



Artery Academy

Ayah Rabba'

CHOLINOCEPTOR-BLOCKING DRUGS

Pharmacology 1

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«اللهم هَوِّنْ عَلَيْنَا سَعْيَنَا فِي مَنَاكِبِ الْحَيَاةِ ،
وَاطْوِ عَنَّا بُجْدَ الْمَوْتِ» ♥

Cholinoceptor antagonist.

* ادوية بتعمل inhibition لل Receptor وبالتالي بتكون effects عكس مفعول agonist.

Anticholinergic drugs

Anti-muscarinic

Non-selective
(Atropine)

له غير انتقائي
لا يرتبط مع جميع
أنواع Receptors

M₁-selective
(Pirenzepine)

له انتقائي على M₁
(لا يرتبط بالـ M₂)

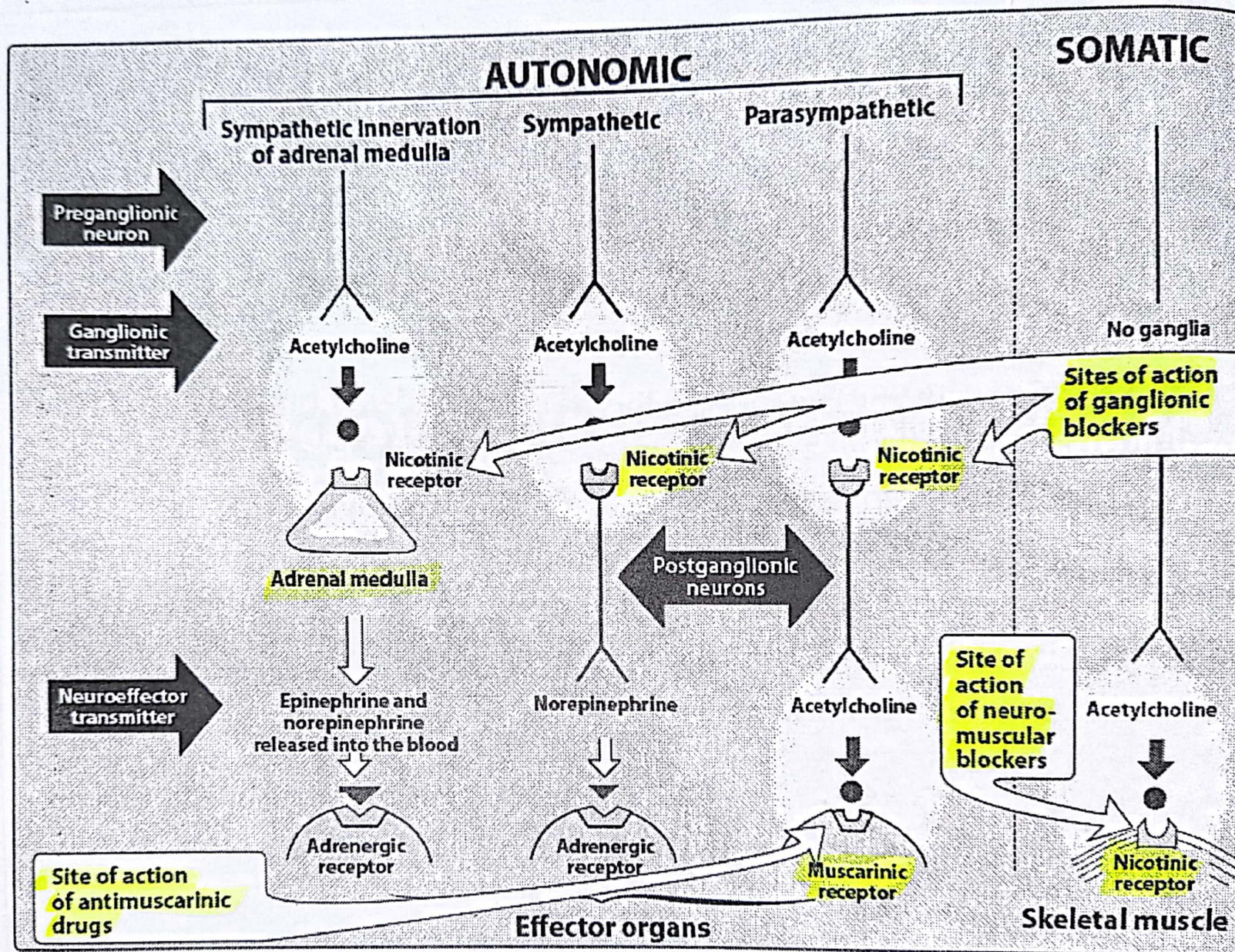
Anti-nicotinic

Ganglionic blockers
(Hexamethonium)

