



PHARMACOLOGY

Lecture: anticholinergic drugs

OBJECTIVES:

- 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.

Before studying this lecture, we recommend revising the lectures of the MSK block: muscle relaxants & cholinergic agonists



- Important.
- Extra notes.

Anticholinergic drugs

Definition: Are drugs that **block cholinergic receptors**.

They oppose their parasympathetic actions to produce actions similar to the sympathetic system's.

Classification

Anti-muscarinics

Mechanism of action of Antimuscarinic drugs:
reversible competitive blockade of muscarinic receptors.

Anti-nicotinics

Ganglionic blockers
used to treat hypertension, but not any more

Neuro-muscular blockers
e.g. muscle relaxants

Naturally occurring alkaloids

synthetic atropine substitutes

Suffix ine:

Definition

Esters of tropic acid and **tertiary amines**

Pharmacokinetics

Lipid soluble

Good oral absorption

Good distribution

Cross BBB → **have CNS actions**

Examples

Atropine
(prototype)

Hyoscine

More specific
less side effects

Benztropine

Homatropine

Tropicamide

Pirenzepine

Ipratropium

Glycopyrrolate

Oxybutynin

Mechanism :

Atropine & hyoscine can block all muscarinic receptors (**non selective**), Thus have many ADRs

Sensitivity:

1. Salivary, bronchial, & sweat glands (the most)
2. Smooth muscle & heart
3. Gastric glands & Smooth muscle

Cholinergic VS anticholinergic drugs

Action on:	Cholinergic actions Parasympathetic "Rest and digest"	Anticholinergic actions Sympathetic "Fight and flight"
Eye	<p>There will be 2 Contractions:</p> <ol style="list-style-type: none"> 1. Circular muscle of iris → Contraction(miosis) Parasympathetic stimulation on eye: Circular muscles(M receptor)→ contraction → Active miosis 2. Ciliary muscles → Contraction <p>Result in:</p> <ul style="list-style-type: none"> • Accommodation for near vision • Reduce intraocular pressure 	<p>There will be 2 Relaxations:</p> <ol style="list-style-type: none"> 1. Circular muscle of iris → relaxation(mydriasis) "Dilatation of eye pupil" Atropine: Blocking muscarinic receptors→ relaxing <u>circular muscles</u> → <u>Passive Mydriasis</u>. Sympathetic stimulation: <u>Radial muscles</u> (alpha receptor) → contraction → <u>Active mydriasis</u> 2. Ciliary muscles → relaxation (cycloplegia) "paralysis of the ciliary muscle of the eye" <p>Result in:</p> <ul style="list-style-type: none"> • loss of accommodation for near vision. • Loss of light reflex. • Increase I.O.P , thus contraindicated in glaucoma.
CVS	Bradycardia (decreased H.R.)	<ul style="list-style-type: none"> • Tachycardia (increase in heart rate) • ↑ Conduction speed in the AV node of the heart (+ ve dromotropic effect)
Urinary tract	Contraction of smooth muscles Relaxation of sphincter Urination	Relaxation of smooth muscles of urinary bladder. contraction of sphincter Urinary retention
Exocrine glands	Increase of : sweat, saliva, lacrimal, bronchial, intestinal secretions	Decrease all secretions: ↓ Salivary secretion → Dry mouth. ↓ Sweating → dry skin → Fever and hyperthermia in infants and children. ↓ Bronchial secretion → ↑ Viscosity ↓ Lacrimal secretion → Sandy eye, dry eye
GIT	Increase peristalsis Increase secretion Contraction of smooth muscles Relaxation of sphincter Result in: Diarrhea	Decrease peristalsis (↓ GIT motility → Antispasmodic effect) Decrease secretion Relaxation of smooth muscles Contraction of sphincter Result in: constipation
Respiratory system	1. Bronchoconstriction 2. Increase bronchial secretion Contraindicated in Asthma	1. Relaxation of bronchial muscles (Bronchodilatation) 2. Decrease bronchial secretion (↑ viscosity)

