

Anticholinergics Drugs

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Anti-cholinergic drugs / Parasympatholytics/ Atropinic

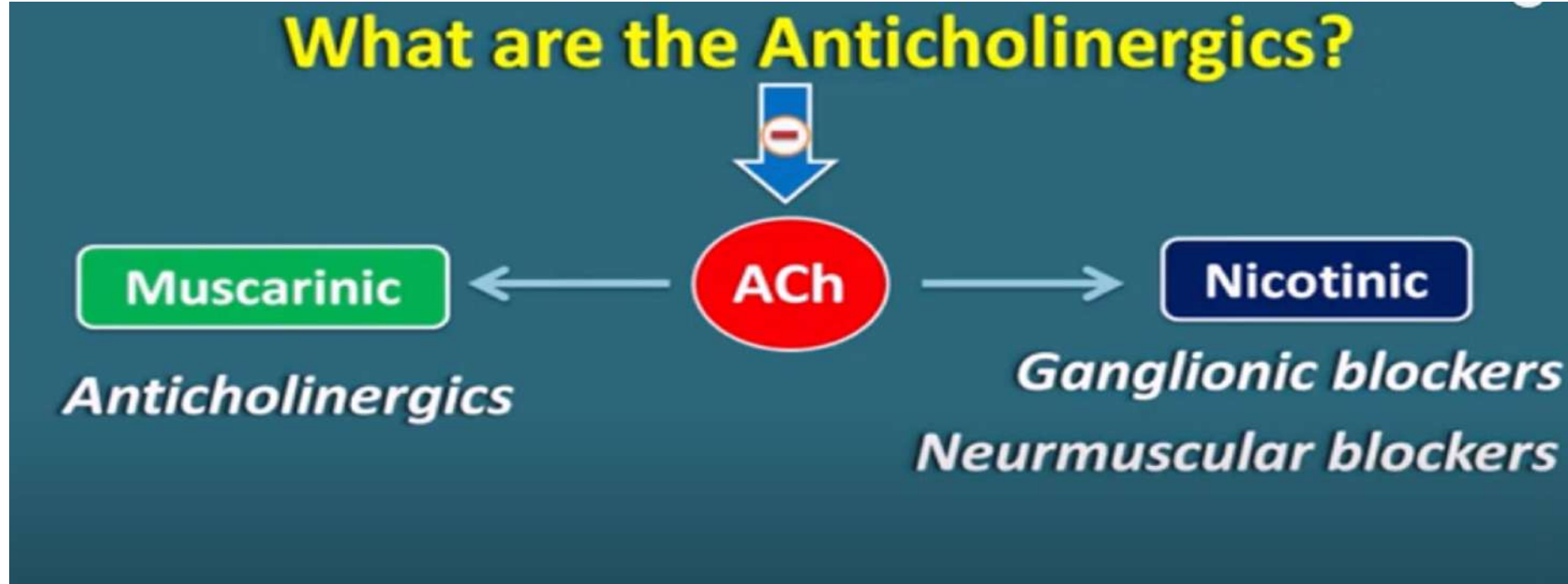
- The term 'anticholinergic drugs' is restricted to those which block actions of Ach on autonomic effectors and in the CNS exerted through **muscarinic receptors**.
- Though nicotinic receptor antagonists also block certain actions of ACh, they are generally referred to as '**ganglion blockers**' and '**neuromuscular blockers**'.

