
بسم الله الرحمن الرحيم

Anticholinergic drugs;

Cholinergic antagonists,

Cholinergic blockers,

Cholinergic receptor blocking drugs,

By

Dr. Muhammad Sarwar

PHARMACOLOGICAL EFFECTS;

CNS; (M_1, M_2, M_3, M_4, M_5 Receptors);

- **Atropine** has a ***stimulant action on the CNS*** *especially at high doses*.
- Atropine **stimulates medullary centers** – vagal, respiratory and vasomotor.
- **High doses** cause **cortical excitation**, restlessness, disorientation, hallucinations and delirium followed by respiratory depression and coma.
- By blocking the relative cholinergic over-activity in basal ganglia, it **suppresses tremors and rigidity in parkinsonism.**
- ***Hyoscine*** *produces* ***central depressant effects*** even at low doses. **Amnesic action**—block short term memory.

CVS; (M_2 Receptors);

- Atropine causes ***tachycardia*** due to blockade of M_2-receptors on SA node.
  - *The tachycardia is more **marked in young adults** than* in children and the elderly.
- Atropine ***shortens the refractory period of AV conduction***, especially if it has been depressed by high vagal tone.
- Atropine does **not influence BP.**
  - Normal dose has **no effect on blood vessels.**
- **Dilatation of cutaneous vessels** of the **face,** head, neck and trunk **----** **Atropine flush** **--- red as a beet** **---** diagnostic of overdose.

- **Atropine causes -- Transient initial bradycardia**, especially at low doses.
  - By **blocking Presynaptic M_1 receptors** (autoreceptors) on vagal postganglionic fibers that normally limit ACh release in the SA node and other tissues.
  - Transient **initial vagal stimulation (in CNS).**
  - **Clinical significance** – when used along with neostigmine for reversal **(Atropine + neostigmine** to antagonize curare like drugs) may cause bradycardia.
    - Atropine to be given a few minutes before neostigmine to avoid summation.

Eye; (M_3 Receptors);

- **Circular constrictor muscles of iris, Ciliary's muscles, Lacrimal gland.**

- Topical instillation of atropine (0.1%) causes
  - ***mydriasis, abolition of light reflex*** *and* ***cycloplegia,*** *lasting 7–10 days*.
    - ❖This results in **photophobia** and ***blurring of near vision***.
    - ❖The ***intraocular tension rises*** specially in narrow angle glaucoma.
  - **Lacrimal secretion is decreased.**
    - ***"Dry & Sandy Eyes"***
- Conventional systemic doses produce minor ocular effects.

Duration of effects of Antimuscarinic Drugs used in eye;

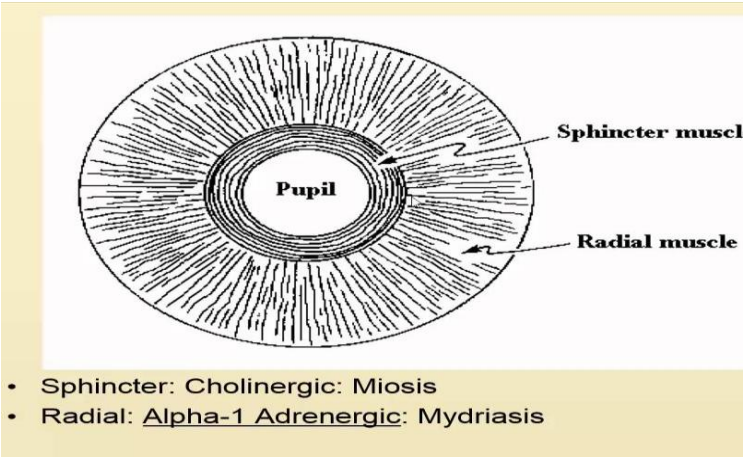
	duration of effects (in days)	%
Atropine	**7-10 (>72 h)**	**0.5-1 %**
Scopolamine	**3-7**	**0.25 %**
Homatropine	**1-3 (24 h)**	**2—5 %**
Cyclopentolate	**1 (2-12 h)**	**0.5-2 %**
Tropicamide	**0.25 (0.5-4 h)**	**0.5-1 %**

Atropine --- Mechanism of passive mydriasis;

Circular constrictor muscles (M_3) of iris are blocked & **radial dilator muscles (α)**

