokinase.
Anti Hyperlipidemias	
Limits	LDL<160mg/dl……HDL>60mg/dl……Total Cholesterol<200mg/dl
Types of hyperlipidemias	Type-1=↑Cholimicron, Type2=↑LDL, Type3=↑LDL & VLDL, Type4=↑IDL, Type5=↑VLDL &Cholimicron
HMG CoA Reductase Inhibitor Atorvastatin, Simvastatin, Rosuvastatin, Fluvastatin, Pravatatin	Analogs of HMG, the precursor of cholesterol. Competitive Inhibition of HMG CoA reductase. ↓ of intracellular cholesterol causes the cell to ↑ the number of specific cell-surface LDL receptors that can bind and internalize circulating LDLs Thus, the end result is a reduction in plasma cholesterol, both by lowered cholesterol synthesis and by increased catabolism of LDL.
Niacin	Converted into Nicotinamide and inhibits lypolisis in adipose tissue resuling in ↓ free fatty acids for vldl sysnthesis Adverse: Intense cutaneous flush
Fibrates Fenofibrate, Gemfibrozil	Act on PPARs to ↓ LDLs. Gastrointestinal effects, Lithiasis, Myositis
Bile Acid Sequestrants, Cholistyramin, Cholestipol	anion-exchange resins that bind to bile acids and bile salts. the resulting resin/bile acid complex is excreted in the feces.↓ bile acid concentration causes hepatocytes to increase conversion of cholesterol to bile acids, ↓ cholesterol levels. Adverse: Gastrointestinal effects
Cholestrol absorption Inhibit Ezitimibe	Ezetimibe selectively inhibits intestinal absorption of dietary and biliary cholesterol in the small intestine, leading to a decrease in the delivery of intestinal cholesterol to the liver.

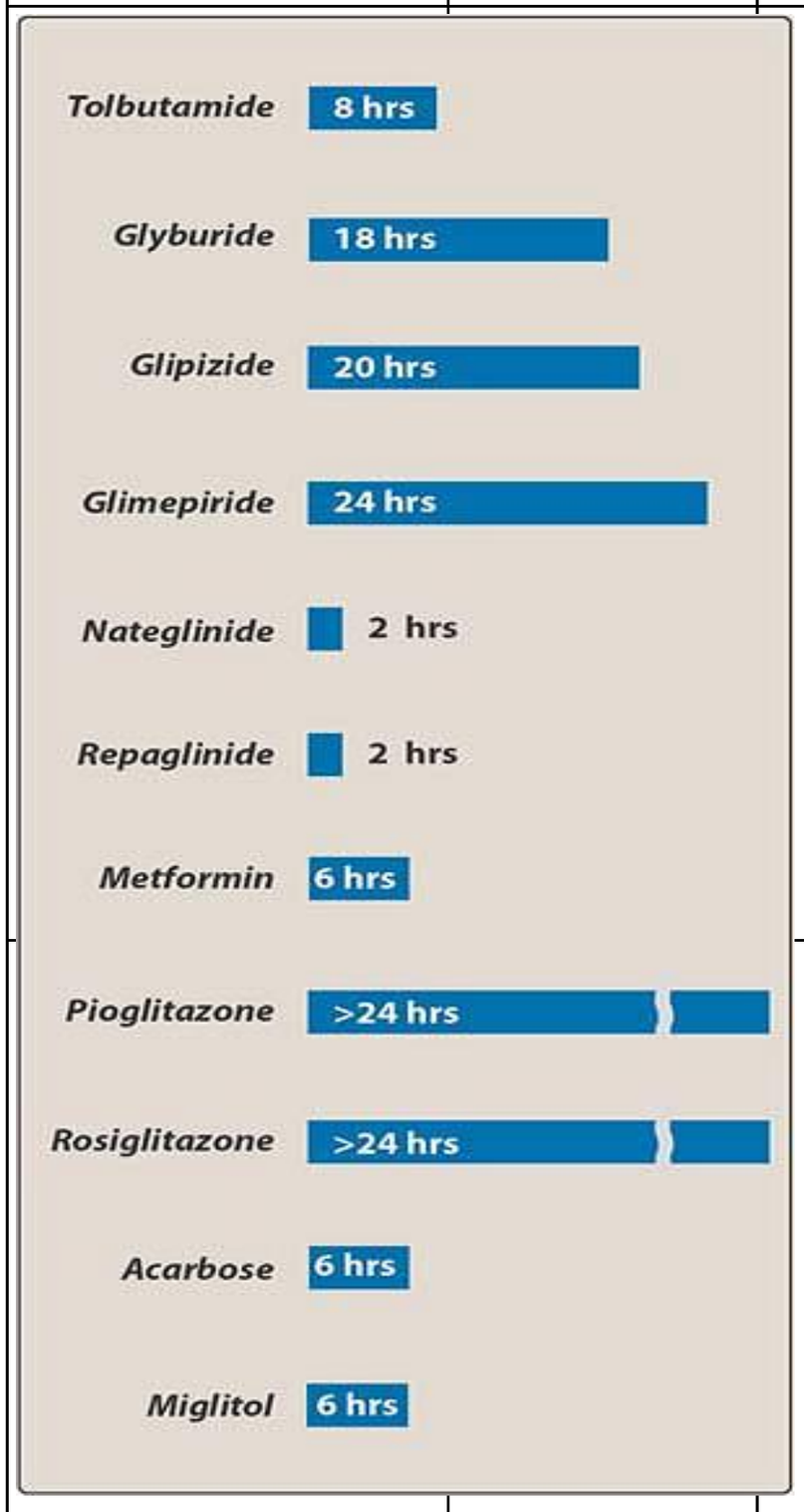
	Type 1	Type 2
Age of onset	Usually during childhood or puberty	Frequently over age 35
Nutritional status at time of onset	Frequently undernourished	Obesity usually present
Prevalence	5 to 10 percent of diagnosed diabetics	90 to 95 percent of diagnosed diabetics
Genetic predisposition	Moderate	Very strong
Defect or deficiency	β Cells are destroyed, eliminating the production of insulin	Inability of β cells to produce appropriate quantities of insulin; insulin resistance; other defects

TYPE OF DRUG	EFFECT ON LDL	EFFECT ON HDL	EFFECT ON TRIACYLGLYCEROLS
HMG CoA reducatase inhibitors (statins)	↓↓↓↓	↑↑	↓↓
Fibrates	↓	↑↑↑	↓↓↓↓
Niacin	↓↓	↑↑↑↑	↓↓↓
Bile acid sequestrants	↓↓↓	↑	Minimal
Cholesterol absorption inhibitor	↓	↑	↓

Insulin Types:	Fast/Short Acting: Regular, Lispro, Aspart, Glulisin------Intermediate:NPH (Neutral Protamine Hagedron)------Long Acting: Glargin, Determir
Synthetic Amylin Analog Pramlintide	Pramlintide is a synthetic amylin analog that is indicated as an adjunct to mealtime insulin therapy in patients with Type 1 or Type 2 diabetes. By acting as an amylinomimetic, pramlintide delays gastric emptying, decreases postprandial glucagon secretion, and improves satiety.Pramlintide is administered by subcutaneous injection and should be injected immediately prior to meals.
Oral Agents:Sulphonylureas Glimepiride, Gliburide, Gliclazide, Gliperide	1) stimulation of insulin release 2)↓ hepatic glucose production; and 3) ↑peripheral insulin sensitivity. Adverse: weight gain, hyperinsulinemia, & hypoglycemia. Should be used with caution in patients with hepatic or renal insufficiency,
Oral Agents:Meglintide Nateglinide, Repaglinide	Same as above. rapid onset and a short duration of action. ketoconazole, itraconazole, fluconazole, erythromycin, and clarithromycin, may enhance the glucose-lowering effect of repaglinide, by inhibiting their metabolism by cyp3a4.
Oral Agents:Biguanides Metformin	Metform ininhibs hepatic gluconeogenesis, ↓ intestinal absorption of sugars &improves peripheral glucose uptake & utilization. LDL, VLDL ↓, ↑ HDL. Metformin is contraindicated in diabetics with renal and/or hepatic disease, acute myocardial infarction, severe infection, or diabetic ketoacidosis. GI Side effects.
Oral Agents:Glitazones Pioglitazone, Rosiglitazone	Act on PPARɣ. Hepatotoxicity, Weight gain.
Oral Agents:α-Glicosidase Inhibitors Acarbose, Miglitol	These drugs are taken at the beginning of meals. They act by delaying the digestion of carbohydrates, thereby resulting in lower postprandial glucose levels. side effects are flatulence, diarrhea, and abdominal cramping.
Oral Agents:Dipeptydil peptidase IV Inhibitors Sitagliptin	Sitagliptin inhibits the enzyme DPP-IV, which is responsible for the inactivation of incretin hormones, such as glucagon-like peptide-1. Prolonging the activity of incretin hormones results in increased insulin release in response to meals and a reduction in inappropriate secretion of glucagon. Adverse effects being nasopharyngitis and headache.
Incretin Mimetic Exenatide	Oral glucose results in a higher secretion of insulin than occurs when an equal load of glucose is given intravenously. Exenatide act like glucose and causes glucose-dependent insulin secretion but also slows gastric emptying time, decreases food intake, decreases postprandial glucagon secretion, and promotes Î²-cell proliferation. Consequently, weight gain and postprandial hyperglycemia are reduced, and HbA1c levels decline. adverse effects consist of nausea, vomiting, and diarrhea.

CLASSIFICATION	BRONCHO-CONSTRICTIVE EPISODES	RESULTS OF PEAK FLOW OR SPIROMETRY	LONG-TERM CONTROL	QUICK RELIEF OF SYMPTOMS
Mild intermittent	Less than two per week	Near normal*	No daily medication	Short-acting β_2 agonist
Mild persistent	More than two per week	Near normal*	Low-dose inhaled corticosteroids	Short-acting β_2 agonist
Moderate persistent	Daily	60 to 80 percent of normal	Low- to medium-dose inhaled corticosteroids and a long-acting β_2 agonist	Short-acting β_2 agonist
Severe persistent	Continual	Less than 60 percent of normal	High-dose inhaled corticosteroids and a long-acting β_2 agonist	Short-acting β_2 agonist

STAGE	CHARACTERISTICS	LONG-TERM CONTROL
I: Mild COPD	FEV_1 greater than 80 percent predicted	Short-acting bronchodilator when needed
II: Moderate COPD	FEV_1 50 to 80 percent predicted	Regular treatment with one or more bronchodilators Inhaled glucocorticosteroid
III: Severe COPD	FEV_1 less than 30 percent predicted	Regular treatment with one or more bronchodilators Inhaled glucocorticosteroid Antibiotics for acute exacerbations of COPD characterized by increased volume and purulence of secretions Long-term oxygen therapy