Mechanism of action

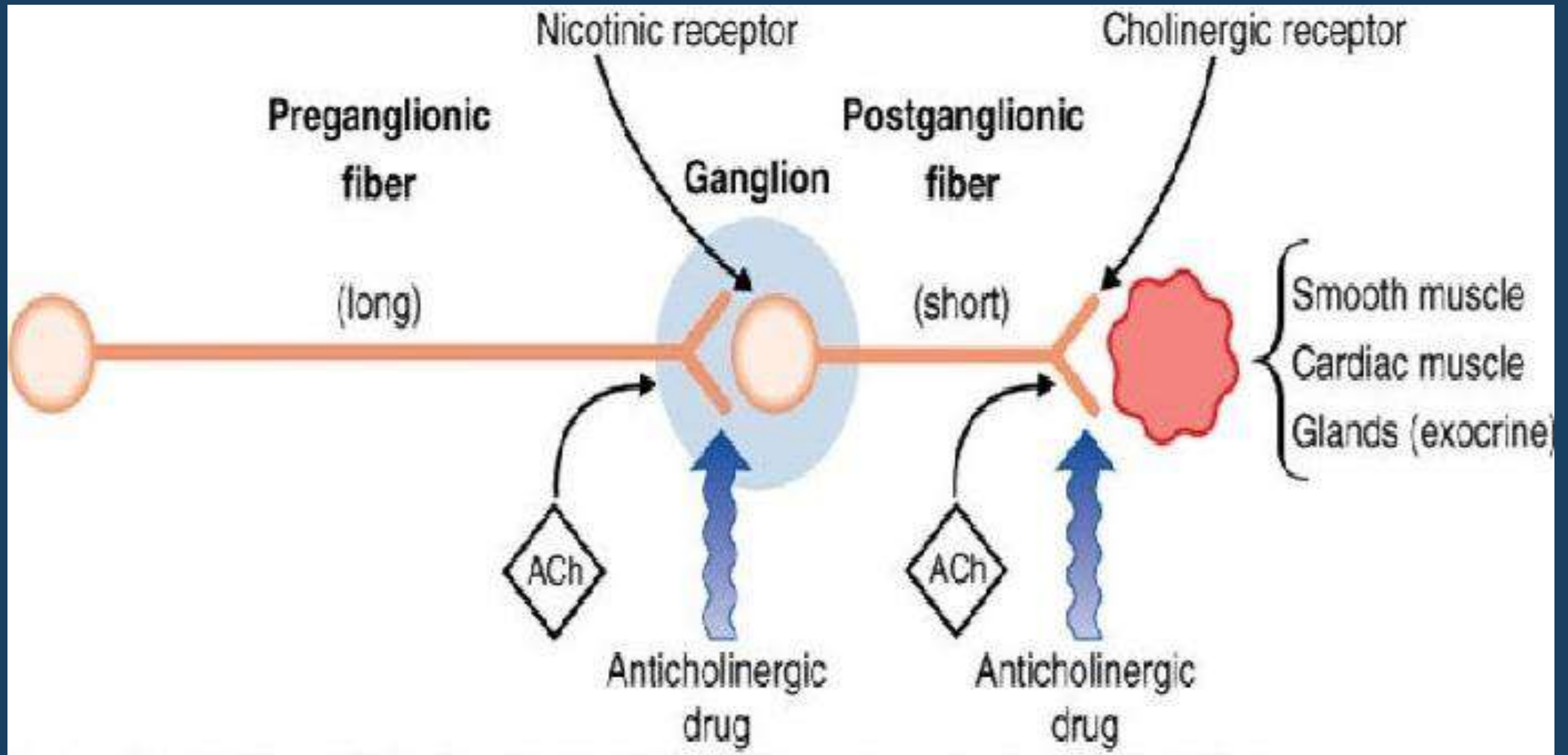
- Anticholinergic are the class of drugs that block the neurotransmitter acetylcholine in CNS and PNS.
- Anticholinergic drugs combine reversibly with muscarinic cholinergic receptors thus preventing access of neurotransmitter acetylcholine in these sites.

Anticholinergics

- **Anticholinergics** are drugs that oppose the effects of acetylcholine.
- In essence, they also lyse and block the effects of parasympathetic [nervous system](#) (PNS) so they are also called as **parasympatholytics**.
- **Atropine** is currently the only widely used anticholinergic drug. Other common examples include meclizine, scopolamine and ipratropium.



Anticholinergics (cholinergic blocking drugs)



