

# Parasympathetic system

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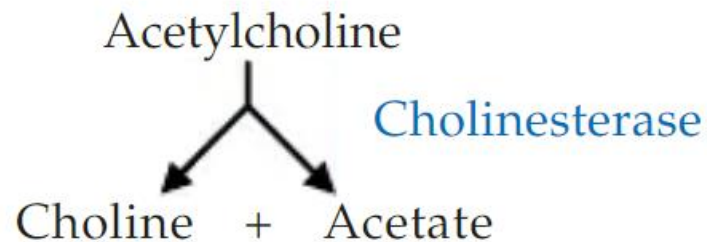
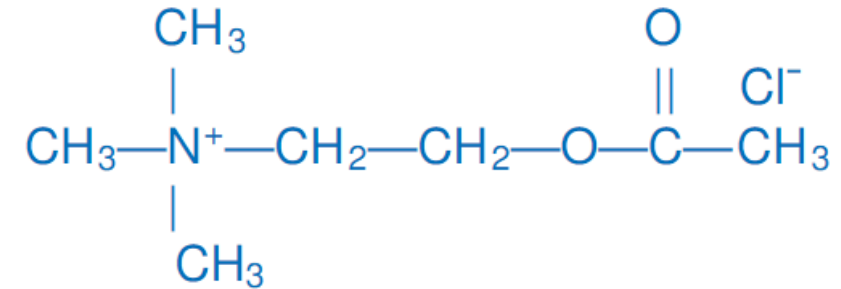
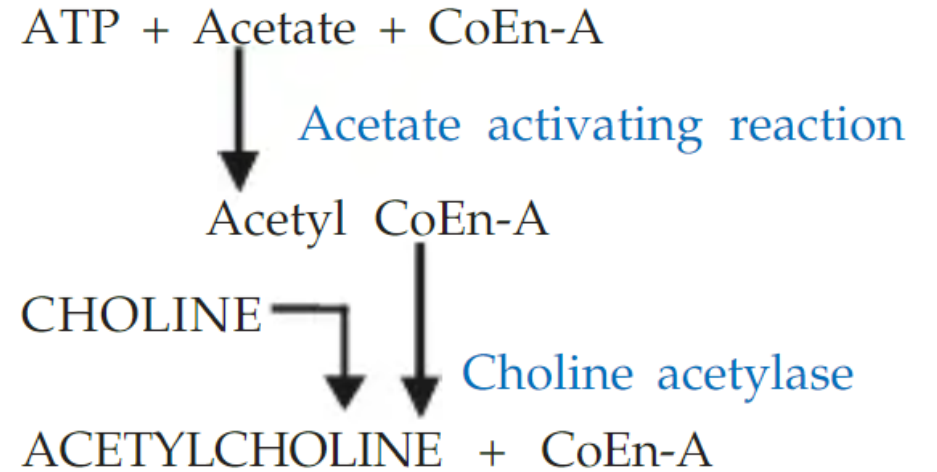


# Synthesis and metabolism of ACh

Acetylcholine (ACh) is a major neurohumoral transmitter at autonomic as well as somatic sites

Choline is actively taken up by the axonal membrane and acetylated with the help of ATP and coenzyme-A by the enzyme cholineacetylase

ACh is hydrolyzed by the enzyme cholinesterase, and choline is recycled immediately after release



# Cholinoceptors

Two classes of **cholinoceptors** are **muscarinic** and **nicotinic**

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## Muscarinic

These receptors are selectively stimulated by muscarine and selectively blocked by atropine

They are located in the heart, blood vessels, eye and glands of the gastrointestinal, respiratory, and urinary tracts, sweat glands, and in the CNS

The muscarinic receptors have been divided into 5 subtypes **M1**, **M2**, **M3**, **M4**, and **M5**

# Muscarinic cholinceptors

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The first 3 have been functionally characterized

**M1:** has a major role in mediating gastric secretion and relaxation of the lower esophageal sphincter caused by vagal stimulation

**M2:** Cardiac muscarinic receptors are predominantly M2 and mediate vagal bradycardia

**M3:** Visceral smooth muscle contraction and glandular secretions are elicited through M3 receptors

# Muscarinic actions

All blood vessels are dilated, though only a few (skin of face, neck) receive cholinergic innervation

Smooth muscle contraction in most organs

Secretion from all parasympathetically innervated glands is increased (sweating, salivation, lacrimation, and gastric secretion)

Bronchial muscles constrict (asthmatics are highly sensitive)

Contraction of circular muscle of iris → miosis

Contraction of ciliary muscle → reduction in intraocular tension (especially in glaucoma patients)

# Nicotinic

Based on location and selective agonists and antagonists two subtypes  $N_M$  and  $N_N$

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**$N_M$ :** are present in the skeletal muscle, mediate skeletal muscle contraction  
are selectively stimulated by phenyl trimethyl ammonium (PTMA)  
blocked by tubocurarine

**$N_N$ :** are present on ganglionic cells of ANS, adrenal medullary cells,  
in the spinal cord and certain areas of the brain

They are selectively stimulated by dimethyl phenyl piperazinium (DMPP)  
blocked by hexamethonium

# Nicotinic actions

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## **Autonomic ganglia**

High dose ACh stimulates both sympathetic and parasympathetic ganglia causing tachycardia and a rise in BP