له لا تستعمله لأنه يعمل
التيقاف كامل في PNS.

Neuromuscular
blockers
(Tubocurarine)

له في Somatic system.

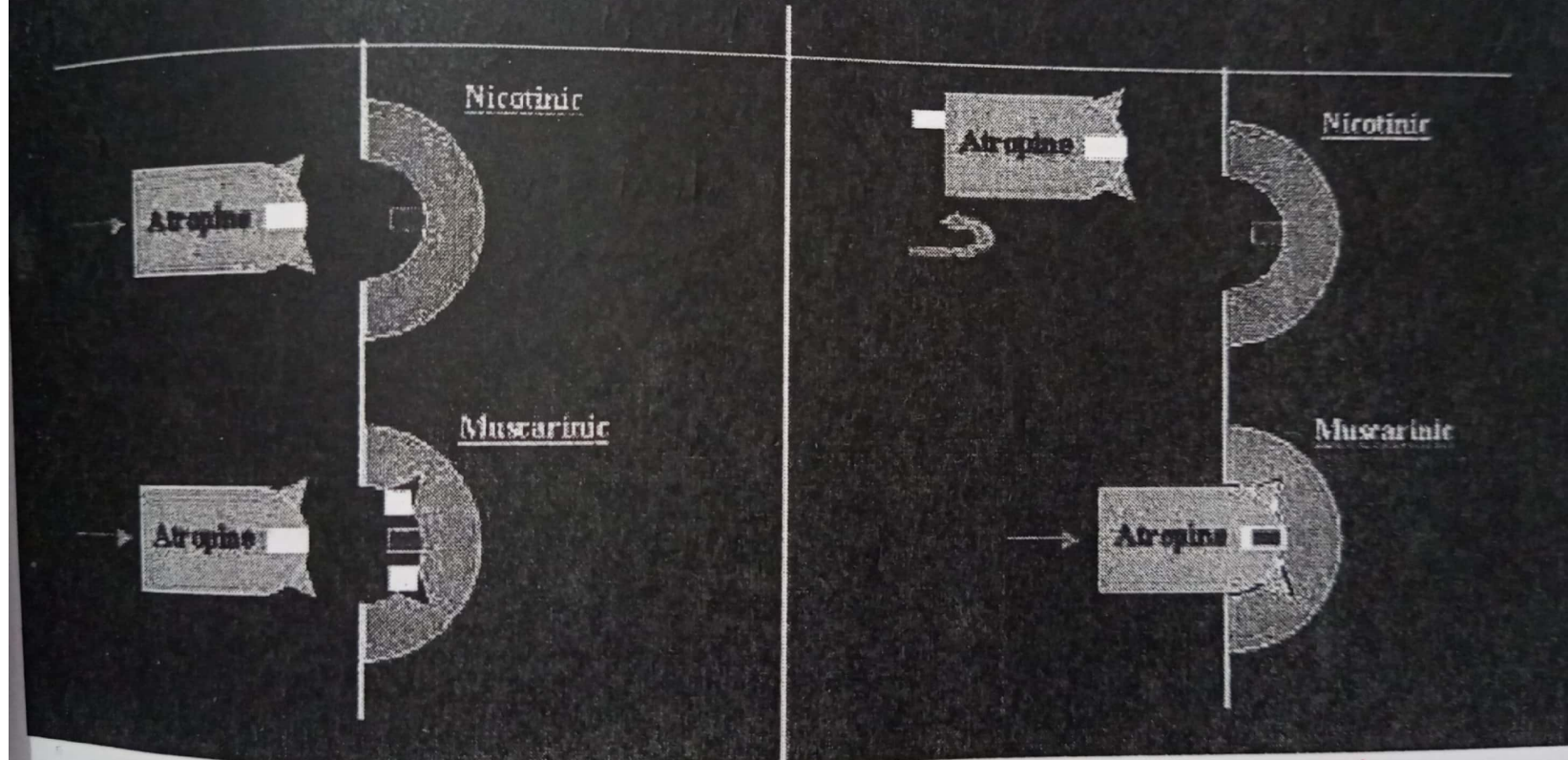


Anti-muscarinic Drugs

- Only two M_1 -selective antagonists have been developed (eg, pirenzepine, telenzepine)
- **Atropine** is the prototypical (classical) nonselective muscarinic blocker.

Atropine is the prototypical anti-muscarinic drug

Atropine at Receptors

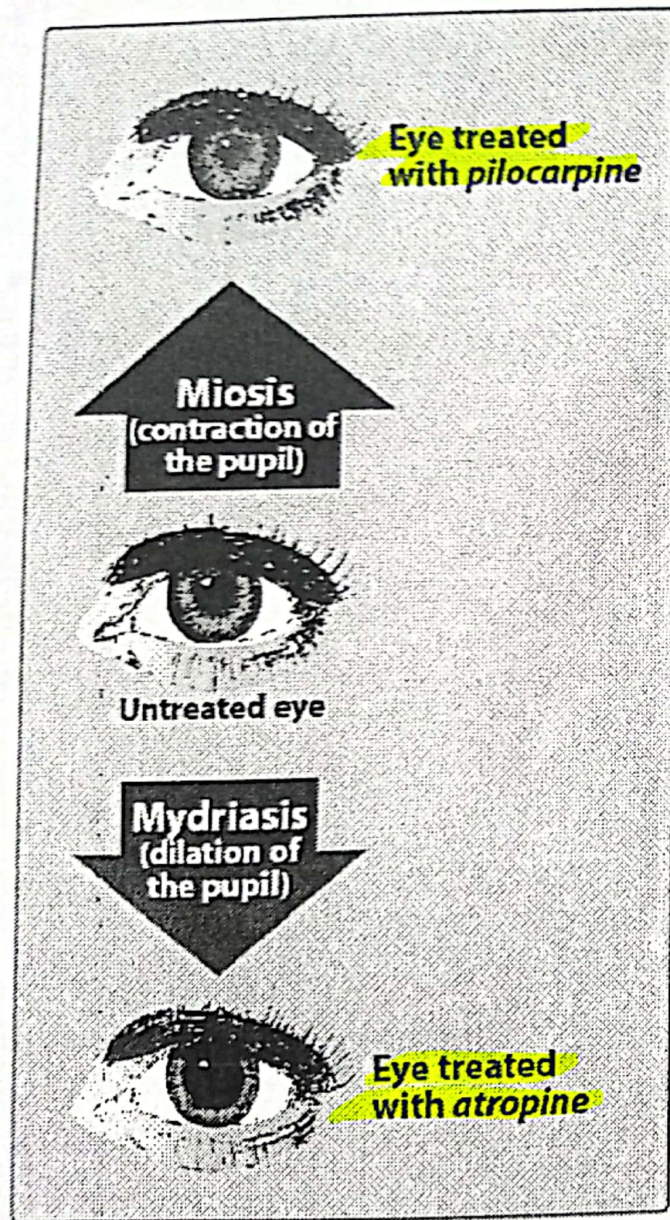


رسمه توضیح ارتباط Atropine علی muscarinic receptors و عدم ارتباطه مع nicotinic receptor

Anti-muscarinic Drugs

- Only two M_1 -selective antagonists have been developed (eg, pirenzepine, telenzepine)
- **Atropine** is the prototypical (classical) nonselective muscarinic blocker.
- Atropine is found in the plant *Atropa belladonna* (mainly) and many other plants.
- The species name "belladonna" ("beautiful woman" in Italian) comes from the original use of this plant to dilate the pupils of the eyes for cosmetic effect.