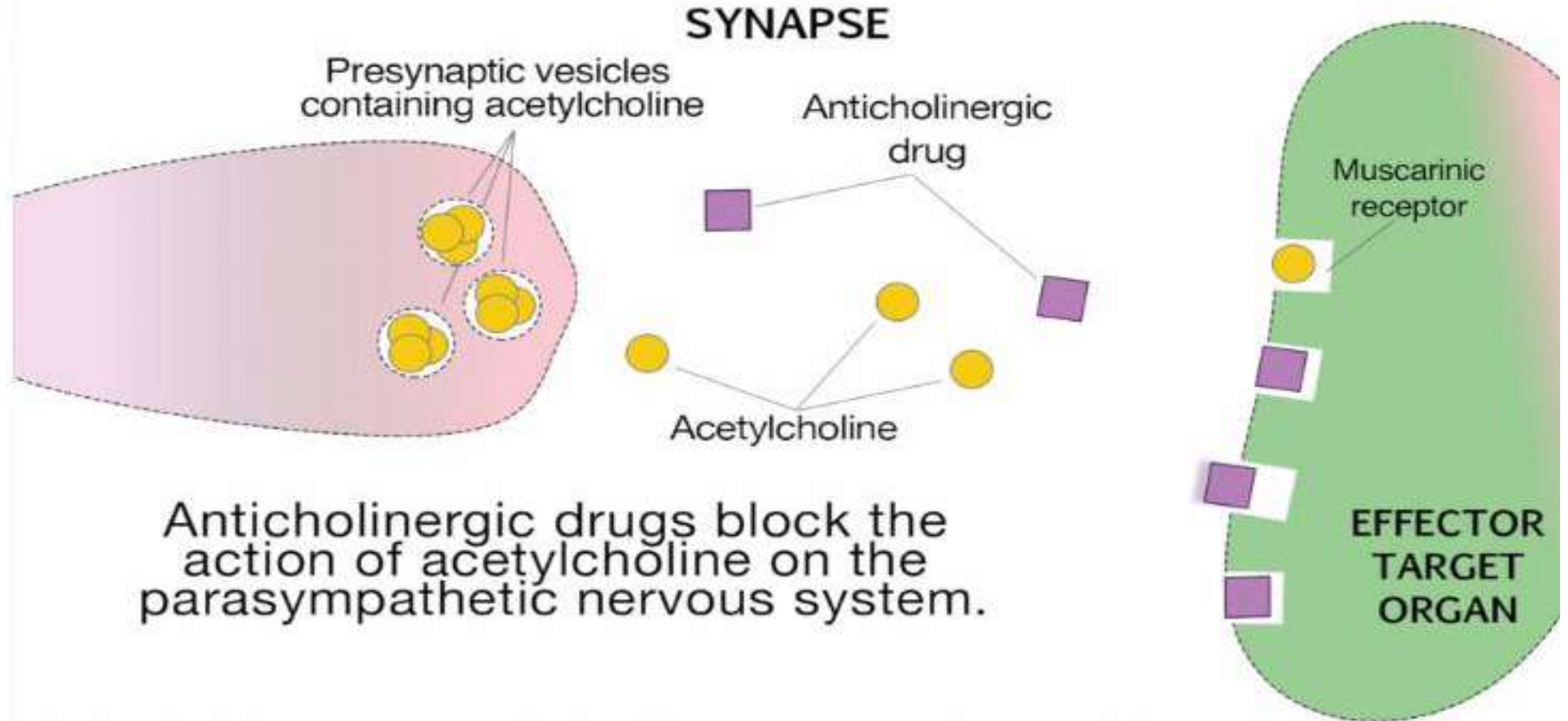
Parasympathetic Nervous System

- **Parasympathetic Nervous System** 75% of all parasympathetic nerve fibers are in the vagus nerves.
- These nerves supply the thoracic and abdominal organs, which innervate the heart, lungs, esophagus, stomach, small intestine, proximal half of the colon, liver, gallbladder, pancreas and upper portions of the ureters.
- **Parasympathetic Nervous System** Also supply the muscles of the eyes, lacrimal, nasal, submaxillary, and parotid glands; descending colon and rectum; lower portions of the ureters, bladder and genitalia.
- All are regulated by acetylcholine-exerts excitatory effects at nerve synapses and neuromuscular junctions; and inhibitory effects at peripheral sites e.g. heart
-

What is an anticholinergic?

- Anticholinergics are a type of medication that blocks the action of a neurotransmitter, a chemical messenger in the brain, called acetylcholine. Acetylcholine is responsible for transferring signals between certain cells that affect specific bodily functions.
- The medication blocks acetylcholine from causing involuntary muscle movements in the lungs, gastrointestinal tract, urinary tract, and other areas of the body.
- As anticholinergics can affect a variety of functions, including digestion, urination, salivation, and movement, they can help treat many conditions.

Cholinergic and Anticholinergic Drugs



Anticholinergic drugs block the action of acetylcholine on the parasympathetic nervous system.

Anticholinergic drugs

Antimuscarinics
(Parasympatholytics)

Antinicotinics

Naturally occurring
alkaloids

synthetic atropine
substitutes

Ganglionic
blockers

Neuromuscular
blockers

Atropine as Prototype

Atropine (hyoscyamine) is found in the plant *Atropa belladonna*, or **deadly nightshade**

Also in *Datura stramonium*, also known as jimson-weed (Jamestown weed) or **thorn apple**