--- *unopposed contraction.*

Pupil become **unresponsive to light.**



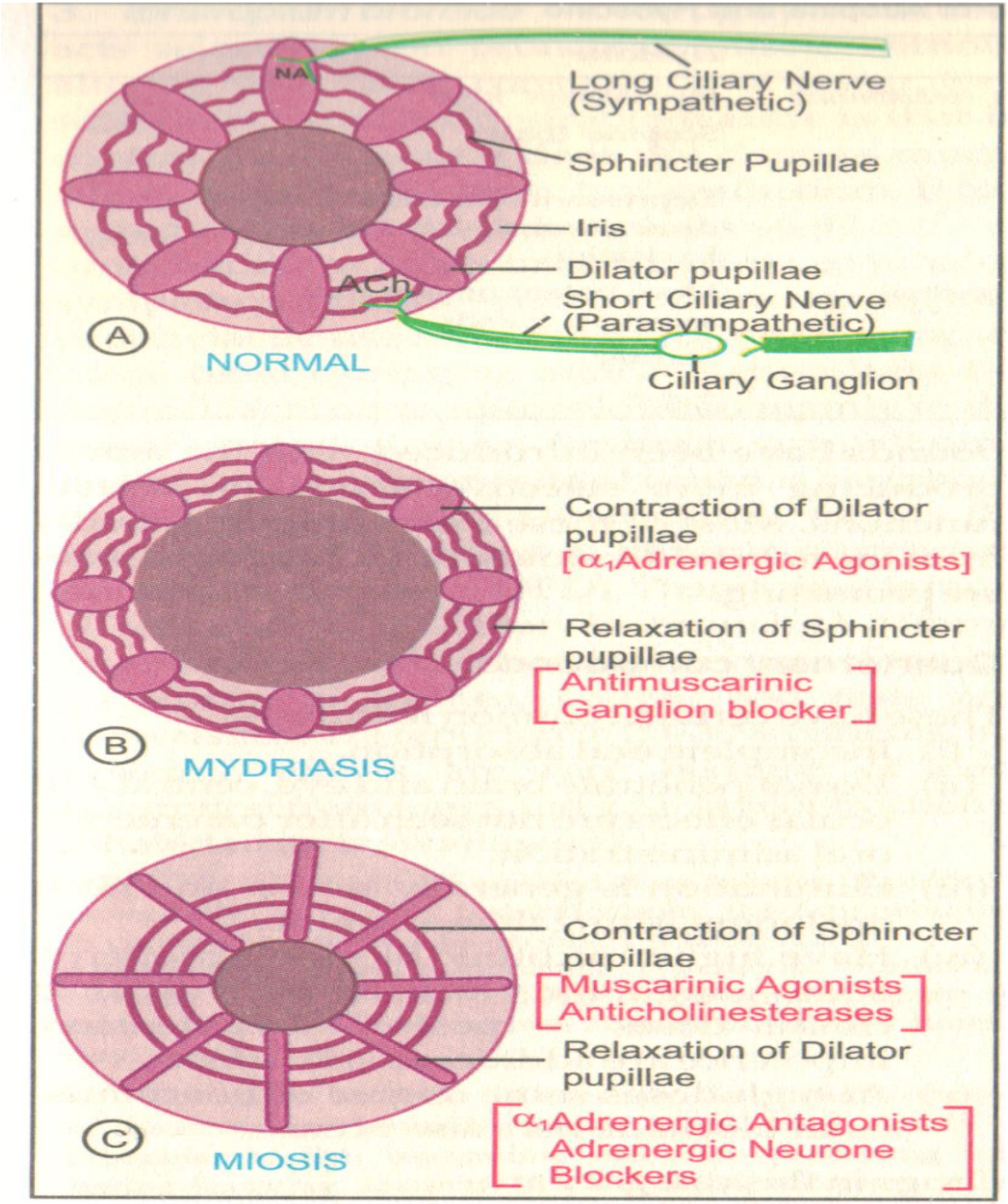
Ancient cosmetic use;

Belladonna (beautiful lady).

