Drugs Acting on the Peripheral Nervous System

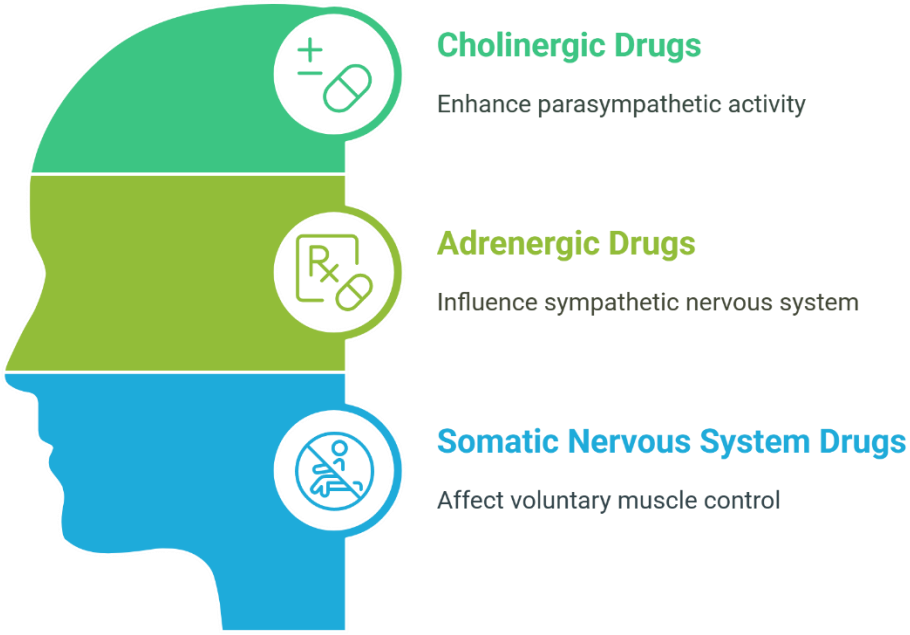
Drugs Acting on the Peripheral Nervous System (PNS)

Overview of the Peripheral Nervous System

- The **Peripheral Nervous System** (PNS) includes all the nerves outside the brain and spinal cord. It is divided into:
    - **Somatic Nervous System** (controls voluntary movements, like skeletal muscle)
    - **Autonomic Nervous System (ANS)** (controls involuntary actions, like heart rate, digestion)
- The **ANS** is further divided into:
    - **Sympathetic Nervous System (SNS)** – "fight or flight"
    - **Parasympathetic Nervous System (PNS)** – "rest and digest"

Drugs Acting on the PNS

- Drugs affecting the PNS either **stimulate** or **inhibit** the transmission of nerve impulses.
- They act on **neurotransmitters** and their **receptors**.



1. Cholinergic Drugs (Affecting Acetylcholine)

➢ These act on **parasympathetic nerves** or **somatic motor nerves**.

- **Cholinergic agonists (parasympathomimetics)**: Mimic acetylcholine (ACh).
    - Example: *Pilocarpine* – stimulates salivation in dry mouth.

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- **Anticholinergics (parasympatholytics)**: Block ACh receptors.
  - Example: *Atropine* – used to dilate pupils or treat bradycardia.
- **Cholinesterase inhibitors**: Prevent breakdown of ACh.
  - Example: *Neostigmine* – used in myasthenia gravis.

2. Adrenergic Drugs (Affecting Norepinephrine/Epinephrine)

- These act on **sympathetic nerves**.
  - **Adrenergic agonists (sympathomimetics)**: Mimic norepinephrine (NE) or epinephrine.
    - Example: *Salbutamol* – bronchodilator for asthma.
  - **Adrenergic antagonists (sympatholytics)**: Block adrenergic receptors.
    - Example: *Propranolol* – beta-blocker for hypertension.

