

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.



Important



In male and female slides



Only in male slides



Only in female slides



Extra information

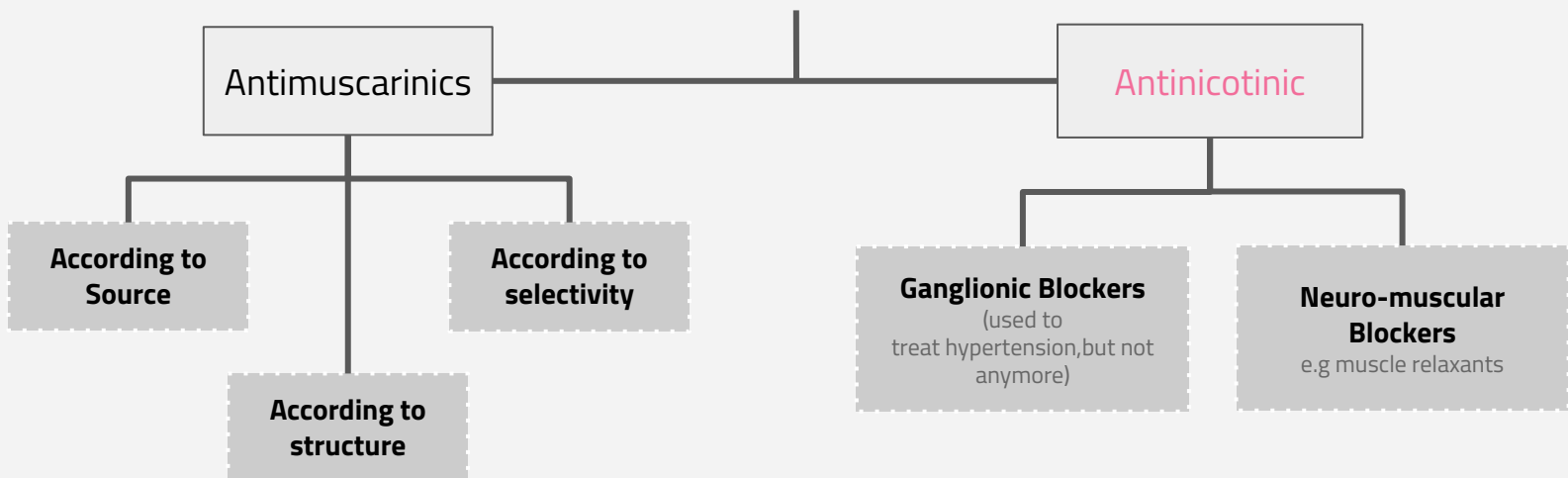


[helpful video](#)

Editing file

Anticholinergic Drugs

Classifications:



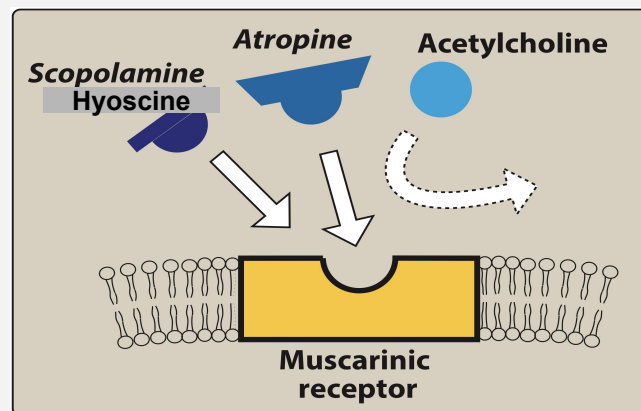
Antimuscarinics

Antimuscarinics			
According to source	Natural non-selective, block all the muscarinic receptors (M1, M2, M3, M4 and M5)	<ul style="list-style-type: none"> Atropine (Hyoscyamine) Extracted from a plant called <i>Atropa belladonna</i> Hyoscine (Scopolamine) from a plant called <i>Hyoscyamus nigra</i> 	Pharmacokinetics of Atropine and Hyoscine <ul style="list-style-type: none"> Lipid Soluble Good Oral Absorption Good distribution Can cross BBB (cause CNS effect) Hyoscine has better BBB penetration 50% of ATROPINE is metabolized in liver and 50% excreted unchanged in urine HYOSCINE is more completely metabolized ATROPINE has $t^{1/2}$ of 3-4h
	Synthetic/Semi-synthetic atropine substitutes Very Selective to muscarinic receptors	<ul style="list-style-type: none"> Homatropine (Semisynthetic) Tropicamide Ipratropium Pirenzepine Benztropine Oxybutynin Darifenacin Glycopyrrolate 	
According to structure	Tertiary amine	<ul style="list-style-type: none"> Atropine (Hyoscyamine) Hyoscine (Scopolamine) 	<ul style="list-style-type: none"> (Can cross BBB, Lipid Soluble)
	Quaternary ammonium	<ul style="list-style-type: none"> Glycopyrrolate Ipratropium 	<ul style="list-style-type: none"> (Can't cross BBB, Water Soluble)
According to selectivity	Non-selective	<ul style="list-style-type: none"> Atropine (Hyoscyamine) Hyoscine (Scopolamine) Ipratropium 	-
	Selective	<ul style="list-style-type: none"> Pirenzepine (M1) Darifenacin (M3) 	-

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 sensitive**.
- Smooth muscle and heart are **intermediate**.
- Atropine & hyoscine can block all muscarinic receptors (M1,M2,M3,M4,M5) because they are **(not selective)**.



only in female slide :

System or organ	Cholinergic actions (Parasympathetic)	Anticholinergic actions (Sympathetic)
Eye	Circular muscle of iris Contraction (miosis) . Ciliary muscle Contraction . Result in: 1/ Accommodation for near vision 2/ ↓ Intraocular pressure	Circular muscle of iris Relaxation (mydriasis) . "Dilatation of eye pupil" Ciliary muscles Relaxation (cycloplegia) . Result in: 1/ Loss of accommodation for near vision. 2/ Loss of light reflex. 3/ ↑ Intraocular pressure(I.O.P), thus contraindicated in glaucoma
CVS	Bradycardia (↓H.R.)	1/ Tachycardia (↑H.R.) 2/ ↑Conduction speed in AV node of the heart
Urinary bladder	Contraction of smooth muscles, Relaxation of sphincter. (Urination).	Relaxation of smooth muscle, Contraction of sphincter (Urinary retention)
Exocrine glands	Increase of: sweat, saliva, lacrimal, bronchial and intestinal secretions.	↓ all secretions.
GIT	↑ peristalsis, ↑ secretion, Relaxation of sphincter (Diarrhea)	↓ peristalsis, ↓ secretion, Contraction of sphincter (constipation) إمساك
Respiratory system	1/ Bronchoconstriction 2/ ↑ bronchial secretion	1/ Bronchodilatation 2/ ↓ bronchial secretion

