

Autonomic Nervous System

- **Parasympathomimetic drugs**
- **Parasympatholytics**
- **Sympathomimetics**
- **Sympatholytics**

	Sympathetic	Parasympathetic
Anatomy:		
1- Origin	From 1 st thoracic to 3 rd lumbar segments	-Cranial: (III, VII, IX & X) -Sacral: (S2,3,4)
2- Ganglia	Close to spinal cord	Near or embedded in organs
3- Preganglionic	Short	Long
4- Postganglionic	Long	Short
5- Innervation:	<i>Sympathetic only</i>	<i>Parasympathetic only</i>
<ul style="list-style-type: none"> • Most organs receive dual nerve supply <u>except:</u> 	<ul style="list-style-type: none"> • Dilator pupillae muscle [DPM]. • Erector pili M. • Sweat glands • Adrenal medulla. • Ventricles • Blood vessels 	<ul style="list-style-type: none"> • Constrictor pupillae muscle [CPM]
Physiology:		
<ul style="list-style-type: none"> • Tone 	Blood vessels & sweat glands.	All organs except blood vessels & sweat gland.

Autonomic Nervous System

The autonomic nervous system (ANS) is concerned primarily with visceral functions such as cardiac output, blood flow to various organs, and digestion, which are necessary for life.

**The autonomic nervous system has two divisions:
sympathetic & parasympathetic.**

	Sympathetic	Parasympathetic
• Actions	They are antagonistic except for atrial conduction and salivation [both↑]	
• Cardiovascular: - Heart	↑all cardiac properties.	↓ all cardiac properties.
- Blood vessels	-VC of skin & mucous membrane blood vessels. -VD of coronary & skeletal blood vessels	Not innervated
-Blood pressure	Increased	Decreased
• Eye	Active mydriasis [++DPM]	1-Miosis[+++CPM] 2- Accommodation for near vision 3-↓↓IOP
• Bronchi	Bronchodilation	Bronchoconstriction

	Sympathetic	Parasympathetic
• GIT & Urinary tract	Relax wall& contract sphincters	Contract wall& contract sphincters
• Genital	Ejaculation in male Relaxation of uterus in female	Erection in male
• Exocrine glands: - Salivary - Sweat	Thick & viscid Increase	Watery No effect
Neurotransmitters		
• Ganglia	Ach	Ach
• Postganglionic	Norepinephrine(NE) <i>except</i> in sweat glands Ach is released	Ach

Sympathetic

Parasympathetic

- Synthesis

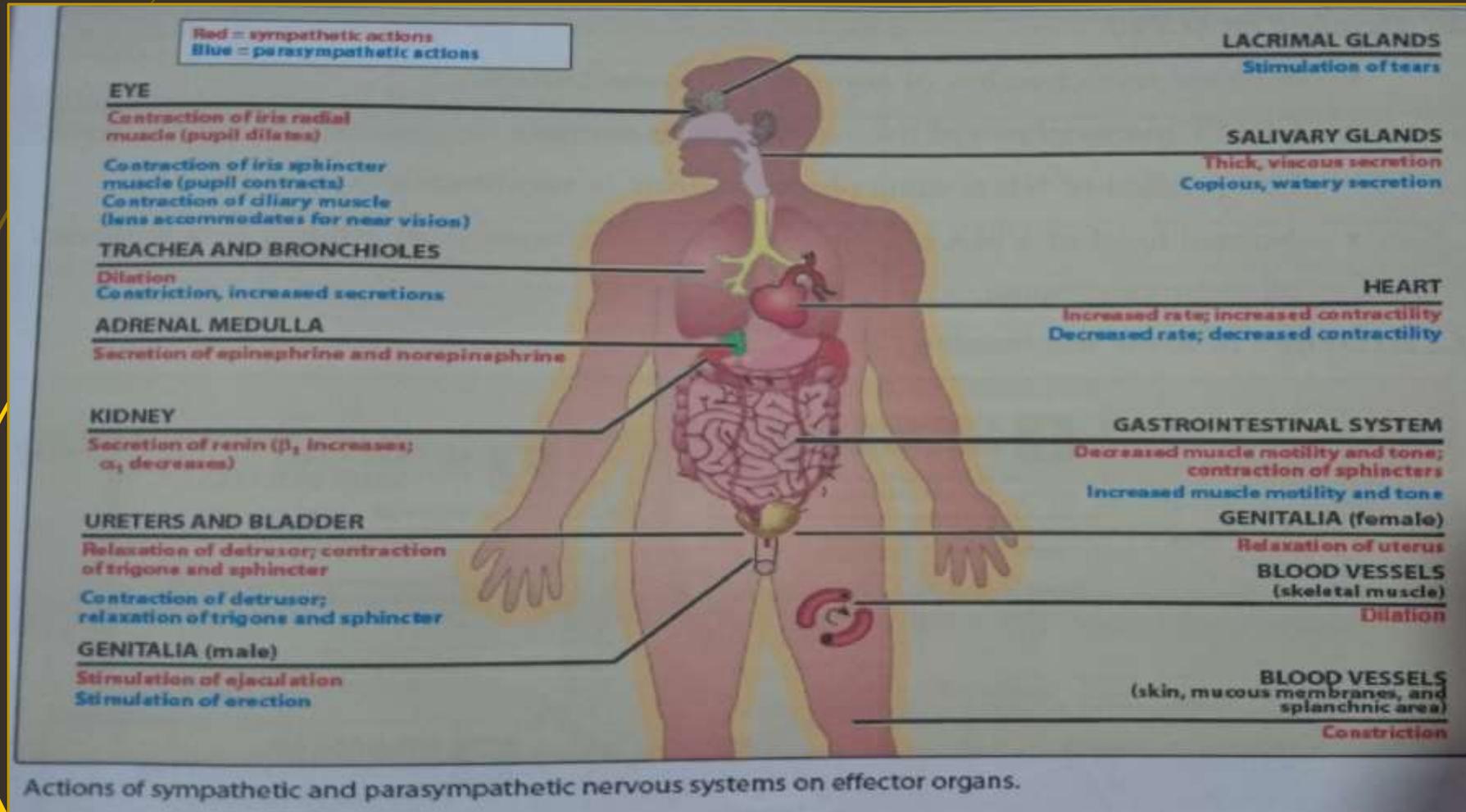
1. Phenylalanine → tyrosine (by hydroxylase)
 2. Tyrosine → DOPA (by tyrosine hydroxylase)
 3. DOPA → dopamine (by dopa decarboxylase)
 4. Dopamine is actively transported into synaptic vesicles by carrier system
 5. Finally, NE is formed by hydroxylation of dopamine (via dopamine B-hydroxylase)
- * In the adrenal medulla & some CNS tracts, epinephrine(adrenaline) is formed via methylation of NE by phenyl ethanolamine N-methyl-transferase [PENMT]

