ANTICHOLINERGIC DRUGS

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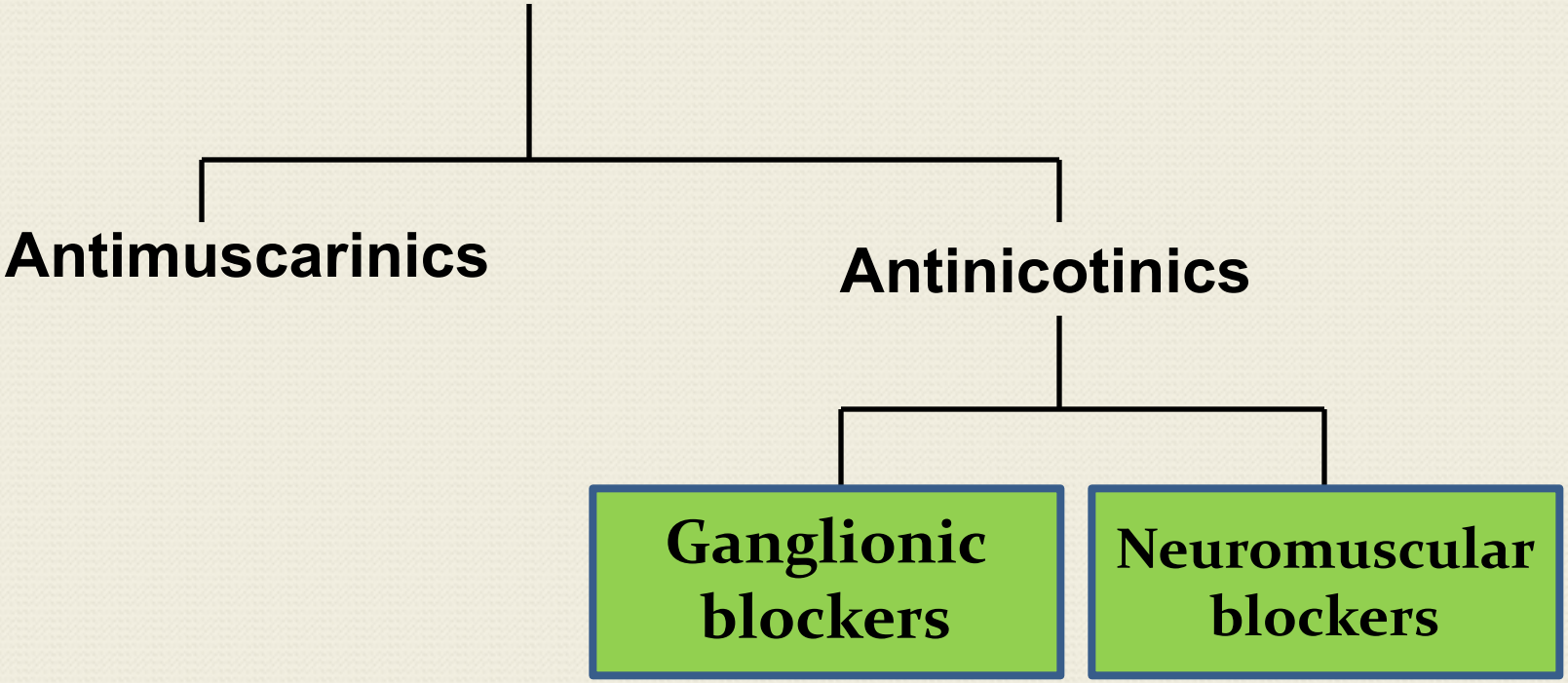
What students should know:

Student should be able to :

- Identify the classification of anticholinergic drugs
- Describe pharmacokinetics and dynamics of muscarinic antagonists
- Identify the effects of atropine on the major organ systems.
- list the clinical uses of muscarinic antagonists.
- know adverse effects & contraindications of anticholinergic drugs.
- Identify at least one antimuscarinic agent for each of the following special uses: mydriasis, cyclopedia, peptic ulcer & parkinsonism.

