

# ANTICHOLINERGIC DRUGS

Revised by  
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## 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 anti-muscarinic agent for each of the following special uses: mydriasis, cycloplegia, peptic ulcer & parkinsonism.

Sleeping more may take away 10% of your day, but if you are 50% more efficient while awake, Who cares?!

- Titles
- Very important
- Extra information
- Doctor's notes

## Cholinergic receptors

Types	Nicotinic	Muscarinic
features	<ol style="list-style-type: none"><li>1. Found centrally.</li><li>2. Almost always excitatory.</li><li>3. acetylcholine is the main neurotransmitter with high affinity to nicotine.</li><li>4. Ion-channel linked receptor.</li></ol>	<ol style="list-style-type: none"><li>1. Found peripherally.</li><li>2. Can be excitatory and inhibitory.</li><li>3. Acetylcholine is the main neurotransmitter.</li><li>4. G-protein coupled receptor.</li></ol>
Location and subclasses	<ol style="list-style-type: none"><li>1. Skeletal muscles</li><li>2. Autonomic ganglia</li><li>3. Adrenal medulla</li><li>4. CNS</li></ol>	<ol style="list-style-type: none"><li>1. M1: CNS.</li><li>2. M2: Heart.</li><li>3. M3: internal organs.</li><li>4. M4 and M5: CNS for memory and attention.</li></ol>

### Don't forget:

- ❖ Activation of M1 causes:
  1. CNS excitation.
  2. Increase Gastric acid secretion.
- ❖ Activation of M2 causes bradycardia.
- ❖ Activation of M3 causes:
  1. Increase secretions of glands.
  2. Smooth muscle contraction.
  3. Vasodilation.

### Remember:

- Odd numbers (1,3,5) are excitatory.
- Even numbers (2,4) are inhibitory.

