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♡

Autonomic Pharmacology

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Autonomic Pharmacology

□ Nervous system:

❖ CNS:

^{a-}
Brain

^{b-}
Spinal cord

❖ Peripheral NS:

^{a-}
Somatic nerves .. Voluntary control
of skeletal muscle

^{b-}
ANS involuntary control.

1- what's the important of ANS?

2- Give an example about it?

3- what does it consist of?

4- what're the structure of it?

Autonomic Pharmacology

□ ANS:

❖ Autonomous

➤ Responsible for visceral involuntary functions

➤ Important to maintain life

➤ E.g. ^{a-}Smooth & ^{b-}Cardiac m., ^{c-}exocrine glands.

❖ Consists of:

1 ➤ Sympathetic system (Thoraco-lumbar) ⇒ Fight and Flight

2 ➤ Parasympathetic system (Cranio-sacral)

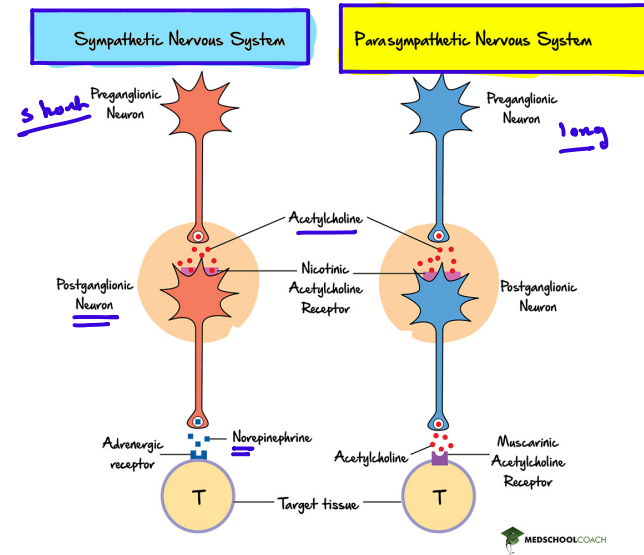
3 ➤ Enteric nervous system

arises from

arises

Autonomic Pharmacology

- ❑ Consists of:
 - ❖ Medullary centers
 - ❖ Preganglionic fibers
 - ❖ Ganglia
 - ❖ Postganglionic fibers



Autonomic Pharmacology

Sympathetic

Parasympathetic

Act at :-

a- Stress, b- trauma, c- hypoglycaemia

acts at rest

d- Cold & e- Exercise

opposes sympathetic

fight or flight response

**regulates digestion, bowel
and urinary function**

Direct-acting Cholinomimetics

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1- what's the CMM?

2- what's the Actt? where we can find it?

Direct-acting cholinomimetics

❖ **Cholinomimetics:-**

Agents that mimic or simulate actions of Ach

❖ Ach is neurotransmitter of cholinergic nerves acts on cholinoceptors in:

➤ Ganglia

➤ Postsynaptic endings of the parasympathetic sys

➤ Adrenal medulla

➤ NMJ endplates

1- Explain the mechanism of its synthize?

2- where does it started?

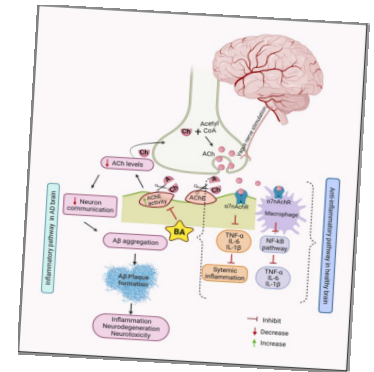
3- Describe the mechanism of releasing?

Pathway of Acetylcholine

4- what's the type of achyle enzymatic? what's the role of them?

- Synthesized in the cytoplasm of cholinergic nerve terminals from Acetyl-CoA & choline:
 - ❖ By the action of choline acetyl transferase enzyme (CAT).