- Choline is transported into cholinergic neurons by carrier system
- Choline is acetylated to Ach by choline acetyltransferase in presence of acetyl CoA

Release of transmitters:

Arrival of impulse to the nerve ending.

- Opening of voltage-activated Ca^{2+} channel → calcium influx into nerve ending.
- Fusion of vesicles with membrane of the nerve ending and exocytosis of the transmitter.



Fate of NE & epinephrine:

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A] Reuptake:

1- Neuronal reuptake [uptake I], 65-70% :

- Active reuptake by neuronal membrane monoamine transporter (MAT).
- **Inhibited by** cocaine, tricyclic antidepressants (TCAs) and guanethedine & guanidril.

2- Vesicular reuptake [uptake III]:

- Follows uptake I to protect NE from monoamine oxidase [MOA].
- **Inhibited by** reserpine.

3- Tissue reuptake [uptake II], 7-13%:

- NE is taken by the target tissue where it is inactivated by MAO (in the mitochondria) & catechol orthomethyltransferase [COMT] in cytoplasm.
- **Inhibited by** corticosteroids

B] Metabolism (15%):

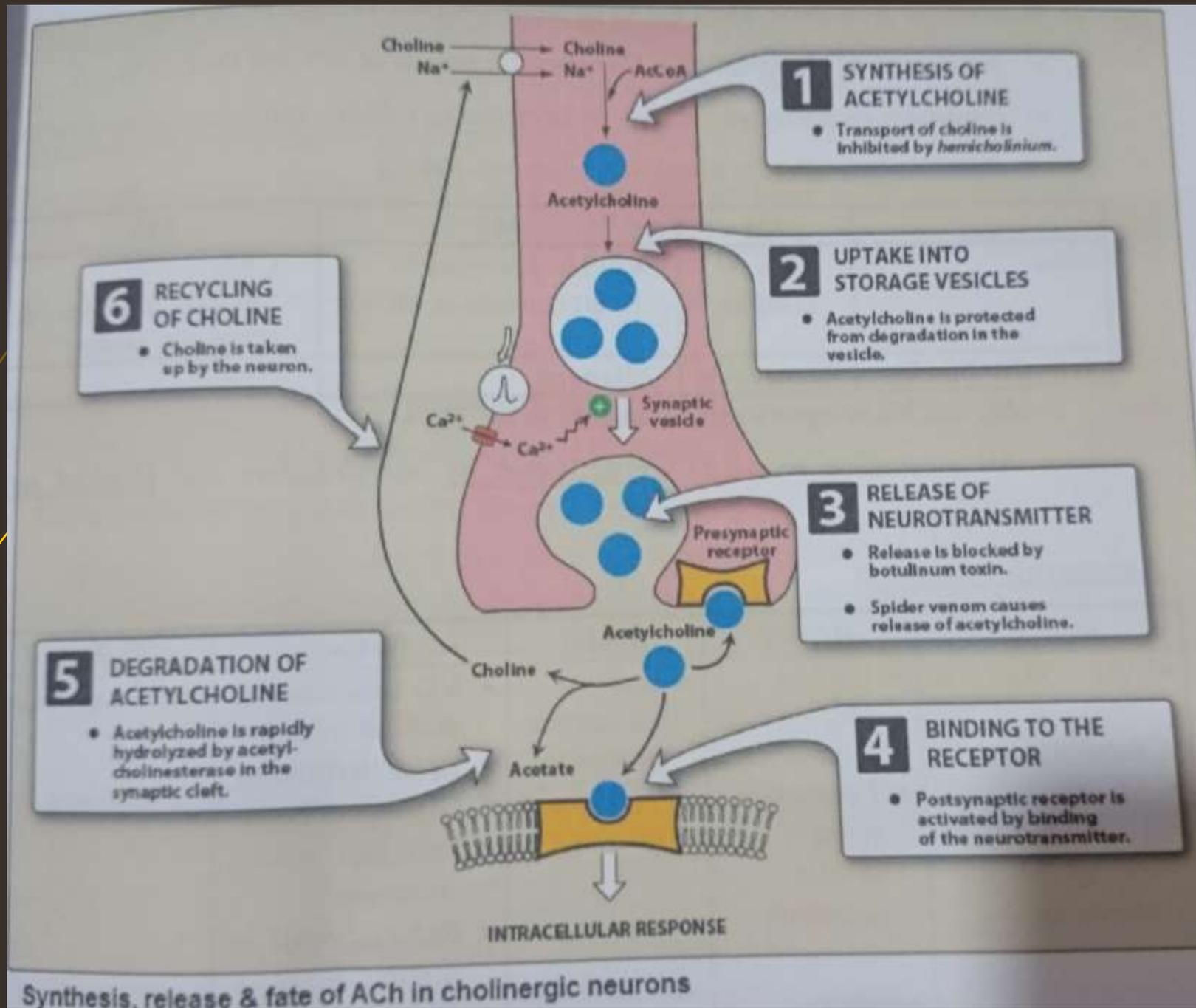
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- MAO in mitochondria of nerve endings and tissues.
- COMT in cytoplasm of tissues but not in nerves.
- End product of NE & epinephrine in urine is vanilmandelic acid [VMA]
- Normal level of VMA is 2-6mg/24hrs. VMA more than 50mg/24hrs indicates pheochromocytoma.

C] Excretion in urine unchanged (5%)

Fate of ACh: Metabolism by cholinesterase [2types]

	True cholinesterase	Pseudo-cholinesterase
Sites	Cholinergic structures, RBSs and CNS.	Contract wall & contract sphincters
Specificity	ACh, Methacholine	Non specific- destroys Ach, procaine and succinylcholine.
Regeneration	In 3 months	In 3 weeks