ANTICHOLINERGIC DRUGS



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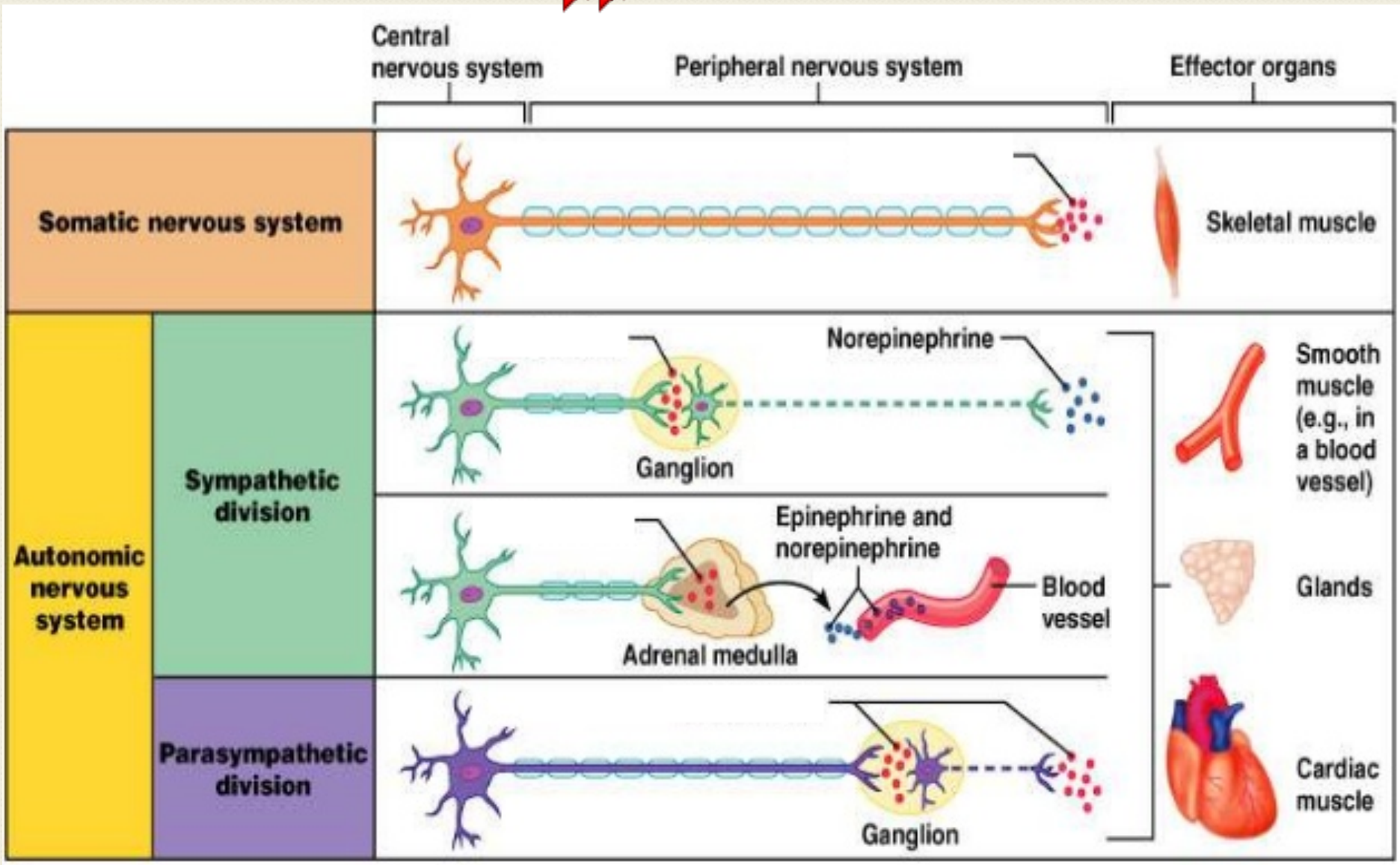

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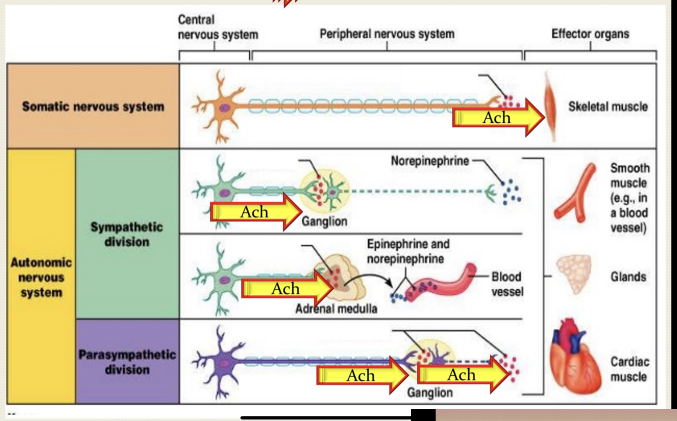

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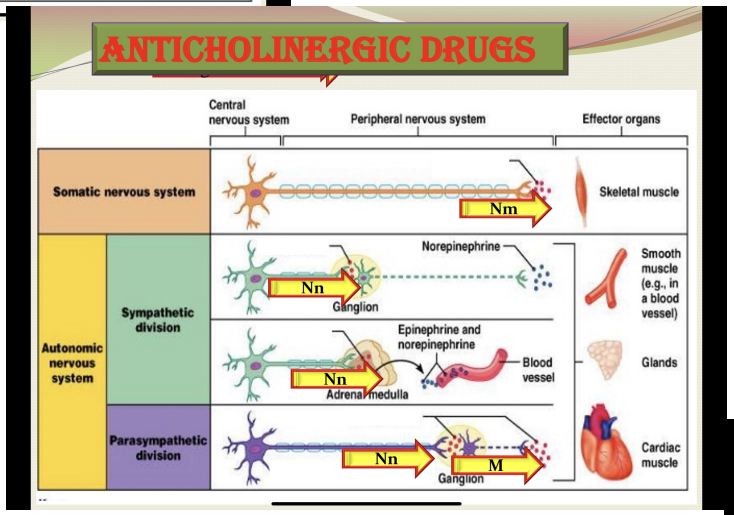