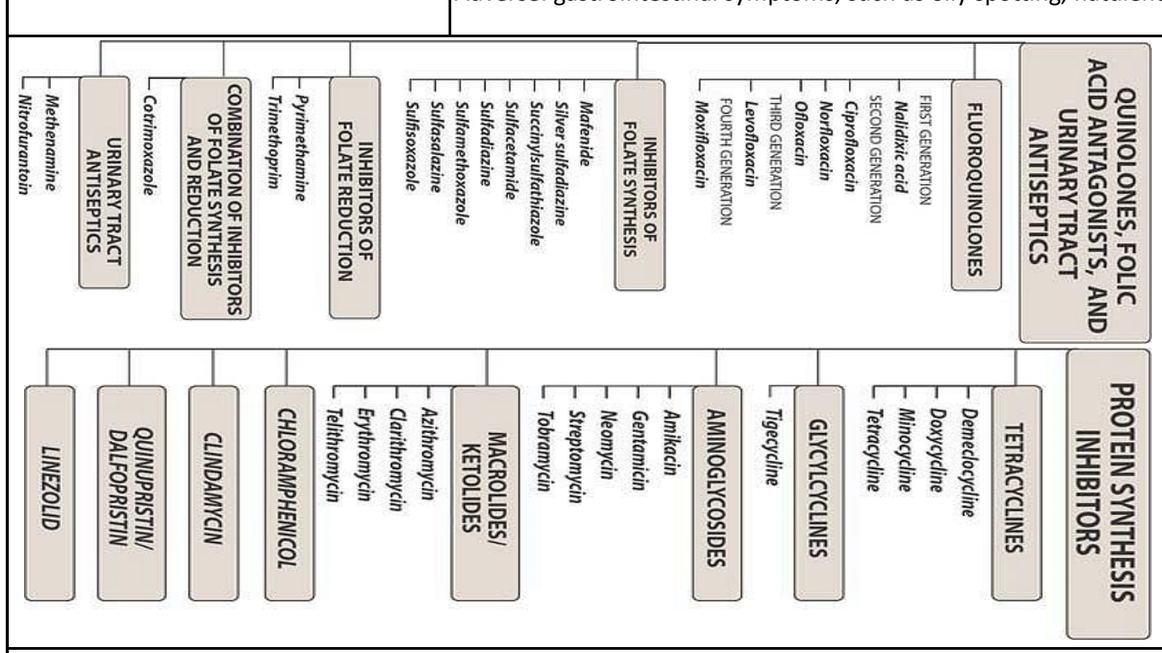


DRUG CLASS	MECHANISM OF ACTION	EFFECT ON PLASMA INSULIN	RISK OF HYPO-GLYCEMIA	COMMENTS
First-generation sulfonylureas *Tolbutamide*	Stimulates insulin secretion	↑	Yes	Well-established history of effectiveness. Weight gain can occur.
Second-generation sulfonylureas *Glipizide* *Glyburide* *Glimepiride*	Stimulates insulin secretion	↑	Yes	Well-established history of effectiveness. Weight gain can occur.
Meglitinides *Nateglinide* *Repaglinide*	Stimulates insulin secretion	↑	Yes (rarely)	Short action with less hypoglycemia either at night or with missed meal. Post-prandial effect.
Biguanides *Metformin*	Decreases endogenous hepatic production of glucose	↓	No	Preferred agent for Type 2 diabetes. Well-established history of effectiveness. Weight loss may occur. Convenient daily dosing. Many contraindications. Monitor renal function.
Thiazolidinediones (glitazones) *Pioglitazone* *Rosiglitazone*	Binds to peroxisome proliferator–activated receptor-γ in muscle, fat and liver to decrease insulin resistance.	↓↓	No	Effective in highly insulin-resistant patients. Once-daily dosing for *pioglitazone* Monitor liver function.
α-Glucosidase inhibitors *Acarbose* *Miglitol*	Decreases glucose absorption	⇔	No	Taken with meals. Adverse gastro-intestinal effects.
DPP-IV inhibitors *Sitagliptin*	Increases glucose-dependent insulin release, decreases secretion of glucagon	↑	No	Once-daily dosing. May be taken with or without food. Well tolerated.

Diuretics	
Thiazide Chlorthiazide, Hydrochlorthiazide	Act on Distal convoluted tubule, by Blocking Na/Cl Transport System. Because the site of action of the thiazide derivatives is on the luminal membrane, these drugs must be excreted into the tubular lumen to be effective. Therefore, with decreased renal function, thiazide diuretics lose efficacy. Adverse: HypoKalemia, HypoNatremia, HypoMagnesemia, HyperGlycemia, HyperUricemia
Tiazide like Metolazone, Chlorthalidone, Indapamide	
loop Furosimide, Bumetanide, Ethacranic acid, Torsemide	Loop diuretics inhibit the cotransport of Na+/K+/2Cl- in the ascending loop of Henle. loop diuretics are most efficacious, because the ascending limb accounts for the reabsorption of 25 to 30 percent of filtered NaCl. They are also effective in patients with poor renal function. Adverse: Ototoxicity, HypoKalemia, HypoNatremia, HypoMagnesemia, HyperUricemia
K-Sparing-Aldosterone Anta Spironolactone, Eplirinone	They antagonizes aldosterone at intracellular cytoplasmic receptor sites, resulting in ↓ Na+ reabsorption &,↓ K+ & H+ excretion. gastric upsets & peptic ulcers, gynecomastia in males and menstrual irregularities in females
K-Sparing-Other Amiloride, Triametrene	They block Na+ transport channels, resulting in a ↓ in Na+/K+ exchange in collecting ducts. Adverse: Leg Cramps

Carbonic Anhydrase Inhibitor Acetazolamide	Acetazolamide inhibits carbonic anhydrase, which catalyzes the reaction of CO2 & H2O, leading to H2CO3, which ionizes to H+ and HCO3(bicarbonate). The ↓ability to exchange Na+ for H+ results in a mild diuresis. Additionally, HCO3- causes marked ↑ in urinary pH & hyperchloremic metabolic acidosis &↓ diuretic efficacy following several days of therapy. Used in Glacoma & Mountain Sickness Adverse:Metabolic acidosis (mild), potassium depletion, renal stone formation, drowsiness, and paresthesia
Osmotic- Mannitol, Urea	Cause Some Degree of Diuresis due to Osmotic effect. Adverse effects include extracellular water expansion and dehydration as well as hypo- or hypernatremia.
Anti-Asthmatics	
β-Agonists:Short-Acting Albuterol, Terbutaline, perbuterol	rapid onset of action (5â€“30 minutes) and provide relief for 4 to 6 hours Adverse effects, as tachycardia, hyperglycemia, hypokalemia, and hypomagnesemia are minimized with dosing via inhalation versus systemic routes.
β-Agonists:Long-Acting Salmetrol, Formetrol	have a long duration of action, providing bronchodilation for at least 12 hours.
Corticosteroids Beclomethasone, Fluticasone, Triamcinolone, Flunisolide	Inhaled corticosteroids (ICS) are the drugs of first choice in any degree of persistent asthma (mild, moderate, or severe(; ICS do not directly affect the airway smooth muscle. Instead, they directly targets underlying airway inflammation by decreasing the inflammatory cascade. Adverse: Osteoprosis, ↓Growth in Kids, ↑ Apetite, peripheral edema, Gaucoma, Hypotension, Ulcers
Leukotriene antagonists Zileuton, Montelukast, Zafirlukast	Ziluton inhibits Synthesis of ILb4. other inhibit Cistenyl IL Receptors. approved for the prophylaxis of asthma but are not effective in situations where immediate bronchodilation is required. Adverse: ↑ serum hepatic enzymes, eosinophilic vasculitis (Churg-Strauss syndrome)
Cromolyn Na, Nedocromil	prophylactic anti-inflammatory agents. Inhibit Histamine release from mast cells. Short acting, bitter taste & irritation of the pharynx & larynx.
Cholinergic antagonists Ipratropium,	useful in patients who are unable to tolerate adrenergic agonists. Ipratropium is slow in onset and nearly free of side effects. These agents are not traditionally effective for patients with asthma unless COPD is also present.
Theophylline	bronchodilator that relieves airflow obstruction in chronic asthma and decreases its symptoms.
Omalizumab	Antibody that selectively binds to IgE--> ↓ binding of IgE to IgE receptor on mast cells & basophils--> ↓release of mediators of the allergic response.
Drugs Used to Treat Allergic Rhinitis	
H1-receptor blockers	diphenhydramine, chlorpheniramine, loratadine, and fexofenadine,
α-Adrenergic agonists	Short-acting phenylephrine, constrict dilated arterioles in the nasal mucosa and reduce airway resistance. Longer-acting oxymetazolin.
Corticosteroids	Beclomethasone, budesonide, fluticasone, flunisolide, and triamcinolone, are effective when administered as nasal sprays.
Drugs Used to Treat Peptic Ulcer	
Anti-Microbials	Triple therapy consisting of a PPI with either metronidazole or amoxicillin plus clarithromycin, or quadruple therapy of bismuth subsalicylate and metronidazole plus tetracycline plus a PPI, are administered for a 2-week course.
H2-Receptor Antagonists Cimetidine, Famotidine, Ranitidine, Nizatidine	Ranitidine--5-10time potent than Cimet. Famotidine--20-50time potent than cimt. Adverse: headache, dizziness, diarrhea, and muscular pain. Cimetidine (Gynecmastina, Glactorhea)
Inhibitors of the H+/K+-ATPase proton pump omeprazole, Lansoprazole, Pentoprazole, Esomeprazole	The superiority of the PPIs over the H2 antagonists for suppressing acid production and healing peptic ulcers has made them the preferred drugs for treating erosive esophagitis and active duodenal ulcer and for long-term treatment of pathologic hypersecretory conditions (for example, Zollinger-Ellison syndrome, in which a gastrin-producing tumor causes hypersecretion of HCl). Adverse:Increased concentrations of viable bacteria in the stomach have been reported with continued use of these drugs. Omeprazole inhibits the metabolism of warfarin, phenytoin, diazepam, and cyclosporine.
Prostaglandin Analogue Misoprostol	A stable analog of prostaglandin E1. Dose-related diarrhea and nausea are the most common adverse effects and limit the use of this agent.
Antimuscarinic agents	DiCyclomine can be used as an adjunct in the management of peptic ulcer disease and Zollinger-Ellison syndrome
Antacids Al(OH)3, Mg(OH)2, CaCO3, NaHCO3	Antacids are weak bases that react with gastric acid to form water and a salt, thereby diminishing gastric acidity. Aluminum hydroxide tends to be constipating, and magnesium hydroxide tends to produce diarrhea
Mucosal protective agents Sucralfate, Bismuth subsalicylate	sucralfate by forming complex gels with epithelial cells, creates a physical barrier that prevents degradation of mucus by pepsin and acid. This agent does not prevent NSAID-induced ulcers, nor does it heal gastric ulcers. Bismuth Subsalicylate effectively heal peptic ulcers.
Drugs Used to Control Chemotherapy-Induced Emesis	
Phenothiazines Prochlorperazine	Blocks Dopamine Receptors. Effective against low or moderately emetogenic chemotherapeutic agents. Side effects, including hypotension and restlessness, are dose limiting
5-HT3 Antagonists Ondansetron, Granisetron, Palonosetron, Dolasetron	L.ong duration of action. Efficacious against all grades of emetogenic therapy. Doses should be adjusted in patients with hepatic insufficiency. Headache is a common side effect.
Substituted benzamides Metoclopramide	Highly effective at high doses against the highly emetogenic cisplatin, preventing emesis in 30 to 40% of patients and reducing emesis in the majority. Antidopaminergic side effects, including sedation, diarrhea, limit its high-dose use.
Butyrophenones--Droperidol, Haloperidol	Act by blocking dopamine receptors. Moderately effective antiemetics.
Benzodiazepines--Alprazolam, Lorazepam	Their beneficial effects may be due to their sedative, anxiolytic, and amnesic properties. These same properties make benzodiazepines useful in treating anticipatory vomiting.
Corticosteroids Dexamethasone, Methylprednisolone	When used alone, are effective against mild to moderate emetogenic chemotherapy. Most frequently, however, they are used in combination with other agents. Their antiemetic mechanism is not known. These drugs can cause insomnia as well as hyperglycemia in patients with diabetes mellitus.
Cannabinoids Dronabinol, Nabilone	Effective against moderately emetogenic chemotherapy. seldom first-line antiemetics because of their serious side effects, including dysphoria, hallucinations, sedation, vertigo, and disorientation.
Sub P/ Neurokinin Blockers- Aprepitant	Targets the neurokinin receptor in the brain and blocks the actions of the natural substance. Aprepitant is usually administered orally with dexamethasone and palonosetron.
Anti-Diarials	
Anti Motility Diphenoxylate, Loperamide	Both are analogs of meperidine and have opioid-like actions on the gut, activating presynaptic opioid receptors in the enteric nervous system to inhibit acetylcholine release and decrease peristalsis. Side effects include drowsiness, abdominal cramps, and dizziness.
Adsorbants	Bismuth subsalicylate, Methylcellulose, and Aluminum hydroxide are used to control diarrhea. Bismuth subsalicylate, used for traveler's diarrhea
Anti - Constipation	
Irritants and stimulants	**Senna** is a widely used stimulant laxative. Its active ingredient is a group of sennosides, a natural complex of anthraquinone glycosides. Taken orally, it causes evacuation of the bowels within 8 to 10 hours. **Bisacodyl**, available as suppositories and enteric-coated tablets, is a potent stimulant of the colon. It acts directly on nerve fibers in the mucosa of the colon. Adverse effects include abdominal cramps and the potential for atonic colon with prolonged use. **Castor oil** is broken down in the small intestine to ricinoleic acid, which is very irritating to the gut, and promptly increases peristalsis. It should be avoided by pregnant patients, because it may stimulate uterine contractions.
Bulk Laxatives	Hydrophyllic Colloids, Methylcellulose, Psyllium seeds, & Bran.

