

Autonomic pharmacology

Anticholinergic drugs

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- Sources
- **Lippincott Illustrated Reviews: Pharmacology 7th Edition**
- **Katzung ; Basic & Clinical Pharmacology 14th Edition**
- **Bennett & Brown ; Clinical pharmacology 11th edition**
- **Essentials of Medical Pharmacology; Lafi 09**

A night landscape with a bright light reflecting on water and a curved light streak in the sky. The scene is dark blue, with a bright light source on the horizon creating a vertical reflection on the water. A curved light streak arches across the sky from the horizon towards the top right. The text 'Anticholinergic drugs' is overlaid in white serif font on the left side of the image.

Anticholinergic drugs

Anti-ACh - Anti-Cholinergics

MOA:

So, if cholinergics agonize M3.....
an Anti-ACh will **ANTAGONIZE** M3

Antagonizing M3 will cause:

- **Decreased** exocrine gland secretions
- **Decreased** gut motility
- **Bronchodilation**
- **Bladder relaxation**



Anti-ACh



A-TROP-ine: Mydriasis w/ Cyclopegia,
Management of Anti-AChE "poisoning:

Benz-TROP-ine/Trihexyphenidyl: Lipid-soluble
(CNS Entry) for Parkinson's, and EPS
Symptoms due to antipsychotics

Ipra-TROP-ium: Safe to use in Asthma and
COPD



Anticholinergic prototype:

Atropine

Effects

- Decreased secretion
- Mydriasis
- Cycloplegia
(decreased accommodation)
- Hyperthermia
- Tachycardia
- Sedation
- Urinary retention and constipation
- Behavioural excitation and hallucinations

Antimuscarinic agents

Selected therapeutic uses and important remarks*

Atropine (click)

- to produce mydriasis & cycloplegia prior to **refraction** (7 days)
- spastic disorders of GI and lower urinary tracts
- **organophosphate poisoning**
- **premedication prior to surgery**, to suppress respiratory secretion in children

Antimuscarinic agents	Selected therapeutic uses and important remarks*
Atropine (click)	<ul style="list-style-type: none">• to produce <u>mydriasis & cycloplegia</u> prior to refraction (7 days)• <u>spastic disorders</u> of GI and lower urinary tracts• <u>organophosphate poisoning</u>• <u>premedication prior to surgery</u>, to suppress respiratory secretion in children
Homatropine	<ul style="list-style-type: none">• <u>Cycloplegic for refraction</u> in children (24 hr)
Tropicamide	<ul style="list-style-type: none">• Fundus examination (3 hr)

Antimuscarinic agents

Selected therapeutic uses and important remarks*

Scopolamine (hyoscine)

- In obstetrics with morphine to produce **amnesia and sedation**
- **Motion sickness**

Ipratropium

- **Asthma** (inhalation)

Antimuscarinic agents

Selected therapeutic uses and important remarks*

Clidinium

- With chlordiazepoxide (**Librax[®]**) in GI disorders like
 - **peptic ulcer,**
 - nervous dyspepsia,
 - **irritable bowel syndrome,**
 - spastic colitis,
 - mild ulcerative colitis

Isopropamide

- With trifluoperazine (**Stelabid[®]**) in
- **peptic ulcer,**
 - visceral spasm



Antimuscarinic agents	Selected therapeutic uses and important remarks*
Pirenzepine	<ul style="list-style-type: none"> • Peptic ulcer (inhibits acid secretion), • poorly enters the CNS, thus, no or little CNS side-effects
Propantheline	<ul style="list-style-type: none"> • Peptic ulcer, • irritable bowel syndrome, & • urinary disorders of storage (urinary frequency, incontinence, nocturnal enuresis)
Emepronium (Cetiprin®)	<ul style="list-style-type: none"> • Urinary disorders of storage (as above)

CNS Agents

Benzotropine

Procyclidine

Benzhexol-HCl

Orphenadrine

(Centrally acting antimuscarinic antagonists)

- **Drug induced dystonias**
- **Parkinson's disease**

Adverse-effects commonly observed with **cholinergic antagonists**:

blurred vision, mydriasis, tachycardia, constipation, urinary retention, and confusion.