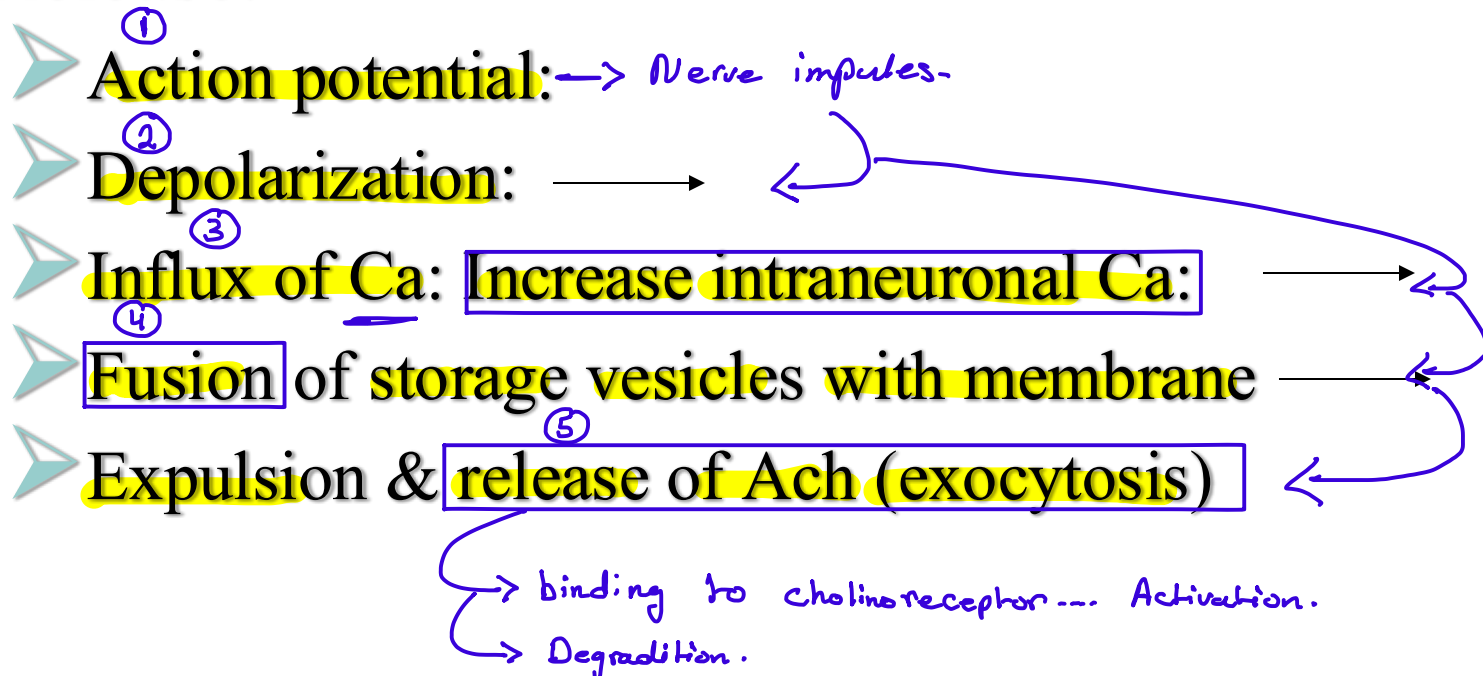
→ in nerve ending.