Anti-muscarinic drugs: natural alkaloids

ATROPINE VS HYOSCINE

Atropine (Hyoscyamine)	Hyoscine (scopolamine)
Long duration ($t_{1/2} = 4h$)	Shorter duration than Atropine
<p>More CVS effect</p> <p>Therapeutic dose:</p> <ol style="list-style-type: none"> ↓ Vasodilation induced by cholinomimetics Cutaneous vasodilation in children by releasing prostaglandins (atropine flush). initial bradycardia followed by tachycardia <p>Toxic dose: atropine flush in adults.</p>	<p>Less CVS effect</p> <p>POTENTIAL RELEVANCE:</p> <p>Hyoscine may represent an alternative to atropine as a PRE-ANESTHETIC MEDICATION for preventing bradycardia during operations.</p>
<p>Less CNS effect</p> <ul style="list-style-type: none"> CNS depression (Sedation). Antiemetic effect (block vomiting center) Antiparkinsonian effect (block basal ganglia). Toxic dose: Hyperthermia - excitement-hallucination followed by respiratory depression and coma 	<p>More CNS effect</p> <ul style="list-style-type: none"> better sedation Better antiemetic action (only Hyoscine is used for motion sickness) * (anti-vomiting) Can produce Amnesia (loss of recent memory) Used as pre- anesthetic

Scopolamine or hyoscine is preferable than atropine as antiemetic because it has more effect on CNS. It is also preferable as pre-anesthetic medication as it has amnesic and more sedative action than atropine.

Amnesia: a deficit in memory caused by brain damage

Q: Can antimuscarinic drugs reverse the action of neostigmine on skeletal muscles?

A: No, Because skeletal muscles only have Nicotinic receptors.



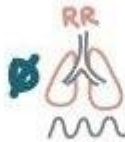
Video : Anticholinergic Agents

Anti-muscarinic drugs side effects

Side effects of anti-muscarinic drugs, specifically atropine :

Remember: effects of a drug other than the desired ones, are regarded as “side effects”

Anticholinergic



1. On the Eyes:

- Blurred vision
- Mydriasis

(dilation of the pupils)

2. Urinary tract

- Urinary retention

3. On the CNS

- Sedation
- Hallucination
- Excitation (at toxic dose)

4. On the CVS

- Tachycardia
- Atropine flush

(dilation of cutaneous blood vessels > hot flushed skin)

5. On the GIT

- Constipation
- Paralytic ileus

(paralysis of the intestines)

6. Secretions

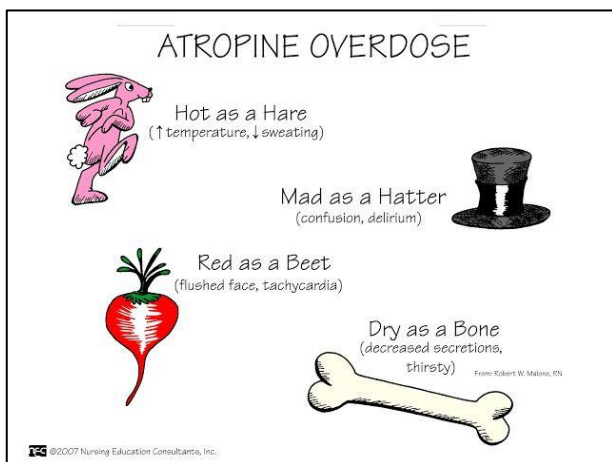
- Dryness of mouth
- Sandy eyes
- Decreased perspiration (sweating) → decreased evaporation → hyperthermia (increased body temperature)

Anti-muscarinic drugs toxicity:

Drug toxicity is caused by overdose or chronic use

Treatment:

- 1) **Gastric lavage.** (Washing out the stomach with water or medications)
- 2) **Anticonvulsant.** For seizures
- 3) **Cooling blanket.** For hyperthermia
- 4) **antidote: Physostigmine**
(anti-cholinesterase = reversible cholinesterase inhibitor)
It is given I.V slowly
Physostigmine is lipid soluble → crosses BBB → blocks the effect of atropine centrally