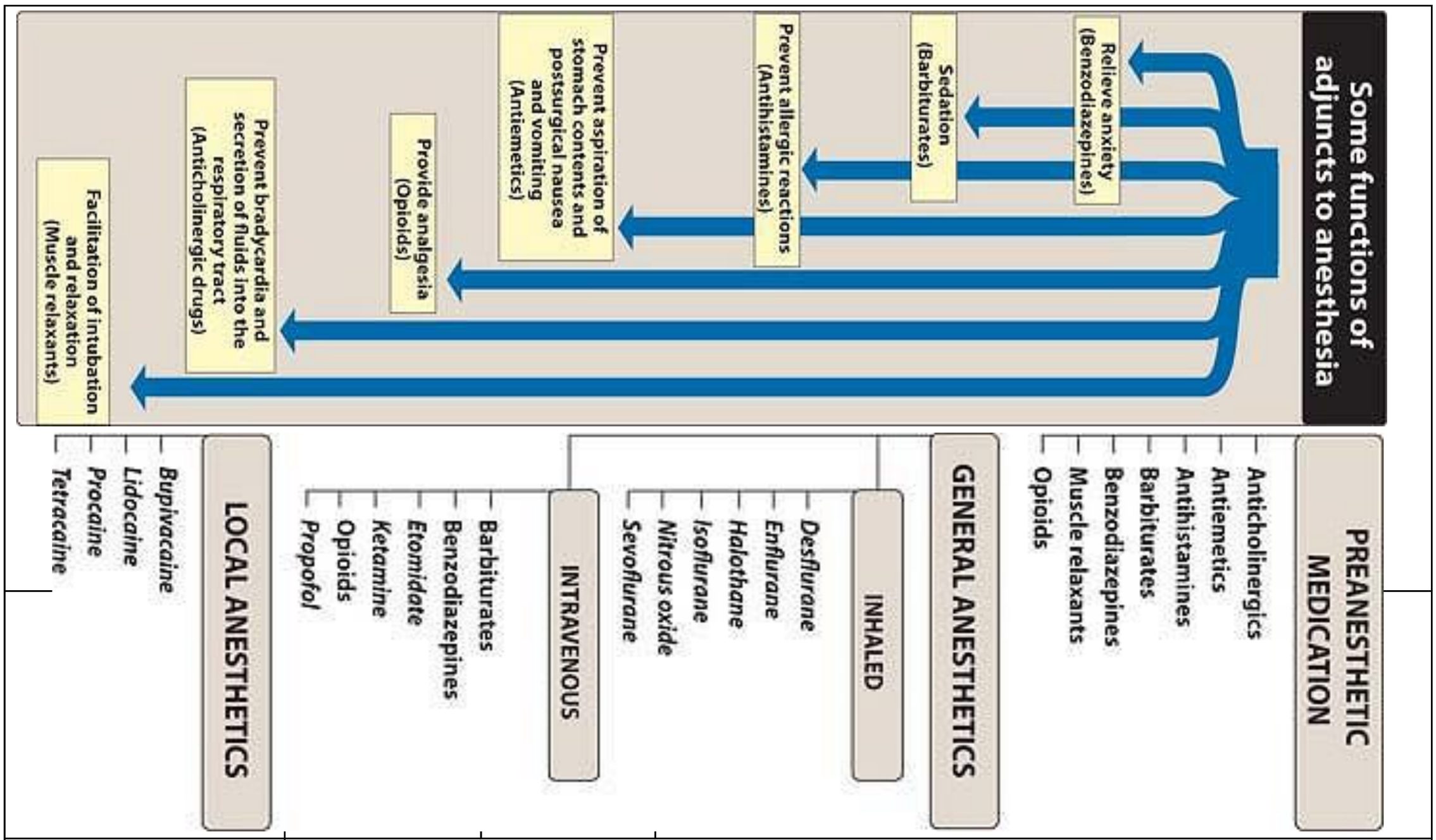
Saline or Osmotic laxatives	Mag. Citrate, Mag. Sulfate, Sodium Phosphate, & Mag. Hydroxide, are nonabsorbable salts that hold water in the intestine by osmosis and distend the bowel, increasing intestinal activity and producing defecation in a few hours. Polyethylene glycol (PEG) are used as colonic lavage solutions to prepare the gut for radiologic or endoscopic procedures. Lactulose is alos used.
Stool Softeners	Docusate sodium, Docusate calcium, and Docusate potassium, act as Surfactants to soften the stool.
Lubricants	Mineral oil and glycerin suppositories are considered to be lubricants. They facilitate the passage of hard stools.
Erectile Dysfunction	Sildenafil, tildenafil, and Verdenafil act by inhibiting PDE-5
Osteoprosis	
Bisphosphonates Etidronate, Risedronate, Alendronate, ibandronate, pamidronate, tiludronate, zoledronic acid	1) inhibition of the osteoclastic proton pump necessary for dissolution of hydroxyapatite, 2) decrease in osteoclastic formation/activation, 3) increase in osteoclastic apoptosis (programmed cell death), and 4) inhibition of the cholesterol biosynthetic pathway important for osteoclast function. Adverse effects: These include diarrhea, abdominal pain, and musculoskeletal pain
Selective estrogen-receptor modulators Raloxifie	Estrogen replacement is an effective therapy for the prevention of postmenopausal bone loss. Raloxifene [rah-LOX-ih-feen]is a selective estrogen-receptor modulator approved for the prevention and treatment of osteoporosis.
Calcitonin	Salmon calcitonin administered intranasally, is effective and well tolerated in the treatment of postmenopausal osteoporosis.
Teriparatide	Recombinant segment of human parathyroid hormone that is administered subcutaneously for the treatment of osteoporosis.
Anti-Obesity Drugs	
Phentermine, diethylpropion, and sibutramine	exerts its pharmacologic action by increasing release of norepinephrine and dopamine from the nerve terminals and by inhibiting reuptake of these neurotransmitters, thereby increasing levels of neurotransmitters in the brain. Thus Apetite is Supresssed. Schedule IV controlled agents due to potential for dependence or abuse. Dry mouth, headache, insomnia, and constipation are common problems.
Orlistat	Orlistat is a pentanoic acid ester that inhibits gastric and pancreatic lipases, thus decreasing the breakdown of dietary fat into smaller molecules that can be absorbed. Adverse: gastrointestinal symptoms, such as oily spotting, flatulence with discharge, fecal urgency, and increased defecation.



AntiMicrobials--Cell Wall Synthesis Inhibitors	
β-Lactam (Penicillins) Penicillins + Aminoglycoside = Synergistic	**Natural Penicillin-G/V**: Gram + Cocci, Gram + Bacilli, Gram - Cocci, Spirochets, Anaerobes **Broad Spectrum** Amoxycillin, Ampicillin: Gram + Cocci, Gram + Bacilli, Gram - Cocci, Spirochets, Anaerobes Plus Gram - Bacilli **Anti-Staphylococcal** Methicillin, Nafcillin, Oxacillin, Dicloxacillin: Penicillinase Producing Staphylococci **Anti-Psuedomonal** Carbenicillin, Piperacillin, Ticarcillin: P. Aeroginosa Adverse: Hypersensitivity, Diarhea, Nephrotoxicity, Neurotoxicity, Heamatological Toxities, Cation Toxicity
β-Lactam (Cephalosporins)	**1st Gen:** Cephadroxil, Cephalexin, Cefazolin, Cephradin: Spectram as Penicliin G , PEcK (Proteus, Escercia Kelbsella) **2nd Gen:** Cefaclor, Cefuroxime, Cefoxitin : Spectram as Penicliin G , HENPEcK (Hemophilus, Enterobacter, Nesseria, Proteus, Escercia Kelbsella) **3rd Gen:** Ceftriaxone, Cefotaxime, Cefixime, Ceftazidime: More activity against G-ve. Ceftri is used in Meningitis **4th Gen:** Cefepime. Non Methicillin resistant Streptococci, Staphylococci. **5th Gen:** Ceftobiprole, Ceftaroline: Anti Psuedomonal
β-Lactam Carbapenims Imipenim/Cilastatin Meropenim, Ertapenim	Widest spectram antibiotics. B-Lactamse resistant. But not metelo ones. Used in the Emperic Therapy. Adverse: Nausea, vomiting, and diarrhea.
β-Lactam Monobactams Eztreonam	Effective against Enterobacteriaceae, but it also acts against aerobic gram-negative rods, including P. aeruginosa.
Other Vancomycin	Vancomycin is effective against gram-positive organisms. It has been lifesaving in the treatment of MRSA and methicillin-resistant Staphylococcus epidermidis (MRSE) infections as well as enterococcal infections. fever, chills, and/or phlebitis at the infusion site.
Other Dapromycin	Daptomycin has a spectrum of activity limited to gram-positive organisms constipation, nausea, headache, and insomnia.
Other Bacitracin	Bacitracin a mixture of polypeptides. Active against gram-positive organisms. Its use is restricted to topical application because of its potential for nephrotoxicity with systemic use.
AntiMicrobials--Protein Synthesis Inhibitors	
Tetracyclines Tetracyclin, Doxicycline, Minocycline, Demeclocycline	Inhibits Protein Synthesis by binding to 50S Subunit of Ribosom. Broad Spectrum G+ (Anthrax), G-(Cholera), Anaerobes, Spirochetes (Lyme Desaese), Chlaymidia, Mycoplasma (Pnemonia) Adverse: Hepatotoxicity, Phototoxicity, Deposition in bones of Children (Growth problems), GIT
Glycycline Tegecycline	Inhibits Protein Synthesis by binding to 50S Subunit of Ribosom. Broad Spectrum. Expanded broad-spectrum activity including methicillin-resistant staphylococci, multidrug-resistant Streptococcus pneumoniae, and other susceptible strains of streptococcal species, vancomycin-resistant enterococci,
Aminoglycosides Gentamycin, Neomycin, Streptomycin, Tobramycin	Inhibits Protein Synthesis by binding to 50S Subunit of Ribosom. Broad Spectrum. Effective in the empirical treatment of infections suspected of being due to aerobic gram-negative bacilli, including Pseudomonas aeruginosa. Adverse: Ototoxicity, Nephrotoxicity, Skin Rash, paralysis
Macrolides Erythromici, Clarithromicin, Azithromicin	50S. G+, G-, Spirochetes, Chlaymidia, Mycoplasma Adverse: Ototoxicity, Hepatotoxicity, GIT.
Chloramphenicol	50S. Only used as alternative to other Drugs. Graybaby Syndrome, GIT, Anemias