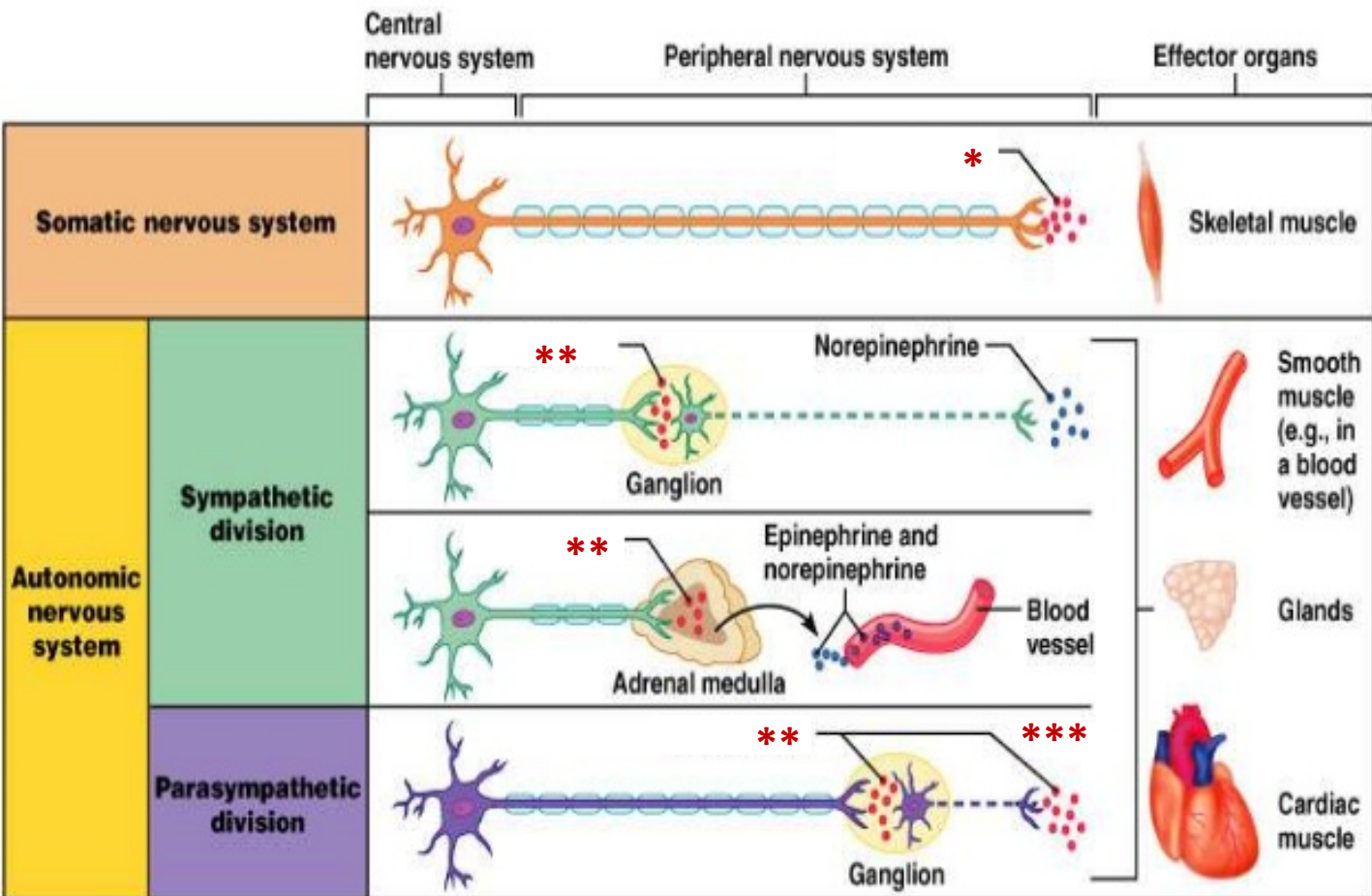
# Anticholinergic Drugs

Anti-muscarinics

anti-nicotinics

Ganglionic Blockers

Neuromuscular blockers



- \* neuromuscular blockers.
- \*\* ganglionic blockers.
- \*\*\* site of action of antimuscarinic drug.

# Antimuscarinic Drugs

Antimuscarinic drugs classified according to:

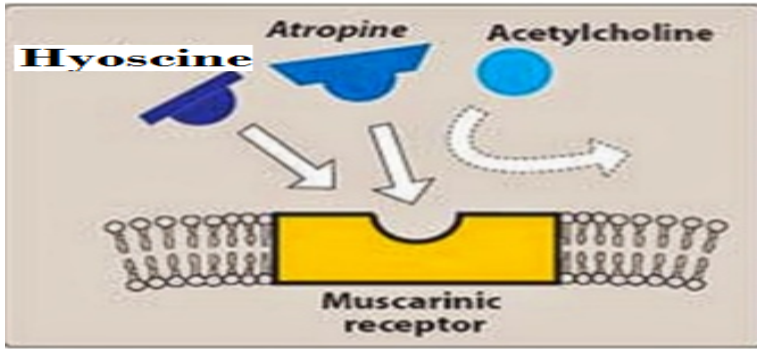
Source	<ul style="list-style-type: none"> <li>Natural: <b>atropine, hyoscine.</b></li> <li>Semisynthetic: <b>Homatropine</b></li> <li>synthetic: <b>Tropicamide, Benztropine, Pirenzepine, Ipratropium, Glycopyrrolate, Oxybutynin, Darifenacin</b></li> </ul>
Structure	<ul style="list-style-type: none"> <li>Tertiary amines ( lipid soluble ): <b>atropine, hyoscine.</b></li> <li>Quaternary ammonium ( water soluble): <b>Glycopyrrolate.</b></li> </ul> <div style="border: 1px dashed orange; padding: 5px; margin-top: 5px; text-align: center;">Glycopyrrolate = glucose = soluble in water</div>
Selectivity	<ul style="list-style-type: none"> <li>Non-selective: <b>Atropine, Hyoscine, Ipratropium.</b></li> <li>Selective: <b>Pirenzepine (M1), Darifenacin (M3)</b></li> </ul>

<p>M3 ونوع الريسبتور هناك M3 وممكن أتذكره من عدد كلمات الجملة "داري فين الأكل"</p>	Darifenacin
<p>نقدر نقرأ أول مقطع باسم الدرق (Piren) باريني يعني ناقسني ، واخر مقطع (pine) باين يعني واضح، قصير الجملة باريني ، باين بأصير الأول (M1)</p>	Pirenzepine =Gastrozepin

## Mechanism of action:

**Competitively block muscarinic receptors.**

Salivary, bronchial, and sweat glands are the most sensitive .  
Smooth muscles and heart muscles are intermediate.  
Gastric glands and muscles are the least sensitive.