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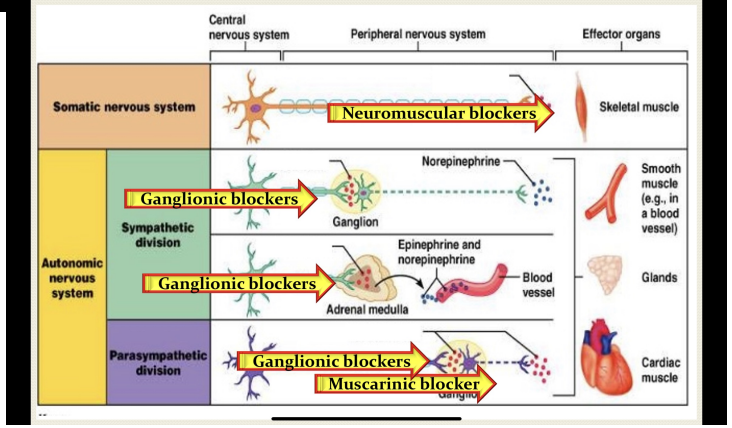


ANTICHOLINERGIC DRUGS

Antimuscarinic Drugs

According to source

Natural

- Atropine (Hyoscyamine)
- Hyoscine (scopolamine)

Semisynthetic

Synthetic

Antimuscarinics
Muscarinic antagonists

Semisynthetic & Synthetic atropine substitutes

Homatropine (semisynthetic)

Tropicamaide

Benztropine

Pirenzepine

Ipratropium

Glycopyrrolate

Oxybutynin, Darifenacin

ANTICHOLINERGIC DRUGS

Antimuscarinic Drugs

According to structure

Tertiary amines

- Atropine (Hyoscyamine)
- Hyoscine (scopolamine)
- lipid soluble

Quaternary ammonium

- Glycopyrrolate
- Ipratropium

ANTICHOLINERGIC DRUGS

Antimuscarinic Drugs

According to selectivity

Non-selective

- Atropine, Hyoscine
- Ipratropium

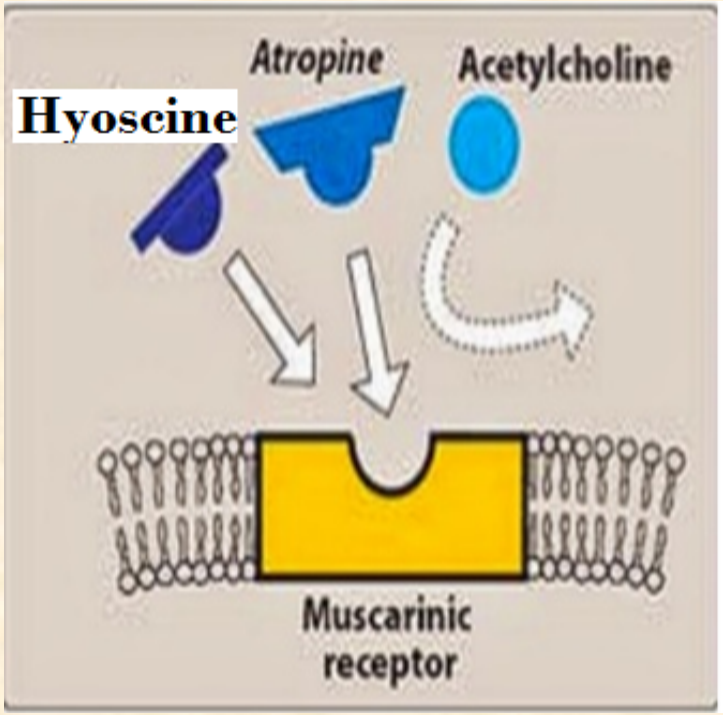
Selective

- Pirenzepine(M1)
- Darifenacin(M3)

MECHANISM OF ACTION

Reversible competitive blockade of muscarinic Receptors (reverses muscarinic effects of cholinergic drugs).

Atropine & hyoscine can block all muscarinic receptors (not selective).



PHARMACOKINETICS

Natural alkaloids

- Atropine (Hyoscyamine)
- Hyoscine (scopolamine)
- Lipid soluble
- Good oral absorption
- Good distribution
- Cross blood brain barrier **(have CNS actions)**

PHARMACODYNAMIC ACTIONS

Cholinergic actions	Anticholinergic actions
Eye **Circular muscle of iris** Contraction **(miosis)** **Ciliary muscles** Contraction **accommodation for near vision**	 relaxation **(mydriasis)** relaxation **(cycloplegia)** **loss of accommodation**
Heart bradycardia (↓ H.R.)	Tachycardia (↑ H.R)
Urinary bladder Contraction of muscles Relaxation of sphincter **Urination**	Relaxation of muscles contraction of sphincter **Urinary retention**

PHARMACODYNAMIC ACTIONS

Cholinergic drugs	Anticholinergic drugs
Exocrine glands Increase of sweat, saliva, lacrimal, bronchial, intestinal secretions	Decrease all secretions
GIT ↑ peristalsis ↑secretion relaxation of sphincter Diarrhea	↓ peristalsis ↓ secretion Contraction of sphincter constipation
Lung Bronchoconstriction ↑bronchial secretion	Bronchodilatation ↓ Decrease secretion

PHARMACODYNAMIC ACTIONS

CNS:

- **Atropine** at clinical dose, initial stimulation followed by depression **(sedative effect).**
- **Hyoscine** →sedative effect
- **Antiemetic effect** (block vomiting center).
- **Antiparkinsonian effect** (block basal ganglia).