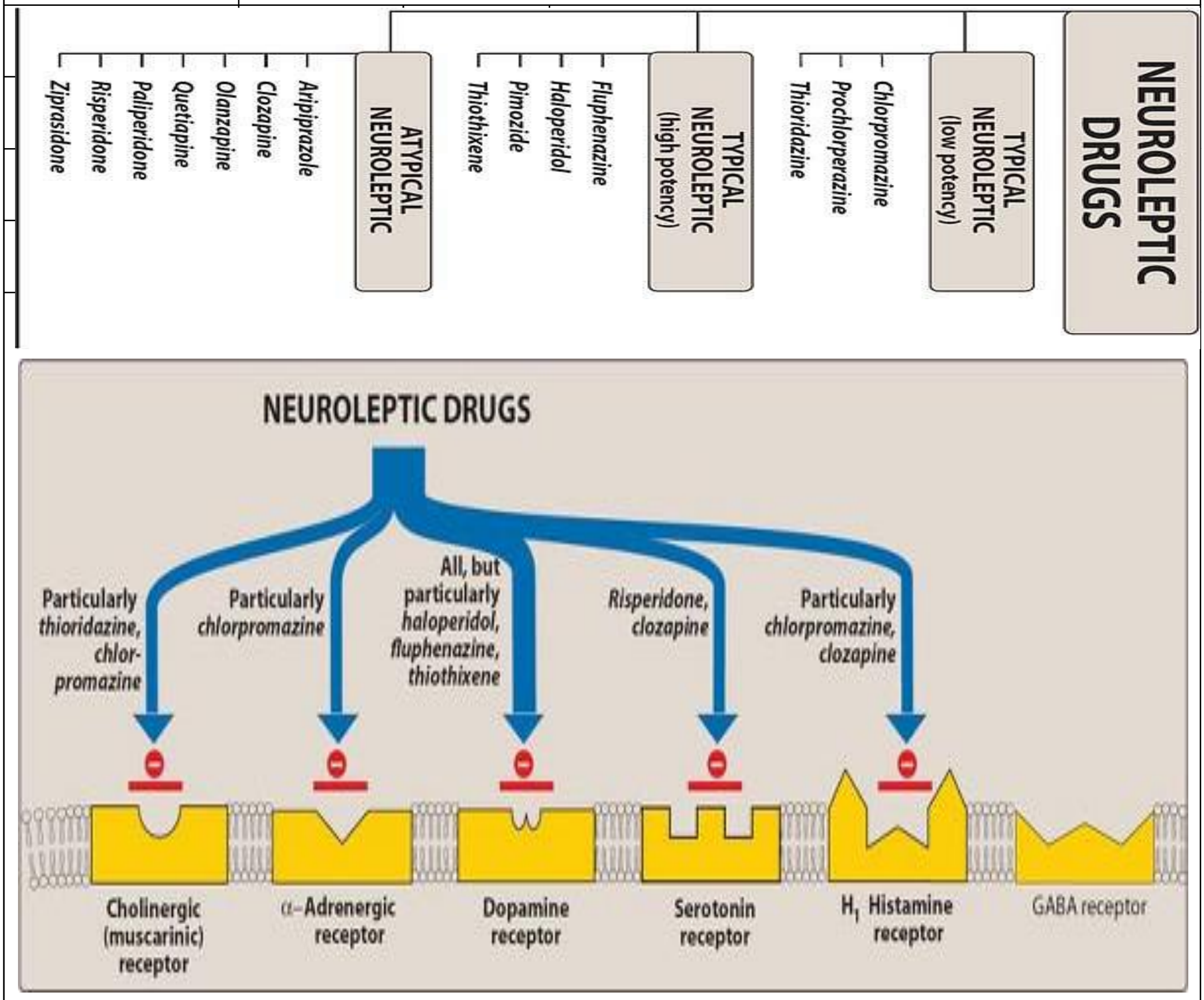
Clindamicin	50S. Clindamycin is employed primarily in the treatment of infections caused by anaerobic bacteria, such as Bacteroides fragilis
Quinpristin/Dalfopristin	50S. A 30/70 mixture of two streptogramins, respectively. Reserved for the treatment of vancomycin-resistant Enterococcus faecium (VRE).
Linezolid	70S. Linezolid against resistant gram-positive organisms, such as methicillin- and vancomycin-resistant Staphylococcus aureus, vancomycin-resistant E. faecium and E. faecalis, and penicillin-resistant streptococci. Linezolid is a totally synthetic oxazolidinone.
AntiMicrobials--Floroquinolones	
1st Gen Nalidixic Acid	Fluoroquinolones enter the bacterium by passive diffusion via water-filled protein channels (porins). Then, they inhibit the replication of DNA by interfering with DNA gyrase (topoisomerase II) & topoisomerase IV during bacterial growth & reproduction causing Cell Death. Like aminoglycosides, quinolones exhibit concentration-dependent bacterial killing. Bactericidal activity becomes more pronounced as the serum drug concentration ↑to approximately 30-fold the minimum inhibitory concentration. 1st: G---------2nd & 3rd:G+/-, Chalmidia, Mycoplasma-------4th: G+/-, Anaerobes Adverse: GIT, Phototoxicity, Connective tissue problems . Not in Pregnanacy.
2nd Gen- Ciprofloxacin, Ofloxacin, Norfloxacin	
3rd Gen-Levofloxacin	
4th Gen-Moxifloxacin	
Synth. Inhibitors Sulphonamides Sufamethoxazole, Sulfadiazine, Ag Sulfadiazine, sulfasalazine, Mefnide	Analogs of PABA, Competetively inhibit dihydropteroate synthetase in Folate synthesis. Sulfa drugs are active against selected enterobacteria in the urinary tract and nocardia. sulfasalazine is not absorbed when administered orally, therefore, is reserved for treatment of chronic inflammatory bowel disease (for example, Crohn's disease or ulcerative colitis). Adverse:Crystalluria, Hypersensitivity, Hemopoietic disturbances, Kernicterus Contraindicated with Methinamine
Reduction Inhibitors Trimethoprim Pyremethamine	Dihydrofolate reductase Inhibitor. Spectrum similar to that of sulfamethoxazole. However, trimethoprim is 20- to 50-fold more potent than the sulfonamide. Adverse: folic acid deficiency symptoms
Co-Trimoxazole	cotrimoxazole has greater activity than equivalent quantities of either drug used alone. broader spectrum, effective for UTIs & RTIs. Adverse: Dermatologic, GIT: Nausea, vomiting, as well as glossitis and stomatitis are not unusual, Hematologic
UTI Antiseptics Methinamine, Nitorfurantoin	UTIs in women of child-bearing age and in the elderly are one of the most common problems seen by primary care physicians. E. coli is the most common pathogen, causing about 80% of uncomplicated upper and lower UTIs. Staphylococcus saprophyticus is the second most common bacterial pathogen causing UTIs, with other common causes including Klebsiella pneumoniae and Proteus mirabilis Methinamine: Converted into Formaldehyde in low Ph urine. used in Lower UTIs. causes GIT disorders. Nitrofurantoin.:Less commonly used in UTIs b/c of its narrow antimicrobial spectrum & its toxicity. Sensitive bacteria reduce the drug to an active agent that inhibits various enzymes and damages DNA. Antibiotic activity is greater in acidic urine.
Anti-TB Drugs	
1st Line- Isoniazid, Rifamycins, Pyrazinamide, Etambutol	INH: Inhibits Synthesis of Mycolic acid by inhibiting enoyl acyl carrier protein reductase (InhA) & **β**-ketoacyl-ACP synthase (KasA). Static in Stationary phase, Cidal for rapidly dividing. INH achieve levels in breast milk high enough to cause a pyridoxine deficiency in the infant unless the mother is supplemented with the vitamin. Peripheral neuritis (Due to Pyridoxine Deficiency it causes), Hepatitis & idiosyncratic hepatotoxicity. Inhibits P450 System
	Rifampin, rifabutin, and rifapentine: Cidal for all. Blocks Transcription of RNA polymerase. rifampin can induce a number of cytochrome P450 enzymes. Rifabutin is the preferred for tuberculosis-with HIV patients. Rifapantine is long acting. Rifampin is derived from the soil mold.
	Pyrazinamide is Cidal. Causes Urate Retention & Gouty Attacks.
	Ethambutol is bacteriostatic. Adverse effect is optic neuritis. Causes Urate Retention & Gouty Attacks.
2nd Line--Streptomycin Capreomycin, Cycloserine Ethionamide, Amino Salycilic Acid, Macrolides Floroquinolones	Aminoglycoside
	peptide that inhibits protein synthesis
	Cycloserine is oral, tuberculostatic agent that antagonize the steps in bacterial cell wall synthesis involving D-alanine.
	Ethionamide is a structural analog of isoniazid,
	Moxifloxacin & Levofloxacin, have an important place in the treatment of multidrug-resistant tuberculosis.
	Azithromycin & clarithromycin, are part of regimen that includes ethambutol & rifabutin for infections by M. avium-intracellulare complex.
Anti-Leprosy	Dapsone, Clofazimine, Rifampicin
Anti-Fungal (Systemic + Cutenious) Amphotericin-B, Flucytosine Keto, Flu, Itraconaxzole Caspo, Mica, Anadula fungin	Amphotericin-B : Naturally occurring, polyene macrolide antibiotic by Streptomyces nodosus. Drug of choice for all life-threatening, systemic mycoses. Bind to ergosterol in Cell membranes of fungal cells, & Creates Pores. fungicidal or fungistatic, depending on the organism and the concentration of the drug. Fevers & Chills, Nephrotoxicity, Anemias, Thrombophlebitis (Adding heparin to infusion alleviate this problem)
	Flucytosine(5-FC) is synthetic pyrimidine antimetabolite fungistatic often used in combination with amphotericin B. Also can Cross to CSF. auses reversible neutropenia, thrombo-cytopenia, and dose-related bone marrow depression.
	Azoles are predominantly fungistatic, inhibit C-14 α-demethylase. Itraconazole has largely replaced ketoconazole for treatment of mycoses b/c of its broader spectrum, greater potency, & fewer adverse effects. ketoconazole, as a second-line drug, is a less expensive alternative for mucocutaneous candidiasis. Fluconazole is clinically important b/c of its lack of the endocrine side effects of ketoconazole & its excellent penetrability into the CSF of both normal and inflamed meninges.
	Echinocandins class interfere with the synthesis of the fungal cell wall. They are not oral.
Anti-Fungal (Cutenious) Terbinafine	Terbinafine is the drug of choice for dermatophytoses & onychomycoses (fungal infections of nails). ↓Ergosterol production by inhibiting fungal squalene epoxidase. Fungicidal. Shorter Treatment Period (3 Months). GIT (diarrhea, dyspepsia, and nausea), headache, and rash.
Anti-Fungal (Cutenious) Mi, Butacona, Clotrimazole	Miconazole, Clotrimazole, Butoconazole, & Terconazole are topically active drugs that are only rarely administered parenterally because of their severe toxicity.
Anti-Fungal (Cutenious) Griseofulvin	Griseofulvin requires treatment of 6 to 12 months in duration. Causes disruption of the mitotic spindle and inhibition of fungal mitosis. **Griseofulvin potentiates the intoxicating effects of alcohol.**
Anti-Fungal (Cutenious)-Nystatin	Nystatin is a polyene antibiotic, and its structure, chemistry, mechanism of action, and resistance resemble those of amphotericin B.
Anti-Amibiasis (Mixed) Metronidazole, Tinidazole	The nitro group of metronidazole is able to serve as an electron acceptor, forming reduced cytotoxic compounds that bind to proteins and DNA, resulting in cell death. Metronidazole is the drug of choice for pseudomembranous colitis. Causes unpleasent Metalic Taste.
Anti-Amibiasis (Luminal) Iodoquinol, Paramomycin, Diloxanide Furoate	After treatment of invasive intestinal or extraintestinal amebic disease is complete, a luminal agent, such as iodoquinol, diloxanide furoate, or paromomycin, should be administered for treatment of asymptomatic colonization state. Iodoquinol is halogenated 8-hydroxy quinolone, Paromomycin is aminoglycoside antibiotic.
Anti-Amibiasis (Systemic) Chloroquine, Emetine, Dehydroemitine	Chloroquine is an Anti-Malarial drug. Emetine & dehydroemetine are alternative agents for the treatment of amebiasis. They inhibit protein synthesis by blocking chain elongation.
Anit- Malarial	Tissue Schizonticide: Primaquine--------Blood schizonticide and sporontocide: Pyrimethamine Blood Schizonticide: Chloroquie, Quinine, Quinidine, Mefloquine, Pyremethamine, Artimisinin, Artemether/Lumefantrine

