Cholinergic Antagonists

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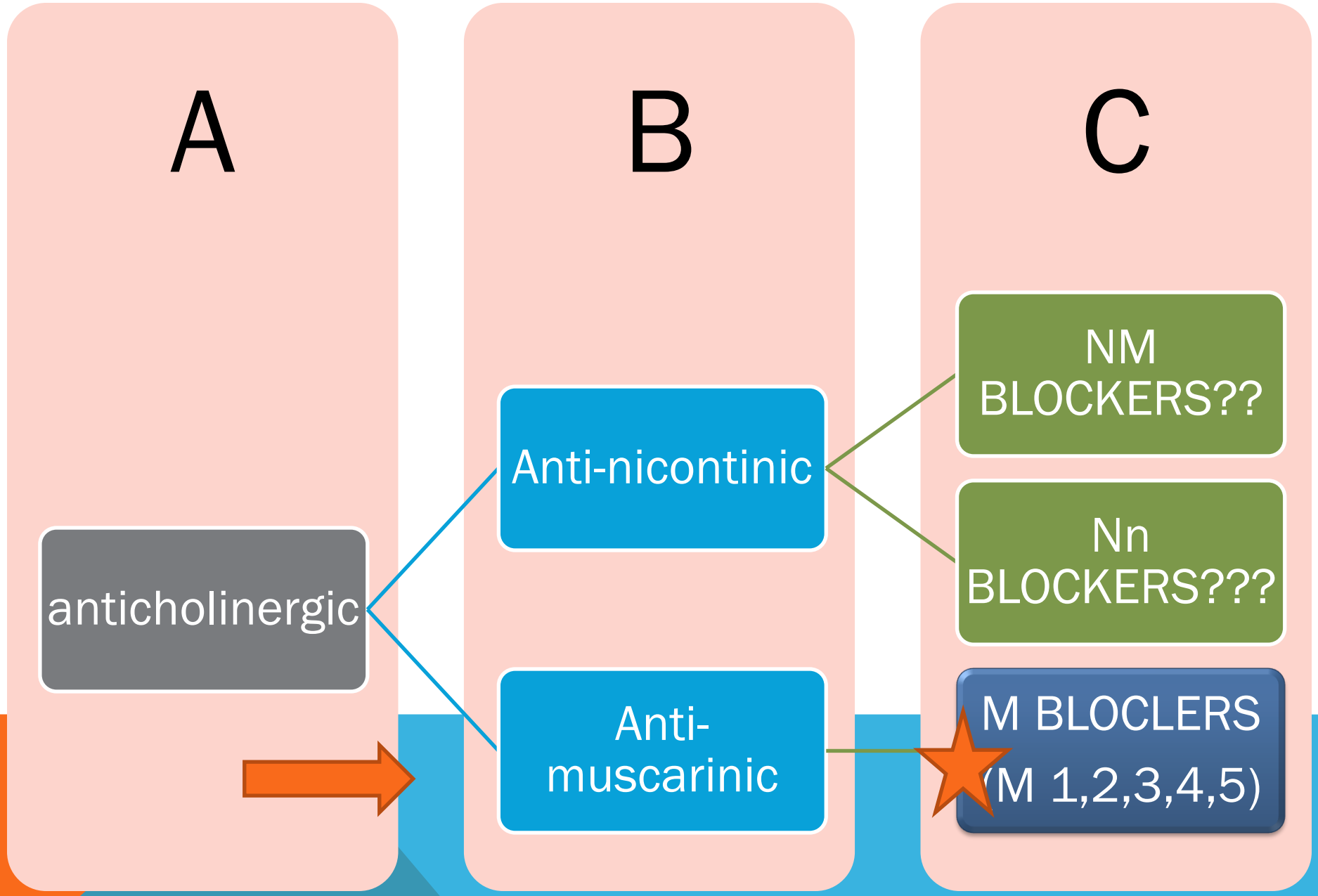

A
B
C
anticholinergic
Anti-nicontinic
Anti-muscarinic
NM BLOCKERS??
Nn BLOCKERS???
M BLOCLERS
(M 1,2,3,4,5)

(ANTI-MUSCARINIC DRUGS)

They are competitive antagonists of ACh at muscarinic receptors.

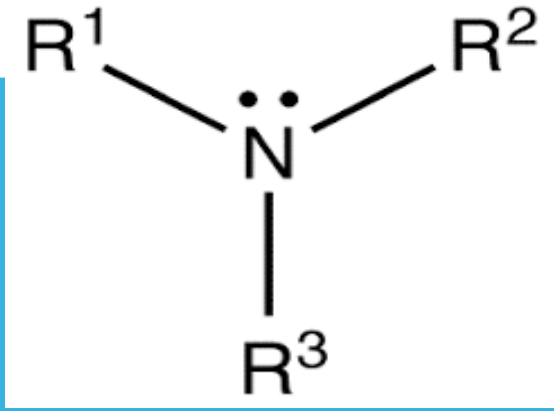
1) **Natural: belladonna alkaloids [atropine & hyoscine]**
2) **Semi-synthetic: (homatropine)**
3) **Synthetic: atropine substitutes.**

