ANS drug summary

Cholinergic and Adrenergic Transmission		
Drug	**Action**	**Consequences**
• **Hemicholinium**	Inhibits choline transporter	Failure of Choline transmission into the presynaptic nerve
• **Vesamicol**	Inhibits VAT	Inhibits the storage of Ach in vesicles Failure of Ach transmission
• **Botulinum toxin**	Inhibits VAMPS and SNAPS action in cholinergic transmission	Vesicles cannot adhere with the right position and no exocytosis of Ach takes place
• **Metyrosine**	Inhibits the enzymatic activity of tyrosine hydroxylase	Tyrosine is not converted to DOPA
• **Reserpine**	Inhibits VMAT	Inhibits the storage of DA in vesicles Depletion of catecholamines
• **Cocaine & Tricyclic antidepressants**	Inhibit NET (norepinephrine transporter)	Inhibits the reuptake of NE into the neuron
• **Guanethidine and bretylium**	Inhibits VAMPS and SNAPS action in adrenergic transmission	Blocks release of NE into the synaptic space
• **ω–Conotoxin GVIA (toxin of marine snails)**	Blocks Ca^{+2} channels	Reduce NE & Ach release
• **α–Latrotoxin (black widow spider venom)**	Acts on vesicles	Explosive release of NE & Ach
Direct-acting Drugs (Choline esters)		
Drug	**Effect**	**Affected by ACE**
• **Acetylcholine**	Highly affects muscarinic and nicotinic receptors	Extremely affected by ACE
• **Methacholine (a methyl group is added)**	Extremely affects muscarinic receptors	Slightly affected
• **Carbacol (the acetyl group is substituted with an amide group)**	-Moderately affects muscarinic receptors -Highly affects nicotinic receptors	Not affected
• **Benthanecol (a methyl group is added, and the acetyl group is substituted with an amide group)**	-Moderately affects muscarinic receptors	Not affected

Direct-acting Drugs (Alkaloids)		
Drug	**Effect**	**Note**
• **Muscarine**	Has a stronger effect than ACh on muscarinic receptors	Natural
• **Pilocarpine**	-Direct acting (muscarinic agent) -Has long been used to increase salivary secretion	Natural alkaloid that comes from plants
• **Nicotine**	Only stimulates nicotinic receptors	
• **Lobeline**	Acts on nicotinic receptors	-Similar to nicotine -Natural alkaloid that comes from plants
• **Cevimeline**	Muscarinic agonist	Used for the treatment of dry mouth associated with Sjögren's syndrome (a systemic autoimmune disease) that's caused by radiation damage of the salivary glands
Indirect-Acting Drugs (cholinesterase inhibitors)		
Drug	**Effect**	**Note**
• **Neostigmine**	-Reversibly inhibits cholinesterase → inhibits degradation of Ach -Used in myasthenia gravis and ileus - Has an additional direct nicotinic agonist effect at the neuromuscular junction	-An ester composed of carbamic acid ([1]) and a phenol bearing a quaternary ammonium group([2]) -Used in reatment of the antimuscarinic effects
• **Physostigmine**	Reversibly inhibits cholinesterase → inhibits degradation of Ach	-A naturally occurring carbamate, is a tertiary amine - Well absorbed from all sites and can be used topically in the eye -It is distributed into the CNS and is more toxic than the more polar quaternary carbamates