Scopolamine (hyoscine) occurs in *Hyoscyamus niger*



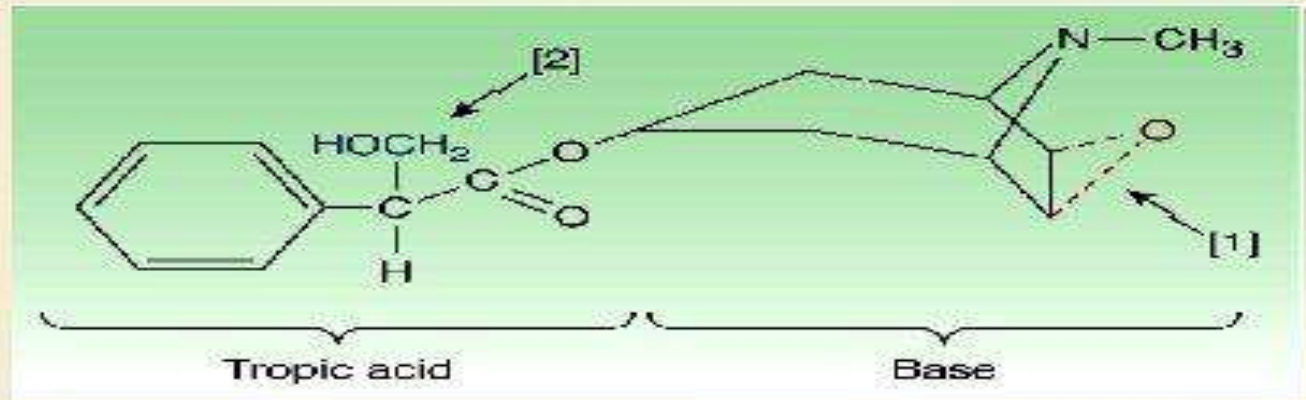
Datura stramonium



Atropa belladonna

Muscarinic antagonists

Natural alkaloids



- History (Thousands of years)
- Atropine (*Hyoscyamine*)
- Hyoscine (*scopolamine*)
- Esters of tropic acid and **tertiary amines**
- Lipid soluble
- Good oral absorption
- Good distribution
- Cross blood brain barrier (**have CNS actions**)

Muscarinic antagonists

Synthetic atropine substitutes

Tertiary amines

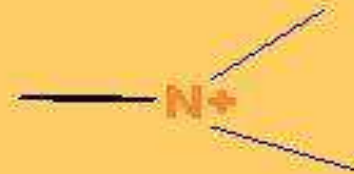
Lipid soluble
central actions

Benztropine
Homatropine
Tropicamide
Pirenzepine
Oxybutynin

Quaternary amines

Polar, water soluble
No CNS effects

Ipratropium
Glycopyrrolate



Antimuscarinic drugs

DRUG	Pharmacokinetics
Natural alkaloids Atropine (Hyosyamine) Hyoscine (scopolamine)	Tertiary amines , lipid soluble, well absorbed, well distributed, good penetration to CNS
Synthetic atropine substitutes	
Benz tropine	Tertiary amine
Tropicamide Homatropine	Tertiary amines
Ipratropium	Quaternary amines, not absorbed well, poor distribution, no CNS effects
Pirenzepine	Tertiary amine
Glycopyrrolate Oxyphenonium	Quaternary amines
Oxybutinin	Tertiary amine

Cholinergic VS Anticholinergic

DEFINITION

Cholinergic agents are chemical compounds that can mimic the function of acetylcholine

Anticholinergic agents are substances that can block the action of acetylcholine

POINT OF ACTION

Act on parasympathetic and sympathetic nervous systems

Act mainly on the central and peripheral nervous system

EXAMPLES

Pilocarpine, physostigmine, etc.

Atropine, clidinium, Cogentin, etc.

Cholinergic & anticholinergic actions

Cholinergic actions	Anticholinergic actions
Eye 1. Contraction of circular muscle of iris (miosis) 2. Contraction of ciliary muscles for near vision	1. Mydriasis 2. Cycloplegia
Heart bradycardia (↓ heart rate)	Tachycardia (↑ heart rate) ↑ force of contraction
Urinary bladder Contraction of muscles Relaxation of sphincter	Relaxation of muscles contraction of sphincter

Cholinergic actions	Anticholinergic actions
Exocrine glands Increase of sweat, saliva, lacrimal, bronchial, intestinal secretions	Decrease of all secretion
GIT ↑ peristalsis ↑ secretion relaxation of sphincter	↓ peristalsis ↓ secretion Contraction of sphincter
Lung 1. Constriction of bronchial smooth muscles 2. Increase bronchial secretion	1. Relaxation of bronchial muscles 2. Decrease secretion

Anticholinergic Drugs (Muscarinic blockers)

Atropine	Preanesthetic medication - Antispasmodic
Hyoscine	Motion sickness - Antispasmodic Pre-anesthetic medication
Pirenzepine	Peptic ulcer
Ipratropium	Asthma
Benztropine	Parkinsonism
Dicyclomine	Antispasmodics
Tropicamide Cyclopentolate	Ophthalmoscope examination of retina

Adverse drug effects

Cholinergic actions	Anticholinergic actions
Nausea	Dry mouth
Vomiting & diarrhea	Blurred vision
Salivation	Tachycardia
Bronchconstriction	Hot flushed skin
	Agitation & confusion
	Increase in body temp
	Constipation
	Urinary retention

Classification

- **CLASSIFICATION**

1. **Natural alkaloids(Belladonna alkaloids):**

- Atropine, Hyoscine (Scopolamine)

2. **Semisynthetic and synthetic antimuscarine agents :**

- Atropine derivatives used as Mydriatics :

- Homatropine, Tropicamide and Cyclopentolate etc

- Atropine derivatives used in COPD and Bronchial asthma :

- Ipratropium bromide, Tiotropium bromide ,oxitropium bromide

- Atropine derivatives used in peptic ulcer:

- Pirenzepine, telenzepine

Classification(cont.)