* اسم النبتة ست الحسن لذنه قديماً كانوا يستقدمونها كحل لعيون النساء ،
فيتسع بؤبؤ العين وتصبح أكثر جمالية



What is
pilocarpine?

Direct acting
cholinomimetic
(cholinceptor agonist)

- when eye treated with pilocarpine, the effect is miosis. (pupil narrowing)

- when eye treated with atropine, the effect is mydriasis. (pupil dilation).

Anti-muscarinic Drugs

Pharmacokinetics

- Atropine and other tertiary anti-muscarinic drugs are well absorbed and well distributed in the body including the CNS.
- In contrast, the quaternary derivatives are poorly absorbed (10-30% of the oral dose) and poorly taken up by the brain and therefore are relatively free of CNS effects. (more safe)
- Atropine and tertiary anti-muscarinic drug more toxic than quaternary.
↳ due to well absorption and distribution in CNS.

Anti muscarinic Drugs

Mechanism of action

- Inverse agonists

Or

- Competitive pharmacologic antagonists

- Their effect can be overcome by increasing the concentration of the muscarinic agonist.

• معلومة على الحاسني

- inverse agonists efficacy $\neq$ Zero %
- antagonists efficacy = Zero %
- agonists efficacy = 100 %

* يمكن الحصول على تأثير antagonist بطريقتين :-

- inverse agonists → دواء يرتبط مع المستقبل نفسه الذي يرتبط عليه agonist drug ويعطي تأثير عكسي للagonist حتى بعدم وجود تأثير agonist فتكون efficacy له بالسالب .

Competitive antagonist → استجابة عكسية عند زيادة تأثير agonist بزيادة الجرعة .

* innervated: supplied of nervous energy or of nerve stimulus.

Organ system effects

Organ	Effect	Receptor involved
CNS	Sedation, anti-motion sickness action, antiparkinson action, amnesia, delirium	Several (M_1, M_4, M_5)
Eye	Cycloplegia (loss of accommodation), mydriasis	M_3
Lung	Bronchodilation, especially if constricted	M_3
GI tract	Relaxation, slowed peristalsis, reduced gastric secretions	M_3 and M_1
Genitourinary	Relaxation of bladder wall, urinary retention	M_3 and M_1
Heart	Initial bradycardia, especially at low doses, then tachycardia	Tachycardia by M_2
Blood vessels	Block of muscarinic vasodilation; not visible unless a muscarinic agonist is present	Uninnervated M_3
Glands	Reduction in secretions (salivation, lacrimation, sweating)	M_3 and M_1
Skeletal muscles	None	None

no stimulant on receptors.

(لأن نوع المستقبلات فيها (nicotonic)

Dose-dependent effect of atropine on the heart

• عند أخذ جرعة

قليلة من atropine

يكون التأثير هو

(bradycardia)

بسبب حجب M_1

receptor

الذي يسيطر من افراز

Ach

وبالتالي هاد

antagonist (Atropine)

مع يعطى تأثير Ach.

• عند أخذ جرعات

عديدة من atropine

يصبح التأثير

tachy

character

بسبب حجب M_2

receptor

والتي يسيطر منها

bradycardia

في هذا الموضع مع

يعكس تأثير M_2

agonist.

At low doses of atropine:

The predominant effect is a decreased cardiac rate (bradycardia).

□ The effect is a result from blockade of the presynaptic M_1 receptors on neurons (which normally inhibits Ach. release), thus permitting increased ACh release.