system	Drugs	Clinical Uses	Pharmacodynamic Actions
CNS	Benztropine and Benzhexol	<p><u>Parkinsonism</u></p> <p>*Mnemonic: To <u>park</u> your car you'll need <u>Benz</u>ene to move it</p>	- Antiparkinsonian effect (block basal ganglia)
	Hyoscine (preventative, taken before symptoms)	<p>- Motion sickness (vomiting) "antiemetic effect"</p> <p>- Pre-anesthetic + an Amnesia effect (شعور الفقدان بالذاكرة عشان المريض ما يتذكر شيء من العملية)</p> <p>- Antispasmodic</p> <p>*Mnemonic: people feel motion sickness as the plane goes Higher (<u>Hy</u>oscine)</p>	<p>-Hyoscine → (sedative effect)</p> <p>-Antiemetic effect (block vomiting center)</p>
	Atropine (I.V/ I.M)	<p>Pre-anesthetic, Antispasmodic</p>	<p>-Atropine at clinical doses, initial stimulation followed by depression (sedative effect)</p> <p>High doses of atropine cause cortical excitation, restlessness, disorientation, hallucination(هذيان) and delirium(confusion) followed by respiratory depression and coma.</p>
<p>Sinus Bradycardia. Used to increase heart rate through vagolytic effects (inhibits action of Vagus nerve to the heart), causing increase in cardiac output.</p> <p>Pain of myocardial infarction → depression of SA, AV node</p>		<p>Atropine cause initial bradycardia followed by tachycardia due to blockade of M2-receptors on SA node.</p> <p>↑ AV conduction (+ ve dromotropic effect).</p> <p>↓ vasodilation induced by cholinergic agonists.</p> <p>Toxic dose: Cutaneous vasodilation will cause → (atropine flush).</p> <p>Atropine shortens the refractory period of AV conduction.</p> <p>Atropine does not influence Blood pressure .</p>	
CVS			
Eye	Tropicamide, Homatropine	<p>Ophthalmic Disorders: Ophthalmic examination of Retina (fundus examination)</p> <p>نحتاج البؤبؤ يتوسع عشان نقدر نشوف قاع العين (الشبكية) بالفحص mydriasis فلازم يصير</p> <p>*Mnemonic: - We have an ophthalmologist in our <u>home</u> - You should visit the ophthalmologist after returning from a <u>tropical</u> country</p>	<p>Passive mydriasis due to paralysis of circular muscle.</p> <p>Cycloplegia (loss of near accommodation) due to paralysis of ciliary muscle</p> <p>Loss of light reflex.</p> <p>↑ Intraocular pressure (I.O.P) contraindicated to Glaucoma.</p> <p>↓ in lacrimal secretion it will cause Dry and sandy eye</p> <p>The reason for Glaucoma is that mydriasis, unlike miosis, blocks drainage of intraocular fluid which leads to increase in IO pressure</p>
Respiratory system	Ipratropium (inhalation)	<p>- Bronchial asthma & chronic obstructive pulmonary disease (COPD)</p> <p>-Pre-operative medication when anaesthetic → ↓secretion & laryngospasm</p> <p>-Hyoscine → amnesia (فقدان الذاكرة) يستخدم قبل العمليات عشان المريض ما يتذكر اي شيء</p>	<p>Relaxation of bronchial muscles (Bronchodilators)</p> <p>- Can not cross BBB</p> <p>- No systemic side effects.</p> <p>- nonselective muscarinic Antagonist</p> <p>↓Bronchial secretion → ↑ Viscosity</p>







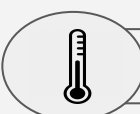
system	Drugs	Clinical Uses	Pharmacodynamic Actions
GIT	Glycopyrrolate, Hyocine butyl bromide	<ul style="list-style-type: none"> - Intestinal Spasm (antispasmodic) - Biliary and renal colics (مغص) - Irritable bowel syndrome (IBS) - Antispasmodics in Hypermotility 	<ul style="list-style-type: none"> - Dryness of mouth - ↓ Gastric acid secretion - Relaxation of smooth muscles - ↓ GIT Motility → Antispasmodic effect
	Pirenzepine	Peptic Ulcer	- ↑ Sphincter contraction
	dicyclomine	Irritable bowel syndrome, colonic diverticular disease	- Constipation
	Atropine + Diphenoxylate (Not important)	Used for treatment of Traveler's diarrhea with opioid (Not important)	
Genitourinary tract (GUT)	Oxybutynin, Darifenacin	Urinary incontinence & Urinary urgency caused by minor inflammatory bladder disorders	<ul style="list-style-type: none"> - Relaxation of smooth muscles of urinary bladder - Sphincter contraction - Urinary Retention - Contraindicated in old men (+60 y.o) with prostatic hypertrophy
Secretions	-	Hyperhydrosis	<ul style="list-style-type: none"> - ↓ Salivary Secretion → Dry mouth - ↓ Sweating (M3 blockage) → dry skin - Contraindicated In Children: modest dose → "Atropine Fever" (Bizarre effect) - ↓ Bronchial secretion → ↑ Viscosity - ↓ Lacrimal secretion → sandy eye

🍄 Cholinergic Poisoning 🍄

- Cause: Cholinesterase inhibitors "insecticides", Mushroom poisoning
- Treatment: **Atropine** reverses muscarinic effects of cholinergic poisoning



