DRUGS ACTING ON AUTONOMIC GANGLIA

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The autonomic ganglia are relay stations in the autonomic nervous system (ANS), transmitting signals between the central nervous system (CNS) and target organs. They contain preganglionic and postganglionic neurons, which communicate through neurotransmitters and receptors.

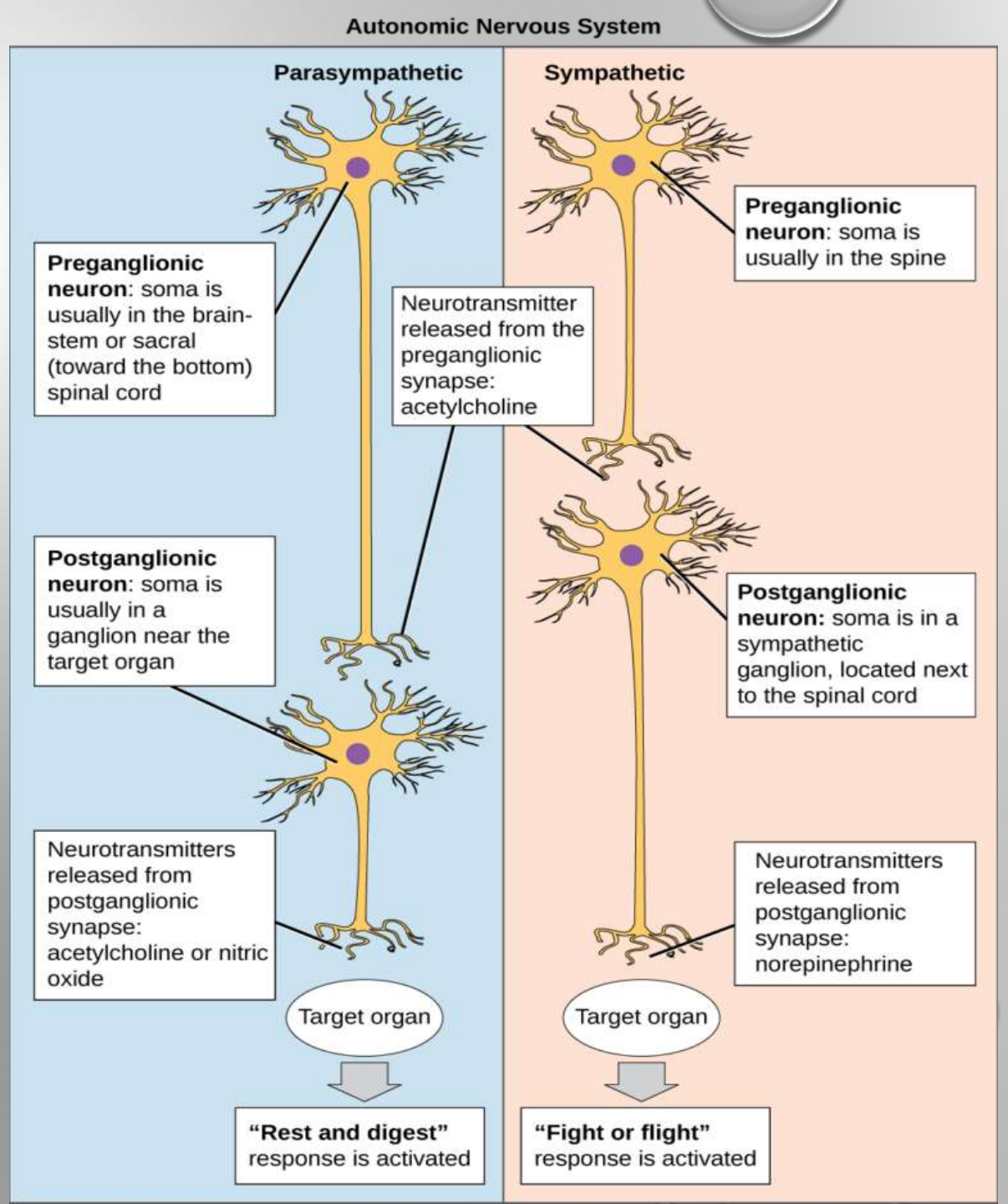
Neurotransmission in Autonomic Ganglia

A. Preganglionic Neurotransmission

- Neurotransmitter: Acetylcholine (ACh)
- Receptor: Nicotinic Acetylcholine Receptors (nAChRs)
  - Nicotinic receptors (N2 or NN type) in ganglia are ligand-gated ion channels.
  - Activation → Na^+ influx → Depolarization → Action potential.