ATROPINE

Source and chemistry

- **Natural belladonna alkaloid.**

- **Tertiary amine.???**



Pharmacokinetics:

- **A: Well absorbed from all sites except intact skin.**
- **T1/2: 2 hours.**
- **D: Passes BBB (tertiary amine) .**
- **M: Metabolized in liver.**
- **E: ⅓ the dose is excreted unchanged in urine.**
- **Urinary excretion is enhanced by acidification of urine.**

Pharmacodynamics

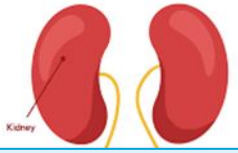
1-Mechanism of actions

2-Pharmacological actions

ACTIVATION OF MUSCARINIC RECEPTORS

Memory stimulations

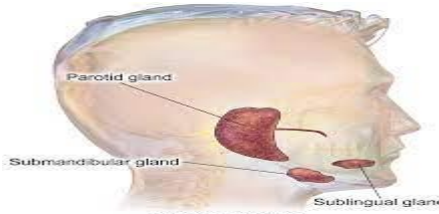
Muscarinic stimulations



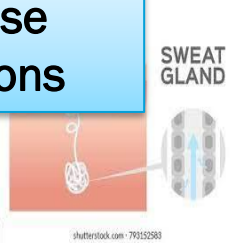
1-Contraction of wall

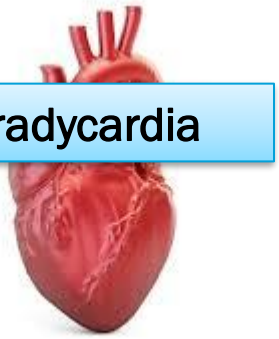
2-Relaxation of sphincters

3-Increase secretions

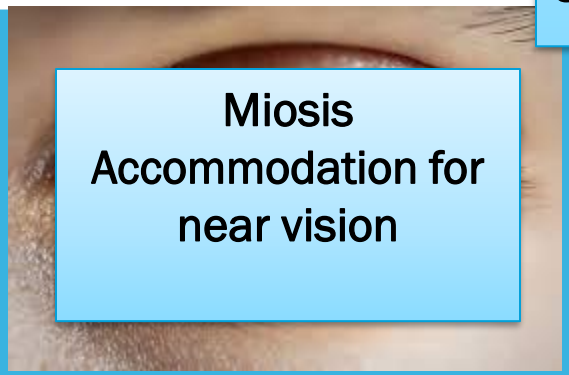


Increase secretions





bradycardia



Miosis
Accommodation for near vision

PHARMACOLOGICAL ACTIONS ATROPINE

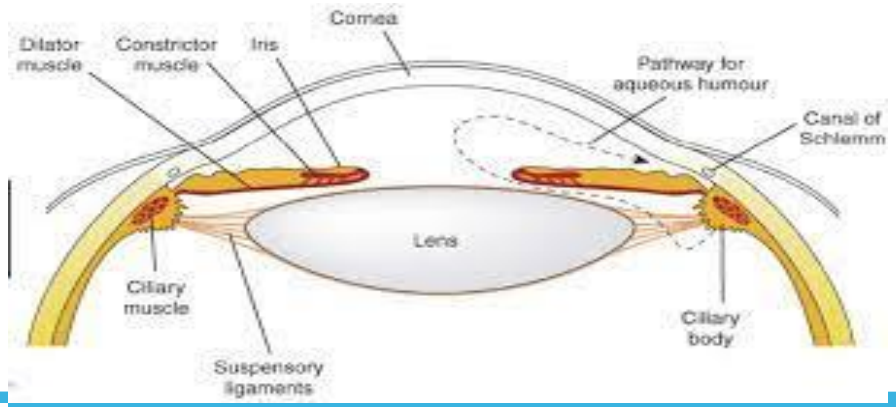
SAD HC

CNS actions

- Has stimulant & depressant actions
- Stimulates respiratory center (RC) & CIC.
- Inhibits basal ganglia & vomiting center
- Sedation, amnesia, delusions
- High doses ⇨ agitation, hallucination, mania & convulsions followed by CNS depression.

Eye

- **Passive mydriasis.**
- **Paralysis of accommodation (cycloplegia) ⇨ impaired near vision.**
- **⬆ IOP ⇨ Contraindicated for patients with narrow-angle glaucoma.**



CVS

i. Heart:

- **Tachycardia**

Especially in young people (high vagal tone)

- **Slowly IV injection ⇨ paradoxical bradycardia followed by tachycardia. This can be explained by:**
  - ✓ **Earlier block of presynaptic M_2 receptors ⇨ relieving the inhibitory effect on ACh release ⇨ ⬆ Ach release.**
  - ✓ **Central stimulation of CIC.**

ii. Blood vessels:

- ✓ Unaffected by therapeutic doses.
- ✓ Toxic doses ⇨ atropine flush.

iii. Blood pressure: unaffected

GIT

- Relaxes wall (antispasmodic action) & constricts sphincters.
- Inhibits secretion ⇨ constipation

Urinary tract

- Relaxes wall & constrict sphincter of the bladder ⇨ urine retention
- Relaxes ureters.