PHARMACODYNAMIC ACTIONS

CNS:

High doses of atropine cause cortical excitation, restlessness, disorientation, hallucinations, and delirium followed by respiratory depression and coma.

Eye:

- **Passive mydriasis**

  due to paralysis of circular muscle

- **Cycloplegia** (loss of near accommodation)

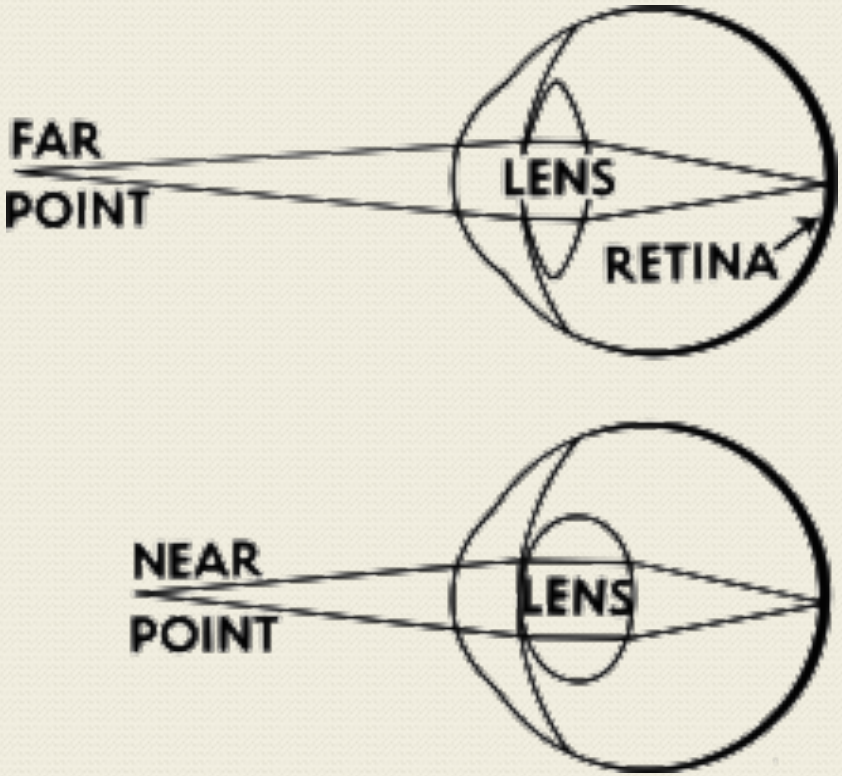
  due to paralysis of ciliary muscle.