Adverse Effects

-  Confusion, agitation, delirium
Hyoscine → amnesia (فقدان الذاكرة)
-  Mydriasis, blurred vision
-  Dry mouth
-  Tachycardia, hot flushed skin
(cutaneous vasodilation)
-  Constipation
-  urinary retention
-  ↑ Body temperature (hyperthermia)

Mnemonics



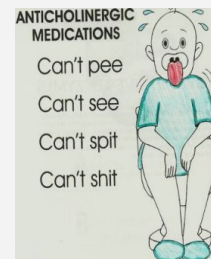
Dry as Bone



Red as Beet



Full as Flask



Mad as hen




Blind as Bat




Hot as Hell fire


Contraindications

 Children in case of Atropine "atropine fever"

 Old patients with prostate hypertrophy

 Tachycardia, secondary to thyrotoxicosis or cardiac insufficiency

 Glaucoma (angle closure)

 Paralytic ileus (↓ motility), Constipation, GI obstructive disease

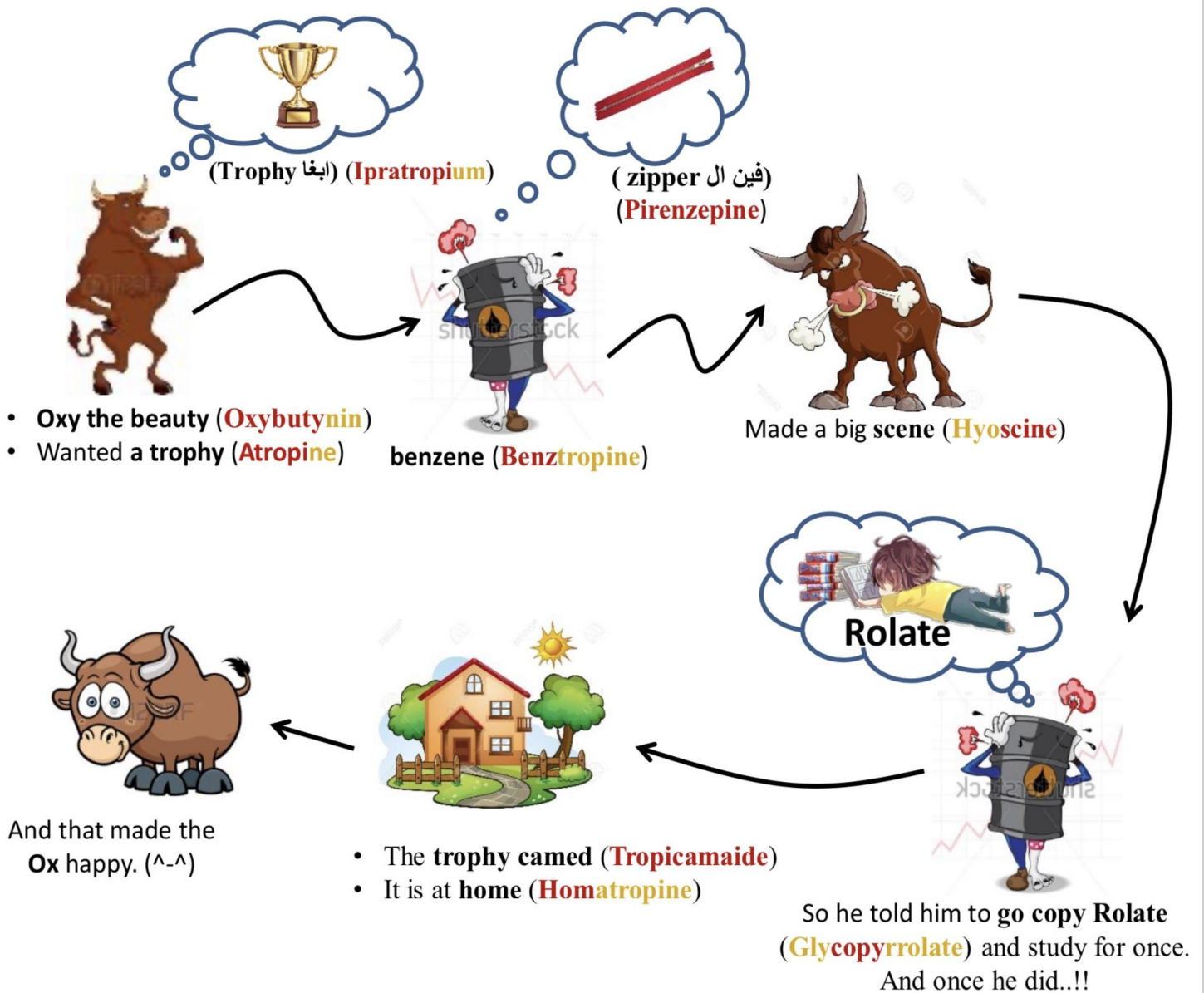
Summary (Female Slides)