Autonomic Receptors

12 Cholinergic receptors: Cholinergic receptors are classified into:

A. Nicotinic receptors: They are directly coupled to Na^+ channels and mediate fast excitatory synaptic transmission at:

1. The neuromuscular junction.
2. Autonomic ganglia.
3. Adrenal medulla.
4. Various sites in CNS

B. Muscarinic receptors: They are **G-protein-coupled receptors** causing :

- Activation of phospholipase C (hence formation of IP3 and DAG) [$\text{M}_{1,3,5}$].
- Inhibition of adenylyl cyclase \longrightarrow decrease in cAMP, activation of potassium channels or inhibition of calcium channels [$\text{M}_{2,4}$].

	M1	M2	M3
Sites	- CNS - Ganglia	- CNS & presynaptic - Heart (mainly of atria)	- CNS - Smooth muscles & secretory glands
Selective blocker	Pirenzepine	Gallamine	

- M₄ and M₅ receptors present mainly in the CNS.
- All muscarinic receptors are activated by acetylcholine and blocked by atropine.

Adrenergic receptors:

α_1 (Gg)	α_2 (Gi)	β_1 (Gs)	β_2 (Gs)	β_3 (Gs)
<ul style="list-style-type: none">• VC(skin& mucous membranes)• Mydriasis• $\uparrow\uparrow$ tone of urinary bladder sphincter	<ul style="list-style-type: none">• Inhibits NE, Ach release• Decreases renin& insulin secretion	<ul style="list-style-type: none">• Increase all cardiac properties• $\uparrow\uparrow$ renin release	<ul style="list-style-type: none">• VD(coronary & skeletal muscle)• Bronchodilation• Glycogenolysis• Increases insulin secretion• Relaxes wall of uterus• Hypokalemia & tremors	<ul style="list-style-type: none">• $\uparrow\uparrow$ Lipolysis

Autonomic drugs

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1. Parasympathomimetics.
2. Parasympatholytics.
3. Sympathomimetics.
4. Sympatholytic.
5. Ganglion stimulants & ganglion blockers.

