



Anticholinergic Drugs

- Red : important
- Black : in male / female slides
- Pink : in female's slides only
- Blue : in male's slides only
- Grey: Extra, Doctor's notes

OBJECTIVES:

By the end of this lecture , you 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, cycloplegia, peptic ulcer & parkinsonism.

Editing File

Anticholinergic Drugs - Antimuscarinic

classifications:

According to Source	
Natural	Synthetic / Semisynthetic
Atropine (Hyoscyamine)	Homatropine (Semisynthetic)
Hyoscine (Scopolamine)	Tropicamide
Pharmacokinetics of Atropine and Hyoscine: <ul style="list-style-type: none"> • Lipid soluble • Good Oral absorption • Good distribution • Can cross BBB (have CNS effect) • Hyoscine has <u>better</u> BBB penetration • 50% of ATROPINE is metabolized in liver and 50% excreted unchanged in urine. • HYOSCINE is more completely metabolized. • ATROPINE has t1/2 of 3–4 h. 	Ipratropium
	Pirenzepine
	Benztropine
	Oxybutynin
	Darifenacin
	Glycopyrrolate

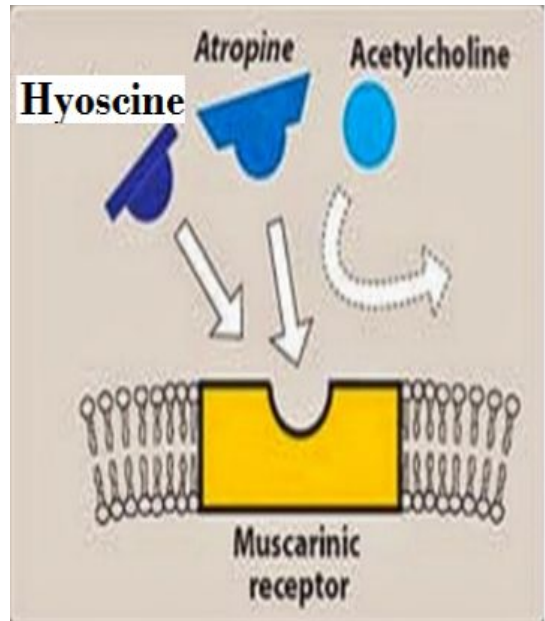
According to structure	
Tertiary amines "Lipid soluble"	Quaternary ammonium "Water soluble"
Atropine (Hyoscyamine)	Glycopyrrolate
Hyoscine (Scopolamine)	Ipratropium

According to selectivity	
Non-selective	Selective
Atropine (Hyoscine)	Pirenzepine (M1)
Hyoscine (Scopolamine)	Darifenacin (M3)
Ipratropium	

Mechanism of action:

Reversible competitive blockade of muscarinic receptors, some like atropine block nicotinic receptors in toxic doses (reverses muscarinic effects of cholinergic drugs).

- Salivary, bronchial, and sweat glands are most sensitive
- Gastric glands and gastric smooth muscles are the least.
- Smooth muscle and heart are intermediate.
- Atropine & hyoscine can block all muscarinic receptors because they are **(not selective)**.



REVIEW For Mechanism of actions: For your understanding only!

★ **Muscle Relaxants “ Neuromuscular Blockers”** peripherally acting :Act by blocking neuromuscular junction or motor end plate “nicotinic receptors” leading to skeletal muscle relaxation. e.g=Atracurium

★ **Cholinomimetics:** Drugs that produce actions similar to stimulation of parasympathetic system or similar to Acetylcholine

Direct:

Cause direct stimulation of cholinergic receptors “muscarinic or nicotinic receptors”

e.g Carbachol

Indirect:

Acts indirectly by inhibiting Acetyl cholinesterase act on both muscarinic and nicotinic receptors.

e.g Neostigmine

Pharmacodynamics Actions:

CNS

- Atropine (clinical dose) → **stimulation** followed by **sedation**
it stimulates medullary centers including vagal, vasomotor, and respiratory
high dose: cortical excitation, restlessness, hallucinations, disorientation, and delirium followed by respiratory depression and coma
- Hyoscine → **Sedation** (both drugs are pre-anesthetics)
- Antiemetic (block vomit center) and Antiparkinsonian effects (block basal ganglia)

CVS

- Bradycardia followed by tachycardia (blocks M2 receptors in SA node)
why initial bradycardia? At low doses, atropine (non-selective) inhibits pre-synaptic M1 receptors that inhibit Ach release. This "double" inhibition leads to an increase of Ach-->bradycardia
- **↑AV conduction**
- No BP influence, but decreases vasodilation caused by cholinergic agonists
- Toxic dose → Cutaneous vasodilation (atropine flush)

Eye

- **Passive mydriasis** (circular muscle paralysis) (active mydriasis is due to radial muscle contraction)
- **Cyclopegia** (ciliary muscle paralysis → loss of near accommodation → blur)
- ↑IOP (not suitable for glaucoma) + ↓Lacrimal secretion (sandy eye).