# Pharmacokinetics:

-Natural Alkaloids:

**Atropine (Hyoscyamine)**

**Hyoscine (scopolamine)**: better BBB Penetration, while passage of atropine is restricted

عشان نتذكر هالمعلومة كأننا ناشر ونقول هيو Hyo السكين scine ، والسكين حاد ويخترق أي شيء. Penetration

- ✓ Lipid soluble.
- ✓ Good oral absorption.
- ✓ Good distribution.
- ✓ Cross blood brain barrier (**have CNS actions**).
- ✓ Rapidly absorbed from the GIT.
- ✓ When applied to the eyes they penetrate the cornea.
- ✓ 50% of atropine is metabolized in the liver and excreted unchanged in urine.
- ✓ Atropine has  $t_{1/2}$  of 3–4 h
- ✓ Hyoscine is more completely metabolized and has better BBB penetration.

# Pharmacodynamics effects of muscarinic drugs

## 1) CNS



### **Atropine:**

**Clinical dose:** initial stimulation followed by depression (sedative effect).

**High dose:** cortical excitation, restlessness, disorientation, hallucinations, delirium followed by respiratory depression, coma.

**Hyoscine:** sedative effect (more)

Antiemetic effect of motion sickness (block vomiting center if they cross BBB).

**Benzotropine:** Antiparkinsonian effect (block basal ganglia).

## 2) CVS



### **Atropine**

- Causes initial bradycardia followed by tachycardia due to blockade of M2-receptors on SA node.

- Higher AV conduction (+ve dromotropic effect) (tachycardia)

\* AV = Atrioventricular

- Does not influence Blood Pressure.

- Decrease (**blunt**) Vasodilatation induced by cholinergic agonists. **Doesn't reach vasoconstriction.**

# Atropine does not influence the blood pressure because it doesn't have any effect on the blood vessels. It only block (**blunt**) the effect of vasodilation induced by cholinergic agonist.

-**Toxic dose:** Cutaneous vasodilatation → atropine flush.

Face appears red

## 3) Eye

- Passive mydriasis (no miosis)

due to paralysis (relaxation) of circular muscle

- Cycloplegia (loss of near vision accommodation)


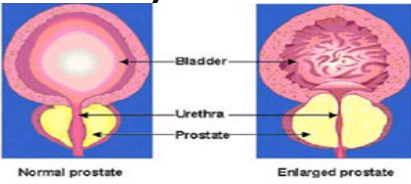
due to paralysis of ciliary muscle.

- Loss of light reflex.

- Increase I.O.P > # glaucoma. (contraindication)

- Lower Lacrimal secretion → sandy eye (dryness)

# Pharmacodynamics effects of muscarinic drugs

<p>4) Respiratory system</p>	<ul style="list-style-type: none"> <li>- Relaxation of bronchial muscles (bronchodilator)</li> <li>- Lower Bronchial secretion leads to higher viscosity</li> </ul>
<p>5) GIT</p> 	<ul style="list-style-type: none"> <li>- Dryness of mouth (low saliva secretion)</li> <li>- ↓ Gastric acid production</li> <li>- Relaxation of smooth muscles.</li> <li>- ↓ GIT motility → <b>Antispasmodic effect.</b></li> <li>- Constipation</li> <li>- ↑ Sphincter contraction.</li> </ul>
<p>6) GUT</p> 	<ul style="list-style-type: none"> <li>- Relaxation of bladder.</li> <li>- Sphincter contraction.</li> <li>- Urinary retention.</li> <li>- Urinary retention (in old men with prostatic hyperplasia)</li> </ul>
<p>7) Secretions</p>	<ul style="list-style-type: none"> <li>↓ Salivary secretion → <b>(Dry mouth)</b>. (xerostomia)</li> <li>↓ Sweating → dry skin, M3 receptor blocker.</li> <li>- Modest dose of atropine: blocks sweat glands → "atropine fever" of children</li> <li>↓ Bronchial secretion → higher Viscosity</li> <li>↓ Lacrimal secretion → Sandy eye</li> </ul>

## Clinical Uses of anti-muscarinic drugs

### Cardiovascular effects:

- Sinus bradycardia.
- Pain of myocardial infarction → depression of SA, AV node.

