

Autonomic Drugs

Subcommittee:

Theobald, Jr., Robert J.	rtheobald@atsu.edu
Bylund, David B.	dbylund@unmc.edu
Dretchen, L. Kenneth	dretchek@georgetown.edu
Gibb, James W.	james.gibb@pharm.utah.edu
Harris, Steven	sharris@pc.edu
Moore, Kenneth E.	moorek@msu.edu
Silinsky, Eugene	e-silinsky@northwestern.edu
Strandhoy, Jack	jstrand@wfubmc.edu
Westfall, David P.	westfall@unr.edu
Westfall, Thomas C.	westfatc@slu.edu

Drugs acting at synaptic and neuroeffector junctional sites autonomic and neuromuscular pharmacology	
Recommended Curriculum Equivalent: 1.0 hr	
Introduction and History	
Neuronal Drugs	
Botulinum toxin Entacapone Reserpine	Cocaine Metyrosine
Learning Objectives	
<p>Physiology and pathophysiology</p> <p>Describe the anatomical projections of the sympathetic and parasympathetic autonomic nervous system.</p> <p>Describe the evidence for the development of the concept of neurotransmitters, cotransmitters and end-organ specificity.</p> <p>Describe homeostasis, fight-or-flight, and rest-and-repair with regard to the autonomic nervous system.</p> <p>Describe the central control of the autonomic nervous system.</p> <p>List and describe the responses of end organs to activation of each division of the autonomic nervous system.</p> <p>Describe the concept of dominant tone.</p>	
<p>Mechanisms of action</p> <p>Block the uptake of choline into cholinergic neurons</p> <p>Inhibits Catechol-o-methyl transferase peripherally</p> <p>Blocks storage vesical transport system</p> <p>Inhibit reuptake of NE into adrenergic neurons</p> <p>Depletes NE by interfering with synthesis</p>	
<p>Notes</p> <p>Define words containing the suffixes, -ergic, -mimetic, -lytic, and -ceptive.</p>	

Drugs acting at synaptic and neuroeffector junctional sites autonomic and neuromuscular pharmacology			
Recommended Curriculum Equivalent: 3.0 hr			
Drug Classes and Drugs to consider			
Direct Acting Cholinergic Ester-Agonists	Direct Acting Cholinergic Alkaloid Agonists	Cholinergic Indirect Acting	Related Drugs
Acetylcholine Bethanechol	PILOCARPINE	Neostigmine Physostigmine Pyridostigmine Echothiophate Edrophonium Malathion Parathion	Pralidoxime Obidoxime Sarin VX series
Learning Objectives			
<p>Physiology and pathophysiology Describe synthesis, storage, release, and inactivation of cholinergic agonists. List the steps in the synthesis, storage, release and inactivation of acetylcholine, and drugs that interface with those processes. List the location of nicotinic and muscarinic receptors. Compare the major cholinesterases as to location and function. Compare the two major cholinesterases: acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE) as to anatomical locations, sites of synthesis and function.</p>			
<p>Mechanism of action Explain the mechanism of actions, including 2nd messenger systems of acetylcholine and related drugs. Explain the differences in onset and duration of action and route of administration for different groups of anticholinesterases. Explain the chemical makeup of the active site of AChE (anionic and esteratic) as to attraction, attachment and rates of breakdown of various substrates and inhibitors. Distinguish the mechanism by which pralidoxime reactivates phosphorylated AChE.</p>			
<p>Actions on organ systems Describe the responses to activation of these receptors. Explain the reason why anticholinesterases are reversible or irreversible.</p>			
<p>Pharmacokinetics Describe the variations of pharmacokinetics of cholinergic drugs. Relate the onset of action of anticholinesterases, routes of administration, and the duration of action of anticholinesterases with sites and type of attachment to the enzyme. Explain why anticholinesterases are reversible or irreversible, and indicate which anticholinesterases are in each category. Explain the role of enzyme aging in the enzyme-inhibitor interaction.</p>			

Adverse effects, drug interactions and contraindications

List the adverse effects of cholinergic drugs.

List and describe the rationale for contraindications of cholinergic drugs.

Therapeutic uses

List the therapeutic uses of cholinergic agonists.

Describe the effects of accumulated acetylcholine at muscarinic and nicotinic receptors in the periphery and the central nervous system.

List therapeutic uses for and adverse side effects of anticholinesterases.

Explain why anticholinesterase agents can be used as insecticides (malathion, parathion) and chemical warfare agents (sarin, VX series).

Explain why pralidoxime is not effective reactivating all phosphorylated AChE.

Explain the concept of differential toxicity of malathion and parathion in different species.