B. Postganglionic Neurotransmission

- Sympathetic Postganglionic Neurons → Norepinephrine (NE) (except sweat glands = ACh)
- Parasympathetic Postganglionic Neurons → Acetylcholine (ACh)

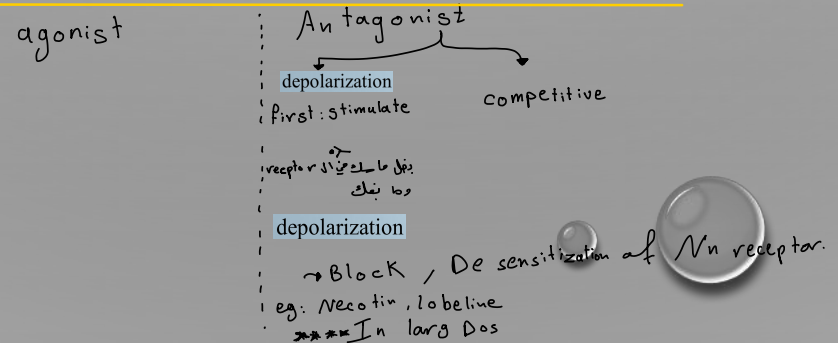


• Drugs acting on autonomic ganglia can either stimulate or block neurotransmission in sympathetic and parasympathetic ganglia. these drugs primarily affect nicotinic acetylcholine receptors (Nn) in the autonomic ganglia.

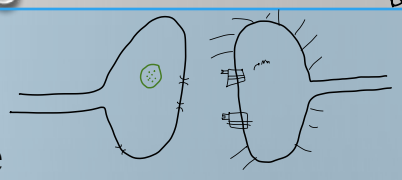
1. **ganglionic stimulants:** these drugs activate nicotinic receptors at the ganglionic level, leading to mixed sympathetic and parasympathetic effects.

2. **ganglionic blockers** (ganglioplegics): → paralysis. side effects

these drugs inhibit synaptic transmission in autonomic ganglia, leading to sympatholytic and parasympatholytic effects, depending on which system predominates in an organ.



Ganglionic stimulants

Drug	Mechanism of Action	Pharmacological Effects	Clinical Use
Nicotine 	Stimulates Nn in autonomic ganglia, adrenal medulla, and CNS; **at high doses**, causes depolarization block	↑ BP,↑HR (sympathetic); ↑ GI motility, salivation, urination (parasympathetic); at high doses, paralysis of ganglia	Smoking cessation (nicotine patches, gum, lozenges)
Lobeline	Similar to nicotine; stimulates Nn	Transient ganglionic stimulation; weak stimulant effects	No therapeutic use; previously used for smoking cessation
Varenicline	Partial agonist at nicotinic receptors (mainly CNS)	Reduces nicotine craving	(Smoking) cessation
Dimethylphenylpiperazinium (DMPP)	Selective nAChR agonist; more potent than nicotine	Strong autonomic effects; BP fluctuations, HR changes	Research use only
Tetramethylammonium (TMA)	Stimulates nAChRs in ganglia	Short-lasting ganglionic stimulation	No clinical use

- **Effects of ganglionic stimulants**

- sympathetic activation: ↑ Bl pressure, heart rat, sweating (adrenal medulla stimulation).

- parasympathetic activation: ↑ git motility, urination, bronchoconstriction.

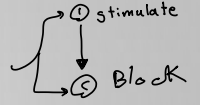
- at high doses, overstimulation leads to depolarization block, causing ganglionic paralysis.

Ganglionic blockers

A. Competitive Nicotinic Antagonists

Drug	Mechanism of Action	Pharmacological Effects	Clinical Use
Hexamethonium	Non-depolarizing nAChR antagonist at autonomic ganglia	Blocks sympathetic and parasympathetic tone; hypotension, tachycardia, cycloplegia, urinary retention	Historical use for hypertension, no longer used
Mecamylamine	Competitive nAChR antagonist (crosses BBB)	Similar to hexamethonium; CNS effects (sedation, tremor)	Tourette's syndrome, nicotine withdrawal
Trimethaphan	Short-acting nAChR antagonist (IV use)	Rapid BP drop, venodilation, prevents baroreceptor reflex	Hypertensive emergencies, aortic aneurysm surgery

B. Depolarizing blockers



these drugs persistently activate nicotinic receptors, causing sustained depolarization and subsequent blockade.

Drug	Mechanism of Action	Pharmacological Effects	Clinical Use
Nicotine (high dose)	Prolonged nAChR activation → depolarization block	Initial stimulation, then ganglionic paralysis	No therapeutic use (toxic in overdose)
Tetraethylammonium (TEA)	nAChR activation, short-acting	Short-lived ganglionic blockade	Early antihypertensive (obsolete)

Effects of Ganglionic Blockers

Because autonomic ganglia regulate both sympathetic and parasympathetic activity, ganglionic blockers remove predominant autonomic tone, leading to:

Organ/System	Predominant Autonomic Tone	Effect of Ganglionic Blockade
Arterioles	Sympathetic (vasoconstriction)	Vasodilation → Hypotension
Veins	Sympathetic (vasoconstriction)	Venodilation → Blood pooling
Heart	Parasympathetic (vagal tone)	Tachycardia
Eye (Iris & Ciliary muscle)	Parasympathetic (pupil constriction, accommodation)	Mydriasis, cycloplegia (blurred vision)
GI tract	Parasympathetic (motility)	Constipation, ↓ secretions
Bladder	Parasympathetic (detrusor contraction)	Urinary retention
Sweat glands	Sympathetic (cholinergic)	Anhidrosis (↓ sweating)