**Ganglionic
blockers**

Mecamylamine

Moderately severe to severe **hypertension**

Trimethaphan

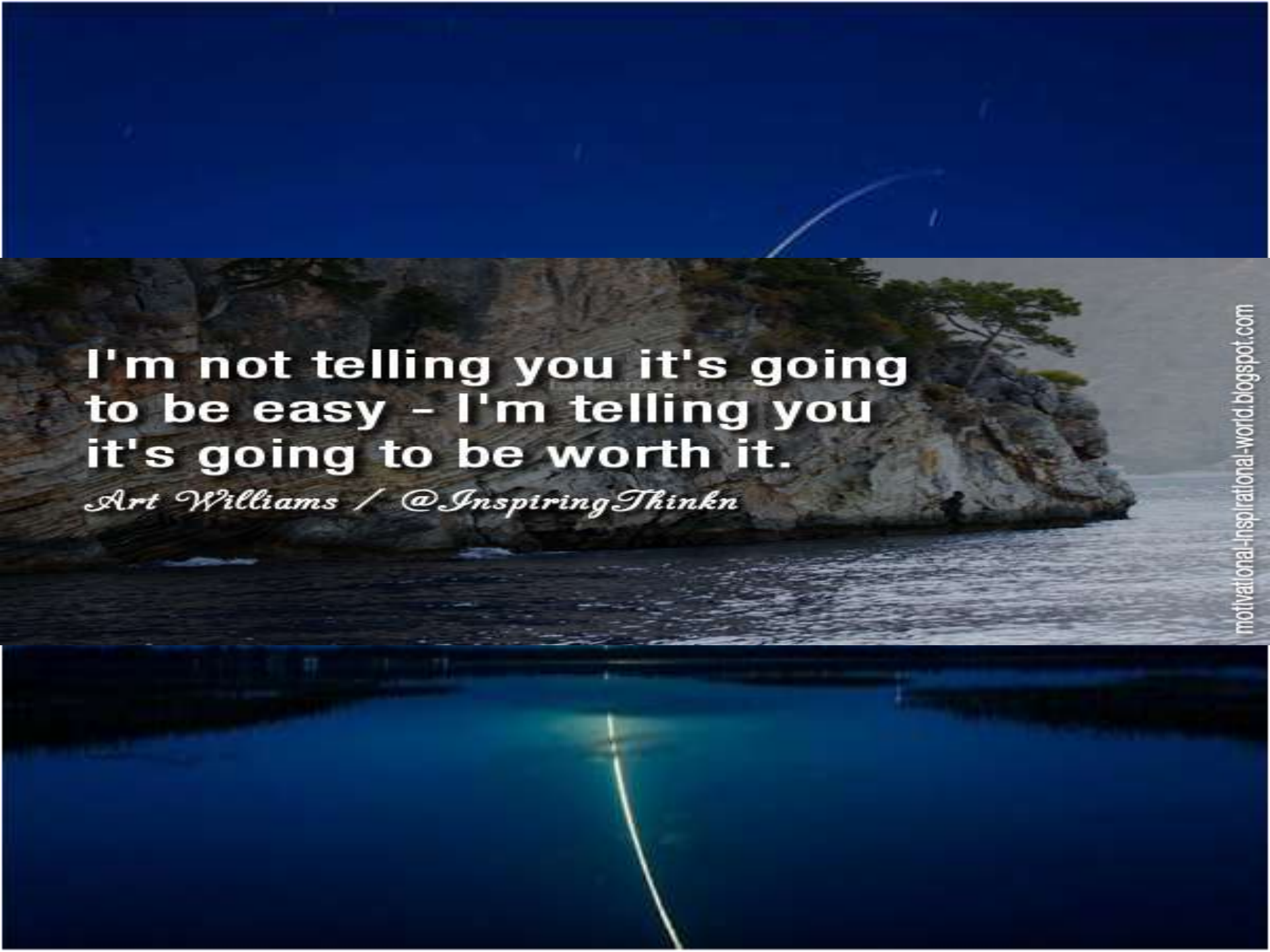
Short-term treatment of **hypertension** (emergency lowering of blood pressure, when other agents cannot be used)



Neuromuscular
blockers

Nondepolarising
(competitive agents)
Depolarising agents

See appropriate section in the chapter on CNS pharmacology (later on)



**I'm not telling you it's going
to be easy - I'm telling you
it's going to be worth it.**

Art Williams / @InspiringThinkn

*Thank
you*



USES OF CHOLINERGIC DRUGS

- For myasthenia gravis, both to diagnose (edrophonium) and to treat (neostigmine, pyridostigmine, distigmine).
- To stimulate the bladder and bowel after surgery (bethanecol, carbachol).
- To lower intraocular pressure in chronic simple glaucoma (pilocarpine).