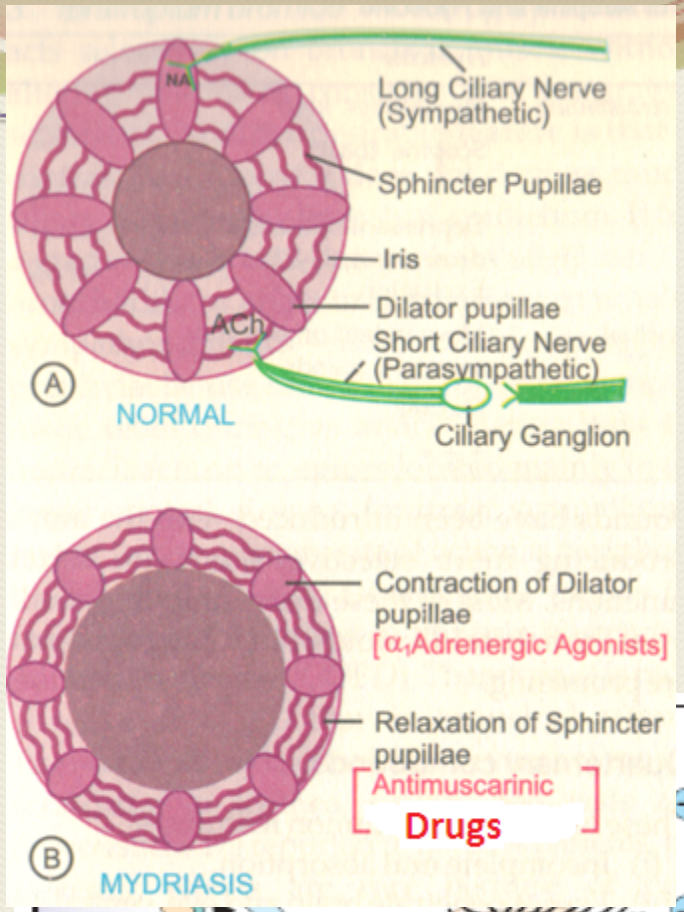
- **Loss of light reflex.**

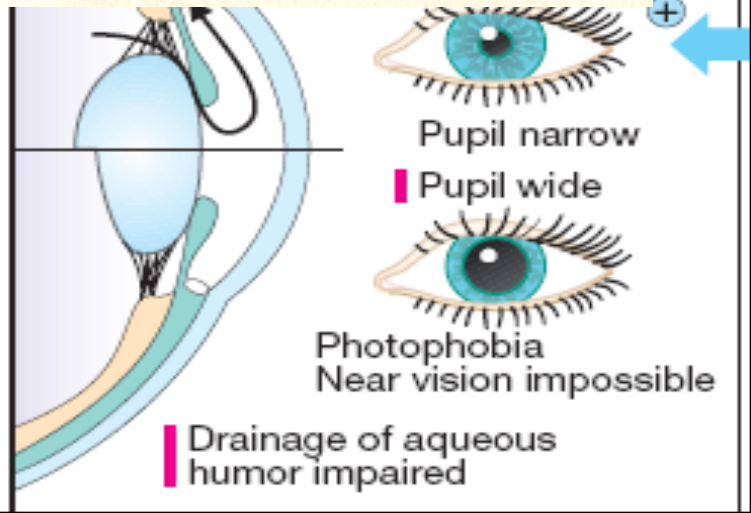
- **Increase I.O.P # glaucoma.**

- **↓ Lacrimal secretion → Dry & sandy eye**

Eye:

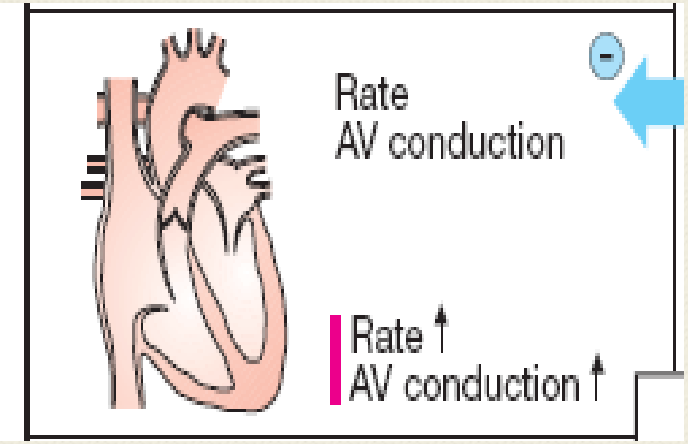

FAR
POINT
LENS
RETINA
NEAR
POINT
LENS

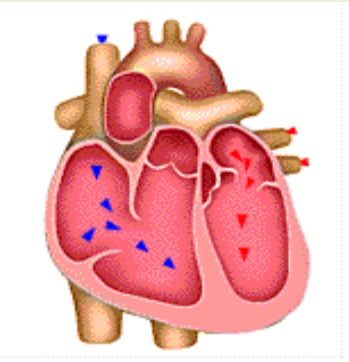

NA
Long Ciliary Nerve
(Sympathetic)
Sphincter Pupillae
Iris
Dilator pupillae
ACh
Short Ciliary Nerve
(Parasympathetic)
A
NORMAL
Ciliary Ganglion
Contraction of Dilator
pupillae
[α1Adrenergic Agonists]
Relaxation of Sphincter
pupillae
Antimuscarinic
Drugs
B
MYDRIASIS


Pupil narrow
Pupil wide
Photophobia
Near vision impossible
Drainage of aqueous
humor impaired

CVS:

- **Atropine** causes *initial bradycardia* followed by *tachycardia* due to blockade of M2-receptors on SA node.
- ↑ **AV conduction** (+ ve dromotropic effect).
- ↓ Vasodilatation induced by cholinergic agonists.
- **Toxic dose:** Cutaneous vasodilatation→ (atropine flush)



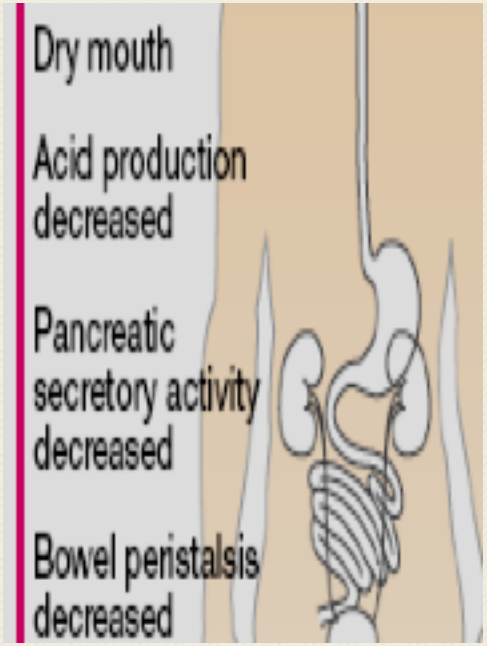


Respiratory system

- Relaxation of bronchial muscles (bronchodilators)
- ↓ Bronchial secretion → ↑ viscosity