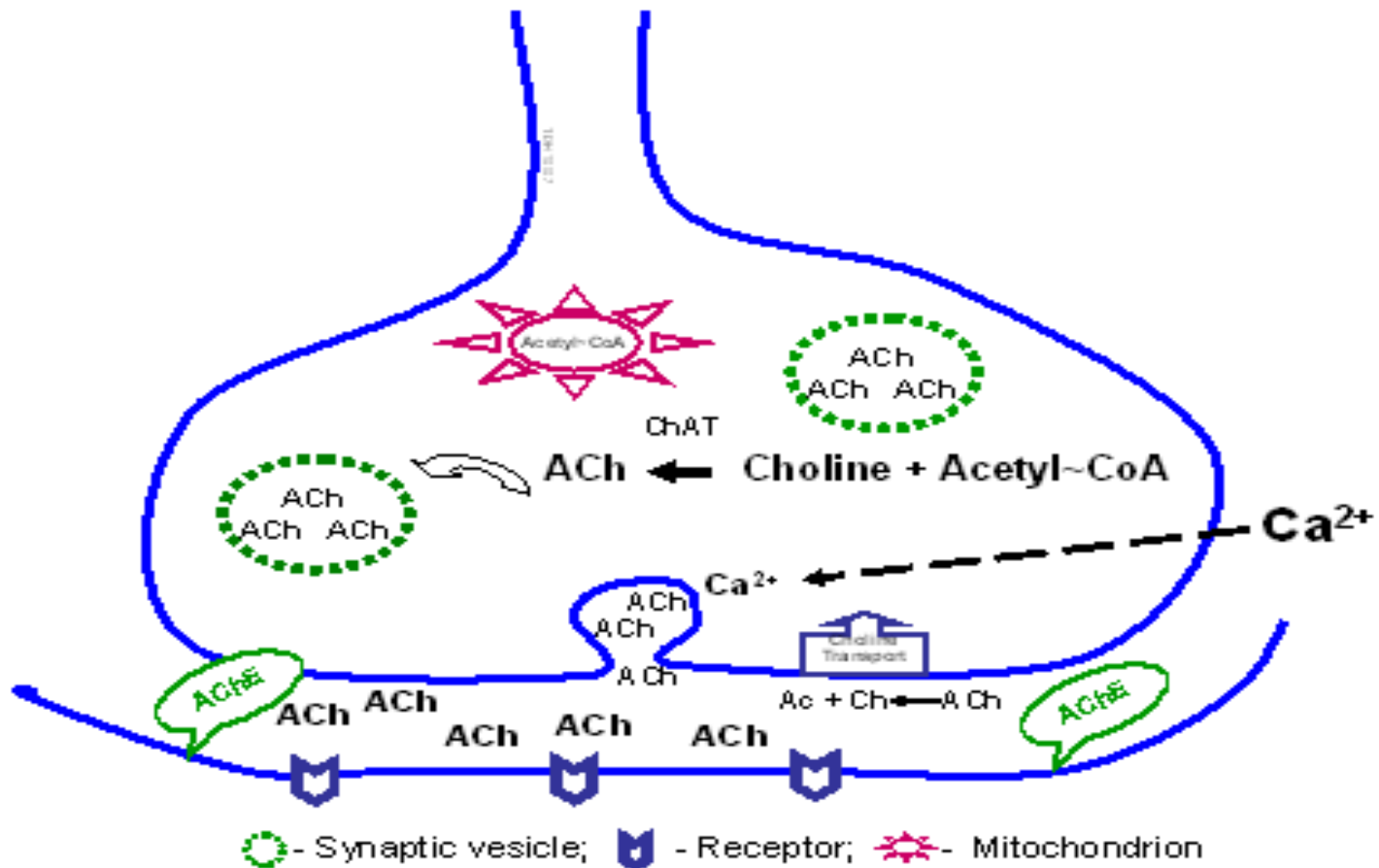
Pathway of acetylcholine:

□ Storage in vesicles

□ Release:



Synthesis & Release Of Ach



Pathway of acetylcholine:

- Binding and activation of cholinoceptors

- Actions

- Degradation:

Cholinesterase

Ach \longrightarrow Choline + Acetate

➤ Cholinesterase is specific to Ach (True) ... degradation of Ach

➤ Pseudocholinesterase (PCE) in plasma and liver is not specific

Acts on others as suxamethonium

➤ Genetic absence PCE \longrightarrow Prolonged apnoea

neurons
⊕
naji

Pathway of Ach: Recycling

□ Recycling of **choline** back into **neurons**

❖ **Inhibitors of Ach Pathway:**

➤ **Release:** Botulinum toxins

➤ **Binding of Ach:** **Anti-cholinergic drugs**

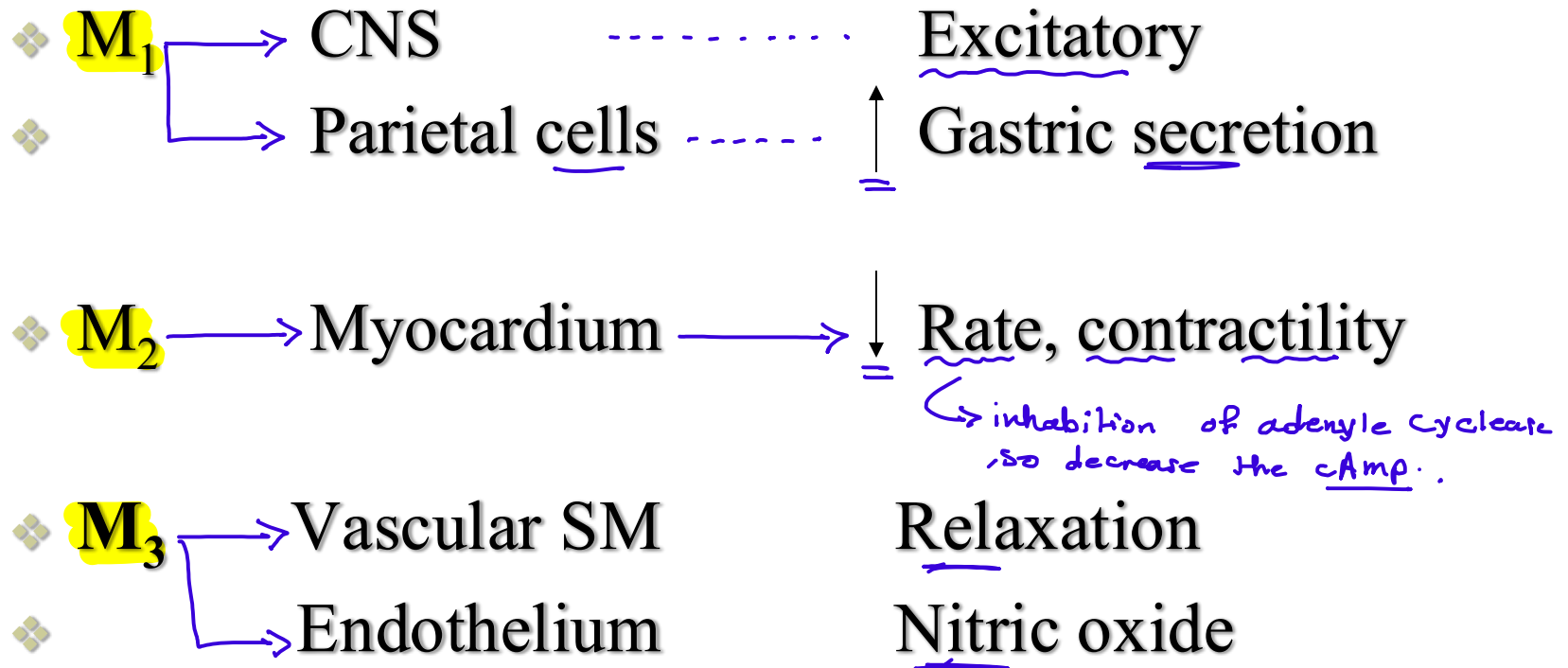
↳ anti-muscarinic receptor
↳ Anti-nicotinic drug.

1- what're the types of cholinergic receptor?

2- what're the subtype of muscarinic?
what's the role of them?

Locations & Function of Cholinoceptors

□ Muscarinic receptors:



Muscarinic cholinceptors

- ❖ M_3 → Circular M of iris → Miosis
- ❖ M_3 → Exocrine, GIT → ↑ Secretions
- ❖ M_3 → GIT & Bladder wall → Contraction
- ❖ M_3 → Sphincters → Relaxation
- ❖ M_3 → Bronchi → Constriction

Muscarinic receptors

- ❖ In corpora cavernosa of penis:
 - Through release of nitric oxide
 - And vasodilatation
 - Leads to erection

1- what're the type of them?
where we can find them?

Nicotinic receptors

❖ Nicotinic N_N

Ganglia (stimulation)

❖ Nicotinic N_N

Adrenal medulla

(Adrenaline & NA

release)

+ CNS

❖ Nicotinic N_M

NMJ endplates

(Muscle contraction)

Mechanism of Ach signal transduction

❖ Muscarinic receptors:

➤ G-protein coupled receptors

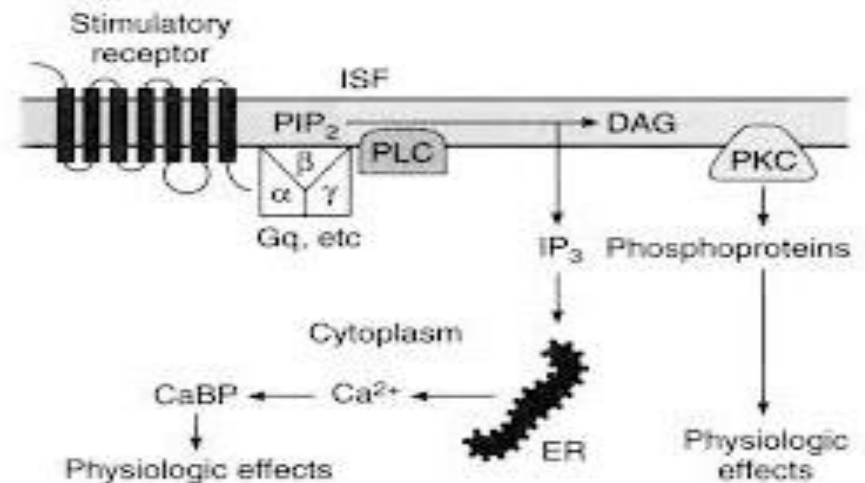
➤ Second messengers (as DAG, IP3, cGMP)

G_q \uparrow second messenger
 G_I inhibit the catalytic
 cycles \downarrow cAMP.