- 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.

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	asthma, COPD, inhalation
Pirenzepine	Stomach	Peptic ulcer
Glycopyrrolate	GIT	Antispasmodics in hypermotility
Oxybutynin Darifenacin	UT	Urinary urgency, Urinary incontinence

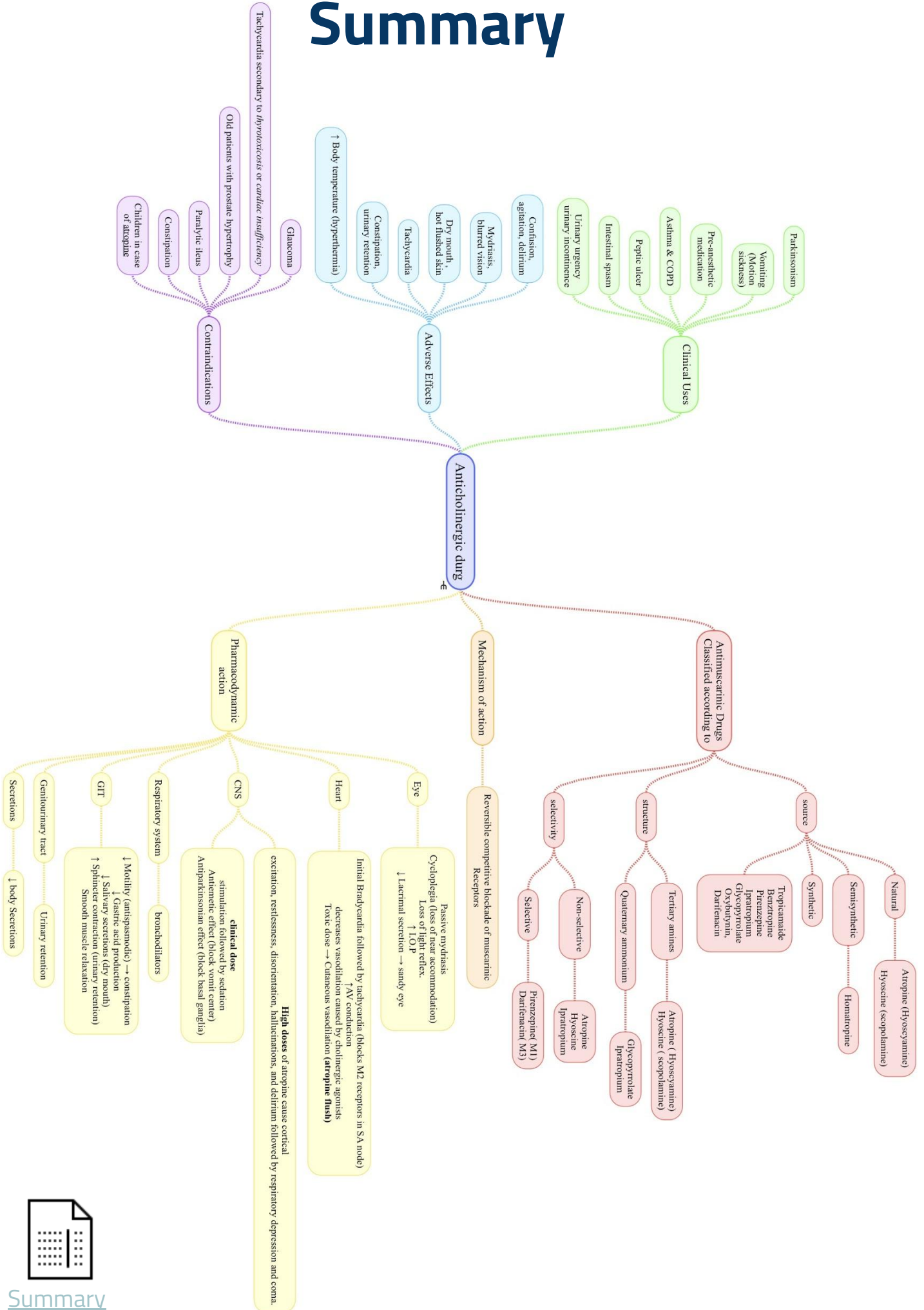
Extra



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

Oxy the buty (**Oxybutynin**) wanted a trophy (**Atropine**) so he went to benzene (**Benzotropine**) and told him (Trophy ابغا) (**Ipratropium**) but he was too busy looking for his zipper and said (فين الزير) (**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) (**Tropicamaide**) its at home (**Homatropine**), and that made him happy.

Summary



MCQ



1- Which ONE of the following drugs is used in ophthalmoscopic examination?			
A- Homatropine	B- Hyoscine	C- Atropine	D- Ipratropium
2- In preanesthetic, a 6 years old boy takes anticholinergic but after taking it he became feverish and exhibited tachycardia, hot skin and his pupil dilated which drug did he use?			
A- Acetylcholine	B- Hyoscine	C- Atropine	D- Benztropine
3- Which one of the following is a contraindication to the use of antimuscarinic drugs?			
A- Asthma	B- Intestinal spasm	C- Peptic ulcer	D- Urinary retention
4- Which of these drugs is used for motion sickness?			
A- Benztropine	B- Scopolamine	C- Ipratropium	D- Piphenoxylate
5- Your 23 year-old patient recently diagnosed with asthma cannot tolerate the CNS side effects of his inhaled albuterol (a beta-2 agonist bronchodilator). As an alternative, you recommend he try an inhaled quaternary antimuscarinic, and prescribe:			
A- Atropine	B- Tropicamide	C- Ipratropium	D- Darifenacin
6- Which of these drugs is best used to treat Irritable bowel syndrome?			