Respiratory system

- Bronchodilatation.
- ⬇ secretions (viscid & difficult to expel).

EXOCRINE GLANDS: الاهم

1) **Inhibition of secretions:**

- **Salivary secretions ⇨ dry mouth.**

- **Lacrimal secretions.**

- **Sweat ⇨ dry skin (atropine fever).**

CLINICAL USES:

A. Preanesthetic medication:

- **Advantages as a pre-anesthetic medication:**

1) **Reduces secretions**
2) **Anti-emetic action**
3) **RC stimulation**
4) **Bronchodilatation**
5) **Counteracts excess vagal tone & bradycardia induced by general anesthetics**

B- Eye:

1. **Mydriatic in iritis (alternatively with miotics to prevent adhesions).**
2. **Accurate measurement of refractive errors in uncooperative patients e.g. young children, who require ciliary muscle paralysis.**
   - **For adults and older children, the shorter-acting atropine substitutes are preferred.**

C-Heart block

due to digitalis, myocardial infarction, verapamil, or β-blockers.

D-Organophosphorus poisoning

(atropine is life-saving)

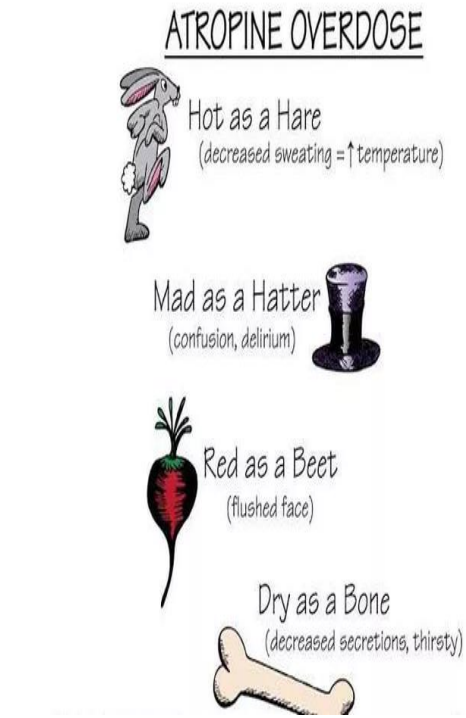
E-GIT:

Antispasmodic in Colic

Anti-emetic.

ATROPINE TOXICITY:

- Dry mouth.
- Hot, dry and flushed skin.
- Mydriasis, blurred vision and ⬆ IOP.
- Tachycardia.
- Urine retention especially in patients with benign prostatic hyperplasia.
- Hyperthermia (fatal in infants).
- Agitation, delirium & convulsions followed by coma and RC depression (cause of death).



❑ Treatment of Atropine Toxicity:

- ❑ Treatment of toxicity is usually **symptomatic.**
- ❑ Severe tachycardia may require cautious administration of small doses of **physostigmine.**
- ❑ Hyperthermia can usually be managed with **cooling blankets or evaporative cooling.**

CONTRAINDICATIONS OF ATROPINE:

1) Narrow angle glaucoma.(eye)
2) Angina and arrhythmias.(CVS)
3) Constipation, ileus and Peptic ulcer (GIT).
4) Benign prostatic hyperplasia (BPH)(UTI).
5) Bronchial asthma (RS)

HYOSCINE (SCOPOLAMINE)

- **Differs from atropine in:**
  1) **Short duration.**
  2) **Dominant effect on eye and secretions with less tachycardia.**
  3) **CNS: both depressant [sedation, amnesia, anti-motion sickness] & stimulant [RC stimulation, hallucination in overdose] (but it is mainly depressant).**

- **Clinical Uses:**

(1) Preanesthetic medication:

❖ **Better than atropine, as it causes:**

a. Less tachycardia.

b. Strong antisecretory action.

c. Strong antiemetic action.

d. More CNS depressant.

e. RC stimulation.

(2) Motion sickness:

Used as transdermal patch.

ATROPINE SUBSTITUTES

Atropine methyl nitrate	**Antisecretory antispasmodics**	**hypertrophic pyloric stenosis.**
Hyoscine N-butyl bromide:	**Antisecretory antispasmodics**	**relax spasm of GIT & urinary tract**
Propantheline & oxyphenonium	**Antisecretory antispasmodics**	**relax spasm of GIT.**
Pirenzepine & telenzepine	**Antisecretory antispasmodics**	Selective M1 blockers. HCl secretion. Used for peptic ulcer
Ipratropium and tiotropium	**Anti-asthmatics**	Given by inhalation. Little effect on secretions and mucociliary movement.
Oxybutynin and tolterodine	For urinary incontinence	**Selective M_3 antagonists**
Benztropine and benzhexol	**Anti-parkinsonian**	

MYDRIATICS

	Atropine	Homatropine	Tropicamide , cyclopentolate
Duration:	**7-10 days**	**24 hours**	**6 hours**
Cycloplegia	**+++**	**++**	**+**
Uses:	**1. Iritis 2. Measurement of refractive errors in children**	**1. Fundus examination 2. Measurement of refractive errors**	


Thank you!