❖ Nicotinic receptors:

➤ Ion channel receptors

↳ \uparrow permeability of Na⁺



1- what's the action of it ?
what's the feature of it?

Acetylcholine

- ❖ Has little therapeutic value
 - Multiple actions
 - Binds & activates muscarinic & nicotinic receptors
 - Short $t_{1/2}$

Pharmacodynamics of Ach

□ Muscarinic stimulation on the CVS:

- Decrease SV & CO

By -ve (chronotropic, inotropic & dromotropic)

- Decrease ABP:

- Stimulation of vascular M₃ receptors
- Increase nitric oxide

Pharmacodynamics of Ach

□ Eye:

❖ Miosis:

- Contraction of the circular muscle of the iris

❖ Accommodation to near vision:

- Contraction of the ciliary muscle

❖ Decrease IOP

Pharmacodynamics of Ach

- ❑ Exocrine glands:
 - Increase secretion
- ❑ Increase intestine movement with relaxation of sphincter: → defecation
- ❑ Contraction of urinary bladder wall with relaxation of the sphincter: → urination

Pharmacodynamics of Ach

- Bronchi:
 - Broncho-constriction
 - Mucosal hypersecretion

Pharmacodynamics of Ach

- ❑ Stimulation of nicotinic cholinceptors:
 - ❖ Effects on ganglia
 - ❖ Adrenal medulla
 - ❖ NM Junction transmission

1- what's the subgroup?

2- what does each group contain?

Direct acting cholinomimetics

❖ Choline esters:

➤ Bethanechol, Carbachol, Methacholine

➤ Resist degradation by cholinesterases

➤ Have longer duration of action than Ach

❖ Natural alkaloid:

➤ Pilocarpine

➤ Acts directly on the eye

Bethanechol :- 1- what's the target of work?

3- what's the indication?

2- what's the mechanism of it?

4- what's the intra indication?

→ it's given For functional obstruction, NOT For organic obstruction
↳ ex. Tumor obstruct the prostate.

Bethanechol ⇒ taken orally and subcutaneous.

- ❖ Derivative of Ach which has little or no nicotinic effect.
- Good muscarinic activity on bladder & GIT
- ❖ Prokinetic agent
- ❖ Leads to easier urination and defecation ↑ Motility.
↳ M₃ ... ↑ opening of sphincter ⊕
- ❖ Used in treatment of:
 - Postoperative or post-labour urinary retention or paralytic ileus (Prokinetic) by increase the opening of sphincter and increase the motility.

Note:- NOT taken (IV) due to high concentration which will affect the heart, especially M₂ ... sever brady cardia.

Carbachol \Rightarrow Long duration because it doesn't get degraded by Acetyl cholinesterase

\rightarrow It's not selective.

- ❖ Derivative of Ach
- ❖ Has muscarinic & nicotinic actions
- ❖ **Limited systemic uses because of its nicotinic stimulatory effects on ganglia & adrenal Medulla with consequent changes in the CVS & other systems.**
- ❖ Used **topically as miotic agent to decrease high IOP in glaucoma** \Rightarrow No Adverse effects.

\rightarrow Given as eye drop \Rightarrow \downarrow Intra ocular pressure.