Trypanosomiasis	Benznidazole, Nifrutimox, Suramine, Pentamidine, Melarsoprol Pentamidine is the drug of choice for pneumonia caused by P. jiroveci who failed to respond to trimethoprim-sulfamethoxazole. Nifurtimox has found use only in the treatment of acute T. cruzi infections (Chagas' disease). Melarsoprol a mersalyl oxide derivative & trivalent arsenical. Used in trypanosomal infection usually in the late stage with CNS involvement and it is lethal to these parasites. CNS toxicities are the most serious side effects. Suramin is used in early ttt & especially, prophylaxis of African trypanosomiasis.
Anti- Leshmeniasis	Na-Stibo gluconate
Anti-Toxoplasmosis	Pyremethamine
Anti-Giardiasis	Metronidazole, Tinidazole, Nitazoxanide
Athelmintics Nematodes	Roundworms DiethyleCarbamazine, Ivermectin, Mebendazole, Thiabindazole, Pyrantal Pamoate
Athelmintics Trematodes	Flatworms or Flukes Praziquental
Athelmintics Cestodes	Tapeworms Albendazole, Niclosamide
CNS Drugs (Anti Parkinson) Destruction of dopaminergic neurons in the substantia nigra	
DOPA Analogs Levodopa/Carbidopa	Levodopa a precursor of dopamine restores dopaminergic neurotransmission by ↑synthesis of dopamine in the surviving neurons of the substantia nigra. The effects lasts only 3-5 years until the neuron count ↓to where they cant store enough dopamine. Carbidopa, a dopa decarboxylase inhibitor that does not cross the blood-brain barrier, ↓metabolism of levodopa in GIT & Periphery therby reducing the required dose of Levodopa by 4-5 times. Vit B6 ↑peripheral breakdown of levodopa & ↓ its effectiveness Anorexia, nausea, vomiting, Hypotension, Visual & auditory hallucinations, Abnormal involuntary movements (dyskinesias)
MAO-b Inhibitors Seligiline, Rasaligiline	Selegiline, also called deprenyl, selectively inhibits MAO Type B at low to moderate doses but above recommended doses, it loses selectivity. Selegiline is metabolized to methamphetamine and amphetamine. Rasagiline, irreversible & selective inhibitor MAO-B, has 5 times the potency of selegiline. it is not metabolized to amphetamine-like substance.
COMT Inhibitors Antacapone, Tolcapone	Inhibition of COMT leads to ↓plasma conc. of 3-O-methyldopa,↑central uptake of levodopa, & greater concentrations of brain dopamine. Diarrhea, postural hypotension, nausea, anorexia, dyskinesias, hallucinations, and sleep disorders. fulminating hepatic necrosis is associated with tolcapone use
DOPA Receptor Agonists Bromocriptine	Derivative of the vasoconstrictive alkaloid, ergotamine, is a dopamine-receptor agonist. Adverse:Same as levodopa, except Hallucinations, confusion, delirium, nausea, & orthostatic hypotension are more common, dyskinesia is less.
DOPA Receptor Agonists Apomorphine, Ropinirol, Pramipixole, Rotigoptine,	Nonergot dopamine agonists that have been approved for the treatment of Parkinson's disease. Apomorphine is used for acute management of the hypomobility phenomenon. Adverse: Nausea, hallucinations, insomnia, dizziness, constipation, and orthostatic hypotension
Amantadine	It was accidentally discovered that Amantadine, which is effective in the treatment of influenza, has an antiparkinsonism action.
Anti Muscarinics	They are much less efficacious than levodopa and play only an adjuvant role. Benztropine, Trihexyphenidyl, Procyclidine, and Biperiden.
CNS Drugs Alzhymer's Desease	
Antichloinestrases Tacrine, Donezepil, Rivastigmine, Galantamine	It is postulated that inhibition of acetylcholinesterase (AChE) within the CNS will improve cholinergic transmission, at least at those neurons that are still functioning.
NMDA-receptor antagonist	Memantine inhibits glutamate NMDA receptors
Anxyiolytics and Hypnotics	
Benzodiazepines Diazepam, Alprazolam, bromazepam, Temazepam, Midazolam	Act on GABA-a Receptors. Anxiolytic & Muscle Rexalatino (α2), Sedation Hypnosis, Anterograde Amnesia, AntiConvulsat (α1). Adverse: Drowsiness and confusion Duration:(Long)Diazepam, Chlordiazepoxide, chlorazepate, flurazepam, quazepam-(Intermediate)Lorazepam, temazepam, estalopam, Alprazolam-(Short) Oxazepam, triazolam
Barbiturates Thiopental, Phenobarbital, Pentobarbital, Secobarbital, Amobarbital	Act on GABA-a Receptors. Thiopental (Ultra short acting), Pento, Seco, Amo (Short), Pheno (Long). At↓ doses, they produce sedation (calming effect, reducing excitement). At higher doses, they cause hypnosis, followed by anesthesia (loss of feeling or sensation), and finally, coma and death. Barbiturates suppress the hypoxic and chemoreceptor response to CO2, and overdosage is followed by respiratory depression and death. Barbiturates induce P450 microsomal enzymes in the liver. Usage in Anethesia, Anxiety and Convulsions. Adverse:drowsiness, impaired concentration, and mental and physical sluggishnes
Other Buspiron	Buspirone acts on 5-HT2A serotonin receptors and DA2 dopamine receptors. Slow Onset of Action
Other Hydroxyzine	An antihistamine with antiemetic activity. Low tendency for habituation & useful for patients with history of drug abuse. Often used for sedation prior to dental procedures or surgery. Drowsiness is a possible adverse effect
Other AntiHistamines Diphenhydramine, Doxylamine	Nonprescription antihistamines with sedating properties, such as diphenhydramine and doxylamine, are effective in treating mild types of insomnia.
Other Zolpidem, Zaleplon, Esxzopiclon	Non benzodiazepine in structure, but act on a subset of the benzodiazepine receptor family, BZ1.
Other Ramelteon	Ramelteon is a selective agonist at the MT1 and MT2 subtypes of melatonin receptors.
Other Chloral Hydrate	Trichlorinated derivative of acetaldehyde that is converted to the active metabolite, trichloroethanol, in the body. Effective sedative and hypnotic that induces sleep in 30 minutes & duration of sleep is about 6 hours. Irritating to the GIT & causes epigastric distress. produces an unusual, unpleasant taste sensation. It synergizes with ethanol.
CNS Stimulants	
MethyleXanthines Theohyline, Theobromine, Cafeine	Act by translocation of extracellular Ca, ↑ in cAMP & cGMP by inhibition of phosphodiesterase, adenosine receptors.1-2 cups coffee (100-200 mg) ↓ fatigue & ↑ mental alertness by stimulating the cortex & other areas of the brain. 12 to 15 cups (1.5 g) produces anxiety & tremors. The spinal cord is stimulated only by very high doses (2-5 g). ↑ dose has positive inotropic & chronotropic effects on the heart. Mild Diuresis & ↑ in GIT HCl Secretions.
Nicotine	It improves attention, learning, problem solving, and reaction time.
Cocaine	powerful stimulation of the cortex and brainstem. ↑ awareess & causes powerful euphoria
Amphetamines	CNS Stimulants that are used in ADHD &Narcolepsy
Vernicline	partial agonist at a4b2 neuronal nicotinic acetylcholine receptors in the CNS. Used in smoking cessestion
Methylephenidate	Similar to Amphetamine and used in ADHD
Narcolepsy Druges Modafnil, Armodafnil	Modafinil & Armodafinil, are new drugs for narcolepsy with few advese effects as compared to amphetamine
Aneasthetics	



Halogenated Carons Halothane, Isoflurane, Enflurane, Desflurane	Enflurane rapid Onset & contraindicated in patients with kidney failure. Isoflurane causes concentration-dependent hypotension due to peripheral vasodilation. Adverse effects: Bradycardia, Arrhythmias, Malignant hyperthermia.
Nitrous Oxide	Nitrous oxide is a potent analgesic but a weak general anesthetic. Frequently employed at concentrations of 30% in combination with oxygen for analgesia, particularly in dental surgery.
IV Barbiturates, Benzodiazepines, Etomidate, Ketamine, Propofol, Opioids	Thiopental, Midazolam etc. Combination of morphine and nitrous oxide provides good anesthesia for cardiac surgery. Etomidate is used to induce anesthesia. It is a hypnotic agent but lacks analgesic activity. Ketamine, a short-acting, induces a dissociated state that patient is unconscious but appears to be awake and does not feel pain. Propofol is an IV sedative/hypnotic used in the induction or maintenance of anesthesia.
Local anesthetics are generally applied locally and block nerve conduction of sensory impulses from the periphery to the CNS. Local anesthetics abolish sensation (and, in higher concentrations, motor activity) in a limited area of the body without producing unconsciousness (for example, during spinal anesthesia). The small, unmyelinated nerve fibers that conduct impulses for pain, temperature, and autonomic activity are most sensitive to actions of local anesthetics. The most widely used of these compounds are bupivacaine [byoo-PIV-ah-kane], lidocaine [LYE-doe-kane], mepivacaine [me-PIV-a-kane], procaine [PRO-kane], ropivacaine [roe-PIV-a-kane], and tetracaine [TET-ra-kane]. Of these, lidocaine is the most frequently employed. At physiologic pH, these compounds are charged; it is this ionized form that interacts with the protein receptor of the Na+ channel to inhibit its function and, thereby, achieve local anesthesia.	
Anti Depressants	
SSRI Flouxeine, Fluvoxamine, Citalopram, Escitalopram, Paroxetine, Sertraline	headache, sweating, anxiety and agitation, gastrointestinal effects (nausea, vomiting, diarrhea), weakness and fatigue, sexual dysfunction, changes in weight, sleep disturbances (insomnia and somnolence),
SNRI--Duloxetine, Venlafexine	Alternatve to SSRis, & in depression with chronic painful symptoms against which SSRIs are also relatively ineffective. Duloxetine is contraindicated in hepatic and renel disorders
Atypical Mertazapine, Bupropion, Nefazodon, Trazodon	Mertazapine does not cause Sexual Dysfunction. It blocks presynaptic α2 & 5-HT2 receptors. Nefazodone and trazodone are weak inhibitors of serotonin reuptake.
TCAs impramine, Trimipramine, Clomipramine, Desipramine, Doxepine, Amoxapine, Amytriptyline,	TCAs block norepinephrine and serotonin reuptake into the neuron. TCAs also block serotonergic,α-adrenergic, histaminic, and muscarinic receptors. Imipramine has been used to control bed-wetting in children (older than 6 years). Amitriptyline, have been used to treat migraine headache and chronic neuropathic pain syndromes. Adverse:blurred vision, xerostomia, urinary retention, constipation, and aggravation of narrow-angle glaucoma, life-threatening arrhythmias on overdoses. Also cause orthostatic hypotension, dizziness, and reflex tachycardia. Sexual Dysfunction.