Drug	Effect	Note
• **Edrophonium**	-Reversibly inhibits cholinesterase → inhibits degradation of Ach -Used in myasthenia gravis and ileus	-Not an ester, it is a quaternary alcohol -Binds electrostatically and by hydrogen bonds to the active site, thus preventing access of acetylcholine - Used as a diagnostic test for myasthenia
• **Pyridostigmine**	-Used in myasthenia gravis	
• **Ambenonium**	-Used in myasthenia gravis	
• **Demecarium**	-Used in glaucoma	
• **(Organophosphates):** **-Echothiophate** **-Parathion** **-Malathion**	-Irreversibly inhibits cholinesterase - Echothiophate is used in glaucoma	-Well absorbed from the skin, lung, gut, and conjunctiva—thereby making them dangerous to humans and highly effective as insecticides. - Parathion and malathion must be activated in the body by conversion to the oxygen analogs - Undergo initial binding and hydrolysis by the enzyme, resulting in a phosphorylated active site - The phosphorylated enzyme complex may undergo a process called aging
• **Pralidoxime**	- Able to break the phosphorusenzyme bond and can be used as "cholinesterase regenerator" drugs for organophosphate insecticide poisoning	- Given before aging has occurred

Central nervous system		
Drug	**Effect**	**Note**
• **Tacrine**	Anticholinesterase used for the treatment of mild to moderate Alzheimer's disease	Its efficacy is modest, and hepatic toxicity is significant
• **Donepezil**	Used in treatment of cognitive dysfunction in Alzheimer's patients	-Newer and more selective than Tacrine - Given once daily because of its long half-life, and it lacks the hepatotoxic effect of tacrine
• **Varenicline**	Partial agonist action at central nicotinic receptors	-It has antagonist properties that persist because of its long half-life - It prevents the stimulant effect of nicotine at presynaptic nicotinic receptors that cause release of dopamine - Its use is limited by nausea and insomnia and also by exacerbation of psychiatric illnesses, including anxiety and depression
Cholinoreceptor-blocking drugs		
Drug	**Effect**	**Note**
• **Scopolamine (hyoscine)**	-Has more marked central effects, producing drowsiness and amnesia -Effective in preventing or reversing vestibular disturbances	-In toxic doses, scopolamine, and atropine, can cause excitement, agitation, hallucinations, and coma - Given by injection or by mouth or as a transdermal patch - Produces significant amnesia for the events associated with surgery and obstetric delivery
• **Pirenzepine & Telenzepine**	-M1 blockers -Reduce gastric acid secretion with fewer adverse effects than atropine	
• **Trihexyphenidyl and benztropine**	-Useful as adjunctive therapy for Parkinson’s disease	

Drug	Effect	Note
• **Atropine**	-Has minimal stimulant effects on CNS -Atropine and other tertiary antimuscarinics cause an unopposed sympathetic dilator activity & mydriasis -Paralysis of the ciliary muscle, or cycloplegia resulting in loss of accommodation the fully atropinized eye cannot focus for near vision. -Causes acute glaucoma in patients with a narrow anterior chamber angle. -Causes tachycardia by vagal block. -Causes some bronchodilation & reduce secretion - Suppresses sweating	-In toxic doses, scopolamine, and atropine, can cause excitement, agitation, hallucinations, and coma - Atropine is used in myocardial infarction - Individuals with hyperactive carotid sinus reflexes benefit from atropine - Atropine is combined with diphenoxylate → (Lomotil) is available in both tablet and liquid form.
• **Phenylephrine**	- Alpha 1stimulant (not blocker) - Produces a short mydriasis	-Used in control of hypotension -Sufficient for funduscopic examination
• **Ipratropium**	- Non selective M blocker - Used as an inhalational drug in asthma with reduced systemic effects	- Useful in chronic obstructive pulmonary disease (COPD) a condition that occurs more frequently in older patients, particularly chronic smokers.
• **Tiotropium**	-Has a longer bronchodilator action and can be given once daily	
• **Oxybutynin**	- More selective for M3 receptors -Used to relieve bladder spasm after urologic surgery	-It reduces involuntary voiding in patients with neurologic disease

Drug	Effect	Note
• **Darifenacin**	Has greater selectivity for M3 receptors	-Long half-life -Used in adults with urinary incontinence
• **Botulinum toxin A**	- An alternative treatment for urinary incontinence refractory to antimuscarinic drugs	By interfering with the release of neuronal acetylcholine, botulinum toxin is reported to reduce urinary incontinence for several months after a single treatment

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