Antimuscarinic Drugs uses & contraindications

	Drug(s)	Organ	Uses
Natural alkaloids	Atropine	CNS	<ul style="list-style-type: none"> Pre-anesthetic medication Antispasmodic Traveler's diarrhea with opioid (Atropine + diphenoxylate)
	Hyoscine		<ul style="list-style-type: none"> Pre-anesthetic medication Antispasmodic Motion sickness (anti-vomiting)
Benztropine (more lipid soluble)	Parkinson's disease – specific on CNS (MNM: Ben took his son to the park)		
Synthetic atropine substitutes	Homatropine	Eye	Fundus examination of eye *because they have shorter action duration <24hrs, while atropine's effect on the eye lasts for about a week
	Tropicamide		
	Ipratropium Selective M3 antagonist	Respiratory System	<ul style="list-style-type: none"> Asthma & COPD (chronic obstructive pulmonary disease) Given by inhalation (to localize the action on the RSP system and limit side effect)
	Pirenzepine	Stomach	Peptic ulcer (blocks M1 at the parietal cells).
	Glycopyrrolate	GIT	Antispasmodics in intestinal hypermotility
	Oxyb UT ynin Selective for UT	UT	<ul style="list-style-type: none"> Urinary urgency Urinary incontinence

Anti-muscarinic drugs contraindications:

1) Glaucoma

(angle closure glaucoma)
paralysis of circular muscle → passive mydriasis → blocking Schlemm's canal → ↑ intraocular pressure

2) Tachycardia

(secondary to thyrotoxicosis or cardiac insufficiency)