### Hyperhydrosis



### Cholinergic poisoning

- Cholinesterase inhibitors "insecticides".
- Mushroom poisoning **it has high constriction of muscarinic.**



# Clinical Uses of anti-muscarinic drugs

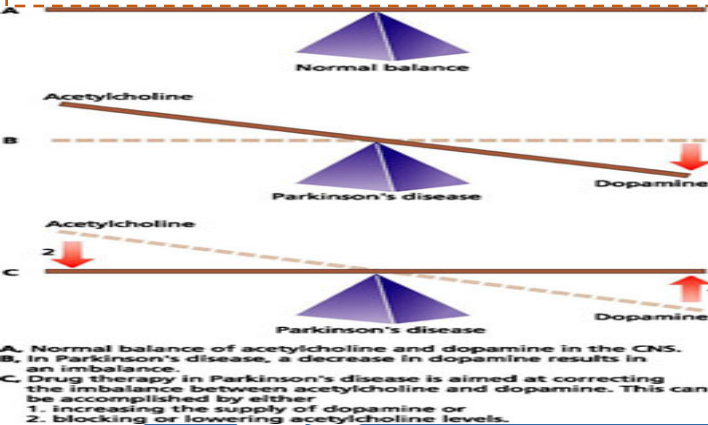
Drugs	organ	Uses
<b>Atropine</b>	CNS	Pre-anesthetic medication, Antispasmodic. Atropine with diphenoxylate used for treatment of Traveler's diarrhea with opioid.
<b>Hyoscine</b>	CNS	Pre-anesthetic medication, Motion sickness, antispasmodic.
<b>Benztropine</b> <b>Benzhexol</b>	CNS	* Parkinson's disease- (benztropine -lipid soluble to cross brain barrier)
<b>Homatropine</b> <b>Tropicamide</b>	Eye	Ophthalmoscopic examination of retina. We can't use atropine because it has long duration effect
<b>Ipratropium</b>	Respiratory system	asthma, COPD, by inhalation because ipratropium is not selective so, to limit the effect we give it by inhalation pre-operative medications when anesthetic → increase secretion & laryngospasm. (Hyoscine for amnesia)
<b>Pirenzepine</b>	Stomach	Peptic ulcer
<b>Oxybutynin</b> <b>Darifenacin (selective)</b>	UT	Urinary incontinence, Urinary urgency caused by minor inflammatory bladder disorders
<b>Glycopyrrolate (water soluble)</b> <b>Hyoscine butyl bromide (solid)</b> <b>dicyclomine</b>	<u>G</u> IT	Antispasmodics in hypermotility, Biliary and renal colics. Irritable bowel syndrome (cause diarrhea and increase mortality) Colonic diverticular disease

Glyco=Glucose which is found in the food in the (GIT)

**Glycopyrrolate**

It is known also as **Gastrozepin**, and as its name suggest its related to decrease the gastric acid in stomach.

**Pirenzepine**



**\* CNS:**



اللي فيهم شلل رعاشي Parkinson's disease صعبة يسوقون سيارة، والسيارة تحتاج بينزين Benz

Benztropine

الرئة Respiratory system كأنها بالونة ما ينفخ ندخل جواتها ليرة Ipra وإلا يتنفخ .