Parasympathomimetics [Cholinomimetic drugs]

Acetylcholine (ACh) receptor stimulants and cholinesterase inhibitors together comprise a large group of drugs that **mimic** Ach (cholinomimetics or parasympathomimetics).

Cholinoceptor stimulants: they are either:

1-Direct-acting cholinomimetic agents bind to and activate muscarinic and/or nicotinic receptors: **1- Choline esters:**

* Ach

* Methacholine

* Carbachol

* Bethanechol

2- Cholinomimetic alkaloids: * Pilocarpine

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II-Indirect-acting agents inhibit cholinesterases → increase the endogenous

Ach in synaptic clefts and neuroeffector junction → stimulate cholinceptors.

The are classified into:

Reversible	Irreversible
<ul style="list-style-type: none">■ Physostigmine & neostigmine.■ Neostigmine substitutes: (edrophonium, pyridostigmine, ambenonium, benzpyrinium and demecarium)	<ul style="list-style-type: none">■ Organophosphorus compounds:<ul style="list-style-type: none">- Echothiophate -Isoflurophate- Ware gases e.g. sarin & soman.- Thiophosphate insecticides e.g. parathion & malathion.

I-Direct Cholinomimetics

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(1) Choline esters

They are poorly absorbed and poorly distributed into CNS (they are hydrophilic).

Choline Ester	Susceptibility to cholinesterase	Muscarinic action	Nicotinic action	Selectivity
Acetylcholine	True and pseudo	+++	+++	No selectivity
Methacholine	True only	+++++	None	Heart
Carbachol	Non	++	+++	Eye,GIT,urinary
Bethanechol	Non	++	None	GIT,urinary

Pharmacological actions:

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Eye:

Muscarinic (M_3)

- 1) Contraction of constrictor pupillae muscle → resulting in miosis.
- 2) Contraction of the ciliary muscle.
 - As a result of 1&2 → the iris is pulled away from the angle of the anterior chamber, and the trabecular meshwork at the base of the ciliary muscle is opened. Both effects facilitate aqueous humor outflow into the canal of Schlemm, and ↓ I.O.P .
- 3) Accommodation for near vision.

Nicotinic: Lid twitches due to activation of nicotinic receptors in the eye lid muscles.

When applied to eye, carbachol → miosis & lid twitches (muscarinic and nicotinic).

Cardiovascular System

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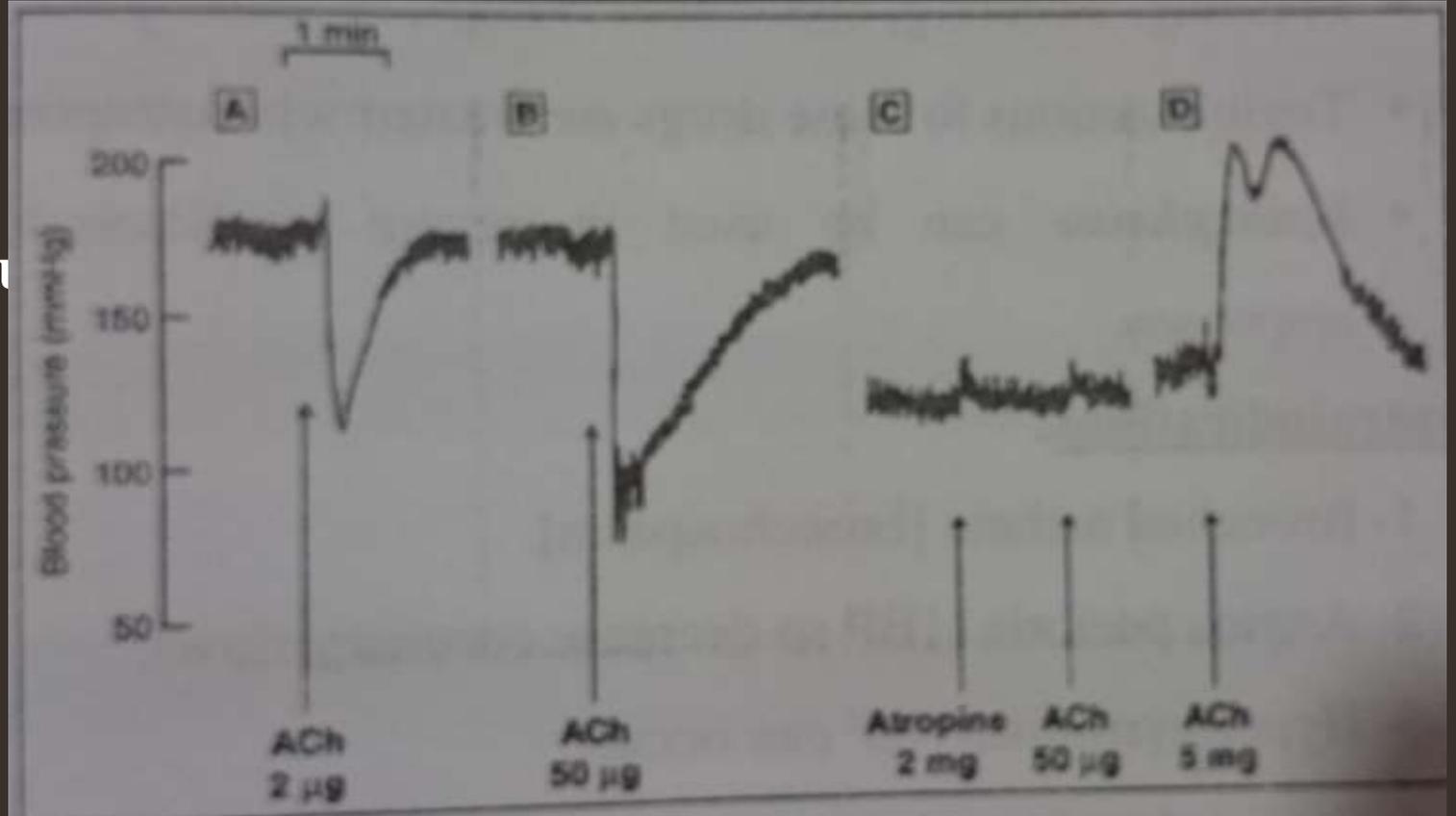
1) Vasodilation: Stimulation of M_3 \longrightarrow production of NO (endothelium – derived relaxing factor), which diffuses to smooth muscles cells of blood vessels \longrightarrow \uparrow cGMP \longrightarrow VD.