Figure 13-2. The effect of neostigmine in myasthenia gravis. (From Grollman, A.: *Pharmacology and Therapeutics*, 6th Ed. Philadelphia, Lea & Febiger, 1965.)

Antimuscarinic agents

Selected therapeutic uses and important remarks*

Atropine (click)

- to produce mydriasis & cycloplegia prior to **refraction** (7 days)
- spastic disorders of GI and lower urinary tracts
- organophosphate poisoning
- premedication prior to surgery, to suppress respiratory secretion in children

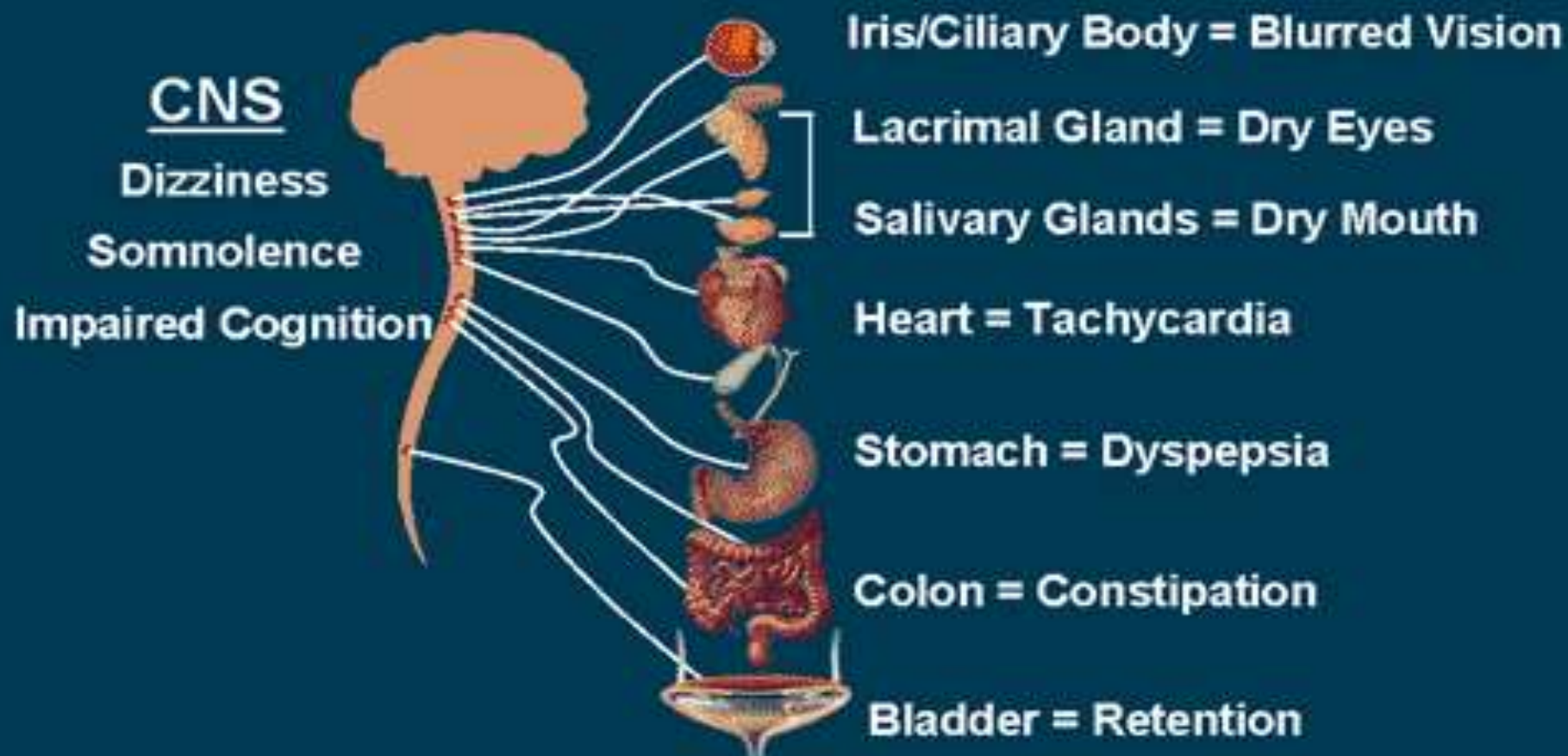
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Scopolamine (hyoscine)	<ul style="list-style-type: none"> • In obstetrics with morphine to produce amnesia and sedation • Motion sickness
Ipratropium	<ul style="list-style-type: none"> • Asthma (inhalation)