Ipratropium

أول مقطع باسم الدرق (Dari) يذكرني ب"إرار البول" يعني يستخدم ل (Genitourinary tract)

Darifenacin

نقدر نقرا أسم الدرق كذا ، اوخص (oxy) عنده بيوتيفل beautiful=(buty) حمام , يعني يستخدم ل (Genitourinary tract)

Oxybutynin

**Oxybutynin and Darifenacin are used for Urinary urgency, urinary incontinence**

لما نحتاج الحمام ويكون فيه أحد جوا يستخدمه نقول له اطلع (oxy)=exit بيه دوري (dari)

نستخدم هالدرق كقطرة عند فحص العيون فنقدر نقرا اسم الدرق كذا بيه القطرة (trop)=drop جت (camide)=came

Tropicamide

أول مقطع بالكلمة يذكرني بكلمة "هم" اللي يحسون فيه من يفقد بصره وفعلا أي مرض بالعين فيه كربة وهم وتنتكر يعقوب عليه السلام لما ابيضت عيناه من الحزن والهجم، فأتذكر ان هالدرق يستخدم عند دكتور العيون بفحص الشبكية.

Homatropine

**Tropicamide and homatropine are used for Ophthalmoscopic examination of retina**

بعد الاختبار عند طبيب العيون رجعت البيت (hom) وما قدرت اشوف حتى التراب (trop)

## Adverse Effects:

- Mydriasis, blurred vision
- Tachycardia
- Constipation, urinary retention
- ↑ Body temperature (hyperthermia)
- Confusion, agitation, delirium
- Dry mouth (even in therapeutic dose) , hot flushed skin

### ANTICHOLINERGIC MEDICATIONS

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



### ATROPINE OVERDOSE



Hot as a Hare  
(↑ temperature, ↓ sweating)



Mad as a Hatter  
(confusion, delirium)



Red as a Beet  
(flushed face, tachycardia)



Dry as a Bone  
(decreased secretions, thirsty)

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## Contra-indications:

- Glaucoma (angle closure glaucoma)
- Tachycardia secondary to thyrotoxicosis ( toxicity of thyroid gland increase production of thyroid gland patients are very thin and very active) or cardiac insufficiency
- Old patients with prostate hypertrophy.
- Paralytic ileus
- Constipation
- Children in case of atropine.
- Non selective M blocker → ulcer

A 39 male works as farmer in rural area is brought to the emergency room with Organophosphate toxicity while using pesticide. The patient has received atropine as an antidote.

**Q1: what is the mechanism of action of atropine to neutralize the toxicity?**

It acts as anti-muscarinic drug so it blocks the muscarinic receptor.

**Q2: Which subtype of muscarinic receptor does this drug act on?**

Atropine is non selective anti-muscarinic drug so it may act on all subtype (M1/M2/M3/M4/M5).

**Q3: Atropine is lipid soluble drug so it has CNS action. Is there any other drugs has better blood brain barrier penetration than atropine?**

Yes , **Hyoscine** has better BBB penetration.

**Q4: Atropine has CNS action so in toxic dose it may lead to?**

cortical excitation, restlessness, disorientation, hallucinations, and delirium followed by respiratory depression and coma.

**Q5: What are the pharmacological actions of atropine at eyes level?**

- 1\ loss of near vision (cycloplegia) due to to paralysis of ciliary muscle
- 2\ Passive mydriasis due to paralysis of circular muscle
- 3\ Loss of light reflex    4\increase intra-ocular pressure    5\ decrease lacrimal secretion

**Q6:What are the pharmacological actions of atropine at GIT level?**

- 1\Dryness of mouth    2\ decrease Gastric acid production
- 3\ Relaxation of smooth muscles.    4\ decrease GIT motility
- 5\ increase Sphincter contractions

**Q7: List 4 contraindication for this drug?**

- 1\ Glaucoma    2\ Paralytic ileus
- 3\ Constipation    4\Children in case of atropine

Zoom in to check  
your answers

# QUIZ



Boys	Girls
عبدالرحمن ذكري	غادة المهنا
عبدالعزيز رضوان	اللولو الصليهم
مؤيد أحمد	روان القحطاني
فيصل العباد	درة الحمدي
فارس النفيسة	شروق الصومالي
خالد العيسى	سما الحربي
عبدالرحمن العريفي	انوار العجمي
عبدالرحمن الجريان	وتين الحمود
محمد خوجة	رنا باراسين
عمر التركستاني	امل القرني

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