MAO Inhibitors Selegiline, Phenelzine, Tranylcypramine	Selegiline, which is the first antidepressant available in a transdermal delivery system. MAO inhibitors are indicated for depressed patients who are unresponsive or allergic to TCAs or who experience strong anxiety.yramine, which is contained in certain foods, such as aged cheeses and meats, chicken liver, pickled or smoked fish such as anchovies or herring, and red wines, is normally inactivated by MAO in the gut. Individuals receiving an MAO inhibitor are unable to degrade tyramine obtained from the diet. Tyramine causes the release of large amounts of stored catecholamines from nerve terminals, resulting in occipital headache, stiff neck, tachycardia, nausea, hypertension, cardiac arrhythmias, seizures, and possibly, stroke.



	Drug	Therapeutic notes
TYPICAL NEUROLEPTICS	*Fluphenazine*	Available as slow-release depot form
	Thioridazine	Strong muscarinic antagonist
	Haloperidol	Little adrenergic or muscarinic activity; available as slow-release depot form; High potential for extrapyramidal effects
ATYPICAL NEUROLEPTICS	*Aripiprazole*	Low potential for extrapyramidal effects; Used in treatment of bipolar depression
	Clozapine	Few extrapyramidal effects; causes a potentially fatal agranulcytosis in 1–2% of patients; weight gain, seizures, nocturnal salivation, myocarditis, anticholinergic symptoms; hypotension; sedation
	Olanzapine	Low potential for extrapyramidal effects; weight gain; Used in treatment of bipolar depression
	Quetiapine	Low potential for extrapyramidal effects; Used in treatment of bipolar depression
	Risperidone	Low potential for extrapyramidal effects; minimal sedation; Used in treatment of autism, bipolar depression
	Ziprasidone	Low potential for extrapyramidal effects; contraindicated in patients with history of cardiac arrhythmias; weight gain minimal; Used in treatment of bipolar depression

Tremors

Parkinsonian effects commonly seen with typical neuroleptics

Weight g ain

Weight gain commonly occurs with atypical neuroleptics

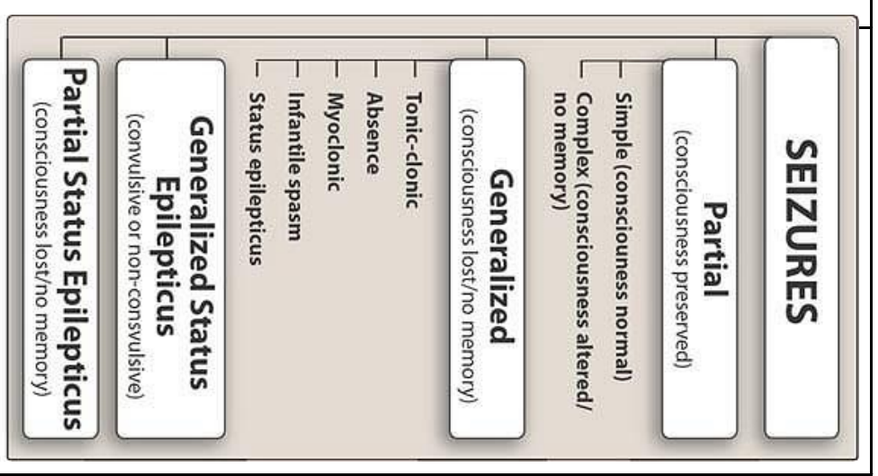
MoA:Dopamine &/or Serotonin receptor blocking activity in the brain.
Antipsychotic actions: All of the neuroleptic drugs can reduce the hallucinations and delusions associated with schizophrenia.
Extrapyramidal effects: Dystonias (sustained contraction of muscles leading to twisting distorted postures), parkinson-like symptoms, akathisia (motor restlessness), and tardive dyskinesia (involuntary movements of the tongue, lips, neck, trunk, and limbs) occur with chronic treatment.
Antiemetic effects: With the exceptions of aripiprazole and thioridazine [thye-oh-RID-a-zeen], most of the neuroleptic drugs have antiemetic effects that are mediated by blocking D2-dopaminergic receptors of the chemoreceptor trigger zone of the medulla.
Antimuscarinic effects: Some of the neuroleptics, particularly thioridazine, chlorpromazine, clozapine, and olanzapine [oh-LAN-za-peen], produce anticholinergic effects, including blurred vision, dry mouth (exception: clozapine increase salivation), confusion, and inhibition of gastrointestinal and urinary tract smooth muscle, leading to constipation and urinary retention. This anticholinergic property may actually assist in reducing the risk of EPS with these agents.

Opioids

Opioid receptors
Brainstem: Opioid receptors influence respiration, cough, nausea and vomiting, blood pressure, pupillary diameter, and control of stomach secretions.
Medial thalamus: This area mediates deep pain that is poorly localized and emotionally influenced.
Spinal cord: Receptors in the substantia gelatinosa are involved with the receipt and integration of incoming sensory information, leading to the attenuation of painful afferent stimuli.
Hypothalamus: Receptors here affect neuroendocrine secretion.
Limbic system: The greatest concentration of opiate receptors in the limbic system is located in the amygdala. They probably do not exert analgesic action, but they may influence emotional behavior.
Periphery: Nerve fibers & their terminals. As in the CNS, they inhibit Ca2+-dependent release of excitatory, proinflammatory substances (for example, substance P) from these nerve endings.
Immune cells: Opioid-binding sites have also been found on immune cells. The role of these receptors in nociception (response or sensitivity to painful stimuli) has not been determined.

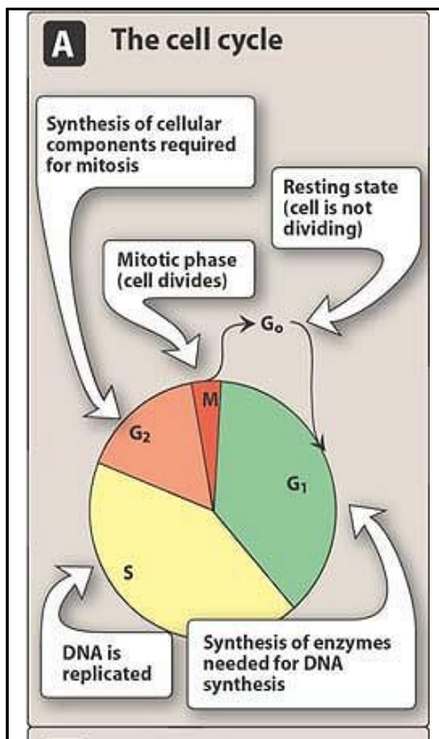
Strong Agonists Morphine, Codiene	Acts on κ receptors in Lamina I and II of the dorsal horn of the spinal cord, and it decreases the release of substance P, which modulates pain perception in the spinal cord. Analgesia, Euphoria, respiratory depression, Depression of cough reflex, Miosis, Emesis, relieves diarrhea and dysentery by decreasing the motility and increasing the tone of the intestinal circular smooth muscle. At large doses, hypotension and bradycardia, Histamine release, ↓ release of GnRH & CRH. Prolong the second stage of labor. Uses: Analgesia, Treatment of diarrhea, Relief of cough, Treatment of acute pulmonary edema. Adverse: Severe respiratory depression, Constipation, Nausa & Vomiting.
Mepridine	Binds to μ & κ receptors. Pupilary dilation. anxiety, tremors, muscle twitches, and rarely, convulsions
Methadone	Synthetics. Similar action of morphine, longer acting, mediated by the μ receptors. used as an analgesic & controlled withdrawal from heroin and morphine.
Fantanyl, Sufentanil, alfentanil, remifentanil	Fentanyl, chemically related to meperidine, has 100-fold analgesic potency of morphine & used in anesthesia. Causes miosis. Sufentanil is even more potent than fentanyl, whereas the other two are less potent but much shorter-acting.
Heroin	Heroin does not occur naturally & produced by diacetylation of morphine, leading to 3-fold ↑ in potency.
Oxycodone	Oxycodone a semisynthetic derivative of morphine.
Moderate Agonists Codiene	Analgesic actions of codeine are due to its conversion to morphine, whereas the drug's antitussive effects are due to codeine itself.
Propoxyphene	Propoxyphene is a derivative of methadone. The dextro isomer is used as an analgesic to relieve mild to moderate pain.
Mixed & Partial Agonists Pentazocine Buprenorphine Nalbuphine and butorphanol	Pentazocine acts as an agonist on κ receptors and is a weak antagonist at μ and δ receptors. Analgesia, Resp. Depression, ↓GI motility. Bupre is used in opiate detoxification, b/c it has a less severe & shorter withdrawal symptoms. causes little sedation, resp. depression, and hypotension, ↑ at high doses.
Other Tramadol	Tramadol is a centrally acting analgesic that binds to the μ-opioid receptor.
Antagonists Naloxone, Naltrexone, Nalmefene	opioid antagonists bind with high affinity to opioid receptors but fail to activate the receptor-mediated response. They r used to reverse the coma and respiratory depression of opioid overdose.

DRUG	MECHANISM OF ACTION	ADVERSE EFFECTS AND COMMENTS
Carbamazepine	Blocks Na^+ channels	Hyponatremia, drowsiness, fatigue, dizziness, and blurred vision. Drug use has as been associated with Stevens-Johnson Syndrome. Blood dyscrasias: neutropenia, leukopenia, thrombocytopenia, pancytopenia, and anemias.
Divalproex	Multiple mechanisms of action	Weight gain, easy bruising, nausea, tremor, hair loss, weight gain, GI upset, liver damage, alopecia, and sedation. Hepatic failure, pancreatitis, and teratogenic effects such have been observed. Broad spectrum of antiseizure activity.
Ethosuximide	Blocks Ca^{2+} channels	Drowsiness, hyperactivity, nausea, sedation, GI upset, weight gain, lethargy, SLE, and rash. Blood dyscrasias can occur; periodic CBCs should be done. Abrupt discontinuance of drug may causes seizures.
Felbamate	Multiple mechanisms of action	Insomnia, dizziness, headache, ataxia, weight gain, and irritability. Aplastic anemia; hepatic failure. Broad spectrum of antiseizure activity. Requires patient to sign informed consent at dispensing.
Gabapentin	Unknown	Mild drowsiness, dizziness, ataxia, weight gain, and diarrhea. Few drug interactions. One-hundred percent renal elimination.
Lamotrigine	Multiple mechanisms of action	Nausea, drowsiness, dizziness, headache, and diplopia. Rash (Stevens-Johnson syndrome—potentially life-threatening). Broad spectrum of antiseizure activity.
Levetiracetam	Multiple mechanisms of action	Sedation, dizziness, headache, anorexia, fatigue, infections, and behavioral symptoms. Few drug interactions. Broad spectrum of antiseizure activity.
Oxcarbazepine	Blocks Na^+ channels	Nausea, rash, hyponatremia, headache, sedation, diplopia.
Fosphenytoin	Blocks Na^+ channels	Gingival hyperplasia, confusion, slurred speech, double vision, ataxia, sedation, dizziness, and hirsutism. Stevens-Johnson syndrome—potentially life-threatening). Not recommended for chronic use. Primary treatment for status epilepticus.
Pregabalin	Multiple mechanisms of action	Weight gain, somnolence, dizziness, headache, weight gain, diplopia, and ataxia. One hundred percent renal elimination.
Primidone	GABA receptor	Sedation, lethargy, behavioral changes, ataxia, hyperactivity, and nausea. Not recommended for chronic use.
Tiagabine	GABA receptor	Sedation, weight gain, fatigue, headache, tremor, dizziness, and anorexia. Multiple drug interactions.
Topiramate	Multiple mechanisms of action	Paresthesia, weight loss, nervousness, depression, anorexia, anxiety, tremor, cognitive complaints, headache, and oligohidrosis. Few drug interactions. Broad spectrum of antiseizure activity.
Zonisamide	Multiple mechanisms of action	Nausea, anorexia, ataxia, confusion, difficulty concentrating, sedation, paresthesia and oligohidrosis. Broad spectrum of antiseizure activity.