Antimuscarinic agents	Selected therapeutic uses and important remarks*
Clidinium	<ul style="list-style-type: none"> • With chlordiazepoxide (Librax[®]) in GI disorders like <ul style="list-style-type: none"> • peptic ulcer, • nervous dyspepsia, • irritable bowel syndrome, • spastic colitis, • mild ulcerative colitis
Isopropamide	<p>With trifluoperazine (Stelabid[®]) in</p> <ul style="list-style-type: none"> • peptic ulcer, • visceral spasm
Pirenzepine	<ul style="list-style-type: none"> • Peptic ulcer (inhibits acid secretion), • poorly enters the CNS, thus, no or little CNS side-effects
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<p><u>CNS Agents</u> Benzotropine Procyclidine Benzhexol-HCl Orphenadrine</p>	<p>(Centrally acting antimuscarinic antagonists)</p> <ul style="list-style-type: none"> • Drug induced dystonias • Parkinson's disease
<p><u>Ganglionic blockers</u> Mecamylamine</p>	<p>Moderately severe to severe hypertension</p>
<p>Trimethaphan</p>	<p>Short-term treatment of hypertension (emergency lowering of blood pressure, when other agents cannot be used)</p>
<p><u>Neuromuscular blockers</u> Nondepolarising (competitive agents) Depolarising agents</p>	<p>See appropriate section in the chapter on CNS pharmacology (later on)</p>

Adverse-effects commonly observed with **cholinergic antagonists**:
blurred vision, mydriasis, tachycardia, constipation, urinary retention, and confusion.

Distribution of Muscarinic Receptors in Various Organs





Metha-CHOL-ine

Acetylcholinesterase (AChE)

Enzymatically degrades acetylcholine at nicotinic and muscarinic synapses.

AChE inhibitors increase amount of acetylcholine in the synaptic cleft.

Acetylcholinesterase Inhibitors

Include

- Neuromuscular reversal agents
- Myasthenia gravis drugs
- Insecticides
- Nerve gases

Poisoning by an acetylcholinesterase inhibitor causes activation of both muscarinic and nicotinic receptors and can be fatal.

Acetylcholinesterase Inhibitors

The clinical effects of AChE inhibitors result from activation of muscarinic *and* nicotinic receptors.

Clinically Important Acetylcholinesterase Inhibitors

Edrophonium (Tensilon®)

Diagnosis of myasthenia gravis (“Tensilon test”)