2) Bradycardia & delay AV conduction are due to stimulation of M_2

- Experimental IV injection of a small dose of Ach \longrightarrow hypotension.
- If large doses of Ach are injected after atropine [muscarinic blocker] \longrightarrow hypertension, due to stimulation of adrenal medulla and autonomic ganglia [nicotinic action of Ach] \longrightarrow release catecholamines into the circulation and at postganglionic sympathetic nerve ending \longrightarrow reversal of action of Ach on blood pressure.

Atropine can reverse the hypotensive action of parasympathomimetics having both nicotinic and muscarinic actions [ACh, carbachol & anticholinesterase], but only abolish the hypotensive effect of drugs having only muscarinic actions [Methacholine & Pilocarpine]

The effect of intravenous injection of ACh on the pressure



Gastrointestinal and Urinary Tracts ($M_{2,3}$) : Stimulation of the wall (M_3) and relaxation the sphincters (M_2).

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Respiratory System:

- Bronchospasm
- Increase bronchial secretion

This combination of effects can cause symptoms, especially in individuals with asthma.

Exocrine Glands (M_3) :

- Stimulate secretion of all glands [sweat, lacrimal, salivary, nasopharyngeal glands, gastric, pancreatic and intestinal].

Neuromuscular Junction (N_m) :

- Activation of N_m receptors results in Na influx and depolarization of skeletal muscle with muscle contraction. High concentration of Ach results in persistent depolarization → muscle weakness and paralysis.

Clinical uses:

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Bethanechol is very occasionally used in post operative urinary retention and paralytic ileus.

- It acts mainly on M₃ receptors and has little effect on the heart.

Ach, Carbachol & methacholine are used as experimental tools.

Side effects:

- Flushing , sweating, abdominal cramps, bronchospasm, headache, and salivation .
- Toxic reactions to these drugs are treated with *atropine*.
- *Epinephrine* can be used in severe cardiovascular or bronchoconstrictor responses.

Contraindications:

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- 1- Bronchial asthma [bronchospasm].
- 2- Angina pectoris [↓ BP so decrease coronary flow].
- 3- Hyperthyroidism [AF can occur].
- 4- Peptic ulcer [++ gastric secretion].
- 5- Hypotension [cause vasodilation].

2) Cholinomimetic alkaloids (Pilocarpine)

- Alkaloid from leaves of Pilocarpus Jaborandi
- Tertiary amine so:
 - well absorbed from most sites of administration.
- Crosses BBB (avoided in Parkinsonism) Not metabolized by Ch.E → long duration.
 - Excreted in urine.
- Has muscarinic action, but no nicotinic actions (*its hypotensive effect is abolished by atropine*)

- Has a specific action on :

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* Eye [no lid twitches].

* Secretions [salivary & sweat].

Clinical uses:

1. Glaucoma.
2. Counteracts action of mydriatics after fundus examination.
3. To cut recent adhesion between iris and lens [alternatively with mydriatics]
4. Promotes hair growth [↑ blood flow to hair follicle].
5. Sialagogue in xerostomia.