- **Autonomic control of pupil. (A)**

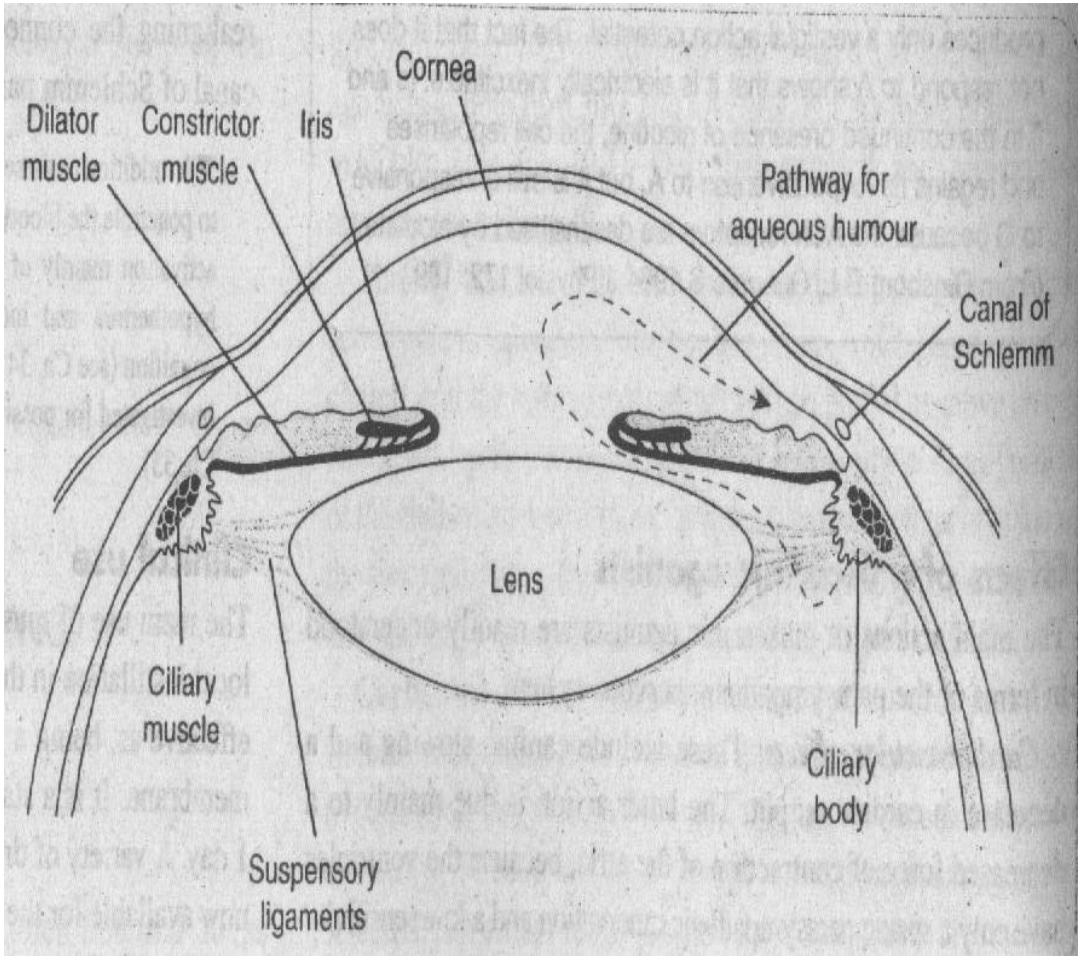
- **Site of action of Mydriatics. (B)**

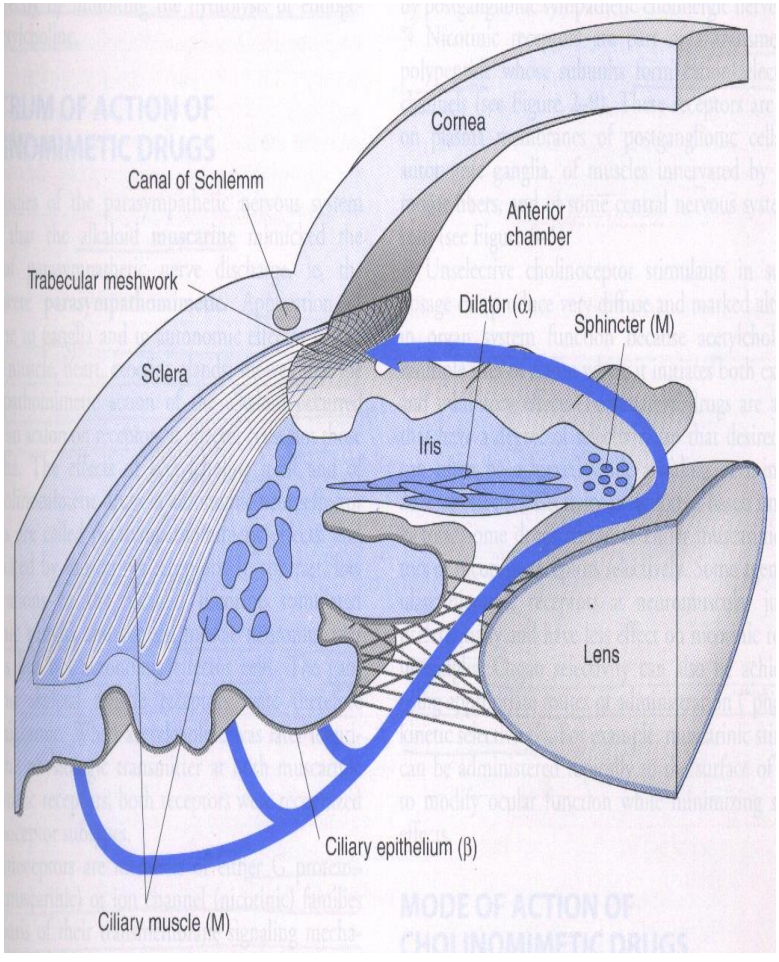
- **Site of action of miotics. (C)**



Mechanism of Cycloplegia;

- **Ciliary's muscles** are **relaxed** so **suspensory ligaments** are **tense** and **lens** is **straightened.**
- ***Eye can't focus for near vision.***





Atropine;