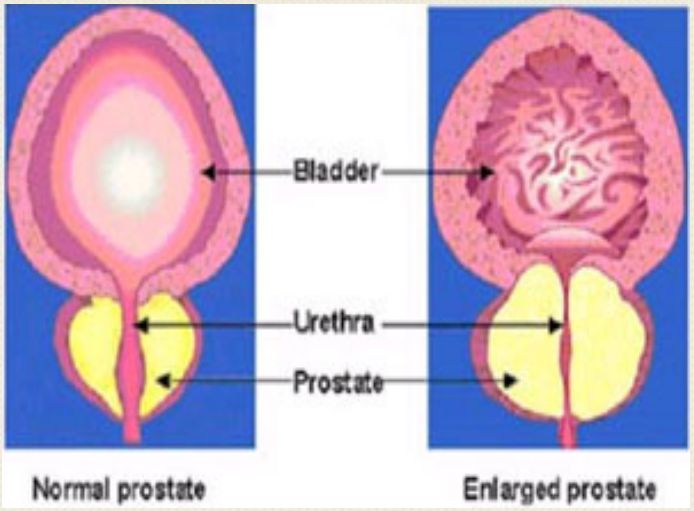
GIT:

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



Genitourinary tract:

- Relaxation of smooth muscles of urinary bladder.
- Sphincter contraction.
- Urinary retention.
- # Contraindicated in old men with prostatic hyperplasia.



Secretions

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

CLINICAL USES

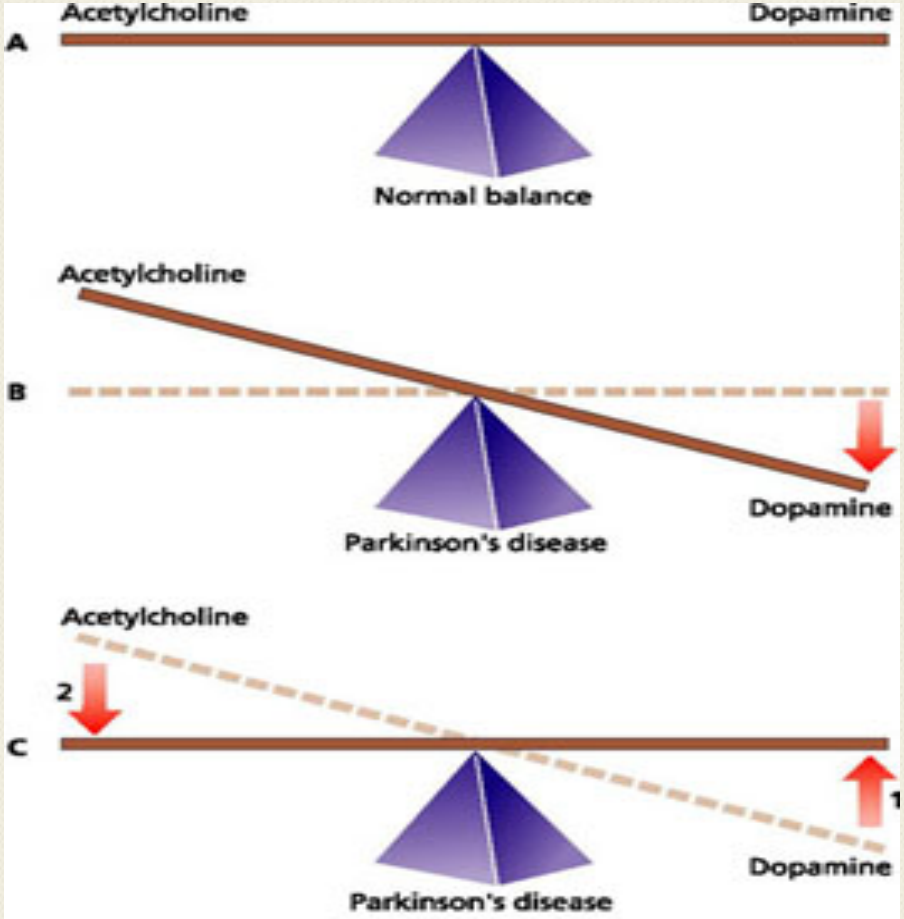
- Parkinsonism
- Vomiting (Motion sickness)
- Pre-anesthetic medication
- Asthma & COPD
- Peptic ulcer
- Intestinal spasm as antispasmodics
- Urinary urgency, urinary incontinence

CLINICAL USES

CNS:

Parkinsonism

e.g. Benztropine



A, Normal balance of acetylcholine and dopamine in the CNS.
B, In Parkinson's disease, a decrease in dopamine results in an imbalance.
C, Drug therapy in Parkinson's disease is aimed at correcting the imbalance between acetylcholine and dopamine. This can be accomplished by either
1. increasing the supply of dopamine or
2. blocking or lowering acetylcholine levels.