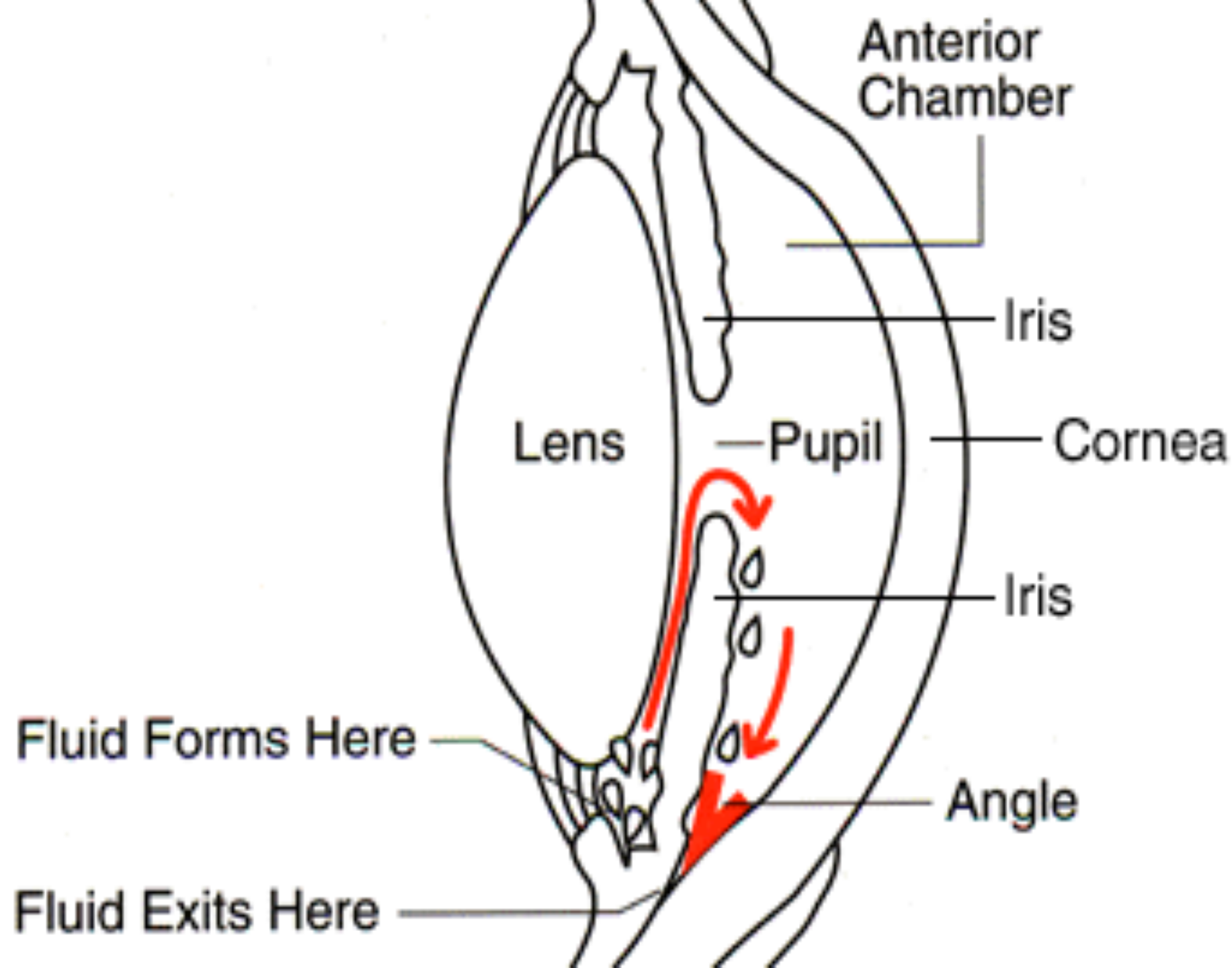
Pilocarpine \Rightarrow Act on M₃

- ❖ Natural alkaloid
- ❖ Resistant to cholinesterase
- ❖ Its muscarinic action in eye result in miosis & contraction of ciliary muscle
- ❖ Used topically in glaucoma
 - To lower high IOP in glaucoma
 - In open or close-angle glaucoma

- ⇒ used to treat a syndrome Xerostomia [dryness of all body secretion]
- ⇒ ↪ ↑ increase sweating and stimulate salivation.

Mechanism of pilocarpine action

- ❖ Improves outflow of aqueous humour
- ❖ Opens fluid pathways / Treatment of dryness
- ❖ Enhances aqueous flow through canal of Schlemm:
 - Contraction of ciliary M & circular muscle of iris
- ❖ Stimulates salivation and sweating



Indications of direct cholinomimetics

- ❖ Stimulate bladder & bowel function after surgery or labour (Bethanechol)
- ❖ Glaucoma (Pilocarpine & Carbachol)
- ❖ Pilocarpine orally to treat xerostomia of Sjogren's syndrome

Adverse effects of direct cholinomimetics

- ❖ Excessive sweating, salivation
- ❖ Flushing, hypotension
- ❖ Abdominal colic, diarrhoea
- ❖ Bronchospasm
- ❖ Pilocarpine: impaired accommodation to far vision & darkness (also carbachol)

Synthesis of NO