- Atropine derivatives used as Antispasmodics:
 - Dicyclomine, flavoxate, oxybutynin , tolterodine
- Atropine derivatives used as a pre-anaesthetic agent :
 - Glycopyrrolate
- Atropine derivatives used in parkinsonism
 - benzhexol, benztropine, biperidin, Procyclidine

In addition, many other classes of drugs, i.e. tricyclic antidepressants, phenothiazines, antihistamines and disopyramide possess significant antimuscarinic actions

Anticholinergics: Generic and Brand Names

Classification	Generic Name	Brand Name
Anticholinergics	atropine	(generic)
	ipratropium	Atrovent
	meclizine	Bonine, Antivert
	methscopolamine	Pamine
	scopolamine	Transderm Scop
	tiotropium	Spiriva

Indications

- Anticholinergics are indicated for the following medical conditions:
- Prevention of nausea, vomiting, and dizziness associated with motion sickness.
- Adjunctive therapy for treatment of GI ulcers
- Decrease secretions before anesthesia or intubation
- Maintenance treatment of bronchospasm associated with COPD.
- Treatment of irritable or hyperactive bowel in adults.

❖ Here are some important aspects to remember for **indication** of anticholinergics in different age groups:

➤ **Children**

- More sensitive to the adverse effects of the drug (e.g. constipation, urinary retention, heat intolerance, confusion).
- **Dicyclomine is not recommended for use in children.**

➤ **Adults**

- Adults should be cautioned of these drugs' adverse effects.
- Use of these drugs among pregnant women is not allowed because they can cross placenta and cause adverse effects to the fetus.

➤ **Older adults**

- Dose adjustment is needed as this age group is also more susceptible to drug side effects.
- They are more likely to have toxic levels of the drug because of renal or hepatic impairments.

□ Pharmacokinetics

- The characteristic interactions of anticholinergics and the body in terms of absorption, distribution, metabolism, and excretion:

Route	Onset	Peak	Duration
IM	10-15 min	30 min	4 h
IV	Immediate	2-4 min	4 h
Subcutaneous	Varies	1-2 h	4 h
Topical	5-10 min	30-40 min	7-14 d
T1/2: 2.5 h Metabolism: liver Excretion: urine			

Contraindications and Cautions

- The following are contraindications and cautions for the use of anticholinergics:
- **Allergy to any component of the drug.** To prevent hypersensitivity reaction
- **Glaucoma.** Can be exacerbated by blockade of PNS.
- **Intestinal atony, paralytic ileus, GI obstruction.** Can be exacerbated with further slowing of GI activity.
- **Pregnancy.** Potential adverse effects on the fetus.

Adverse Effects

- Use of anticholinergic agents may result to these adverse effects:
- CNS: blurred [vision](#), pupil dilation, photophobia, cycloplegia, increased intraocular pressure, weakness, dizziness, [insomnia](#)
- CV: tachycardia, palpitation
- GI: dry [mouth](#), altered taste perception, nausea, heartburn, constipation
- GU: urinary hesitancy and retention, heat prostration

Interactions

- The following are interactions involved in the use of anticholinergics:
- **Antihistamines, antiparkinsonisms, MAOIs (Monoamine oxidase inhibitors) , TCAs (Tricyclic Antidepressants).**
- These drugs also have anticholinergic effects so incidence of anticholinergic effects increases.
- **Phenothiazines.** Decreased effectiveness of this drug.
- **Burdock, rosemary, turmeric.** Risk for exacerbated anticholinergic agents

How Anticholinergics work

- Anticholinergics block acetylcholine from binding to its receptors on certain nerve cells. They inhibit actions called parasympathetic nerve impulses.
- These nerve impulses are responsible for involuntary muscle movements in the:
 - [gastrointestinal tract](#)
 - [lungs](#)
 - urinary tract
 - other parts of your body
- The nerve impulses help control functions such as:
 - salivation
 - digestion
 - urination
 - mucus secretion
- Blocking acetylcholine signals can decrease:
 - involuntary muscle movement
 - digestion
 - mucus secretion
- That's why these drugs can cause certain side effects, such as:
 - retaining urine
 - having a dry mouth