3. Somatic Nervous System Drugs

- These affect **neuromuscular transmission**:
  - **Neuromuscular blockers**: Used during surgery to cause muscle relaxation.
    - Example: *Succinylcholine*
  - **Skeletal muscle relaxants**: Reduce muscle tone or spasms.
    - Example: *Baclofen*

Steps Involved in Neurohumoral Transmission

Neurohumoral transmission is the process by which a nerve impulse leads to the release of a neurotransmitter, stimulating a target cell (neuron, muscle, or gland).

1. Synthesis of Neurotransmitter

- Neurotransmitters like acetylcholine (ACh) or norepinephrine (NE) are synthesized in the nerve terminal.
- Example: Choline + Acetyl-CoA → Acetylcholine (via choline acetyltransferase).

2. Storage in Vesicles

- Neurotransmitters are stored in synaptic vesicles to protect them from degradation and prepare for release.

3. Arrival of Nerve Impulse

- An action potential reaches the nerve terminal, opening voltage-gated calcium channels.

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- Ca^{2+} enters the neuron.

4. Release of Neurotransmitter

- Ca^{2+} influx triggers fusion of vesicles with the presynaptic membrane.
- Neurotransmitter is released into the synaptic cleft via exocytosis.

5. Binding to Receptors

- The neurotransmitter binds to receptors on the postsynaptic membrane:
  - ACh → nicotinic/muscarinic receptors
  - NE → alpha/beta adrenergic receptors

6. Response in Effector Cell

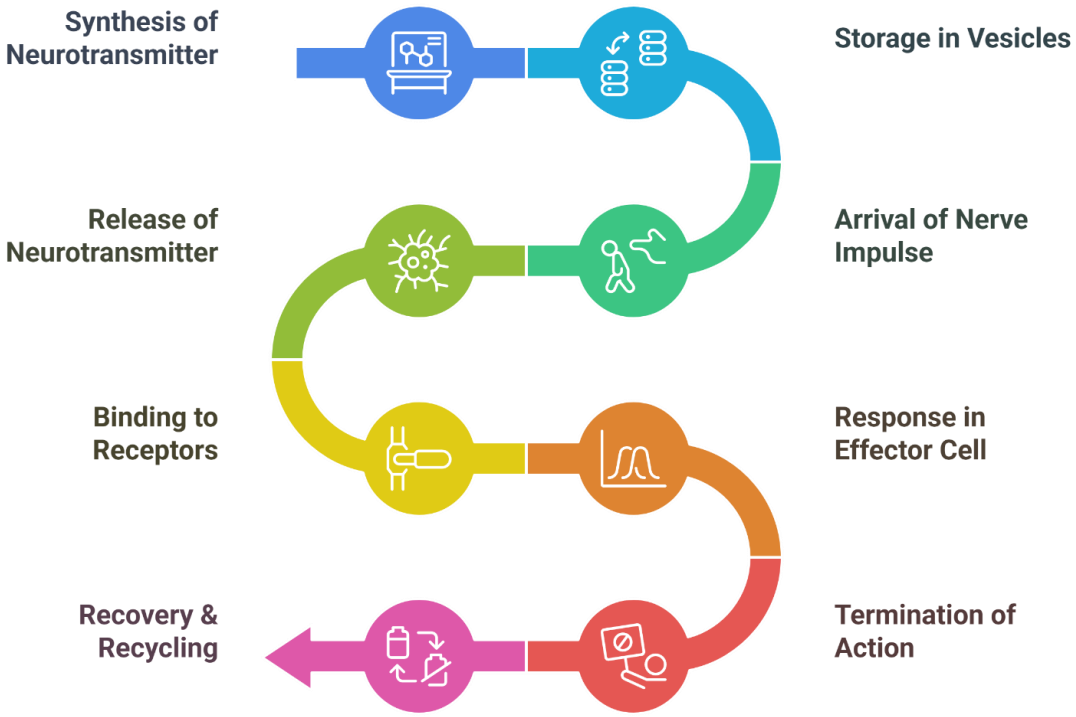
- Receptor binding causes ion channel opening or second messenger activation, triggering a physiological response.