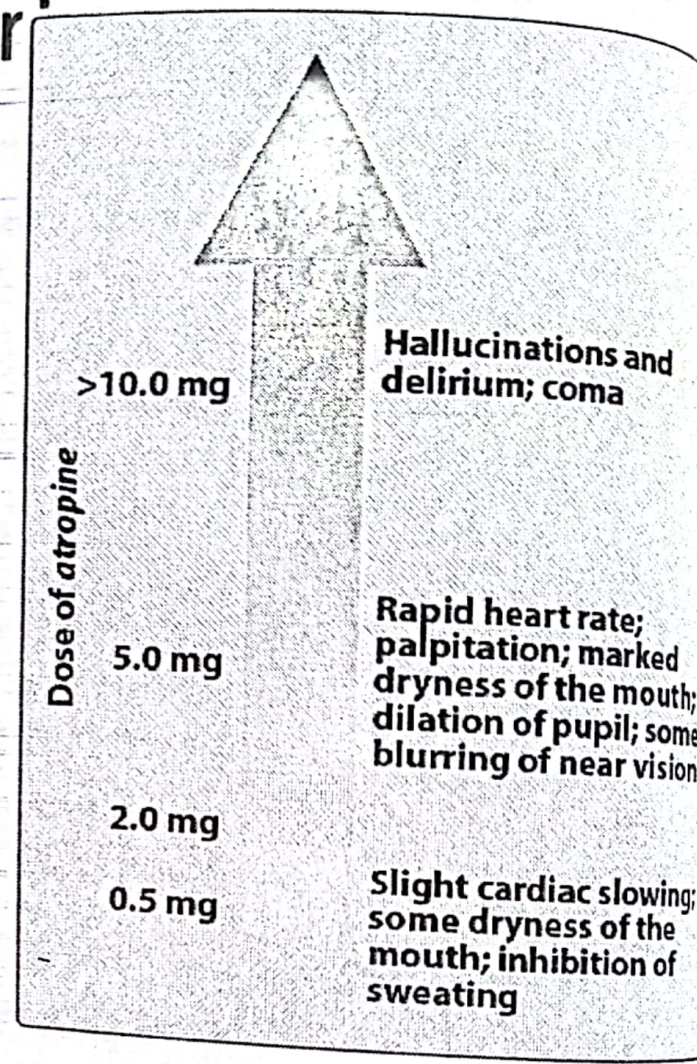
With higher doses of atropine:

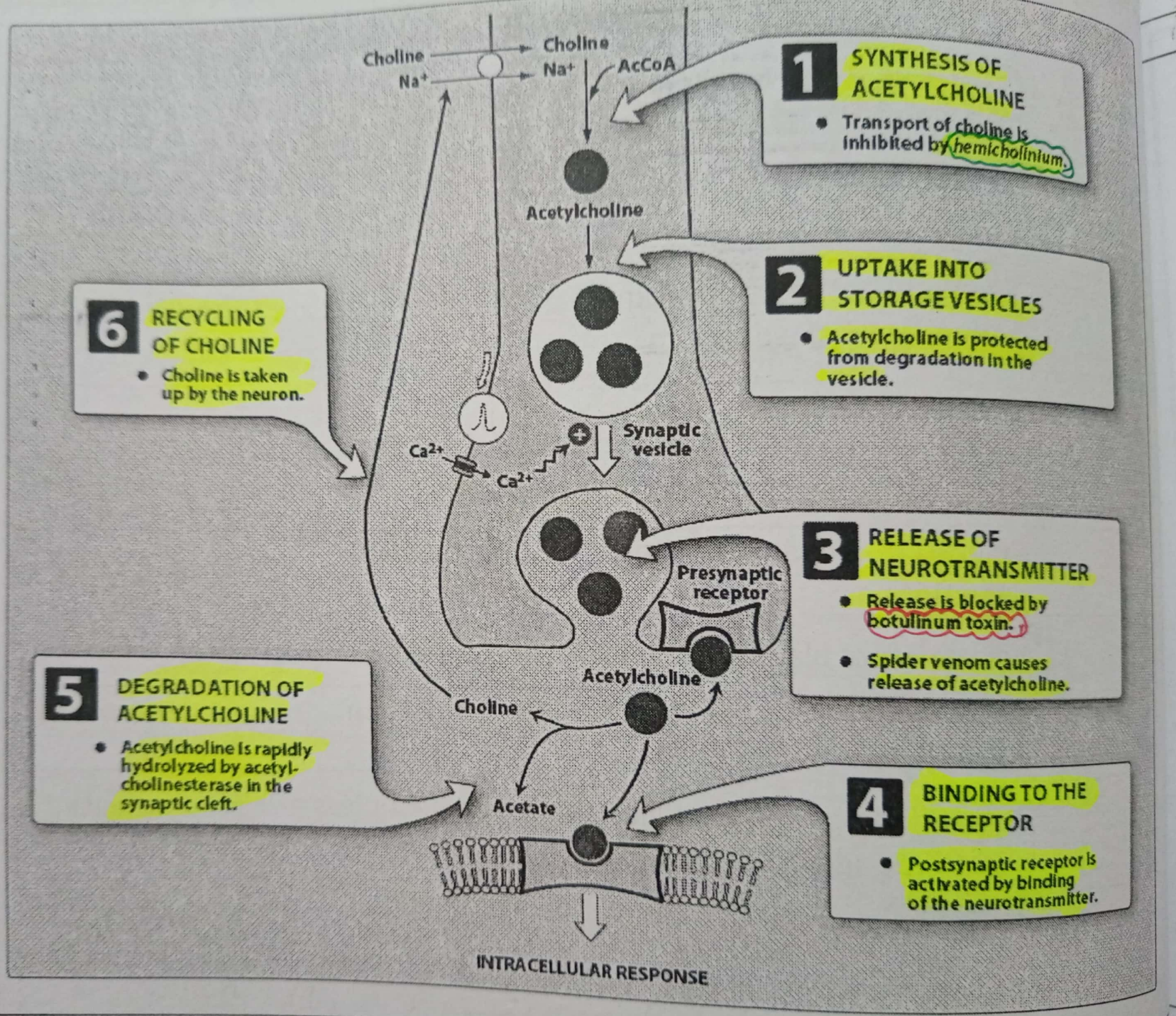
□ The M_2 receptors on the heart are blocked, and the cardiac rate increases (tachycardia).