ANTICHOLINERGIC MEDICATIONS

Can't pee
Can't see
Can't spit
Can't shit



Pharmacological Actions

Pharmacological actions



↑ Rate → Tachycardia

ATROPINE → For treatment of sinus bradycardia

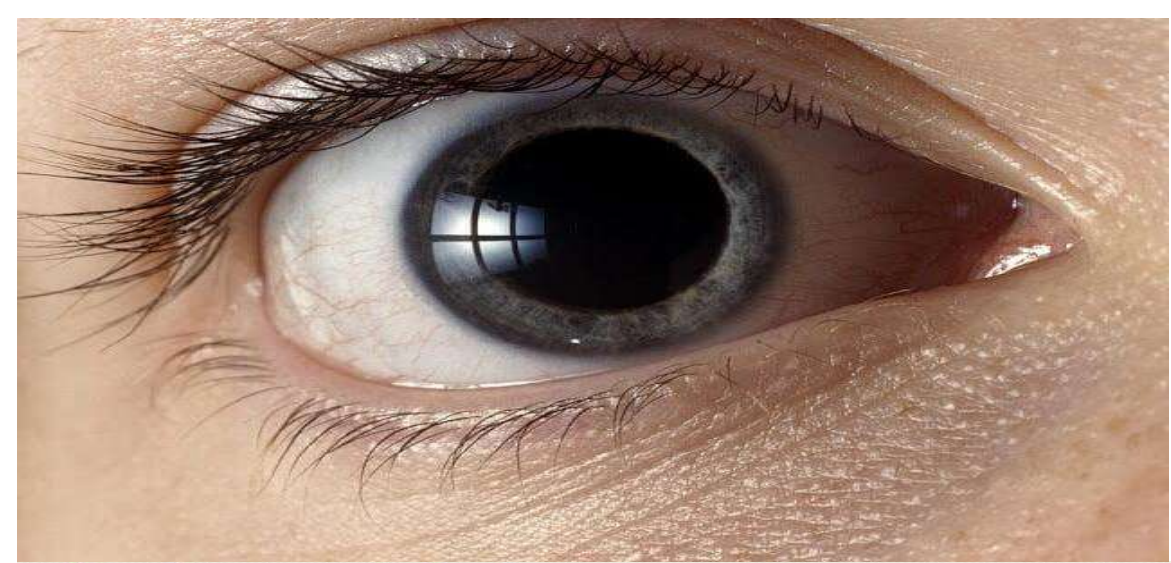
Pharmacological actions



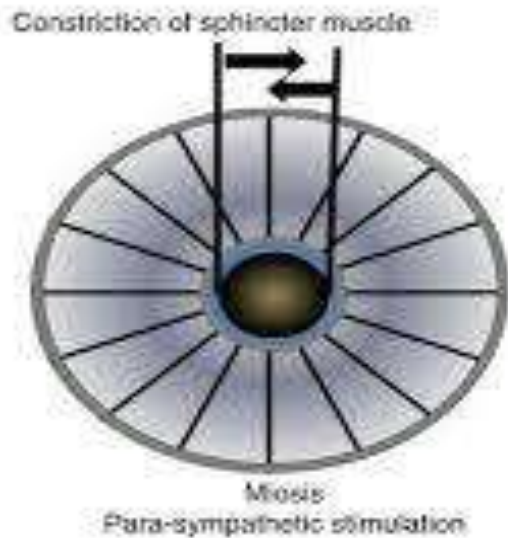
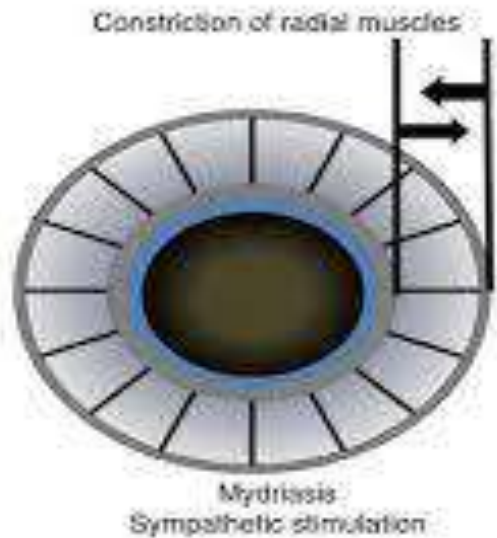
Pupillary dilatation → **Mydriasis**

Cycloplegia → **Paralysis of accommodation**
(Atropine)

↑ **IOP**



- **Passive mydriasis**
_ due to paralysis of circular muscle
- **Cycloplegia** (loss of near accommodation)
due to paralysis of ciliary muscle.
- Loss of light reflex.
- Increase I.O.P # glaucoma.
- ↓ Lacrimal secretion → sandy eye