A- Hyoscine	B- Atropine	C- Pirenzepine	D- Glycopyrrolate
7- DR'S SLIDES: 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
8- DR'S SLIDES: 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

Answers

1	2	3	4	5	6	7	8
A	C	D	B	C	D	C	D

SAQ

Q1) Give 3 antimuscarinic drugs and their clinical uses.

Q2) What are the differences between natural and synthetic/semi-synthetic antimuscarinic

Q3) What is the common clinical use between natural antimuscarinic drugs?

Q4) What are the best drugs used to treat Urinary Incontinence? What is its M.O.A and when is it contraindicated?

Q5) Atropine fever happens in which dose? And who does it affect?

Q6) What causes mushroom poisoning and how does Atropine treat it?

Q7) DR'S SLIDES: Can antimuscarinic drugs reverse the action of neostigmine on skeletal muscles?

Q8) DR'S SLIDES: What is the antidote that can be used in atropine toxicity?

Answers

A1) Benztropine/Parkinsonism . Hyoscine/Motion sickness Ipratropium/Bronchial asthma.

A2) Natural drugs are non-selective to muscarinic receptors and can cross Blood brain barrier, thus it cause CNS effects, Synthetic/semi-synthetic drugs are selective to muscarinic receptors and cannot cross the blood brain barrier.

A3) Pre-anesthetic.

A4) Oxybutynin or Darifenacin. It works by relaxing smooth muscles of urinary bladder and contracting the sphincter which causes Urinary Retention, Contraindicated in old men with prostatic hyperplasia.

A5) modest dose, affects children so it's contraindicated for them.

A6) Cholinesterase inhibitors "insecticides", Atropine reverses muscarinic effects of cholinergic poisoning.

A7) No, because skeletal muscles doesn't contain muscarinic receptors, only nicotinic.

A8) Physostigmine.



GOOD LUCK!

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