

ANS: Pharmacotherapeutics, Medication and  
Neuropharmacology  
NSG-622



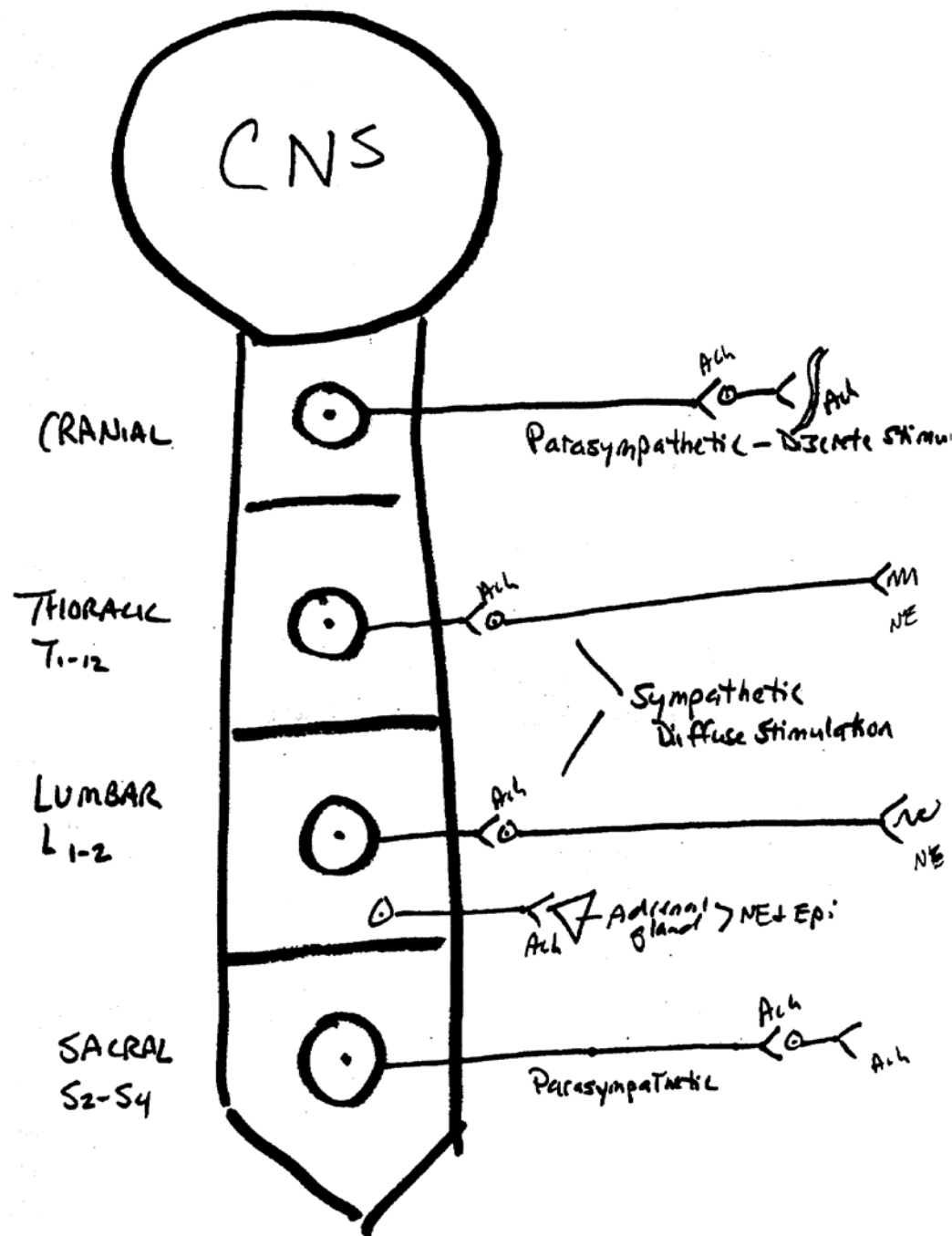
*Jeffrey Fudin, Pharm.D., DAAPM, FCCP*  
*Adjunct Associate Professor, Pharmacy Practice*  
*Albany College of Pharmacy*  
*CEO, NovaPain Associates*  
*Clinical Pharmacy Specialist, VAMC-Albany*  
[www.paindr.com](http://www.paindr.com)

# ANS: Pharmacotherapeutics, Medication and Neuropharmacology

- Pharmacology - Action / Effect
- Pharmacodynamics - Effect of Drugs on Living Systems
  - A. Potency
  - B. Efficacy
  - C. Selectivity
  - D. Structural Specificity

# Physiology Review of Autonomic Nervous System

- A.N.S. - A visceral efferent (coming from C.N.S. to peripheral structures which function automatically)



# Neural System

- Sympathetic - Mediates body response to stress
- Maintenance of normal physiological function
- Terminology:
  - Preganglionic Neuron - Origin in C.N.S.
  - Postganglionic Neuron - Innervate effector cells by chemical transmissions at the neuro-effector junction.
  - Sympathetic - Preganglionic neurons activate a number of postsynaptic neurons (many structures are effected).
  - Parasympathetic - Ganglia / neurons are usually in a 1:1 ratio

# Neurotransmitters

- Parasympathetic - Acetylcholine (very rapidly hydrolyzed and only lasts for seconds)
- Sympathetic - Nor-epinephrine (lasts for minutes)
- Putative neurotransmitters ?