Pharmacological actions



DARIFENACIN
SOLIFENACIN

Selective M₃ blocker used as bladder relaxant

Relaxation of bladder



↓ **Urination**

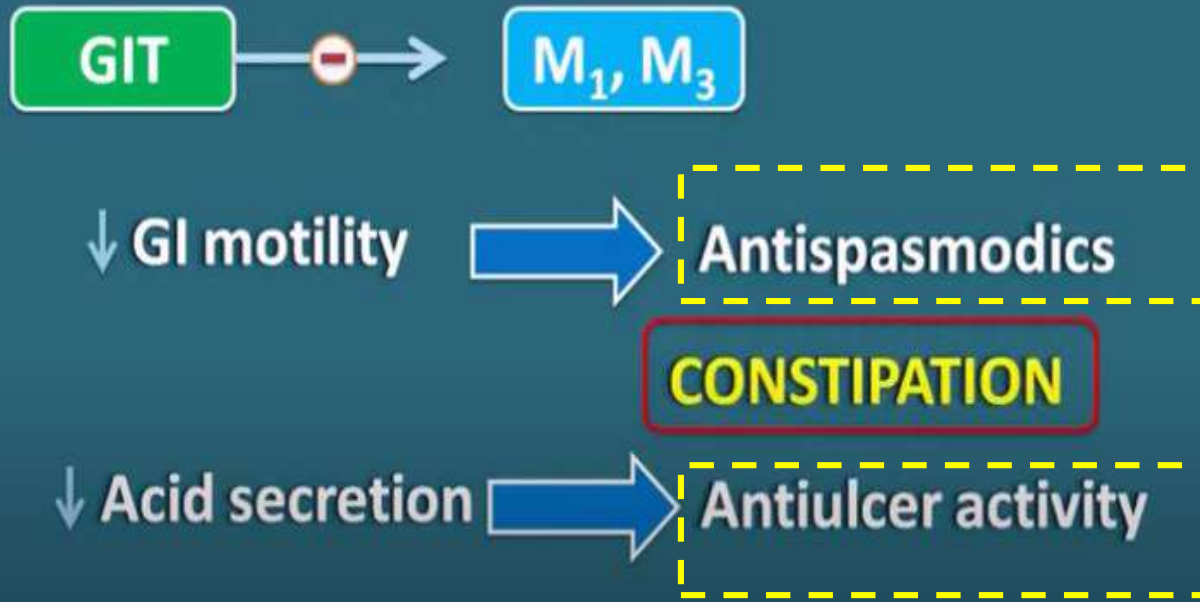


Non-selective anticholinergic / used as bladder relaxants

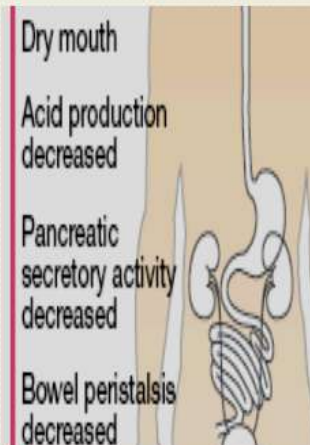
TOLTERODINE
OXYBUTYNIN
FLAVOXATE

Urinary retention

Pharmacological actions



- Dryness of mouth
- ↓ Gastric acid production
- Relaxation of smooth muscles.
- ↓ GIT motility → **Antispasmodic effect.**
- ↑ Sphincter contractions
- Constipation



Disease Spotlight

- **Disease Spotlight:**

- **Gastrointestinal Ulcers**

- **Anticholinergics** were once very widely used to decrease GI activity and secretions. However, more specific and less toxic drugs are available now and the utilization of this drug class is now limited.
- **GI ulcers** are basically erosions in the lining of the GIT caused by increased HCl production most commonly from H. pylori infection (*Helicobacter pylori (H. pylori) infection occurs when H. pylori bacteria infect your stomach. This usually happens during childhood. A common cause of peptic ulcers, H. pylori infection may be present in more than half the people in the world*)
- Patients with GI ulcers suffer from burning abdominal pain, nausea, and acid reflux.

Pharmacological actions



Bronchodilation



Used in COPD

Mucociliary clearance



**Only shown by
atropine**

Pharmacological actions

Glandular secretions



Even the sweat glands are connected with the sympathetic system but the receptors are cholinergic receptors



Secretions

- ↓ Salivary secretion → **(Dry mouth).**
- ↓ Sweating → dry skin
- In children modest doses → "atropine fever"**
- ↓ Bronchial secretion → ↑ Viscosity
- ↓ Lacrimal secretion → Sandy eye



Pharmacological actions

Central actions

↓
Emesis

↓
EPS

➤ Extra pyramidal side effects that are produce antipsychotics

➤ **Benzotropine** and **Benzhexol** are used to decrease Extra pyramidal side effects

