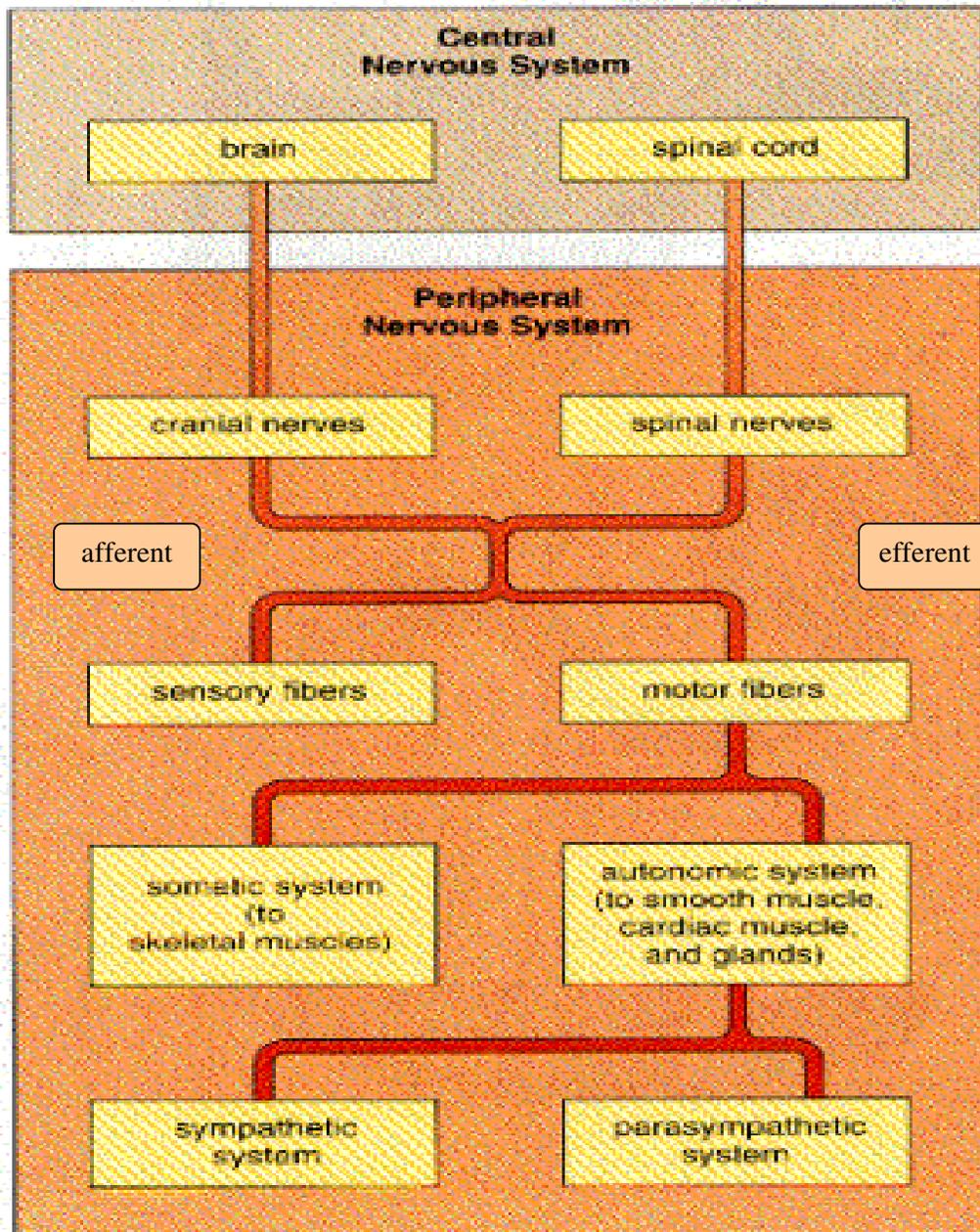
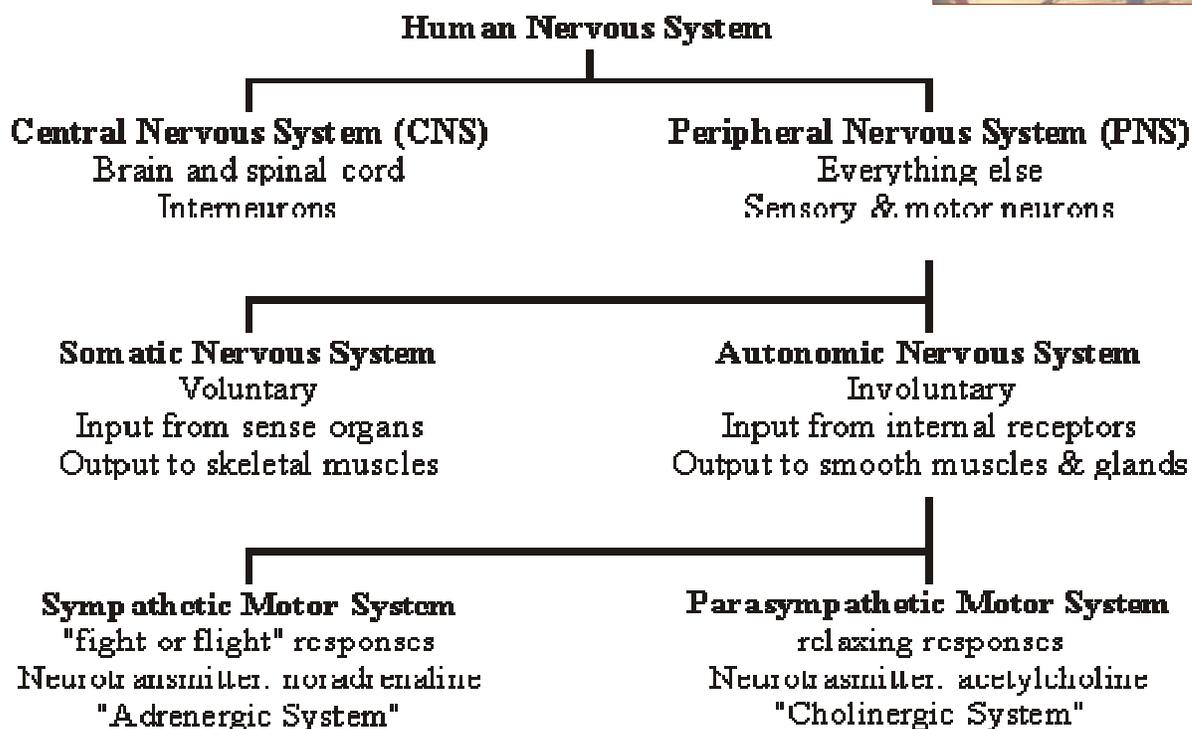