Respiratory System

- Bronchodilation + ↓ Secretion (leads to viscosity)

GIT

- ↓ Motility (antispasmodic) → constipation
- ↓ Gastric acid production
- ↓ Salivary secretions (dry mouth)
- ↑ Sphincter contraction (urinary retention)
- Smooth muscle relaxation

GUT

- Sphincter contraction (urinary retention → can occur in men with prostatic hyperplasia)
- Relaxation of urinary bladder smooth muscles

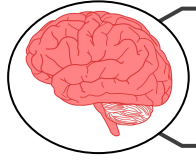
Secretion

- ↓ Sweating (dry skin)
in children, a modest dose can cause atropine fever

Drugs	Organ	Clinical uses
Benztropine AND Benzhexol	CNS	Parkinsonism
Hyoscine		Vomiting (Motion sickness) Preanesthetic
Tropicamide AND homatropine <small>Atropine substitute with short duration of action</small>	Ophthalmic disorders	Ophthalmoscopic examination (fundus examunation) of retina
Glycopyrrolate AND Hyoscine butylbromide	GIT	<ul style="list-style-type: none"> • Intestinal spasm. • Biliary and renal colics. • Irritable bowel syndrome.
Pirenzepine		Peptic Ulcer <small>(because pirenzepine acts on M1 receptors, which are responsible for gastric acid secretion from stomach parietal cells, inhibiting those receptors leads to reduced secretion of gastric acid)</small>
dicyclomine		Irritable bowel syndrome, colonic diverticular disease
Atropine AND diphenoxylate		Used for treatment of Traveler's diarrhea with opioid <small>Extra: Opioid drugs cause constipation.</small>
Oxybutynin AND Darifenacin	GUT	Urinary incontinence & Urinary urgency caused by minor inflammatory bladder disorders.
Ipratropium (inhalation)	Respiratory disorders	Bronchial asthma & chronic obstructive pulmonary disease (COPD).
Atropine	CVS and CNS	Preanesthetic Sinus bradycardia. Atropine IV/IM Used to increase heart rate through vagolytic effects, causing increase in cardiac output.
	Cholinergic poisoning	Mushroom poisoning. Atropine reverses muscarinic effects of cholinergic poisoning. Cholinesterase inhibitors (insecticides)
-	Others	Hyperhydrosis "excessive sweating"

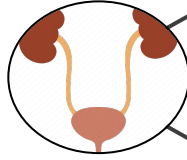
Adverse effects:

Can't pee, Can't See, Can't spit, Can't shit



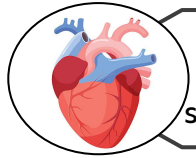
- **CNS:**

- 1-confusion 2-agitation
- 3 -delirium



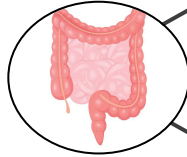
- **Urinary tract:**

Urinary retention



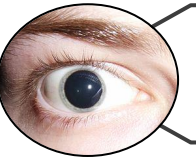
- **CVS:**

- 1-Tachycardia 2-Hot flushed skin(dilation of cutaneous blood vessels)



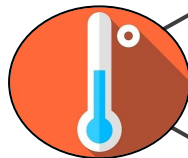
- **GIT:**

Constipation



- **Eyes:**

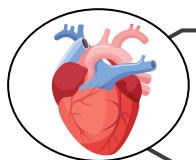
- 1-Blurred vision
- 2-Mydriasis (pupil dilation)



- **Secretions:**

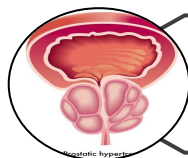
- 1-Dryness of mouth 2-Sandy eyes
- 3-Hyperthermia

Contraindications:



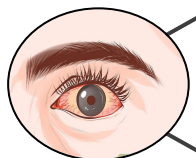
- **Tachycardia**

(secondary to thyrotoxicosis or cardiac insufficiency)



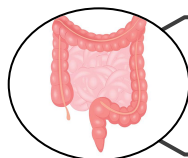
- **Prostate Hypertrophy**

(urinary retention)



- **Glaucoma**

(angle closure glaucoma)



- **Constipation**
- **Paralytic ileus**



- **Children in case of Atropine**

(Atropine flush)

Summary



Drug	Organ	Uses
Atropine	CNS	Pre-anesthetic medication, Antispasmodic
Hyoscine		Pre-anesthetic medication, Antispasmodic, Vomiting (Motion sickness).
Benztropine		Parkinson's disease
homatropine AND Tropicamide	Eye	Fundus examination (ophthalmic examination)
Ipratropium (Inhalation)	Respiratory System	Asthma, COPD
Pirenzepine	GIT	Peptic ulcer
Glycopyrrolate		Antispasmodics in hypermotility
Oxybutynin Darifenacin	GUT	Urinary urgency, Urinary incontinence

QUIZ

MCQs:

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

2-Which of these drugs acts SELECTIVELY?

A-Darifenacin. B-Atropine. C-Hyoscine. 4-Ipratropium.

3-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.

4-One of these cases using Antimuscarinic drugs is contraindicated:

A-Glaucoma. B-Parkinson's disease. C-Sinus bradycardia. D-Bronchial Asthma.

5-Mydriasis is known as:

A-Ciliary Muscle Contraction. B-Pupil Dilation. C-Pupil Constriction. D-Ciliary Muscle Relaxation.

SAQ:

1-What is the mechanism of action of Antimuscarinic drugs?

2-List FOUR Adverse Drug Reactions of Antimuscarinic drugs

3-A patient diagnosed with Colonic Diverticular Disease, what drug can you give him ?

4-Can antimuscarinic drugs reverse the action of neostigmine on skeletal muscles?

5-Enumerate one case in which Antimuscarinic drug is contraindicated:

6-Name TWO drugs used for treatment of Parkinsonism

Answers

MCQs:

1-C

Physostigmine is the treatment for the toxicity because it can cross the BBB therefore it increases the concentration of Ach resulting in treating the toxicity

2-A

3-D

4-A

5-B

SAQ:

1-**Reversible** competitive blockade of muscarinic receptors (reverses muscarinic effects of cholinergic drugs).

2-Constipation, Urinary retention, Mydriasis, Tachycardia.

3-Dicyclomine.

4- No, Neostigmine acts on both (N and M receptors) but in skeletal muscles it acts on the nicotinic receptor

5-Glaucoma.

6-Benzhexol + Benztropine



GOOD LUCK

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Sources:

Team 435.

Dr's slides.