II-Indirect Cholinomimetics

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[Cholinesterase Inhibitors or Anticholinesterases]

They are classified into:

	Reversible	Irreversible
Binding to Ch.E.	Loose	Firm
Activity of Ch.E.	Enzymes can regain activity	Enzymes cannot regain activity
Duration of action	Short	Long(till synthesis of new enzymes)
Examples	Physostigmine, neostigmine and neostigmine substitutes	Organophosphorus compounds

According to the binding with Ch.E. enzymes:

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1- Bind reversible by electrostatic bond with **anionic** site → Edrophonium

2- Bind reversibly with both **anionic & esteratic** sites

Physostigmine, neostigmine.

3- Phosphorylation of the esteratic site → Organophosphorus compounds

(1) Reversible cholinesterase Inhibitors

	Physostigmine	neostigmine
Source & chemistry	Natural plant alkaloid Tertiary amine	Synthetic Quaternary ammonium compound
Absorption & distribution	Complete oral absorption Passes BBB	Partial oral absorption . Cannot pass BBB
Metabolism	Both are metabolized by cholinesterase	
Actions	<p>1-Muscarinic (eye): Miosis, accommodation for near vision, ↓↓ IOP, lid twitches, lacrimation]</p> <p>2- Nicotinic → Muscle twitches (Indirect action only)</p> <p>3- CNS: Stimulation (convulsions in high doses)</p>	<p>1-Muscarinic (mainly GIT & urinary tract)</p> <p>2- Nicotinic → Muscle twitches (direct & Indirect action)</p> <p>3- CNS: no action</p>

Clinical uses:

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Physostigmine :

A) Eye drops:

1- Glaucoma.

2- Counteracts action of mydriatics after fundus examination.

3- To cut recent adhesion between iris and lens [alternatively with mydriatics].

B) Alzheimer dementia **but** newer drugs are better.

C) Atropine toxicity: It antagonizes central and peripheral action **but** not preferred due to CNS toxicity

Neostigmine :

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- 1- Reversal of paralysis induced by non-depolarizing neuromuscular blockers during surgical operations.
- 2- Postoperative retention of urine (Catheterization is better alternative).
- 3- Postoperative paralytic ileus.
- 4- Myasthenia gravis.
- 5- Antidote to atropine toxicity.
- 6- Glaucoma.

Toxicity:

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Muscarinic : Bradycardia, hypotension, bronchospasm, miosis, vomiting, diarrhea and ↑↑ secretions.

Nicotinic : muscle twitches.

CNS: (with physostigmine only)

- Convulsions & collapse
- Coma
- Death from RC depression

Treatment of toxicity:

- 1- Stomach wash.
- 2- Oxygen and artificial respiration.
- 3- Atropine.
- 4- Anticonvulsant in case of seizures.

	Edrophonium	Pyridostigmine Ambenonium	Benzpyrinium	Demecarium
Selectivity	Skeletal muscle	Skeletal muscle	GIT & Urinary tract	Eye
Uses	<p>1- Diagnosis of myasthenia gravis → improves</p> <p>2- Treatment of myasthenia crisis</p> <p>3- Differentiation between myasthenia crisis & cholinergic crisis:</p> <ul style="list-style-type: none"> ▪ Myasthenia crisis improves ▪ Cholinergic crisis worsens 	Treatment of myasthenia gravis (longer duration than neostigmine & more specific)	<p>1- Postoperative urine retention</p> <p>2- Postoperative paralytic ileus</p>	<ul style="list-style-type: none"> • Glaucoma

Myasthenia gravis

Muscle weakness and increased fatigability resulting from a failure of neuromuscular transmission due to formation antibodies against motor end plate
→ loss of nicotinic receptors.

Diagnosis: Edrophonium IV or neostigmine SC + Atropine [to block unwanted muscarinic actions] → improvement.

Treatment :

- 1- Neostigmine or Pyridostigmine + Atropine.
- 2- Adjuvant treatment : ephedrine or caffeine (potentiates neostigmine & facilitate NM transmission
- 3- Others : to decrease antibodies
 - Steroids (e.g. prednisolone) or immunosuppressant drugs e.g. azathioprine.
 - Plasmapheresis to wash antibodies.
 - Thymectomy.

Drugs contraindicated in myasthenia gravis:

1-Skeletal muscle relaxants.

2- Aminoglycosides

3- β -blockers.

N.B.

- **Myasthenia crisis:** severe muscle weakness due to *under treatment* with anticholinesterase drugs \longrightarrow Edrophonium produces muscle improvement.
- **Cholinergic crisis:** severe muscle weakness due to *over treatment* with anticholinesterase drugs [sustained depolarization] \longrightarrow Edrophonium produces more weakness.

Alzheimer's disease

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Alzheimer's disease (AD) is a common age-related dementia.