Introduction to the nervous system

nervous system is divided into :
central and peripheral nervous system





Sympathetic	Parasympathetic
Thoracolumbar Preganglionic fibers leave CNS through first thoracic to second lumbar segments of spinal nerves	Craniosacral Preganglionic fibers leave the CNS through cranial nerves (3,7,9,10) and 2,3,4 sacral segments of spinal cord
Preganglionic is shorter than postganglionic	Longer
Ganglia form chain near the SP cord	Ganglia present near the organ innervated or nearly embedded in it
Ergotropic system Energy expenditure (consumption)	Trophotropic system Growth



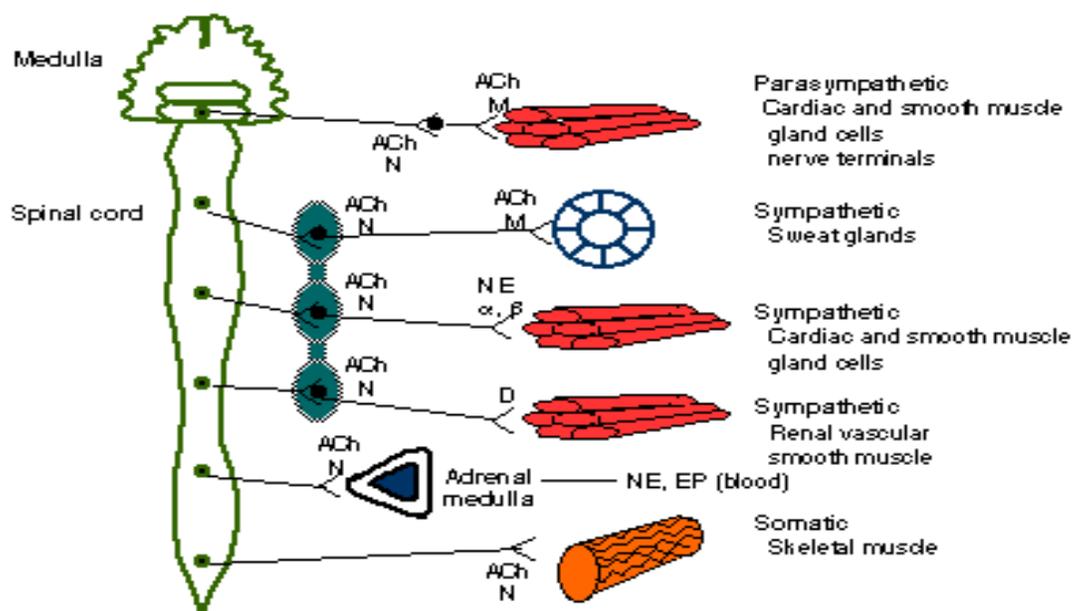
some notes u have to put them in your mind regarding the autonomic nervous system

☐ within the autonomic nervous system 2 neurons are required to reach a target organ preganglionic and postganglionic neuron .

☐ preganglionic neuron originate in the CNS. it forms a synapse with the postganglionic, the cell body of which is located in autonomic ganglia .

☐ all preganglionic neuron release Ach as their transmitter, the acetylcholine (Ach) binds to nicotinic receptors on the postganglionic cell .

☐ all of the parasympathetic postganglionic fibers release Ach . at the target organ Ach interact with muscarinic receptor .



☐ most of the sympathetic postganglionic fibers release NE (norepinephrin). at the target organ NE interacts with a variety of receptor.

☐ most of the vascular smooth muscle is innervated solely by the sympathetic nervous system . this means that blood pressure and peripheral resistance are **controlled by the sympathetic nervous system** .