DRUGS	MAJOR TOXICITIES AND CONCERNS
Atazanavir	Nausea, abdominal discomfort, headache, skin rash
Darunavir	Nausea, abdominal discomfort, headache, skin rash
Fosamprenavir	Nausea, diarrhea, vomiting, oral and perioral paresthesia, and rash
Indinavir	Benign hyperbilirubinemia, nephrolithiasis; take 1 hour before or 2 hours after food; may take with skim milk or a low-fat meal; drink >1.5 L of liquid daily
Lopinavir	Gastrointestinal, hyper-lipidemia, insulin resistance
Nelfinavir	Diarrhea, nausea, flatulence, rash
Ritonavir	Diarrhea, nausea, taste perversion, vomiting, anemia, increased hepatic enzymes, increased triglycerides. Requires refrigeration; take with meals; chocolate milk improves the taste
Saquinavir	Diarrhea, nausea, abdominal discomfort, elevated trans-aminase levels. Take with high-fat meal or within 2 hours of a full meal
Tipranavir	Nausea, vomiting,diarrhea, rash, severe hepatotoxicity, intracranial hemorrhage

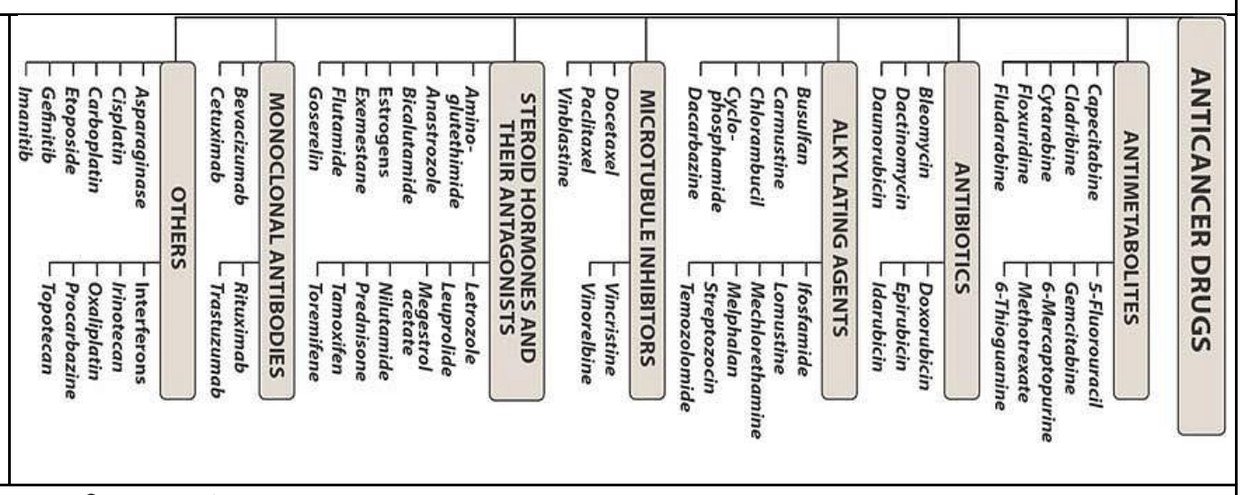
Benzodiazepines Diazepam, Lorazepam	Benzodiazepines bind to GABA inhibitory receptors to reduce firing rate. Diazepam, and lorazepam are most often used as an adjunctive therapy for myoclonic as well as for partial and generalized tonic-clonic seizures. Lorazepam (see p. 108) has a shorter pharmacokinetic half-life but stays in the brain longer than diazepam.
Carbamazepine	Carbamazepine ↓ propagation of abnormal impulses in the brain by blocking Na channels, thereby inhibiting the generation of repetitive action potentials in the epileptic focus and preventing their spread.
Divalproex sodium	Divalproex sodium is a combination of sodium valproate and valproic acid. MOA include Na channel & GABA transaminase blockade, & action at the T-type calcium channels. broad spectrum of activity against seizures. Hepatotoxicity.
Ethosuximide	↓propagation of abnormal electrical activity in the brain, by inhibiting T-type Cachannels. It is effective in treating only primary generalized absence seizures.
Felbamate	Has a broad spectrum of anticonvulsant action. MOA include 1) blocking Na channels, 2) competing with the glycine-coagonist binding site on the N-methyl-D-aspartate (NMDA) glutamate receptor, 3) blocking ca channels, 5) potentiation of GABA actions. Reserved for use in refractory epilepsies (particularly Lennox-Gastaut syndrome) b/c of the risk of aplastic anemia (about 1:4000) and hepatic failure.
Gabapentin	analog of GABA. However, moa is not known. adjunct therapy for partial seizures and for treatment of postherpetic neuralgia.
Lamotrigine, Levetiracetam, Oxcarbazepine, Phenobarbital, Phenytoin and fosphenytoin, Pregabalin, Primidone, Tiagabine, Topiramate, Zonisamide	
Epilepsy in Pregnancy	All women should be on high doses of folic acid prior to conception. Divalproex and barbiturates should be avoided.
Anti-Viral	
Respiratory Viral Inf	Oseltemivir, Zanamivir- Neuraminase Inhibitors-Influenza A & B-Osaltamivir is oral & causes GI Problems & nausea. Zanamivir is inhalation only & causes Bronchial irritation. Amantadine, Rimantadine-Block Vial mebrane Matrix Portien M2 resulting in viral fusion inhibition. CNS Side Effects insomnia, dizziness, ataxia, hallucinations & seizures. no go for Pregenancy. Ribavirin-Guanosine analog against broad spectrum of RNA & DNA viruses. Used in infants & children for severe RSV. Dose-dependent transient anemia & ↑bilirubin.
Hepatitis	Interferon-Glycoproteins that interfere with the ability of viruses to infect cells. α is used in Hepatitis A & B, Lukimias, Kapsosi Sndrome & Pappiloma Virus. Rever, chills, myalgia, arthralgia, & gastrointestinal disturbances. β in multiple sclerosis. Lamivudine, Telbivudine- Lami is used in Hepatitis with HIV. Telbi is not. Dose adj required in renel insufficiency. Adefovir, Entecavir-Dose adj required in renel insufficiency. Adefe in Hep B with HIV



Antiviral drug	Mechanism of action	Viruses or diseases affected
Acyclovir	Metabolized to acyclovir triphosphate, which inhibits viral DNA polymerase	Herpes simplex, varicella-zoster, cytomegalovirus
Amantadine	Blockage of the M2 protein ion channel and its ability to modulate intracellular pH	Influenza A
Cidofovir	Inhibition of viral DNA polymerase	Cytomegalovirus; indicated only for virus-induced retinitis
Famciclovir	Same as penciclovir	Herpes simplex, varicella-zoster
Foscarnet	Inhibition of viral DNA polymerase and reverse transcriptase at the pyrophosphate-binding site	Cytomegalovirus, acyclovir-resistant herpes simplex, acyclovir-resistant varicella-zoster
Ganciclovir	Inhibits viral DNA polmerase	Cytomegalovirus
Interferon-α	Induction of cellular enzymes that interfere with viral protein synthesis	Hepatitis B and C, human herpesvirus 8, papilloma virus, Kaposi's sarcoma, hairy-cell leukemia, chronic myelogenous leukemia
Lamivudine	Inhibition of viral DNA polymerase and reverse transcriptase	Hepatitis B (chronic cases), human immunodeficiency virus type 1
Oseltamivir	Inhibition of viral neuramidase	Influenza A
Penciclovir	Metabolized to penciclovir triphosphate, which inhibits viral DNA polymerase	Herpes simplex
Ribavirin	Interference with viral messenger RNA	Lassa fever, hantavirus (hemorrhagic fever renal syndrome), hepatitis C (in chronic cases in combination with *interferon-α* RSV in children and infants
Rimantadine	Blockage of the M2 protein ion channel and its ability to modulate intracellular pH	Influenza A
Valacyclovir	Same as acyclovir	Herpes simplex, varicella-zoster, cytomegalovirus
Vidarabine	inhibits viral DNA synthesis	HSV-1, HSV-2, and VZV; its use is limited to treatment of immunocompromised patients with HSV keratitis
Zanamivir	Inhibition of viral neuramidase	Influenza A

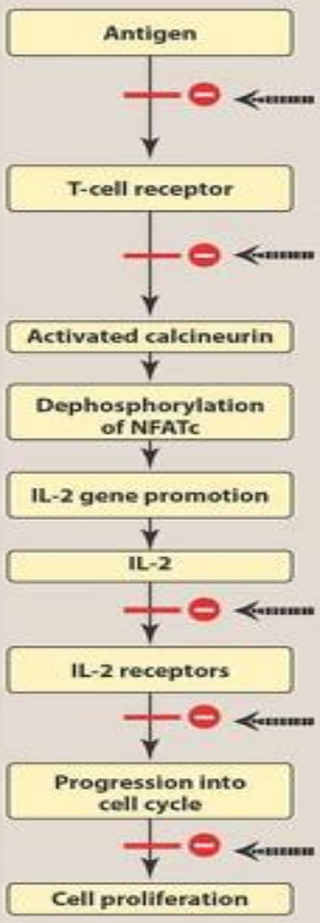
Herpes Simples, CMV, VZ	Acyclovir, gancyclovir, pencyclovir, famcyclovir, Cidofovir, famovirsin, foscarnet, vidarabine, trifluridine
HIV NRTI	Zidovudine, stavudine, lamivudine, zalcitabine, emtricitabine, Tenofovir, Abacavir: Nucleoside and nucleotide reverse transcriptase inhibitors (NRTIs) once enter cells, are phosphorylated to triphosphate analog, which is incorporated into the viral DNA by virus reverse transcriptase causing DNA chain elongation termination. NRTIs are primarily renally excreted, and all require dosage adjustment in renal insufficiency except abacavir, which is metabolized in liver. Adverse: Peripheral neuropathy, pancreatitis, lipoatrophy. Abacavir has Hypersensitivity reactions.
NNRTI	Nevirapine, Delavirdine, Efavirinz- Rash is the most common adverse effect, also fevers and chills. Etravirine is 2nd Gen-Rash.
Protease Inhibitors	Rotinavir, Saquinavir, Indinavir, Fosamprinavir-Parathesias, nausea, vomiting, & diarrhea. Disturbances in glucose & lipid metabolism, including diabetes, hypertriglyceridemia, & hypercholesterolemia. Chronic administration results in fat redistribution, including loss of fat from the extremities and its accumulation in the abdomen and the base of the neck (buffalo hump).
Entry Inhibitor	Efuvirtide, Maraviroc- Enfuvirtide is a fusion inhibitor, given SC. Pain, erythema, induration, and nodules. Maraviro is oral & well tolerated.
Intregrase Inhibitor	Raltegravir
Anti-Cancer	
Anti-Metabolites Methotrexate	Inhibits Follic acid to Tetrahydrofollat by dihydrofollate reductase leading to↓ production of compounds that depend on these coenzymes for their biosynthesis as nucleotides adenine, guanine, thymidine and the amino acids. used in combination with other drugs, in acute lymphocytic leukemia, choriocarcinoma, Burkitt's lymphoma in children, breast cancer, & head and neck carcinomas. MTX is used with Misoprotol to cause abortion. Adverse: Nausea, vomiting, & diarrhea, stomatitis, myelosuppression, erythema, rash, urticaria, & alopecia. Some effects can be prevented or reversed by administering leucovorin. Renal damage (due to high-dose & Alkalinization of the urine and hydration help to prevent this problem), Hepatotoxicity, Pulmonary toxicity in childern, Neurologic toxicities: These are associated with intrathecal administration.
Anti-Metabolites 6-Mercaptopurine, 6-Thioguanine	They r converted to the nucleotide analog, resulting in inhibition o fpurine syntesis & Incorporation into nucleic acids resulting in non functional DNA 6-MP is used in maintenance of remission in acute lymphoblastic leukemia. Bone marrow depression is the principal toxicity, anorexia, nausea, vomiting, and diarrhea. 6-TG is used in acute nonlymphocytic leukemia in combination with daunorubicin and cytarabine. Bone marrow depression is the dose-related.
Ant-Metabolites Fludarabine, Cladribine	Fludarabine is useful in chronic lymphocytic leukemia & may replace chlorambucil, the present drug of choice. Nausea, vomiting, & diarrhea, myelosuppression, Fever, edema, and severe neurologic toxicity. Cladribine is effective against hairy-cell leukemia, chronic lymphocytic leukemia, and non-Hodgkin's lymphoma. Bone Marrow Supression, Fever, peripheral Neuropathy.