□ This generally requires at least 1 mg of atropine, which is a higher dose than ordinarily given.

له عند زيادة 1 mg على الجرعة الاعيانية

المريض.





Anti-muscarinic Drugs

Therapeutic applications

1. Motion sickness
2. Parkinson disease (تقليل أعراض المرض علاجاً)
3. COPD
4. Urinary incontinence

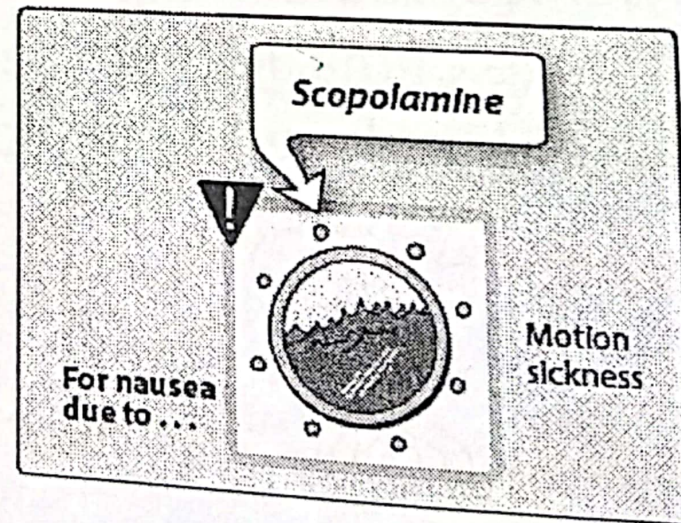
Motion sickness

هو الدواء (المؤقتة) المضاد للحكة

Scopolamine is standard therapy for motion sickness.

It can be given by injection or by mouth or as a transdermal patch.

* لأن قاتل Anti-muscarinic على CNS هو anti motion sickness drug



* أدنى يكون عنقازينين قاشرين

cholinergic and dopaminergic.

Parkinson disease

الجمود في الحركة
وهو الرجفة بالذراعان

- **Parkinsonian tremor and rigidity seem to result from a relative excess of cholinergic activity** because of a deficiency of dopaminergic activity.

هو يعمل ضد الدوية
على شبيه على
cholinergic activity
(antagonists).

Benztropine, biperiden, trihexyphenidyl are representative of several **antimuscarinic agents** used in parkinsonism. Although not as effective as **levodopa**.