Cholinergic drugs

Cholinergic Transmission:

- 1- synthesis of acetylcholine (ACh)
- 2- storage
- 3- release
- 4- metabolism (fate)

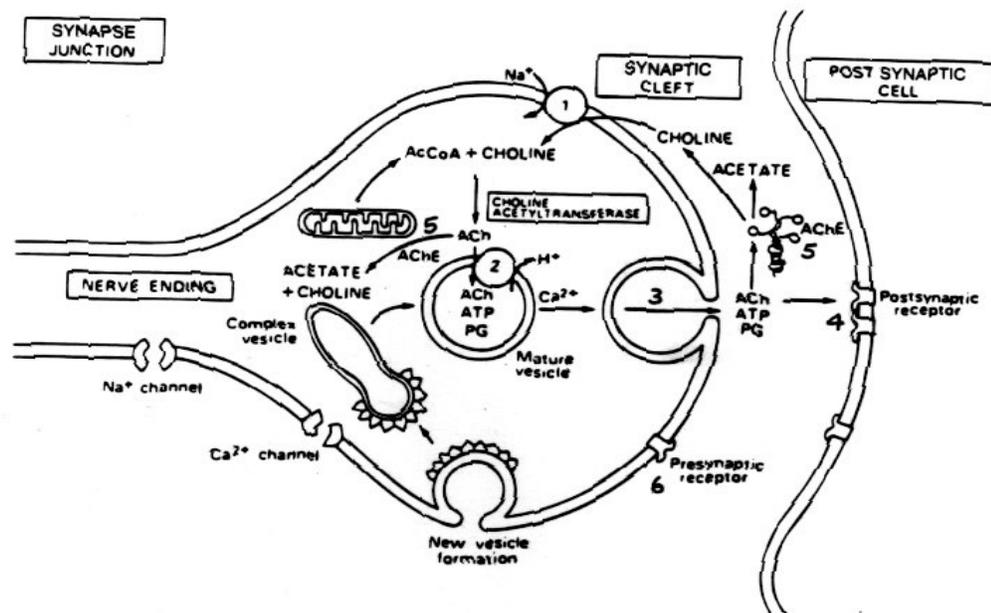


Fig. 17-2. General cholinergic nerve junction showing location of receptor sites and biosynthesis, storage, release, and hydrolysis of acetylcholine. (From B. G. Katzung, Introduction to autonomic pharmacology, in *Basic and Clinical Pharmacology*, B. G. Katzung, Ed., Norwalk, CT, Appleton & Lange, 1992.)

Synthesis:

- choline is transported into presynaptic nerve terminals by carrier (inhibition by: hemicholinium, triethylcholine).
- Choline + acetyl CoA \Rightarrow ACh + CoA

Storage :

- ACh is transported into the storage vesicles by second carrier (inhibited by: vesamicol).

Release:

- ACh is released upon stimulation.
- Stimulation \Rightarrow influx of Ca \Rightarrow exocytosis of ACh (inhibited by: Mg, aminoglycosides).

Fate:

- acetylcholinesterase enzyme (degrades it).



Sites of Ach Release:

- 1- Neuromuscular junction (motor end plate).
- 2- Autonomic ganglia: all preganglionic nerve fibers of both sympathetic and parasympathetic nerves.
- 3- Parasympathetic post ganglionic fibers.
- 4- Sympathetic post-ganglionic fibers to sweat glands.
- 5- Preganglionic sympathetic nerve to adrenal medulla.

Acetylcholinesterase:

found on both presynaptic and post synaptic membrane

<u>True</u>	<u>Pseudocholinesterase</u>
Specific cholinergic fiber	Non-specific
RBC,s , CSF	Plasma, liver, skin, intestine.
Slow turnover, 120 days	Rapid turnover
Ach, methacholine	Succinylcholine. Butyryl-choline

Cholinergic receptor :

- 1- Central cholinergic receptors (nicotinic – since they are stimulated by low nicotinic concentration-).
- 2- Peripheral cholinergic receptors (muscarinic).

Nicotinic Receptors:

It is cation channels- linked receptors (fast). Remember that ion channel act in millisecond

When nicotinic receptor are stimulated Na channels will open causing depolarization (that's why we said that the nicotinic receptors are cation channels linked receptors)

it's classified into 2 subtypes

- 1- *Nm (muscle)* : found at site of neuromuscular junction
- 2- *Nn (nerve)* : found at autonomic ganglion–sympathetic or parasympathetic ,brain and Adrenal medulla

Peripheral Cholinergic Receptors (Muscarinic)

- $M_1 \Rightarrow M_5$: $M_{1,3,5} \Rightarrow$ excitatory (odd).
 $M_{2,4} \Rightarrow$ inhibitory (even).
- is G-protein linked receptors.
- **Found at:**
CNS, exocrine glands, smooth muscle (GIT, UT, RT).