# Confusing Terminology

- Cholinomimetic
- Cholinolytic
- Anticholinergic
- Adrenergic
- Adrenolytic
- Sympathomimetic
- Anti-adrenergic

# Variability of Autonomic Receptors (1)

- Cholinergic receptors
  - Muscarinic type - Effector cells in smooth muscle, cardiac muscle and glands (ie. Atropine)
  - Nicotinic type - Post synaptic cells in ganglia and neuromuscular junction (ie. Nicotine)



# Variability of Autonomic Receptors (2)

- Adrenergic receptors
  - Alpha - stimulating activity
  - Beta - Relaxing activity

# Enzymes Effecting Neurotransmitters

- Cholinesterase
- M.A.O. and C.O.M.T.
- Drug actions

# M/A Examples

- Enzyme Inhibitors - Interfere with enzymes that take up neurotransmitters
- Uptake Inhibitors - Cocaine interferes with Amine reuptake, providing an intense activity of nor-epinephrine at the post neurojunctional membrane
- Receptor Blockers – Atropine (cholinergic) / propranolol (adrenergic)
- Amine depletors - Reduces quantity of nor-epinephrine, ie. Reserpine
- Release Inhibitors - Interferes with release of neurotransmitter, ie. Bretylium (no longer available)

# Ocular Net Effects

- Miosis => Cholinergic
- Anti-adrenergics => Allows parasympathetic dominance
- Mydriasis => Adrenergics - used to reduce production of intraocular pressure by vasoconstriction (wide angle only)

# Quaternary Amines (1)

- Acetylcholine (as prototype)
  - Cardiovascular - Fall in BP due to vasodilation  
Reflex tachycardia possible
  - Other smooth muscles - Will contract
  - GI and Bladder contraction of mitotic sphincter muscles  
Contraction of ciliary muscles
  - Gland Secretions
    - Salivary secretions Mucous gland secretions  
Digestive and GI secretions
  - Nicotinic effects - Require higher doses. We will effect all of ANS and NMJ's.

# Quaternary Amines (2)

- Bethanechol
  - Manipulated Ach chemical structure adding -CH<sub>3</sub> and -NH<sub>2</sub>. This protects against cholinesterase.
  - By adding a second methyl group, chemical will only effect muscarinic
  - Uses: Urinary retention, gastric and intestinal atony
  - S.E.: Flushing, sweating, salivation

# Quaternary Amines (3)

- Carbachol - Longer lasting
- Methacholine - Chemical manipulation protects chemical against plasma cholinesterase. Very little nicotinic activity, but cholinesterase at the N.M.J.'s will break it down.
- Uses: Acute glaucoma, vascular disease
- Muscarine - Historical interest. Source of poison in mushrooms

# Tertiary Amines

- Pilocarpine
- Toxicity and precautions in systemic administration
- Asthmatics - Hypersensitive to muscarinic-type cholinergic drugs
- IV/IM - Serious S.E. may occur
- Peptic ulcers - Worsens due to motility
- **Atropine - Should always be available as antidote due to muscarinic effects Constipation - Don't use due to mechanical obstruction of bowels**



# Anticholinesterase or Cholinesterase Inhibitors (1)

- Physostigmine - 1% solution for glaucoma
  - Antidote for Atropine - like poisoning drugs it's a quaternary amine (very fat soluble), therefore a good antidote for cholinergic syndrome (Atropine, muscarinic and CNS effects will be antagonized)
- Neostigmine (Prostigmine) - Synthetic Quat causing muscarinic and nicotinic effects. It has a positive charge and therefore won't cause any CNS effects because it won't pass B.B.B.
  - Use: Myasthenia gravis

# Anticholinesterase or Cholinesterase Inhibitors (2)

- Edrophonium (Tensilon):
  - A Quat (short acting neostigmine)
  - Uses:
    - Curare antidote
    - diagnostic agent for M.G. - given IV if M.G. symptoms get better, if not, symptoms get worse.
- Neostigmine Substitutes:
  - Pyridostigmine (Mestinon), Ambenonium (Mytelase)
  - Uses: Myasthenia Gravis
- Irreversible Anti-cholinesterase : organophosphates
  - These form irreversible covalent bonds
- New acetyl cholinesterase enzymes must be formed

# Cholinergic Blocking Drugs

- Consist of two types:
  - Muscarinic - smooth muscle, glands, heart
  - Nicotinic - ganglions, NMJ
  - ie.: Atropine, Scopolamine

# Net Effects of Cholinergic Blockers

- M/A: Competitive antagonist at muscarinic site. Affinity, but no efficacy
- Effects: Xerostomia
- Anhydrosis
- Decreased bronchial secretions
- Mydriasis and cycloplegia
- Sympathetic tone takes over=> Inhibition of cardiac vagal tone
- Inhibition of GI and GU smooth muscle
- Inhibition of gastric secretion

## Cholinergic Blockers (continued)

- Side Effects: Bradycardia, cutaneous vasodilation
- Precautions: Don't use in glaucoma patients Hyperpyrexia due to inhibited sweating Possible CNS depression orthostatic hypotension