The main pathological features of AD comprise amyloid plaques & loss of neurons (*particularly cholinergic neurons of the basal forebrain*).

Drugs approved for the treatment of AD:

1- Cholinesterase inhibitors:

- **Tacrine** is a drug with anticholinesterase activity, has been used for the treatment of mild to moderate Alzheimer's disease but hepatotoxic.
- **Donepezil, galantamine, and rivastigmine** are newer, more selective and lack the hepatotoxic effect of tacrine.

2- Memantine [NMDA receptor antagonist] → inhibiting glutamate-induced excitotoxicity and neuronal damage. The drug improves cognitive function in moderate-to-severe AD.

(2) Irreversible cholinesterase Inhibitors

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- Echothiophate & Isoflurophate → eye drops for glaucoma.
- Ware gases [e.g. sarin & soman].
- Thiophosphate insecticides [e.g. Parathion & Malathion]

Pharmacokinetics:

- All organophosphates (except for **echothiophate**) are well absorbed from the skin, lung, gut, and conjunctiva and distributed to all parts of the body, including CNS.
- The thiophosphate insecticides (parathion & malathion) are prodrugs. They are rapidly activated in insects and vertebrates. **Malathion** (not parathion) is rapidly metabolized by other pathways to **inactive products** in **birds** and **mammals** but **not in insects** (considered to be relatively safe).

N.B. **Fish** cannot detoxify malathion

Pharmacodynamics:

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- They cause irreversible inhibition of cholinesterase by formation of *covalent bond* with its esteratic site.
- At first loose then non-competitive block [aged enzyme].
- Accumulation of huge amount of Ach → over-activation of cholinceptors at NM junction and at autonomic and central nervous system.
- Their actions ended by resynthesis of new cholinesterases.

Organophosphorus poisoning

Causes :

- 1- **Occupational** inhalation or contamination of skin, clothes and food with insecticides.
- 2- **Suicidal.**
- 3- **Wars.**

Clinical manifestations:

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- **Muscarinic** : Salivation, miosis, sweating, vomiting, colic, bradycardia and bronchospasm.
- **Nicotinic** : Muscle fasciculation then muscle weakness and paralysis.
- **CNS** : Confusion, convulsions the CNS depression.
- **Cause of death** : Respiratory failure.

Treatment:

1. Remove contaminated clothes and wash the skin by soap or NaHCO₃.
2. Aspiration of secretion and artificial respiration.
3. Gastric lavage.
4. **Atropine** 1 mg IV every 10 minutes till full atropinization [dryness of mouth, mydriasis and tachycardia]. The patient is kept full atropinized for 24 hrs.

5. Cholinesterase reactivators [oximes]:

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❖ **Pralidoxime (PAM):** [30mg/kg bolus dose then 8mg/kg/hr IV infusion until clinical improvement] can break the bond between organophosphates and the enzyme, so the enzyme becomes free and hydrolyzes Ach at the receptors.

❖ **Diacetylmonoxime (DAM):** like pralidoxime but can cross BBB and reactivate central cholinesterase.

6. Diazepam for convulsions, and artificial ventilation for respiratory failure.

Note:

- Early after intoxication and formation of organophosphate-enzyme complex → spontaneous reactivation of the enzyme can occur that can be hastened by oximes.
- Within a few hours, the organophosphate-enzyme complex loses one alkyl group and is no longer susceptible to reactivation → ageing. So cholinesterase reactivators should be administered as early as possible.

Parasympatholytics

[Muscarinic Antagonists or Antimuscarinics]

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Muscarinic receptors blockers are *competitive antagonists*.

1. Natural belladonna alkaloids [atropine and hyoscine]
2. Synthetic atropine substitutes.

Atropine

- Natural belladonna alkaloids .
- Tertiary amine.

Pharmacokinetics :

- Well absorbed from all sites except intact skin.
- Passes BBB.
- Metabolized in liver.
- Excreted in urine [1/3 unchanged], enhanced by *acidification of urine*.

Pharmacodynamics :

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A. Antimuscarinic actions:

- 1) Inhibition of secretions [↓↓ all secretion except milk, bile and urine]:**
 - ↓↓ Salivary secretion → dry mouth.
 - ↓↓ Lacrimal secretion.
 - ↓↓ Sweat → dry skin [atropine fever].
 - Gastric secretion is only slightly reduced.
 - Mucociliary clearance in the bronchi is inhibited, so that residual secretions tend to accumulate in the lungs. **Ipratropium** lacks this effect.