CLINICAL USES

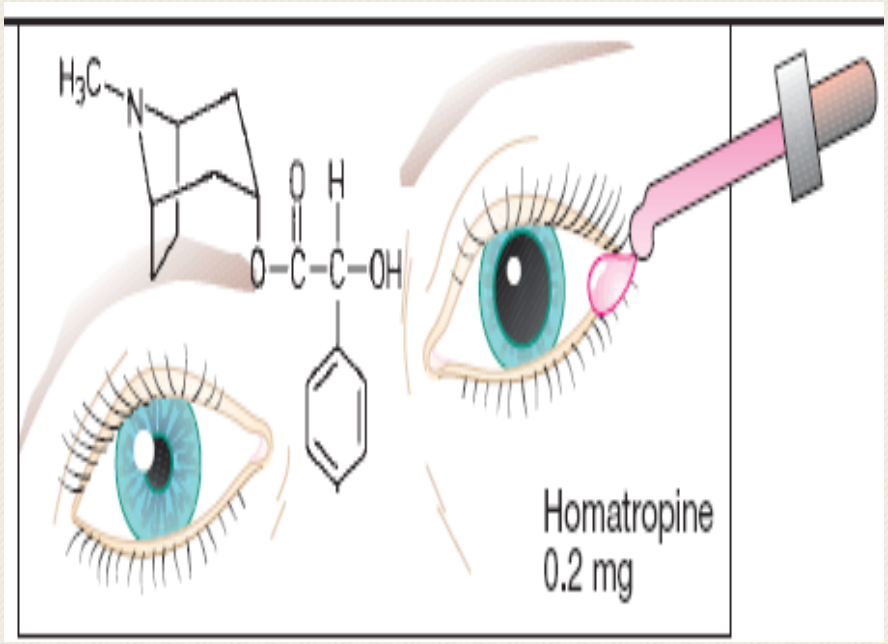
CNS:

Motion sickness e.g. Hyoscine

Ophthalmic disorders:

Ophthalmoscopic examination of retina

e.g. Tropicamide, homatropine



GIT:

e.g. **Glycopyrrolate, Hyocine butyl bromide**.

- Intestinal spasm
- Biliary and renal colics.
- Irritable bowel syndrome

- **Atropine + diphenoxylate**

  used for treatment of Traveler's diarrhea with opioid

GUT:

Urinary incontinence & Urinary urgency caused by minor inflammatory bladder disorders

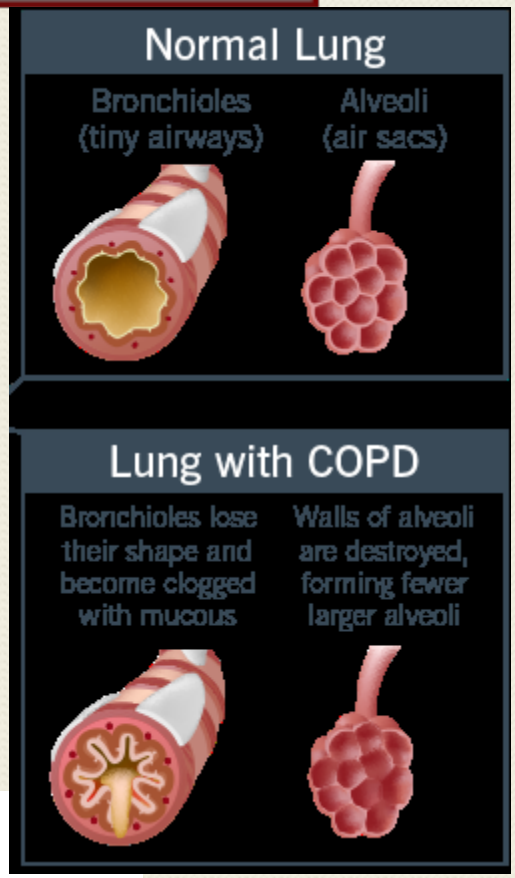
e.g. Oxybutynin

e.g. Darifenacin

Respiratory disorders:

e.g. Ipratropium (inhalation)

- a nonselective muscarinic antagonist
- Can not cross BBB
- Bronchial asthma & chronic obstructive pulmonary disease (COPD)
- No systemic side effects.



Cardiovascular uses:

Sinus bradycardia

atropine IV/IM

Used to increase heart rate through vagolytic effects, causing increase in cardiac output.