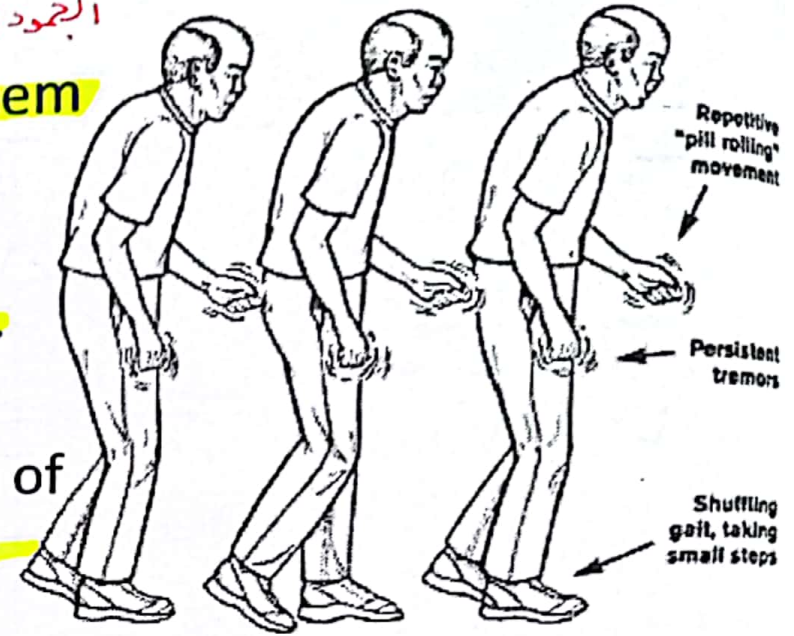
للتقليل أعراض
المرض وليس
لحلاجه كاملاً

- These agents may be useful as **adjuncts** or when patients become **unresponsive to levodopa**.

مضادات
لعدم استجابة المريض للعلاج

→ treatment of the disease.

- increase dopaminergic activity.



* لذن تاثير antagonist
على lung هو
bronchodilation.

Asthma and Chronic obstructive pulmonary disease (COPD)

- Ipratropium and tiotropium are used as bronchodilators for maintenance treatment of bronchospasm associated with asthma and COPD.
- These drugs are quaternary amines and so they poorly absorbed into the systemic circulation and do not enter the CNS (less side effects).
- The aerosol route of administration (inhalation) has the advantage of maximal concentration at the bronchial target tissue with reduced systemic effects.

له استخدام البخاخات لهذه الدوية تزيد من التركيز الذي يصل الى Lungs
و تقلل من الآثار على باقي أجهزة الجسم .

* تستخدم هذه الدوية بشكل رئيسي لمرضى الربو (COPD) ولكن لمرضى (asthma)
هناك بدائل عنها .

Urinary incontinence

سلس البول

- Could be due to different reasons:
 - by minor inflammatory bladder disorders, after urologic surgery or in patients with neurologic disease.
- Oxybutynin, tolterodine and fesoterodine are available for use for urinary incontinence.

* use it for its urinary retention effect.

Anti-muscarinic Drugs

Adverse effects

Blurred vision

النظر مخفّيش



Confusion

الد رتباك



Mydriasis

استلح بؤبؤ العين



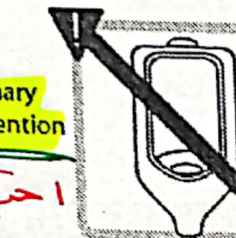
Constipation

الامساك



Urinary Retention

احتباس البول



Anti-muscarinic Drugs Toxicity

- A traditional mnemonic for atropine toxicity is "Dry as a bone, red as a beet, mad as a hatter."

← الجفاف

Dry: due to inhibition of secretions

– "Atropine fever" is common especially in children

← الحرارة المرتفعة بسبب تثبيط إفراز العرق المتحكم به رغبة حرارة الجسم

due to inhibition of thermoregulatory sweating.

– Patients occasionally complain of dry or "sandy" eyes when receiving large doses of antimuscarinic drugs.

ANTICHOLINERGIC SIDE EFFECTS



sketchy medicine



← الاحمرار بسبب اتساع الأوعية الدموية

Red: due to dilation of the cutaneous vessels of the arms, head, neck, and trunk

"atropine flush". The mechanism is unknown

← الجنون

Mad: due to CNS toxicity which includes

sedation, amnesia, and delirium or hallucinations.