☐ note : in CNS we found both muscarinic and nicotinic receptors



Receptor	Location	Effect
<u>M1 (neural)</u> <u>Excitatory</u>	CNS Autonomic ganglia Gastric parietal cell	CNS excitation Gastric acid secretion Activation of phospholipase C increase IP3 & DAG → ↑ Ca
<u>M2 (cardiac)</u> <u>Inhibitory</u>	Heart Presynaptic cholinergic fiber	Cardiac inhibition Presynaptic inhibition Inhibition of adenylcyclase (↓cAMP) Opening of K channels
<u>M3 (glandular)</u> <u>Excitatory</u>	Exocrine glands Smooth muscles Vascular endothelium	Secretion Smooth muscle contraction Vasodilation (via nitric oxide NO) Activation of phospholipase C increase IP3 & DAG

■ **Note :** ALL Muscarinic receptors are coupled to G-protein receptor

» activation of M1, M3, M5 lead to → increase inositol triphosphate (Ip3) which lead to increase Ca⁺ (Excitatory effect)

» activation of M2, M4 lead to → decrease adenylate cyclase (Inhibitory effect)

Pharmacological Actions of Ach:

- Nicotinic action.
- CNS action.
- Muscarinic action.

Nicotinic actions:

1- Neuromuscular junction :

- ✓ stimulation => muscle contraction (twitching).
- ✓ High concentration => persistent depolarization and spastic paralysis.

2- Ganglia:

- ✓ stimulation of sympathetic and parasympathetic ganglia.

3- Adrenal medulla:

- ✓ release of catecholamines (A+ NA).

CNS Actions:

1- Nicotinic actions:

- ✓ anti-diuretic hormone secretion from hypothalamus.
- ✓ Activation of Renshaw cells.
- ✓ Inhibition of motor fibers.

2- Muscarinic actions:

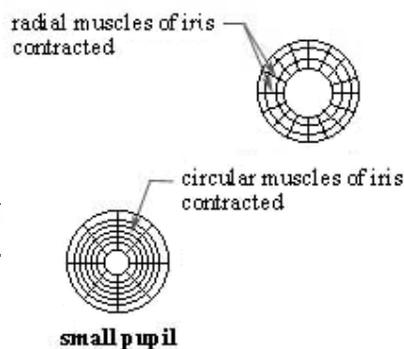
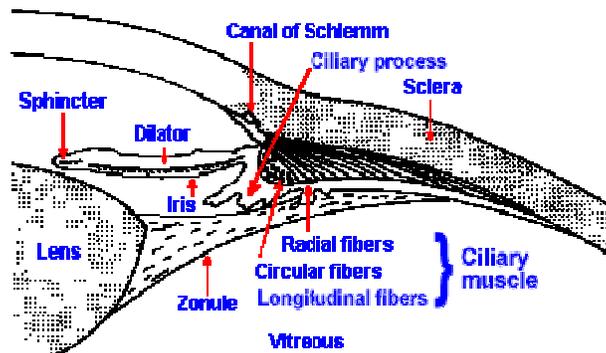
- ✓ Ach is involved in memory and arousal.
- ✓ Parkinsonism. (↓ in dopamine and ↑ in Ach)



<u>Organs</u>	<u>Response</u>
Eye: - sphincter muscle of iris. - ciliary muscle	- contraction (miosis). - contraction for near vision.
Heart: - S.A. node. - Atria. - A.V.node. - Ventricles.	- decrease in rate (negative chronotropy). - ↓ Contractile strength (-chronotropy) + ↓ refractory period. - ↓ Conduction velocity(-dromotropy) + ↑ refractory period. - Small in contractile strength.
Blood vessels: - artery. - vein.	} Dilation via EDRF (endothelium derived relaxing factor) } Constriction (high dose direct effect).
Lung: - bronchial muscle. - bronchial glands.	- constriction (bronchconstrictor). - stimulation
GIT: - motility. - sphincters. - secretion	- increase. - relaxation. - stimulation.
Urinary bladder: - detrusor. - trigone + sphincter	- contraction. - relaxation.
Glands: Sweat, salivary, lacrimal, nasopharyngeal glands.	Secretion

■ some notes regarding the responses of the eye :

» the responses in the eye can trip up . so there's one way to remember these responses is to recognize that radial muscle causes dilatation (mydriasis) and the circular muscle causes constriction (miosis). that is , there are no d's in any of the words relating to constriction.
 » note there are two muscle of the iris one is the radial the another is the circular . the one that concerned with the mydriasis is the radial as we mention before and it look as a radiation from the pupil (look at the pictures)
 now imagine how each muscle do its action





Cholinomimetic drug (cholinergic drugs):

- ▶ we can call it *Parasympathomimetics* because it produce effect like the parasympathetic.
- ▶ in fact, cholinergic drug (agonist) considers all the drug that ↑ activity in cholinergic neurons.
- ▶ cholinomimetic is called so, because they mimic the action of Ach (does what Ach does).

Types:

1- Direct cholinomimetic (act on the receptors directly):

- ✓ act by direct stimulation of nicotinic or muscarinic receptors.

Activation of muscarinic receptors results in the following responses:

Eye	Miosis (constriction of pupil)
Cardiovascular	Decrease in heart rate
Respiratory	Bronchial constriction and increased secretions
Gastrointestinal (GI)	Increased motility, relaxation of sphincters
Genitourinary (GU)	Relaxation of sphincters and bladder wall contraction
Glands	Increased secretions

Activation of nicotinic receptors results in muscle contraction (fasciculations and weakness).

2- Indirect cholinomimetic:

- ✓ act indirectly by inhibiting Acheesterase thus prevent the degradation of Ach (prolong action of Ach).