- **Clinical uses of ganglionic blockers**

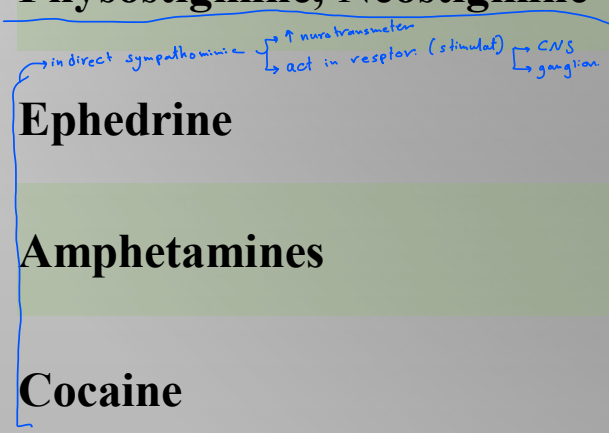
- ganglionic blockers are rarely used today due to better alternatives. however, they had historical and niche applications:

- trimethaphan: rapid BP control in hypertensive crises. aortic aneurysm
- mecamylamine: Tourette's syndrome, nicotine withdrawal. بعدي الد دمر
- hexamethonium: first antihypertensive (no longer used due to severe side effects).

Drugs with Ganglionic Stimulation as a Side Mechanism

These drugs stimulate nicotinic receptors in the autonomic ganglia, leading to sympathetic or parasympathetic effects.

Drug	Primary Action	Ganglionic Effects	Clinical Relevance
Varenicline (Chantix)	Partial nAChR agonist (α4β2 subtype)	Mild ganglionic stimulation, autonomic fluctuations	Smoking cessation
Acetylcholine (ACh, exogenous use)	Direct muscarinic & nicotinic agonist	Stimulates both autonomic ganglia	Used experimentally
Carbachol	Non-selective cholinergic agonist	Enhances ganglionic transmission	Used in ophthalmology
Pilocarpine	Muscarinic agonist (M3)	Indirectly stimulates ganglia via vagal effects	Treats glaucoma, xerostomia
Physostigmine, Neostigmine	Acetylcholinesterase (AChE) inhibitors	Increases ACh at ganglia, leading to overstimulation	Myasthenia gravis, reversal of neuromuscular blockade
Ephedrine	Indirect adrenergic agonist	Mild ganglionic stimulation	Used for hypotension, nasal congestion
Amphetamines	CNS stimulant, releases NE & DA	Indirectly enhances ganglionic transmission	ADHD, narcolepsy
Cocaine	Blocks NE, DA, and serotonin reuptake	Causes sympathetic ganglionic stimulation (↑ BP, HR)	Recreational drug, local anesthetic



2. Drugs with ganglionic inhibition as a side mechanism

these drugs block or desensitize autonomic ganglia, leading to hypotension, tachycardia, and autonomic suppression.

Drug	Primary Action	Ganglionic Effects	Clinical Relevance
Nicotine (high dose, toxicity)	Overstimulation → desensitization	Ganglionic blockade → hypotension, paralysis	Nicotine toxicity
Botulinum Toxin (Botox)	Blocks ACh release	Prevents ganglionic neurotransmission	Used for dystonia, spasticity
Curare (Tubocurarine, Pancuronium, Atracurium)	Non-depolarizing NMJ blocker	Weak ganglionic inhibition (↓ BP)	Muscle relaxation (surgery, ICU)
Succinylcholine (high dose, prolonged use)	Depolarizing NMJ blocker	Can cause ganglionic blockade	Short-term muscle paralysis (intubation)

β-Blockers (Propranolol, Atenolol, Labetalol)	Blocks β-adrenergic receptors	May cause reflex ganglionic inhibition	Hypertension, angina, arrhythmias
Reserpine	Depletes NE, DA in presynaptic terminals	Reduces sympathetic ganglionic tone	Hypertension (historical use)
Guanethidine	Inhibits NE release	Sympatholytic effects, ganglionic suppression	Hypertension (obsolete)
Lidocaine (high doses, IV use)	Na^+ channel blocker (local anesthetic)	Can inhibit ganglionic transmission	Antiarrhythmic, local anesthetic
Magnesium Sulfate	Blocks Ca^{2+} channels, NMJ transmission	Weak ganglionic blockade, hypotension	Preeclampsia, eclampsia treatment
Calcium Channel Blockers (Verapamil, Diltiazem)	Inhibits L-type Ca^{2+} channels	May inhibit ganglionic neurotransmission	Hypertension, arrhythmias
α2-Agonists (Clonidine, Methyldopa)	Central sympatholytic	Reduces ganglionic outflow	Hypertension, opioid withdrawal


Thank you!