← التقيؤ

فقدان الذاكرة

لهذه الهذيان

← العلوسة



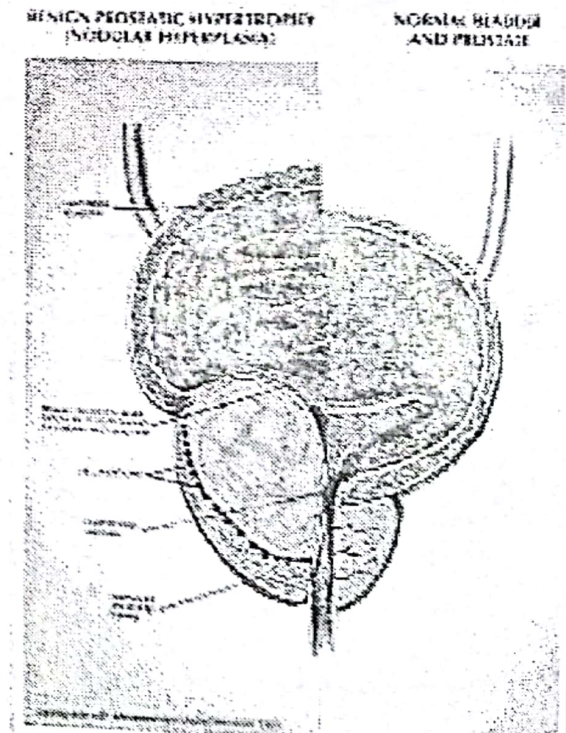
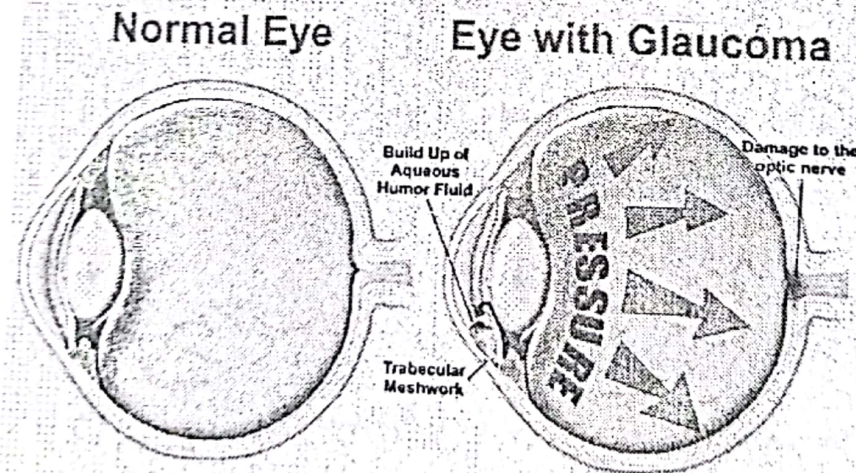
لأنه يسهلها امصاصها
من كل متقوم
بأنه يتر عليه

Anti-muscarinic Drugs

Contraindications

يجوز وتعليمات من الطبيب

- The antimuscarinic agents should be used cautiously:
 - ① in infants because of the danger of hyperthermia.
 - ② in persons with glaucoma
 - ③ in men with prostatic hyperplasia.



Anti-muscarinic Drugs

Tertiary amines (more toxic)

- Atropine
- Scopolamine
- Benztropine
- Trihexyphenidyl
- Biperiden
- Oxybutynin
- Tolterodine
- Eseterodine
- Pirenzepine
- Telenzepine

Quaternary amines ~~more~~

- Ipratropium and tiotropium

Anticholinergic drugs

Anti-muscarinic

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Anti-nicotinic

Ganglionic blockers
(Hexamethonium)

Neuromuscular blockers
(Tubocurarine)

Were used to treat hypertension but not any more

They are important for producing complete skeletal muscle relaxation in surgery

۱۰ بنیادی دیکرو
۱۰ عشان ۲۰ نوقتی
۱۰ کی علی
PMS