Direct cholinomimetic:

- a. Natural occurring alkaloid, e.g. pilocarpine. note most of the drugs end with the suffix -ine ,it will be alkaloids (plant derivative)
- b. Choline ester (not natural), e.g.:
 - ✓ Ach.
 - ✓ Methacholine.
 - ✓ Carbachol.
 - ✓ Bethanichol.



Indirect Cholinomimetics (anti-cholinesterase):

a. Reversible:

▣ **note** : also called cholinesterase inhibitors : they compete with Ach for the active site on cholinesterase enzyme .

- ✓ edrophonium.
- ✓ Ambenonium.
- ✓ Physostigmine.
- ✓ Pyridostigmine.
- ✓ Neostigmine.
- ✓

b. Irreversible:

▣ **note** : phosphorylate the enzyme and inactivate it

- ✓ ecothiophate.
- ✓ Isoflurophate.

Mechanism of Action of Cholinomimetic:

Muscarinic agonist: (G-protein linked receptor)

- activation of phospholipase C => increases IP_3 + DAG => contraction of smooth muscles.
- Increase cGMP => NO (nitric oxide) release => relaxation.
- Inhibition of adenylyl cyclase => hyperpolarization.

Nicotinic agonist: (ion channel linked receptor)

- opening of ion channels => depolarization (because of Na influx).

▣ **note** : the muscarinic type uses G protein , whereas the nicotinic type uses the Na/K ion channel.



before we starting the drugs there are rules or notes u have to read them to understand the next pages

- » Ach and cholinergic drugs affect the urinary bladder by : destrutor contraction , sphincter relaxation
thus → cholinergic drugs enhance the urination
- » any drug that block the action of cholinergic , produce urinary retention .
- » cholinergic drugs increase salivation, secretions in the body and sweating.

» drugs may have quaternary structure or tertiary structure :

a- quaternary

it's a nitrogen with 4 carbon atoms (NC₄⁺) so, it contains positive charge , therefore, it's polar e.g. Ach (natural product) , methacholine , carbachol , bethanechol (non-natural product)

b- tertiary

they are all natural product (uncharged) ,non-polar (lipid soluble) e.g. pilocarpine , nicotine , lobeline .

pharmacokinetics

quaternary group

▶ **Ach**

- low-lipid solubility because it's polar, therefore , poorly absorbed and poorly distributed in the CNS
- it is hydrolyzed in the GIT becoming not active
- it's **not suitable by giving in oral route** because of 3 reasons
 - i- poorly absorbed
 - ii- if it's absorbed it hydrolysed very rapidly by esterases in plasma (becuase very sensitive to esterases 2-3 seconds)
 - iii- it digested by intestinal enzymes

methacholine is 3 times more resistant to hydrolyzed by cholinesterase

▶ **other compounds**

carbamic are completely resistance to be hydrolyzed by cholinesterase such as carbachol , bethanechol

presence of methyl group on bethanechol reduce it potency at nicotinic junction , so it's muscarinic

tertiary cholinomimetics

they are well-absobed from site of administration because it's non-polar compound

- **nicotin** is lipid-soluble, it's absorbed across the skin
- excretion by kidney . the clearence of tertiary amines can be enhance by acidification of urine
- pilocarpine is pure muscarinic & completely resistant to cholinesterase , and it's rapidly absorbed by the corona of the eye & it can cross blood-brain barrier
- Muscarinic quaternary amines is less absorbed in GIT but still toxic when ingested the mushroom

☉ **note :**

- ▶ the *action of the direct drugs* is mostly **muscarinic receptors**
- ▶ the *action of the indirect drugs* is mostly **on both kinds of the receptors.**



Pilocarpine: -MCQ-

- Direct cholinomimetic drugs => direct (+) the receptors.
- Natural occurring alkaloid.

Chemistry:

- tertiary amine.
- Non-polar (non-ionized).

Pharmacokinetics:

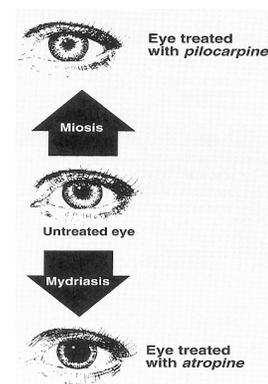
- well absorbed orally.
- Cross BBB.
- Good distribution.
- Not metabolized by cholinesterase.
- Long duration of action.
- Excreted unchanged in urine (acidification => increased excretion).

Pharmacodynamics:

- direct muscarinic agonist mainly on eye and secretion.
- No nicotinic action.
- CNS action (can cross BBB).

Uses:

- glaucoma
- Xerostomia (dry mouth) => increase secretion of saliva.
- To counteract mydriasis after fundus examination => contraction of sphincter of the iris.



glaucoma: group of eye disease characterized by an ↑ in intraocular pressure, causing pathological changes in the optic disk and typical visual field defects.

MCQ :

a patient with an acute attack of glaucoma is treated with pilocarpine. the primary reason for its effectiveness in this condition is its :

- action to terminate acetylcholinesterase
- selectivity for nicotinic receptors
- ability to inhibit secretions. such as tears, saliva , and sweat.
- ability to lower intraocular pressure
- inability to enter the brain .

the answer is : d

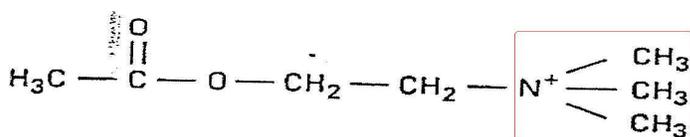


Acetylcholine:

- direct cholinomimetic drug.