↓ Memory



Dementia

CNS excitation



Agitation

Hyperactivity

Disorientation

Side effects

Dry mouth

Blurred vision

Constipation

Urinary retention

Tachycardia

Toxic doses

Restlessness

Agitation

Hyperthermia

Disorientation

Clinical uses

- ✓ Preanesthetics
- ✓ Antispasmodics
- ✓ Mydriatics
- ✓ Bladder relaxants
- ✓ Bronchodilators
- ✓ Anti-emetics
- ✓ Anti-ulcer agents
- ✓ Anti-parkinsonian agents
- ✓ Sinus bradycardia
- ✓ Physostigmine poisoning

Uses of antimuscarinic drugs

Drugs	organ	Uses
Atropine	CNS	Pre-anesthetic medication Antispasmodic
Hyoscine	CNS	Pre-anesthetic medication, Motion sickness, antispasmodic
Benztropine	CNS	Parkinson's disease
Homatropine Tropicamide	Eye	Fundus examination
Ipratropium	Respiratory system	asthma, COPD, inhalation
Pirenzepine	Stomach	Peptic ulcer
Glycopyrrolate	GIT	Antispasmodics in hypermotility
Oxybutynin Darifenacin	UT	Urinary urgency, Urinary incontinence

Hyoscine (SCOPOLAMINE)

What is difference between atropine and hyoscine?

Hyoscine has

- **Shorter duration of action**
- **More CNS depressant action**
- **Antiemetics action in motion sickness**
- **Amnesic action.**
- **Less CVS effect**

Medication / Atropine

- ATROPINE injection, for intramuscular use 2 mg Atropine single-dose autoinjector
- The 2 mg Atropine autoinjector is for use only in adults and children weighing over 90 pounds (41 kg) (generally over 10 years of age).
- Do not use the 2 mg Atropine autoinjector for children weighing 90 pounds (41 kg) and less (generally 10 years of age and younger).

Uses

- **As anti-secretory :**
 - Pre-anesthetic medication : reduces excessive salivation & respiratory secretions.
 - Peptic ulcer : decreases gastric secretions & provide symptomatic relief in peptic ulcer now been superseded by H2 blockers.
- **As anti-spasmodic :**
 - If there is no mechanical obstruction intestinal & renal colic, abdominal cramps symptomatic relief is affordable.
 - Gastritis, gastric hypermotility.
 - To relieve urinary frequency & urgency.
- Can be given in patients of Bronchial Asthma
- As mydiatric & cycloplegic.
- As cardiac vagolytic
- For central actions in Parkinsonism as an adjuvant to levodopa.
- To antagonise muscarinic effects of anti-Cholinesterase i.e OP Poisoning with dose 2mg IV with repeated doses and early mushroom poisoning.

Side effects

- Belladonna poisoning due to drug overdose.
- Dry mouth, difficulty in swallowing and talking.
- Dry, flushed and hot skin.
- Fever, difficulty in micturition, decreased bowel sounds.
- Dilated pupil, photophobia, blurring of near vision.
- Excitement, ataxia, delirium, hallucination.
- Convulsion and coma may occur in severe poisoning.

Atropine overdose Treatment

- Supportive treatment should be administered as indicated.
- If respiration is depressed, artificial respiration with oxygen is necessary. Ice bags, alcohol sponges, or a hypothermia blanket may be required to reduce fever, especially in pediatric patients.
- Catheterization may be necessary if urinary retention occurs.
- Since atropine elimination takes place through the kidney, urinary output must be maintained and increased if possible; however, dialysis has not been shown to be helpful in overdose situations.
- Intravenous fluids may be indicated.
- Because of atropine-induced photophobia, the room should be darkened.

Glycopyrolate

- Glycopyrolate is a synthetic product that differs from atropine in being a quaternary amine.
- The pre-medication dose is 0.005 – 0.01 mg/kg upto 0.2-0.3 mg in adults.
- **Clinical consideration :**
- Because of its quaternary structure, glycopyrolate can't cross BBB & is almost devoid of CNS & Ophthalmic activity.
- Potent inhibition of salivary gland & respiratory tract secretions is the primary rationale for using glycopyrolate as pre-medication.
- Heart rate increases after IV administration.
- It has longer duration of action than atropine sulphate i.e 2-4 hrs.

Scopolamine

- Scopolamine is a naturally occurring tertiary amine.
- It's dose is 0.3-0.5 micro gram I/M.
- **Clinical Consideration :**
- Lipid soluble.
- Easy penetrate BBB.
- More potent antisialagogue than Atropine & causes greater CNS effects
- Clinical doses results in restlessness, drowsiness, amnesia, dizziness & delirium.
- It has the added virtue of preventing motion sickness.
- The lipid solubility allows trans-dermal absorption & has been used to prevent post-operative nausea & vomiting
- Best avoided in patients with closed angle glaucoma.