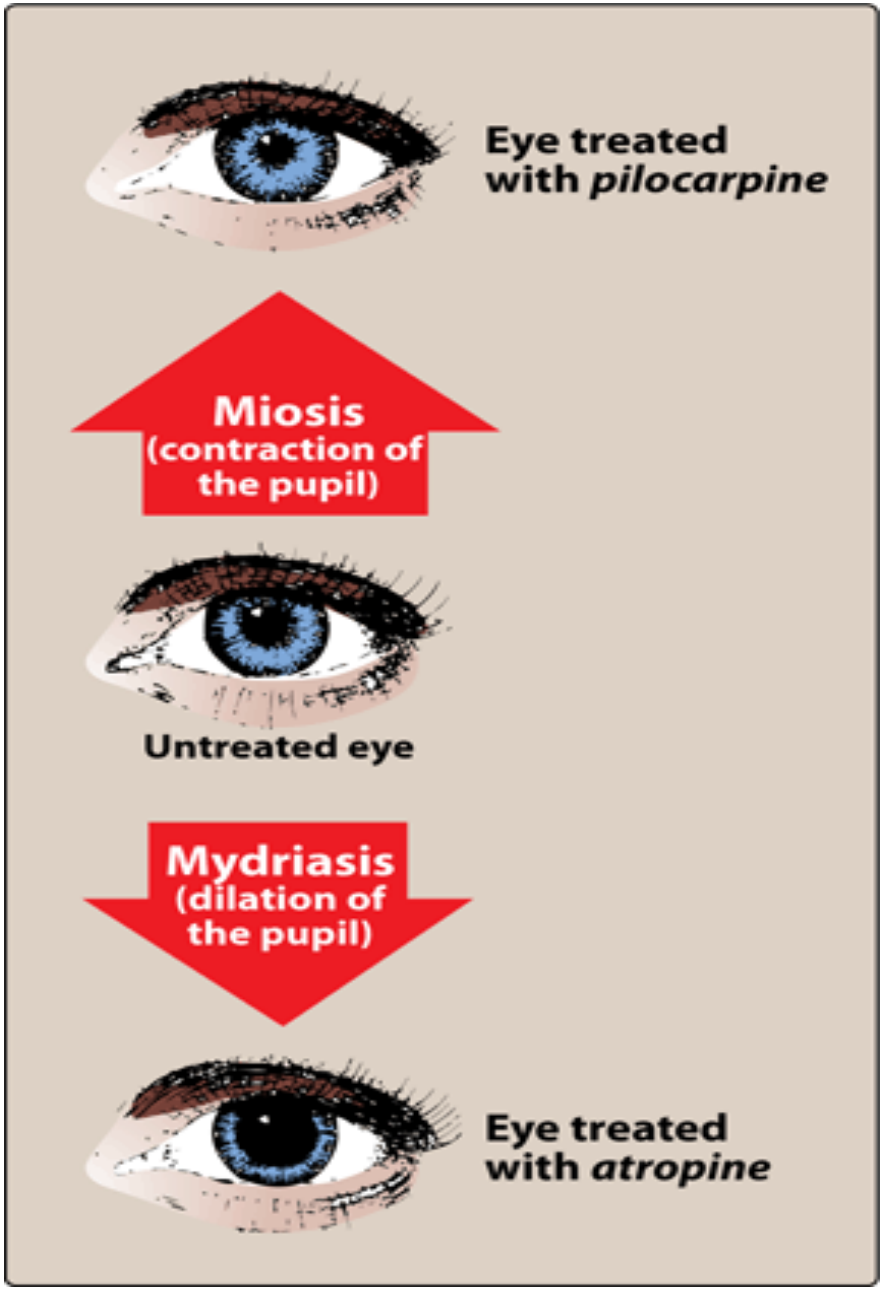
- Passive mydriasis.
- Ciliary muscles relaxed.
- Cycloplegia -- *loss of accommodation.*
  - Ciliary's muscles are relaxed so suspensory ligaments are tense and lens is straightened.
- *Eye can't focus for near vision.*
- Glaucoma precipitated.
  - Intra ocular pressure may ↑ in patients with narrow angle glaucoma.
- Lacrimal secretion is decreased.
- *"Dry & Sandy Eyes"*