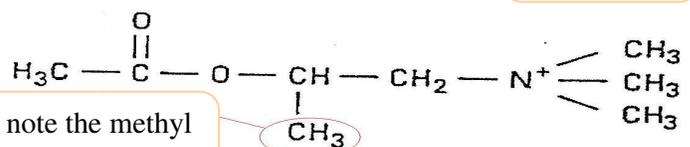
Examples:

- methacholine (Ach + methyl group).
- Bethanichol (choline + carbonic acid + CH₃).
- Carbachol (choline + carbonic acid).



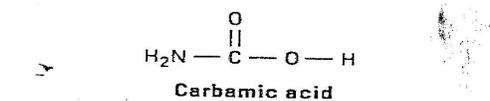
Acetylcholine

note the quaternary

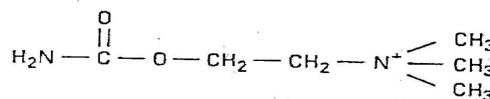


note the methyl group

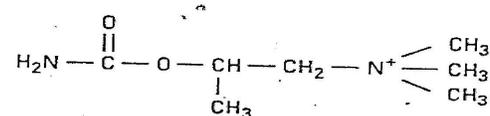
Methacholine (acetyl-β-methylcholine)



Carbamic acid



Carbachol (carbamoylcholine)



Bethanechol (carbamoyl-β-methylcholine)

Acetylcholine

- natural.
- Polar.
- Not absorbed orally.
- Muscarinic and nicotinic agonist.
- Not used due to:
 - ✓ Non-selective.
 - ✓ Short duration of action. [cuz it will rapidly hydrolyzed by the true and pseudo cholinesterase (nonspecific cholinesterase)]

Synthetic choline esters (methacholine, Carbachol, Bethanechol):

Chemistry:

- Quaternary ammonium compound.

Kinetics:

- polar.
- Poor distribution.
- No cross BBB => no CNS actions.
- Metabolism by cholinesterases (true, pseudo..).

Dynamics:

- muscarinic agonists: methacholine, bethanichol (both have CNS action).
- Muscarinic and nicotinic agonists: acetylcholine, carbachol.



Comparison between Ach and synthetic choline esters: -MCQ-

- all are quaternary ammonium compound (=polar).
- More specific (the synthetic).
- Less metabolized => they have longer duration of action (the synthetic).
- Never given I.V. or I.M => given S.C. (the synthetic).

Methacholine:

- Polar => irregular absorption (can be taken: orally, S.C.).
- Metabolized by true cholinesterase only.
- Long duration of action.
- More specific (for CVS).
- Muscarinic action on CVS than GIT and urinary tract.
- No nicotinic actions.
- **Used for:**
 - ✓ Peripheral vascular disease.
 - ✓ Paroxysmal atrial tachycardia.

Carbachol:

-MCQ-

- Quaternary: good absorption than Ach (orally, S.C).
- Not metabolized by cholinesterase.
- Longer duration of action than Ach.
- Selective muscarinic actions on eye, GIT, UT.
- Nicotinic action.
- **Used for:**
 - ✓ Glaucoma.
 - ✓ Urinary retention + paralytic ileus.

Bethanechol:

-MCQ-

- Similar to carbachol but **no nicotinic actions.**
- More preferred than carbachol for paralytic ileus and urinary retention.

presence of the methyl group on the drug make it selective to muscarinic only

Uses: Glaucoma (pilocarpine).

Paralytic ileus (bethanichol).

Urinary retention (bethanichol).

Contraindications: Bronchial asthma (because it acts as bronchoconstrictor).

Peptic ulcer (because it increases the gastric acid secretion).

Angina pectoris (because it causes bradycardia).



Indirect Cholinomimetics (Anti-Cholinesterase):

Inhibit acetylcholinesterase thus increase the Ach concentration at cholinergic receptors.

1- First step (initial binding):

Ach bind to enzyme's active site and is hydrolyzed => choline + acetylated enzyme.

2- Second step (hydration step):

acetylated enzyme bond is broken by hydration (+ H₂O) => enzyme + acetic acid.

Reversible Indirect Cholinomimetics :

- 1) Edrophonium (Quaternary alcohol)
- 2) Carbamates (Ester) :
 - Physostigmine
 - Pyridostigmine
 - Neostigmine
 - Ambenonium

Irreversible Indirect Cholinomimetics :

- 1) Organophosphorous esters:
 - Ecthiophate
 - Isoflurophate

Theses drugs are used in the treatment of Glucoma.

These drugs are irreversible because the organophosphorous esters combines with the Choline esterase with a covalent bond and if left for some time, it will become even stronger and last for more than 100 hours.

They are very well-absorbed from the skin, lungs, gut and conjunctiva except for Ecthiophate which is less stable in Aqueous solutions.