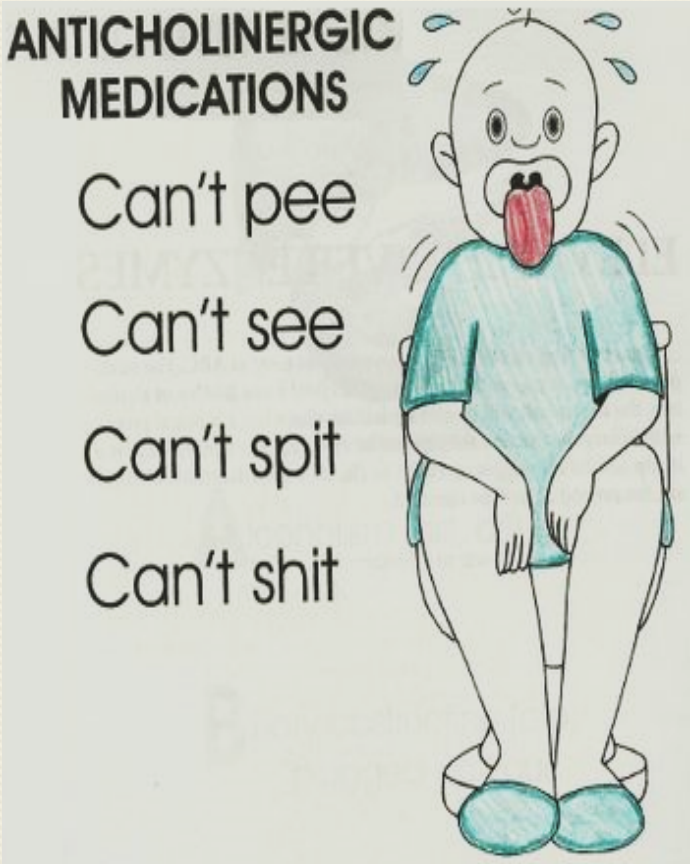
Cholinergic poisoning

Cholinesterase inhibitors “insecticides”.
Mushroom poisoning.

Atropine reverses muscarinic effects of cholinergic poisoning.

ADVERSE EFFECTS

- Confusion, agitation, delirium
- Mydriasis, blurred vision
- Dry mouth , hot flushed skin
- Tachycardia
- Palpitation
- Constipation, urinary retention
- Skin flushing
- ↑ Body temperature (hyperthermia).



THE MNEMONIC

Red as a beet

THE MNEMONIC

Full as a Flask

THE MNEMONIC

Mad as a hen

THE MNEMONIC

Blind as a bat

THE MNEMONIC

Hot as Hell fire

THE MNEMONIC

Dry as a bone

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
Glycopyyrolate	GIT	Antispasmodics in hypermotility
Oxybutynin Darifenacin	UT	Urinary urgency, Urinary incontinence

CONTRA-INDICATIONS

- **Glaucoma** (acute angle-closure glaucoma)
- **Tachycardia** secondary to thyrotoxicosis or cardiac insufficiency
- **Old patients with prostate hypertrophy.**
- **Paralytic ileus**
- **Constipation**
- **Children in case of atropine.**

SUMMARY

- **Antimuscarinics reverse action of cholinomimetics on muscarinic receptors.**
- **Are useful in many applications including intestinal spasm, urinary urgency, vomiting, parkinsonism, asthma and peptic ulcer.**
- **Are contraindicated in constipation, Prostate hypertrophy, tachycardia and glaucoma.**

Quiz 1?

- **A patient is brought into the emergency room. Upon examination you find the following: a high fever, rapid pulse, no bowel sounds and dilated pupils that do not respond to light. His lungs are clear. His face is flushed and his skin is dry. He is confused, disorientated and reports 'seeing monsters'. Based on these symptoms, you suspect he has been 'poisoned'. Which of the following, is the MOST obvious cause of poisoning?**
- A. Neostigmine
- B. Physostigmine
- C. Atropine sulfate
- D. Acetylcholine

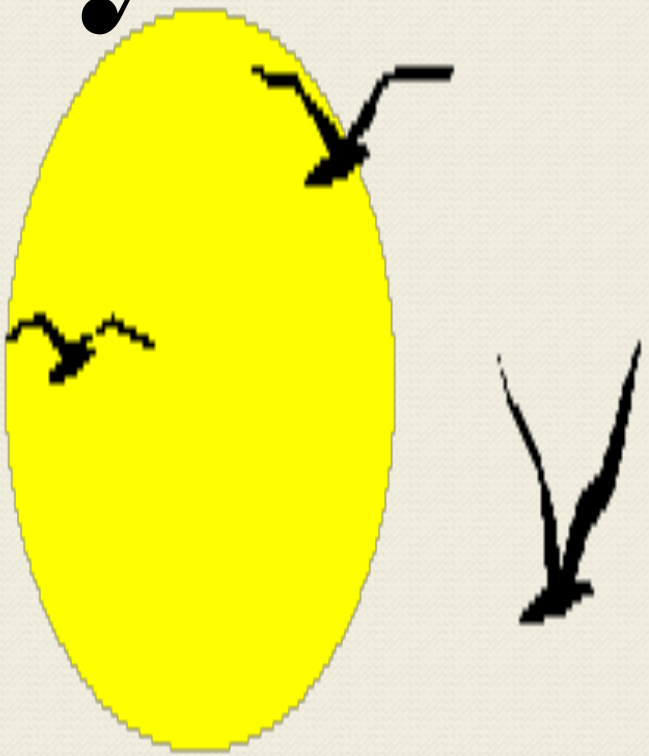
Quiz 2?

- **You are working in the post anesthesia care unit of a hospital. You have just received a patient back from surgery and you are monitoring his status. Knowing that the patient has received atropine, which of the following statements/observations is UNEXPECTED?**
- A. The patient is complaining of extreme thirst.
- B. The patient complains he is unable to clearly see the clock located just across from him.
- C. The patient's heart rate is elevated.
- D. The patient reports he has cramping and diarrhea.

Can antimuscarinic drugs reverse the Action of neostigmine on skeletal muscles?

What is the antidote that can be used in atropine toxicity?

Thank you



Questions ?