Anti-Metabolites 5-flurouracil, Capcitabine, Floxuridine	5-FU a pyrimidine analog, has a fluorine atom in place of a hydrogen atom at position 5 of the uracil ring. Inhbits the synthesis of thynmidine resulting in DNA synthesis inhibition. 5-FU is used in slowly growing solid tumors (colorectal, breast, ovarian, pancreatic, & gastric carcinomas). Nausea, vomiting, diarrhea,alopecia, severe ulceration of oral & GI mucosa, bone marrow depression. Capecitabine is metabolised into 5-FU to be effective. Floxuridine is 5-FU analog.
Anti-Metabolites Cyatarabine, Gemcitabine	Cytarabine, pyrimidine antagonist. used in acute nonlymphocytic leukemia combination with 6-TG & daunorubicin. Nausea, vomiting, diarrhea, myelosuppression, Hepatic dysfunction. Gemcitabine deoxycytidine analog is used for locally advanced or metastatic adenocarcinoma of the pancreas. nausea, vomiting, alopecia, rash, flu-like syndrome, mylosupression
Anti-Biotics Dactinomycin	Intercalates into the minor groove of the double helix between guanine-cytosine base pairs of DNA, forming a stable dactinomycin-DNA complex thus unhibiting DNA synthesis. Bone marrow depression, nausea, vomiting, diarrhea, stomatitis, and alopecia.
Anti-Biotics (Anthracyclines) Doxo-, Dauno-, Ida-, Epi-rubicin	Intercalation in the DNA, Binding to cell membranes, Generation of super oxide and hydrogen per oxide ions. Doxorubicin is one of the most important & widely used anticancer drugs used in combination with other agents for sarcomas & variety of carcinomas (breast, lung), as well as for acute lymphocytic leukemia & lymphomas. Daunorubicin and idarubicin are used in the treatment of acute leukemias. Irreversible, dose-dependent cardiotoxicity, apparently a result of the generation of free radicals and lipid peroxidation
Anti-Biotics Bleomycin	a mixture of different copper-chelating glycopeptides that, like the anthracycline antibiotics, cause scission of DNA by an oxidative process. Used in testicular cancers with vinblastine or etoposide. Pulmonary toxicity is the most serious adverse effect, with fevers and chills.
Alkylating Agents Mechlorithamine	developed as a vesicant (nitrogen mustard) during WW I. Cause lymphocytopenia which led to its use in lymphatic cancers. it covalently attaches to two guanine on 1 or both strands of DNA (so called bifunctional agent) resulting in DNA strand breakage. Proliferating cells are more sensitive, especially in G1 & S phases. Nausea, Vomiting, Myelosupression, Immunosupression, extravasation (isotonic sodium thiosulfite should be used).
Alkylating Agents Cyclofosfamide, Ifosfamide	Both ar e also mustard agents, Cyclofosfamide is most widely used. Both are converted to active compounds in liver. alopecia, nausea, vomiting, and diarrhea) are bone marrow depression. Used in wide variety of neoplastic diseases, such as Burkitt's lymphoma and breast cancer.
Alkylating Agents, Nitrosoureas Carmustine,Lomustine	Because of their ability to penetrate into the CNS, the nitrosoureas are primarily employed in the treatment of brain tumors. Streptozocin is another nitrosourea that is specifically toxic to the β cells of the islets of Langerhans, hence its use in the treatment of insulinomas.Carmustine IV, lomustine oral.Streptozocin is also diabetogenic
Alkylating Agent- Dacarbaine	Dacarbazine an is used in the treatment of melanoma. administered by IV. Major adverse effects are nausea, vomiting, myelosuppression.
Alkylating Agents Temozolomide	A dacarbazine related triazene agent, used against treatment-resistant gliomas & anaplastic astrocytomas of brain. Taken orally for 5 days & repeated every 28 days. Its effects are nausea & vomiting, myelosuppression.
Alkylating Agent- Melphalan	A phenylalanine derivative of nitrogen mustard, used in multiple myeloma. is a bifunctional alkylating agent given orally.
Microtubule Inhibitors Vincristine VX, Vinblastine VBL, Vinorelbine VRB	Vinca alkaloids derived from periwinkle plant, Vinca rosea. They bind to microtubuler protein, tubulin and block the mitosis in phase M. VX is used in acute lymphoblastic leukemia, Wilms' tumor, Ewing's soft-tissue sarcoma, Hodgkin's & non-Hodgkin's lymphomas, & other rapidly proliferating neoplasms. VBL is used with bleomycin & cisplatin for metastatic testicular carcinoma, Hodgkin's & non-Hodgkin's lymphomas. VRB is used in advanced small cell lung cancer. Adverse: phlebitis or cellulitis, nausea, vomiting, diarrhea, & alopecia in all. Mylosupression in VBL, Constipation & Peripheral Neuropathies in VX, Granulocytopenia with VRB
Microtubule Inhibitors Paclitaxel, Docetaxel	they bind to tubulin and inhibit mitosis in pahse G2 & M. Advanced ovarian cancer & metastatic breast cancer. Neutropenia, Peripheral neuropathy with either of these drugs. A transient, asymptomatic bradycardia is sometimes observed with paclitaxel, & fluid retention is seen with docetaxel.

Steroid Hormones & Anta. Prednisone Tamoxifen (estrogen antag.) **Aromatase inhib. for Breast cancer (Aminoglutethimide, letrozole, Anastrozole, Exemestane)** Progestins (Megestrol) Leuprolide & goserelin Estrogens (estradiol or diethylstilbestrol) Flutamide, nilutamide, & bicalutamide	Monoclonal Antibodies Trastuzumab Rituximab Bevacizumab Cetuximab , gemtuzumab ozogamicin, wis a monoclonal antibody conjugated with a plant toxin, alemtuzumab, tositumomab	Platinum coordination complexes (Cisplatin, carboplatin) Irinotecan and topotecan Etoposide (VP-16) Imatinib Gefitinib Procarbazine L-Asparaginase Interferons	

Immuno Suppressants

Selective Inhibitors of Cytokine Production and Function Cyclosporine is a lipophillic cyclic polypeptide composed of 11 amino acids extracted from a soil fungus. Used in organ transplants. Nephrotoxicity Tacrolimus is a macrolide that is isolated from a soil fungus. approved for the prevention of rejection of liver and kidney transplants. Nephrotoxicity and neurotoxicity Sirolimus (SRL) is a recently approved macrolide obtained from fermentations of a soil mold, also for transplants. hyperlipidemia	
Immunosuppressive Antimetabolites Azathioprine first agent to be used in organ transplantation. bone marrow suppression. mycophenolate mofetil	Antibodies---Antithymocyte globulins, Muromonab-CD3 (OKT3), IL-2-receptor antagonists--Basiliximab, Daclizumab, Alemtuzumab Corticosteroids--- prednisone, methylprednisolone,



DRUG	ACTION	ADVERSE EFFECTS
Alemtuzumab	Depletion of T lymphocytes	Cytokine release syndrome; neutropenic, pancytopenia
Antithymocyte globulins	Destruction of T lymphocytes	Profound immunosuppression
Muromonab-CD3	Destruction of T lymphocytes	Cytokine release syndrome
Cyclosporine	Blocks calcineurin and inhibits IL-2 synthesis	Nephrotoxicity, neurotoxicity, hepatotoxicity
Tacrolimus (FK506)	Blocks calcineurin and inhibits IL-2 synthesis	Nephrotoxicity, neurotoxicity, diabetes
Basiliximab	Blocks the IL-2 receptor	Gastrointestinal disorders
Daclizumab	Blocks the IL-2 receptor	Gastrointestinal disorders
Sirolimus	Blocks cytokine-stimulated cell proliferation	Hyperlipidemia, thrombocytopenia, leukopenia, headache, nausea
Azathioprine	Inhibits purine synthesis	Bone marrow suppression, hepatotoxicity, thrombocytopenia, anemia, neoplasia
Mycophenolate mofetil	Inhibits purine synthesis	GI upset, nausea, diarrhea, leukopenia, tumors, increases susceptibility to infection

	MIGRAINE	CLUSTER	TENSION TYPE
Family history	Yes	No	Yes
Sex	Females more often than males	Males more often than females	Females more often than males
Onset	Variable	During sleep	Under stress
Location	Usually unilateral	Behind or around one eye	Bilateral in band around head
Character and severity	Pulsating, throbbing	Excruciating, sharp, steady	Dull, persistent, tightening
Duration	2–72 hours per episode	15–90 minutes per episode	30 minutes to 7 days per episode
Associated symptoms	Visual auras, sensitivity to light and sound, pale facial appearance, nausea and vomiting	Unilateral or bilateral sweating, facial flushing, nasal congestion, lacrimation, pupillary changes	Mild intolerance to light and noise, anorexia

POISON OR SYNDROME	ANTIDOTE(S)
Acetaminophen	*N-Acetylcysteine*
Anticholinergic agents	*Physostigmine*
Benzodiazepine	*Flumazenil*
Carbon monoxide	*Oxygen (+/– hyperbaric chamber)*
Cyanide	*1) Amyl nitrite pearls 2) Sodium nitrite 3) Sodium thiosulfate*
Digitalis	*Digoxin immune Fab*
Methanol Ethylene glycol	*Fomepizole*
Heparin	*Protamine sulfate*
Lead	*Dimercapto-succinic acid*
Mercury Arsenic Gold	*Dimercaprol*
Methemo-globinemia	*Methylene blue*
Opiates	*Naloxone, nalmefene, or naltrexone*
Organo-phosphates Carbamates Nerve gases	*1) Atropine 2) Pralidoxime*

Rituximab (Rheumatoid arthritis, Cancers)-------Adalimumab (Rheumatoid arthritis)---Infliximab (Rheumatoid arthritis)---Alemtuzumab (Leukimias, immunosupresant in renel transplants)
Muromonab-CD3 (immunosupresant in renel transplants)----Trastuzumab (Cancers)---Bevacizumab (Cancers)---Cetuximab (Cancers)---Omalizumab (Asthma)