2) Cardiovascular system:

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- Tachycardia is most pronounced in young people, in whom vagal tone at rest is highest; it is often absent in the elderly.
- If injected *slowly IV* → **paradoxical bradycardia** followed by tachycardia

This, possibly, is due to:

- ✓ Earlier M₂ inhibition (relieves the inhibitory effect on Ach release) → ↑↑ Ach release.
- ✓ Central action [stimulation of CIC].
 - Blood vessels are unaffected at therapeutic doses.
- ✓ Toxic doses → atropine flush (actual cause is unclear, but it may be due to compensatory VD in blush area to increase heat loss to compensate inhibition of sweat).
 - Blood pressure is unaffected.
 - Atropine reverses hypotension of Ach, carbachol n& neostigmine [M&N].
 - It abolishes hypotension of methacholine, bethanechol & pilocarpine [M].

3) eye:

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- Passive mydriasis.
- Paralysis of accommodation(**cycloplegia**), so that near vision is impaired.
- ↑↑ IOP → dangerous in patients suffering from *narrow-angle glaucoma*.

4) Gastrointestinal tract:

- Relaxes wall [antispasmodic] and constricts sphincters.
- Inhibits secretion → constipation.

5) Urinary tract:

- Relaxes wall and constrict sphincters of the bladder.
- Relaxes ureter.

6) Respiration :

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- Bronchodilation and reduced secretions [viscid and difficult to expel].

B. Effects on the CNS:

It has both stimulant and depressant actions (mainly stimulant).

- Stimulates RC (respiratory center) & CIC (cardiac inhibitory center).
- Mild restlessness; higher doses cause agitation, hallucination, mania, convulsions followed by CNS depression.
- Inhibit basal ganglia and *vomiting center*.

Clinical uses:

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1) Preanesthetic medication: (Atropine is usually used, but hyoscine is preferred in thyrotoxicosis as it causes less tachycardia).

- Reduces secretions.
- ++ RC.
- Bronchodilatation .
- Counteracts excess vagal tone & bradycardia induced by general anesthetics

2) CVS: heart block due to digitalis, infraction, verapamil, or β -blockers.

3) Organophosphorus poisoning [atropine is life-saving].

4) GIT: In colic, peptic ulcer and antiemetic[in motion sickness, hyoscine is used]

5) CNS: Parkinson`s disease.

6) Respiration: not preferred in bronchial asthma (inhibits mucociliary movement and bronchial secretion becomes viscid and difficult to expel).

7) *Eye* : mydriatic in *children* & in iritis (alternatively with miotics to prevent adhesions).

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- Accurate measurement of refractive error in uncooperative patients e.g. young children, requires ciliary muscle paralysis. For adults and older children, the shorter acting drugs are preferred.
- α -adrenoceptor stimulant drugs e.g. phenylephrine, produce a short-lasting mydriasis that is usually sufficient for fundoscopic examination. So, atropine & its substitutes are preserved for cases when cycloplegia or long duration is needed

Atropine toxicity:

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- Dry mouth and hot, dry and flushed skin.
- Mydriasis, blurred vision and ↑↑ IOP.
- Tachycardia.
- Urine retention especially in patients with benign prostatic hyperplasia.
- Body temperature is frequently elevated. Unfortunately, children, especially infants, are *very sensitive* to the hyperthermic effects of atropine.
- Agitation, delirium, convulsions followed by coma and depression of RC [cause of death]

Treatment:

- Gastric lavage with tannic acid.
- Artificial respiration with oxygen.
- Cold fomentation.
- Diazepam.
- Neostigmine 1mg SC [antidote]- physostigmine is dangerous.

Contraindications:

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1. Narrow angle glaucoma.
2. Patients with benign prostatic hyperplasia (BPH).
3. Angina and arrhythmia.
4. Constipation and ileus.

Atropine substitutes

1) Antisecretory antispasmodics:

- a- Atropine methyl nitrate → to relax pylorus in hypertrophic pyloric stenosis.
- b- Hyoscine N-butyl bromide → to relax spasm of GIT and urinary tract.
- c- Propantheline and oxyphenonium → to relax spasm of GIT.
- d- Pirenzepine & telenzepine → in peptic ulcer [selective M_1 blockers, reduce gastric secretion]

2) Antiasthmatic: (Ipratropium & tiotropium) given by inhalation with little effect on secretion & ciliary movement.

Drugs having atropine-like action:

1. Atropine substitutes.
2. Tricyclic antidepressants.
3. Pethidine.
4. Some:
 - Antipsychotics [typical group]
 - Antihistaminics [first generation]
 - Antiarrhythmics [quinidine and disopyramide]

3) For urinary incontinence: Oxybutynin, emepronium and tolterodine (M_3 -selective).

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4) Antiparkinsonian: Benztropine and benzhexol.

5) Mydriatics:

	Atropine	Homatropine	Tropicamide & Cyclopentolate
Duration	7-10 days	24hrs	6hrs
Cycloplegia	+++	++	+
Uses	<ul style="list-style-type: none">■ Iritis■ Measurement of refractive errors in children	<ul style="list-style-type: none">■ Fundus examination■ Measurement of refractive errors	