## **Skeletal muscles**

ACh causes contraction of the skeletal muscle fiber

# **Cholinergic drugs (Parasympathomimetic)**

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# Cholinergic drugs

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They act similarly to ACh, either **directly** by interacting with cholinergic receptors (**agonists**) or **indirectly** by increasing the availability of ACh (**anticholinesterases**)

## CHOLINERGIC AGONISTS

### Choline esters

Acetylcholine  
Methacholine  
Carbachol  
Bethanechol

### Alkaloids

Muscarine  
Pilocarpine  
Arecoline

# Cholinergic alkaloids -1

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**Pilocarpine** obtained from the leaves of *Pilocarpus microphyllus*

It has prominent muscarinic actions

It causes marked sweating, salivation

Applied to the eye, it penetrates the cornea and causes miosis, ciliary muscle contraction ↓ **intraocular tension** (i.o.t.) (lasting 4–8 h)

Used primarily in glaucoma (0.5–4% drops)

## Cholinergic alkaloids -2

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**Muscarine** occurs in poisonous mushrooms *Amanita muscaria* and *Inocybe* species

has only muscarinic actions

It is not used therapeutically

It is of toxicological importance in mushroom poisoning, Antidote is **atropine**

### **Arecoline**

It is found in betel nut *Areca catechu*

It has both muscarinic and nicotinic actions

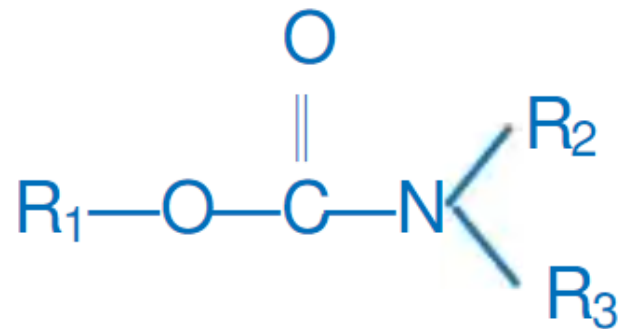
Prominent CNS effects

# Anticholinesterases (anti-ChEs)

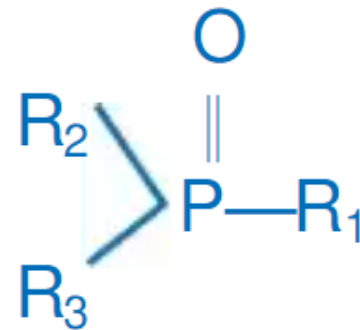
Agents which inhibit ChE thus protect ACh from hydrolysis → cholinergic effects

They have similar but more intense actions as directly acting cholinergic stimulants

Anti-ChEs are either esters of carbamic acid or derivatives of phosphoric acid



Carbamates



Organophosphates

## Reversible

### *Carbamates*

Physostigmine

Neostigmine

Pyridostigmine

Edrophonium

Rivastigmine, Donepezil

### *Acridine*

Tacrine

### **Physostigmine**

Applied to the eye, it penetrates the cornea freely  
It crosses **BBB**

### **Neostigmine**

Is poorly absorbed orally; the oral dose is 20–30  
times higher than the parenteral dose  
It does **NOT** penetrate the cornea or cross **BBB**

### **Organophosphates**

Are absorbed from all sites skin and lungs

## Irreversible

### *Organophosphates*

Dyflos<sup>†</sup>

Echothiophate

Malathion\*

Diazinon\*

Tabun<sup>£</sup>, Sarin<sup>£</sup>

### *Carbamates*

Carbaryl\*

Propoxur\*

\*Insecticides

£Nerve gases

# Therapeutic uses of anti-ChEs -1

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**Glaucoma** is a progressive form of optic nerve damage associated with raised i.o.t.

Miotics like pilocarpine and physostigmine are used to:

Lower i.o.t.

Reverse the effect of mydriatic after refraction testing

Prevent adhesions between the iris and lens/ cornea

# Therapeutic uses of anti-ChEs -2

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**Cobra bite:** To antagonize the action of cobra neurotoxin

**Belladonna poisoning:** Physostigmine is the drug of choice for poisoning with atropine and other anticholinergic drugs

**Alzheimer's disease:** a neurodegenerative disorder affecting primarily the cholinergic neurons in the brain.

The relatively **cerebroselective** anti-ChEs (Tacrine, rivastigmine, and donepezil) improve some symptomatic improvement

# Anti-ChEs poisoning

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**Anti-ChEs** are easily available and extensively used as agricultural and household insecticides

Accidental as well as suicidal and homicidal poisoning are common

Local muscarinic manifestations at the site of exposure (skin, eye, GIT) occur immediately

Followed by complex systemic effects due to muscarinic, nicotinic and central actions



## Differences between sympathetic and parasympathetic divisions of the autonomic nervous system

	<i>Sympathetic</i>	<i>Parasympathetic</i>
Origin	Dorso-lumbar (T <sub>1</sub> to L <sub>2</sub> or L <sub>3</sub> )	Cranio-sacral (III, VII, IX, X; S <sub>2</sub> -S <sub>4</sub> )
Distribution	Wide	Limited to head, neck and trunk
Transmitter (neuroeffector)	Noradrenaline (major) Acetylcholine (minor)	Acetylcholine
Stability of transmitter	NA stable, diffuses for wider actions	ACh—rapidly destroyed locally
Important function	Tackling stress and emergency	Assimilation of food, conservation of energy

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Thank you