Notes

Drugs acting at synaptic and neuroeffector junctional sites autonomic and neuromuscular pharmacology		
Recommended Curriculum Equivalent: 2.0 hr		
Drug Classes and Drugs to consider		
Antagonists at Muscarinic Receptors	Antagonists at Nicotinic Receptors	Drugs Acting at Autonomic Ganglia
Atropine Ipratropium Scopolamine Tolterodine	Nicotine Succinylcholine Tubocurarine MIVACURIUM	Mecamylamine
Learning Objectives		
Physiology and pathophysiology List the locations of and the differences between muscarinic and nicotinic receptors. Explain rationale for original uses in treatment of hypertension and autonomic hyperreflexia.		
Mechanism of action Describe the mechanism of action. Describe nicotine's agonist and antagonist properties.		
Actions on organ systems Contrast and compare the depolarizing the competitive NMJ blocking drugs.		
Adverse effects, drug interactions and contraindications Explain why muscarinic antagonists cause xerostomia, blurred vision, photophobia, tachycardia, anhidrosis, difficulty in micturition, hyperthermia, glaucoma and mental confusion in the elderly. Explain why muscarinic antagonists are contraindicated in glaucoma, obstructive disease of the gastrointestinal tract or urinary tract, intestinal atony. List the adverse side effects of drug acting at autonomic ganglia. Competitive antagonists at NMJ – List the adverse side effects.		
Therapeutic uses Explain the rationale for the therapeutic use in diseases such as bronchoconstriction, excessive salivation, and motion sickness. Explain the rationale for the therapeutic use to produce mydriasis and cycloplegia. Explain why it is not used clinically (except as a smoking deterrent), and its historical, social and toxicological significance. Depolarizing agent – Explain the uses and limitations.		
Notes		

Drugs acting at synaptic and neuroeffector junctional sites autonomic and neuromuscular pharmacology				
Recommended Curriculum Equivalent: 3.5 hr				
Drug Classes and Drugs to consider				
Nonselective Alpha Adrenergic Agonists	Selective Alpha₂ Adrenergic Agonists	Nonselective Alpha₁ Alpha₂ Antagonists	Selective Alpha₁ Adrenergic Antagonists	Indirect and Mixed Acting Agents
Epinephrine Norepinephrine Pseudoephedrine Phenylephrine Dopamine	CLONIDINE BRIMONIDINE METHYLDOPA	Phenoxybenzamine Phentolamine	Prazosin Tamsulosin Terazosin	Amphetamine Ephedrine Tyramine Methamphetamine
Learning Objectives				
<p>Physiology and pathophysiology</p> <p>List steps in the synthesis, storage, release and inactivation of norepinephrine and epinephrine.</p> <p>Describe types and subtypes of adrenergic receptors, their locations, and physiologic response to activation.</p> <p>Describe receptor selectivity of norepinephrine and epinephrine.</p> <p>Describe the differences between direct and indirect acting adrenergic drugs.</p>				
<p>Mechanism of action</p> <p>Direct Agonists bind to receptor with intrinsic activity</p> <p>Indirect Agonists release neurotransmitters from neuron.</p> <p>Antagonists bind to receptor with no intrinsic activity</p>				
<p>Actions on organ systems</p> <p>Explain why alpha-1 adrenergic antagonists are used to treat hypertension and benign prostatic hypertrophy.</p> <p>Explain why alpha-1 adrenergic agonists are important in the treatment of nasal congestion, hypotension, paroxysmal atrial tachycardia, and are used to cause mydriasis and vasoconstriction (with local anesthetics).</p> <p>Explain the mechanism for the use of alpha-2 adrenergic agonists in the treatment of hypertension, and for topical treatment of glaucoma.</p>				
<p>Adverse effects, drug interactions and contraindications</p> <p>List the adverse side effects of alpha₁ and alpha₂ agonists.</p> <p>Explain drug interactions with oxytocic drugs and monoamine oxidase inhibitors.</p> <p>List the contraindications for alpha₁ adrenergic agonists.</p> <p>List the adverse side effects of nonselective alpha and selective alpha adrenergic antagonists.</p>				

Therapeutic uses

Explain why alpha-1 adrenergic agonists are important in the treatment of nasal congestion, hypotension, paroxysmal atrial tachycardia, and are used to cause mydriasis and vasoconstriction (with local anesthetics).

Explain the mechanism for the use of alpha-2 adrenergic agonists in the treatment of hypertension, and for the topical treatment of glaucoma.

Explain the limitations of the use of nonselective alpha-1, alpha-2 adrenergic antagonists in the treatment of hypertension.

Notes

Drugs acting at synaptic and neuroeffector junctional sites autonomic and neuromuscular pharmacology				
Recommended Curriculum Equivalent: 1.5 hr				
Drug Classes and Drugs to consider				
Nonselective Beta Adrenergic Agonists	Selective Beta Adrenergic Agonists	Nonselective Beta Adrenergic Antagonists	Selective Beta Adrenergic Antagonists	Alpha and Beta Adrenergic Antagonists
Isoproterenol	ALBUTEROL	Propranolol Timolol Salmeterol	Metoprolol Atenolol	Labetalol
Learning Objectives				
<p>Mechanism of action</p> <p>Nonselective beta-adrenergic agonists – Compare and contrast the pharmacology of epinephrine and isoproterenol.</p> <p>Selective beta-adrenergic agonists – Compare and contrast the pharmacology of beta selective adrenergic agonists isoproterenol, albuterol, salmeterol, and dobutamine.</p> <p>Beta-adrenergic antagonists – Compare and contrast the pharmacology of propranolol, metoprolol, and atenolol.</p> <p>Compare and contrast the pharmacology of the nonselective alpha and beta blocking drug labetalol, with selective beta blocking drugs.</p>				
<p>Adverse effects, drug interactions and contraindications</p> <p>List the adverse side effects of beta₂ adrenergic agonists.</p> <p>List the adverse side effects of beta adrenergic antagonists.</p>				
<p>Therapeutic uses</p> <p>Selective beta-adrenergic agonists – Explain the mechanisms for the use of these drugs in diseases such as cardiac decompensation, asthma, premature labor, bronchospasm and emphysema.</p>				
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