3) Constipation

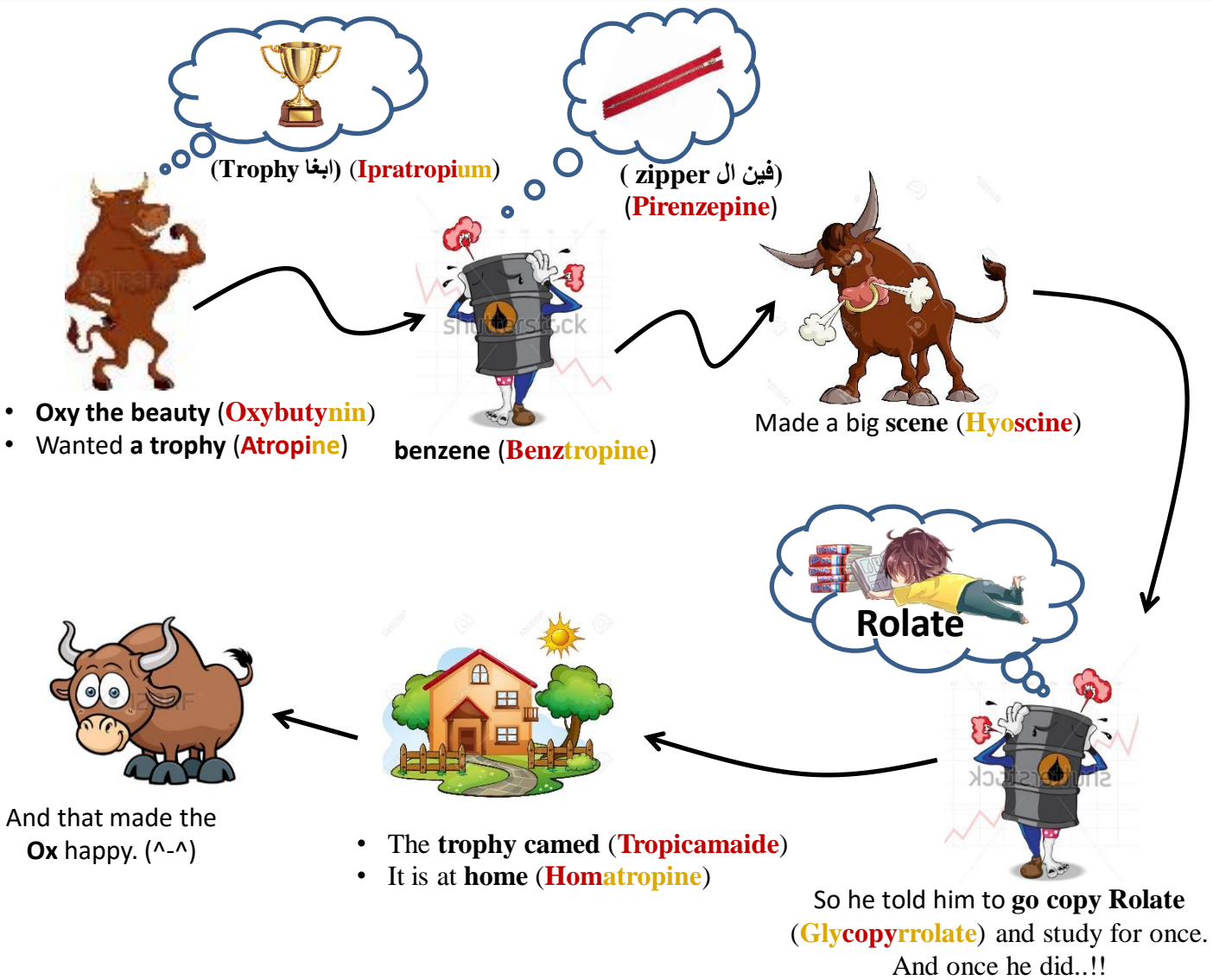
4) Prostate hypertrophy in old patients

since they already experience urinary retention

5) Children in case of atropine

Causes atropine flush, even at therapeutic doses

Anti- muscarinic drugs

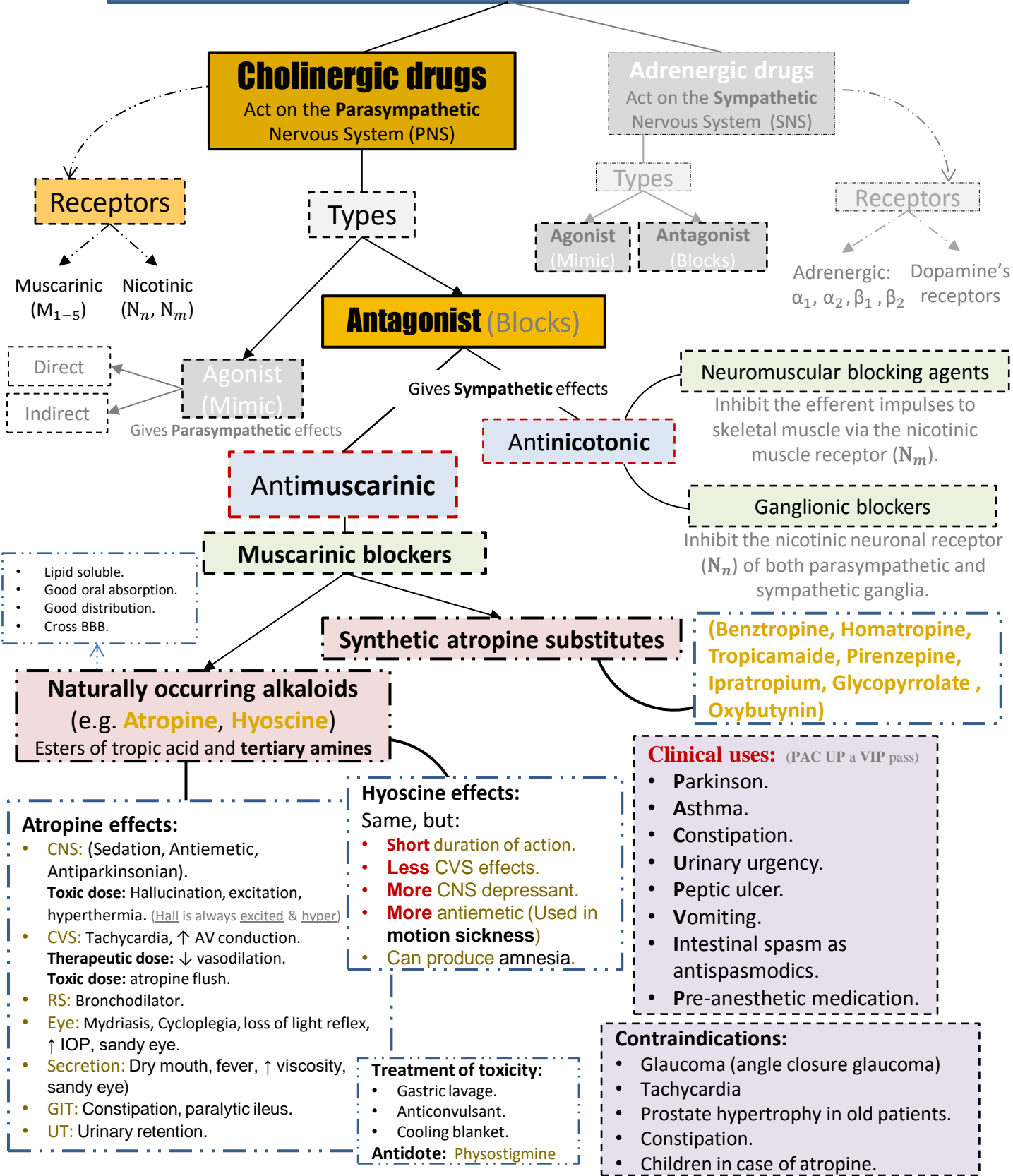


❖ A short story to remember the names of the drugs:

Oxy the buty (Oxybutynin) wanted a **trophy (Atropine)** so he went to **benzene (Benztropine)** and told him **(Trophy ابغا) (Ipratropium)** but he was too busy looking for his zipper and said **(zipper ال zipper) (Pirenzepine)** he made a big scene (**Hyoscine**), he got angry and tolled him why don't you **go copy Rolate (Glycopyrrolate)** and study for once if you really want it that bad. when he did, he told him (the **tropi camaide) (Tropicamide)** its at **home (Homatropine)**, and that made him happy.

Mind map

Drugs on the Autonomic nervous system



Drugs summary: Cholinergic Antagonist

Cholinergic Antagonist drugs – Anti-muscarinic

Mechanism

- Reversible competitive blockade of muscarinic receptors.
- **Atropine & hyoscine** can block all muscarinic receptors (**not selective**).

Naturally occurring alkaloids (Esters of tropic acid and tertiary amines)

Drug	Atropine	Hyoscine	
Pharmacokinetic	Lipid soluble, good oral absorption & distribution, cross BBB.		
Pharmacodynamics	Duration	Long	Short
	CNS	Depression (Sedation), Antiemetic , Antiparkinsonian (block basal ganglia). Toxic dose: Hallucination, excitation, hyperthermia. (<u>Hall</u> is always <u>excited</u> & <u>hyper</u>) Uses: Pre-anesthetic medication Antispasmodic.	More CNS depressant action. More antiemetic action Can produce amnesia . Uses: Pre-anesthetic medication, Motion sickness, antispasmodic.
	CVS	Tachycardia , ↑ AV conduction. Therapeutic dose: ↓ vasodilation. Toxic dose: atropine flush.	Less CVS effect
	RS	Relaxation of bronchial muscles (bronchodilator), ↓ Bronchial secretion → ↑ viscosity.	
	Eye	<ul style="list-style-type: none"> • Passive mydriasis → (due to paralysis of circular muscle) • Cycloplegia (loss of near accommodation) → (due to paralysis of ciliary muscle) Loss of light reflex , ↑ I.O.P (glaucoma), ↓ Lacrimal secretion → lead to sandy eye .	
	Secretions	Dry mouth, dry skin leading to <u>fever</u> , <u>increased Viscosity</u> , <u>Sandy eye</u>	
	GIT	<ul style="list-style-type: none"> • Relaxation of smooth muscles, ↑ contraction of sphincter leading to Constipation. • ↓ GIT motility → Antispasmodic effect, may cause paralytic ileus. 	
	UT	Relaxation of smooth muscles, Sphincter contraction → Urinary retention .	
Contraindications	<ul style="list-style-type: none"> • <u>Tachycardia</u>, <u>Glaucoma</u> (angle closure glaucoma), <u>Prostate hypertrophy</u> in old patients, <u>Constipation</u>, <u>Children</u> (in case of atropine). 		

Synthetic atropine substitutes

Benztropine	Homatropine	Tropicamide	Pirenzepine	Ipratropium	Glycopyrrolate	Oxybutynin
CNS	Eye		Stomach	RS	GIT	UT
Parkinson's disease	Fundus examination of eye		Peptic ulcer	<ul style="list-style-type: none"> • Asthma • COPD (by inhalation) 	Antispasmodics in hypermotility	Urinary urgency & Incontinence

QUIZ

THANK YOU FOR CHECKING OUR WORK
THE PHARMACOLOGY TEAM

عبدالرحمن السيارى
خالد الزهراني
عبدالله الجنيدل
أحمد المصعبي
مهند الزيد
معاذ باعشن
عبدالعزيز الشعلان
محمد السحيباني
عصام الوهيبي

لولوه الصغير
شادن العمران
ساره الحسين
لمى الزامل
كوثر الموسى
منيرة السلولي
ديمه الراجحي
أمل العمران
شمام السعد
رهف بن عبّاد
سارة الخليفة
ساره المطوع
فاطمة الدين

For any correction, suggestion or any useful information do not
hesitate to contact us : Pharmacology.med435@gmail.com



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