7. Termination of Action

- Signal ends by:
  - Enzymatic breakdown (e.g., ACh by acetylcholinesterase)
  - Reuptake into presynaptic neuron (e.g., NE)
  - Diffusion away from the synapse

8. Recovery & Recycling

- Components (e.g., choline) are reabsorbed for neurotransmitter resynthesis.



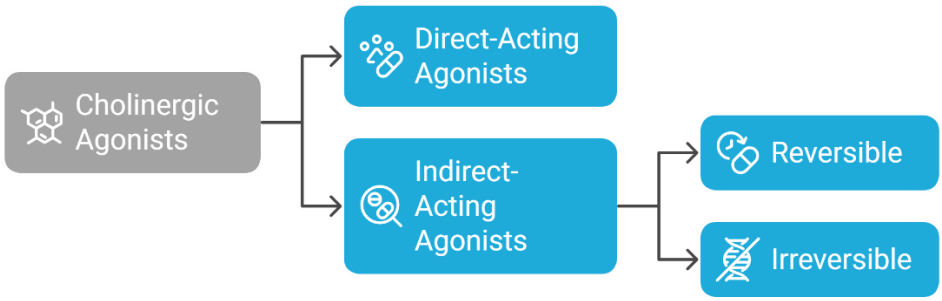
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Cholinergic Drugs (Parasympathomimetics)

Definition:

- Cholinergic drugs are agents that **stimulate the parasympathetic nervous system** (PSNS) by **mimicking the action of acetylcholine (ACh)**, the primary neurotransmitter of cholinergic nerves.
- These drugs either:
    - **Directly activate** cholinergic receptors, or
    - **Indirectly increase** acetylcholine levels by inhibiting acetylcholinesterase (the enzyme that breaks down ACh).

Classification (Based on Mechanism of Action):



A. Direct-Acting Cholinergic Agonists:

- Bind directly to **muscarinic** or **nicotinic receptors**
- Mimic acetylcholine
- Examples:
    - **Muscarinic agonists**: Bethanechol, Pilocarpine, Methacholine
    - **Nicotinic agonists**: Nicotine, Lobeline

B. Indirect-Acting Cholinergic Agonists (Anticholinesterases):

- Inhibit acetylcholinesterase → ↑ ACh at synapse
- Types:
    1. **Reversible**: Neostigmine, Physostigmine, Pyridostigmine
    2. **Irreversible**: Organophosphates (e.g., Malathion, Parathion)

Pharmacological Actions:

System	Effect

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Eye	Miosis (pupil constriction), ↓ intraocular pressure (useful in glaucoma)
Heart	↓ Heart rate (bradycardia), ↓ conduction (via M2 receptors)
GIT	↑ Salivation, ↑ motility, ↑ gastric secretion
Urinary Bladder	Detrusor contraction, sphincter relaxation → promotes urination
Lungs	Bronchoconstriction, ↑ secretions
CNS	Depends on drug; some like physostigmine cross BBB and cause CNS excitation
Skeletal muscle	Stimulated by drugs affecting nicotinic receptors (e.g., neostigmine)

Dose (Examples):

Varies by drug:

- **Bethanechol:** 10–50 mg orally, 2–4 times daily
- **Neostigmine:** 0.5–2.5 mg IV/IM; 15–60 mg orally for myasthenia gravis
- **Pilocarpine:** Eye drops 1–2% for glaucoma; oral tablets 5–10 mg for xerostomia

Indications:

- **Glaucoma** (pilocarpine, carbachol)
- **Urinary retention** (bethanechol)
- **Xerostomia (dry mouth)** (pilocarpine)
- **Myasthenia gravis** (neostigmine, pyridostigmine)
- **Alzheimer's disease** (donepezil, rivastigmine)
- **Anticholinergic toxicity** (physostigmine)
- **Neuromuscular blockade reversal** (neostigmine)

Contraindications:

- **Asthma/COPD** (due to bronchoconstriction)
- **Peptic ulcer** (increased acid secretion)
- **Bradycardia or AV block**
- **Hyperthyroidism** (risk of atrial fibrillation)
- **Mechanical obstruction** in GI or urinary tract
- **Parkinson’s disease** (may worsen tremor)

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