Edrophonium :

- Indirect cholinomimetic
- Simple alcohol
- Reversible anti cholinesterase
- Not substrate for enzyme , attach mainly to anionic site
- Very short duration of action
- **Pharmacokinetics :**
 - Polar
 - Not absorbed orally (should given by injection)
 - Not hydrolyzed by cholinesterase
 - Excreted unchanged in the urine
- **Uses :**
 - Diagnosis of myasthenia gravis (weakness of the skeletal muscles)
to differentiate between myasthenia gravis and toxicity

how to differentiate between myasthenia gravis and toxicity ?

muscle weakness could be due to two causes :

1) myasthenia gravis

2) taking too much anti-cholinergic drugs

we give the patient edrophonium , if cause muscle contraction improvement it means the patient has myasthenia gravis

if the muscle weakness increase ,we will say he has toxicity .

MCQ :

a patient being diagnosed myasthenia gravis would be expected to have improved neuromuscular function after being treated with :

- a. donezepil
- b. edrophonium
- c. atropine
- d. isofluorophate
- e. neostigmine

the answer is : b



Carbamate Derivatives (ester): -MCQ-

- Physostigmine.
- Neostigmine.
- Pyrisostigmine.
- Ambenonium.
- Attach at both sites of the cholinesterase enzyme.
- Substrate for cholinesterase.
- Hydrolyzed at slower rate than Ach.
- All are polar except: physostigmine
- longer half life 4-8 hrs

Physostigmine: -MCQ-

* Tertiary ammonium compound (methyl carbamate)

Pharmacokinetics:

- Non polar
- Good lipid solubility.
- Good oral absorption.
- Good BBB penetration.
- Hydrolyzed by cholinesterase (True & Pseudo)

Pharmacodynamics:

- Attach at both site of the enzyme.
- Intermediate duration of action.
- Indirect action (Reversible anticholinesterase).
- Has muscarinic & nicotinic action.
- CNS (+) action.
- No direct action on NMJ.

Uses:

- Glaucoma.
- To counteract the effect of mydriatics.
- Atropine intoxication.



Neostigmine:

-MCQ-

- * Reversible anticholinesterase.
- * Quaternary ammonium compound (Dimethyl carbamate)

Pharmacokinetics:

- Polar compound.
- Poor lipid solubility.
- Irregular oral absorption.
- No BBB penetration.

Pharmacodynamics:

- Indirect action.
- Has muscarinic & nicotinic action.
(more prominent on GIT & urinary tract than CVS)
- Direct action on NMJ.

Uses:

- Treatment of myasthenia gravis (+ Atropine) → atropine is a muscarinic antagonist , neostigmine has nonspecific action it affects both muscarinic and nicotinic receptors. so if I want to work only on nicotinic I give the patient atropine with the neostigmine to block the action of muscarinic.
- Paralytic ileus & urinary retention.
- Curare intoxication.(skeletal muscle relaxant so we need to give the patient neostigmine to help the muscles contract to alleviate the symptoms and counteract them.)

Amibenonium & Pyridostigmin:

-MCQ-

- * Similar to neostigmine.
- * Treatment of myasthenia gravis.



Indirect Cholinomimetics (Organophosphorous compounds):

-e.g.

* Ecothiophate

* Isoflurophate (DFP), Di isoprobyl fluorphosphate.

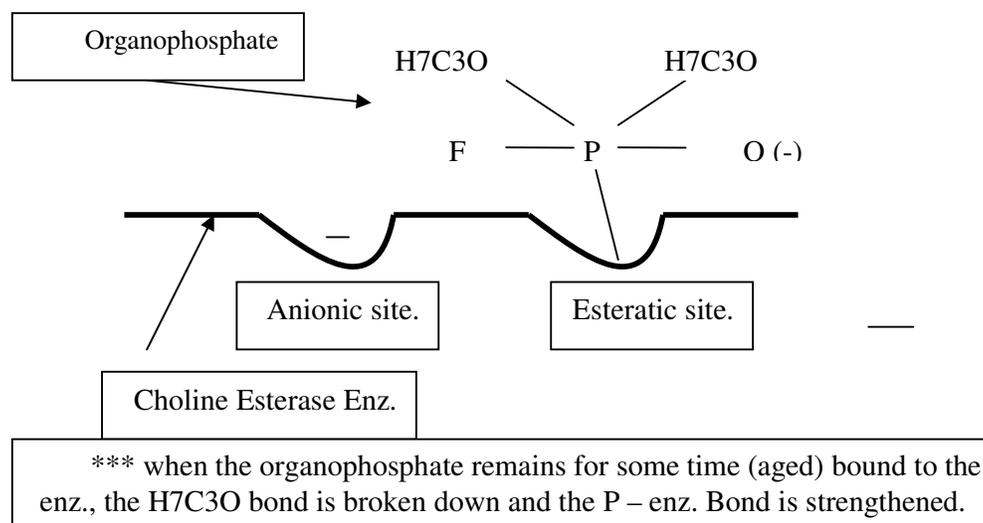
Mechanism: -MCQ-

- Bind only to esteratic site by forming covalent bond with the phosphorous atom.
- Aging make bond extremely stable.
- Long duration of action.
- All are highly lipid soluble **EXCEPT** Ecothiophate (No CVS effect)
- used mainly for Glucoma. (eye drop)

☐ note :

Because organophosphate compounds are lipid-soluble so they can cross the Blood Brain Barrier and they CAN not be easily hydrolysed by the choline esterases, their inhibition will be characteristically permanent which makes them toxic to the body (especially the brain).