Muscarinic agonists, & Anticholinesterases;

- Miosis.
- Ciliary muscles –contract.
- Cyclospasm --- *spasm of accommodation*
  - Ciliary muscles contract so relaxation of suspensory ligaments and bulging of the lens.
- *Accommodation* is fixed for near vision.
- Used for the treatment of glaucoma.
  - Facilitates the flow of aqueous humor and perhaps also by ↓ ing the rate of its secretion.
- Lacrimal secretion is increased.

Pilocarpine (M agonist) Activates pupillary sphincter
----Cause miosis.

Atropine ---
causes passive mydriasis.



Smooth muscles; (M_3 Receptors)

- All **visceral smooth muscles** with parasympathetic innervation are **relaxed** (*M_3-blokade*). **Sphincters ---** are **contracted.**
- **GIT; Tone and amplitude** of **GIT** are **reduced.** ***Spasm*** *may be* ***reduced****,* ***constipation*** *may occur*. **Peristalsis** is only incompletely **suppressed** because it is primarily regulated by local reflexes and other neurotransmitters (serotonin, encephalin, etc.).
- **Airway;** Atropine causes ***bronchodilatation*** and **reduces airway resistance,** especially in asthma patients.
  - **Inflammatory mediators** (histamine, PGs, and kinins) increase vagal activity in addition to their direct action on bronchial muscle and glands. Atropine attenuates their action by **antagonizing the reflex vagal component.**
- **Urinary Tract;** It has a **relaxant action** on the **ureter and urinary bladder**. ***Urinary retention*** can occur in older men with prostatic hyperplasia.

Smooth muscles:

- **Walls of viscera**
  - relaxed. ↓ed tone / peristalsis.
- **Sphincters**
  - contracted.
- **Gastric emptying time & intestinal transit.**
  - prolonged

Secretions:

- **Salivary:**
  - ↓ed ---dryness of mouth
- **Gastric:**
  - blockade of excitatory **M_1 on vagal ganglion**, ↓ed HCl secretion.
- **Pancreatic & intestinal:-----** more control by hormones.

Glands; (*M_3-Receptors*)

- Atropine **decreases sweat, salivary, tracheo-bronchial**, and **lacrimal secretions** (*M_3-blockade*).
  - **Skin and eyes** become **dry**.
  - **Talking** and **swallowing** my be very difficult.
  - Atropine **decreases** less the **secretion of acid and pepsin** and more of the **mucus** in the stomach.

Body temperature;

- **Rise in body temperature** occurs at higher doses and is due to both **inhibition of sweating** as well as **stimulation of the temperature regulating centre** in the hypothalamus.
  - Children are highly susceptible. **(Atropine fever, Hyperthermia)**

Local anaesthetic action;

- Atropine has a **mild anaesthetic action on the cornea.**

The sensitivity of different organs and tissues to atropine;

- The sensitivity of different organs and tissues to atropine varies and can be graded as;
  - **Saliva > sweat > bronchial secretion > eye > bronchial muscles > heart > intestinal and bladder smooth muscles > gastric glands and gastric smooth muscles.**


Thank You