Therefore they are NOT used in the human body except for the Ecothiophate that is not very lipid-soluble, so it cant cross the BBB and can be, thus, used for treatment of glaucoma.



☐ note :

all the *irreversible cholinomimetics* are highly lipid soluble **except** *ecothiophate* so it has no CNS effect because it is non-lipid soluble .

all the *reversible cholinomimetics* are polar (non-lipid soluble) **except** *physostigmine*



Indirect Anticholinesterase:

Pharmacological effect of Organophosphorus:

- 1- Muscarinic action. (see table of Ach)
- 2- Nicotinic action.
 - Ganglia
 - Neuromuscular junction

Therapeutic dose → increase action of Ach, contraction.

Toxic dose → muscle twitching & fibrillation.

- 3- CNS, excitation , convulsion , respiratory failure , coma .

Organophosphate Cholinesterase Inhibition Toxicity:

- Severe bradycardia, hypotension.
- Difficulty in breathing (bronchospasm)
- Increase GIT motility → cramps & diarrhea.
- CNS effect → convulsion, coma and respiratory failure.
- Twitching & fibrillation of skeletal muscle → depolarize block → muscle weakness.

"twitching" is the state at which each muscle fiber contracts alone with no coordination with the other fibers. In other words, it means loss of homogenous contractility.

Treatment of Organophosphate Toxicity : -MCQ-

- 1- Prevent further absorption.
- 2- Support respiration.
- 3- Cholinesterase reactivation which must be taken **BEFORE** aging occurs.
- 4- Atropine (to block muscarinic (peripheral) & central action)

Cholinesterase Reactivation (Oximes).

e.g.

Pralidoxime (PAM): **-MCQ-**

- Accelerate the hydrolytic regeneration of cholinesterase enzyme .
- The reactivate recently inhibited enzyme before aging.

Uses: - I.V → over 15–30 min. for Organophosphate cholinesterase inhibition toxicity.

- Not recommended for use in carbamate toxicity.



New Drug:

*** Cevimeline:**

- Direct acting cholinomimetics.
- Given orally.
- Cholinergic enhancer.
- Increase salivation.
- Use for treatment of dry mouth symptom associated with sjorgren's syndrome.

Anticholinestrase Drug:

Donepezil : -MCQ-

- Given orally.
- Treatment of dementia of Alzheimer's disease.

General Pharmacodynamics about the Indirect Anti-Cholinesterases.

ON CNS:-

In low conc., the high lipid soluble inhibitors cause diffuse activation of the ElectroEncephaloGram leading to mental alertness.

But in high conc, convulsions may result followed by coma and respiratory arrest.

ON CVS:-

It causes increase in the activity of Nicotinic receptors in both Sympathetic and Parasympathetic ganglia and muscurinic receptors in the neuroeffector junction.

In case of the Neuroeffector junction, low conc. Will intensify the effects if endogenous Ach. which will lead to increase in the force of contraction.

But in high conc., fibrillation occurs of the muscle fibers and the membrane depolarization becomes sustained (also called depolarization block).

In the heart, the effect of parasympathetic nervous system predominates so it leads to decrease in the heart rate.

In the AV node, the atrial contractility and the Cardiac Output decrease with modest (slight) change in the Blood Pressure.



difference between pilocarpine and bethanechol :

pilocarpine	bethanechol
Goes to the brain → tertiary ammonium → uncharged → pass through blood brain barrier BBB	Doesn't go to the brain → quaternary amine → charged → doesn't pass through BBB
More effective in secretion than muscle contraction	More effective on muscle contraction than secretion
Used in treatment of secretory problem	Used in the treatment of urinary problem

MCQ

in the comparison of pilocarpine and bethanechol , which one of the following is correct :

- both hydrolyzed by Achesterase
- both inhibit nicotinic receptors
- both may decrease sweating
- both may increase GI motility
- neither causes tachycardia

the answer is : e



Drug	Therapeutic uses
Acetylcholine	None
<i>Bethanechol</i>	Treatment of urinary retention
<i>Carbachol</i>	Miosis during ocular surgery Topically to reduce intraocular pressure in open-angle or narrow-angle glaucoma, particularly in patients who have become tolerant to pilocarpine
<i>Pilocarpine</i>	Reduce intraocular pressure in open-angle and narrow-angle glaucoma
<i>Physostigmine</i>	Increase intestinal and bladder motility Reduce intraocular pressure in glaucoma Reverse CNS and cardiac effects of tricyclic antidepressants Reverse CNS effects of atropine
<i>Neostigmine</i>	Prevent postoperative abdominal distention and urinary retention Treat myasthenia gravis As antidote for tubocurarine
<i>Edrophonium</i>	For diagnosis of myasthenia gravis As antidote for tubocurarine
<i>Isoflurophate</i>	Treatment of open-angle glaucoma

These drugs bind preferentially at muscarinic receptors; other drugs act directly or indirectly at both muscarinic and nicotinic receptors

These drugs are uncharged, tertiary amines that can penetrate the CNS

Long duration of action (2 to 4 hrs)

Short duration of action (10 to 20 min)

Long duration of action (1 week)