Physostigmine

Treatment of glaucoma

Neostigmine

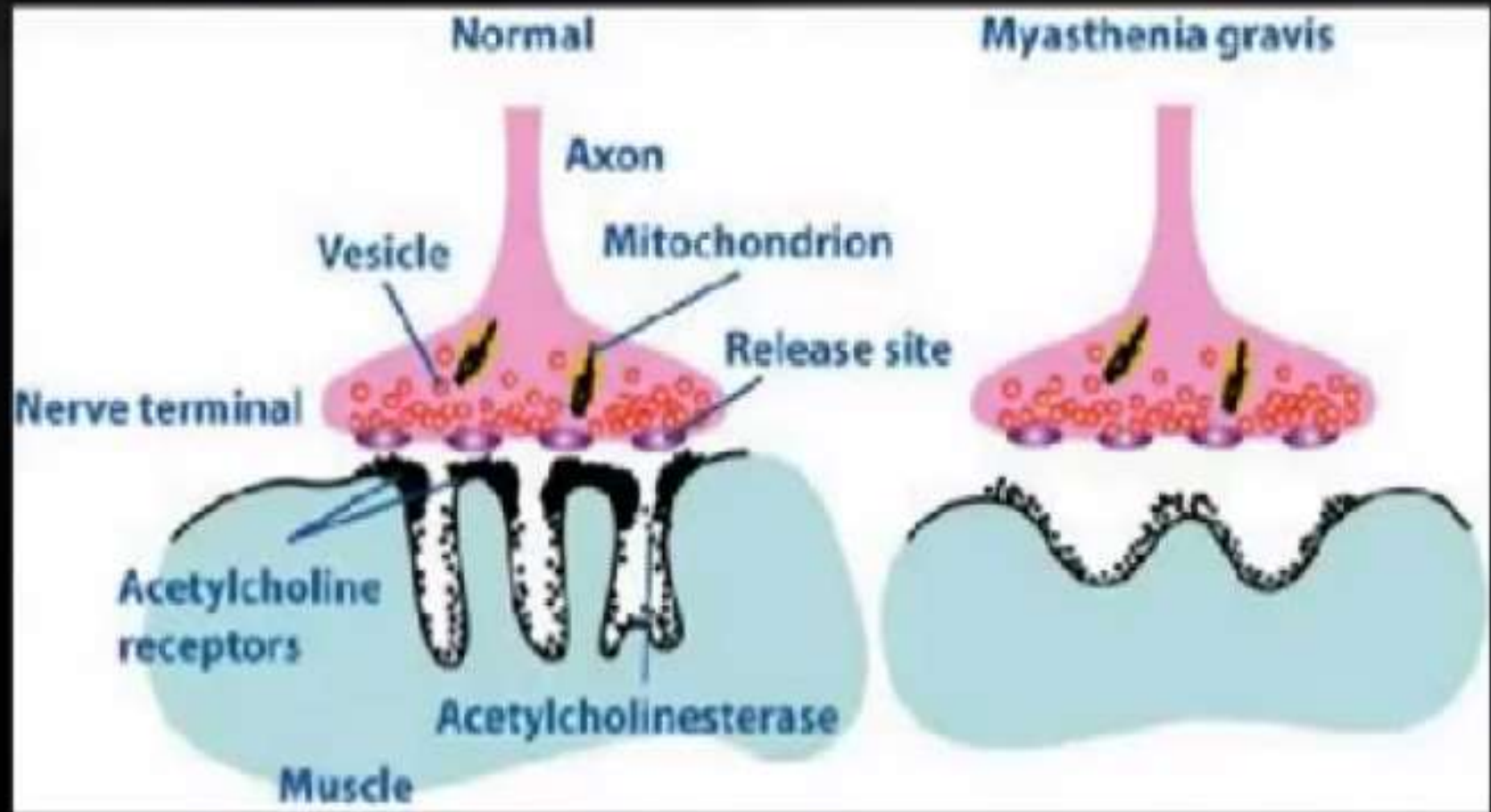
Reversal of non-depolarizing neuromuscular blockers

Treatment of myasthenia gravis

Pyridostigmine

Treatment of myasthenia gravis

Neuromuscular Junction in Myasthenia Gravis





Parasympathetic System

-CHOLinergic

- **M1**- CNS/ENS
- **M2**- Heart
- **M3**- **EG** **BB**
 - Increases **Exocrine** Gland Secretion
 - Increases **Gut** Motility
 - **Broncho**constriction
 - **Bladder** Contraction

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COPD

Muscarinic Antagonists

Atropine

Blocks muscarinic signaling

Treats bradycardia, is an antidote for organophosphate poisoning, and can induce cycloplegia

Atropine makes you "dry as a bone, red as a beet, hot as a pistol, blind as a bat, and mad as a hatter."

Atropine Effects

Decreased secretions

Mydriasis (dilated pupils)

Cycloplegia (decreased accommodation)

Hyperthermia

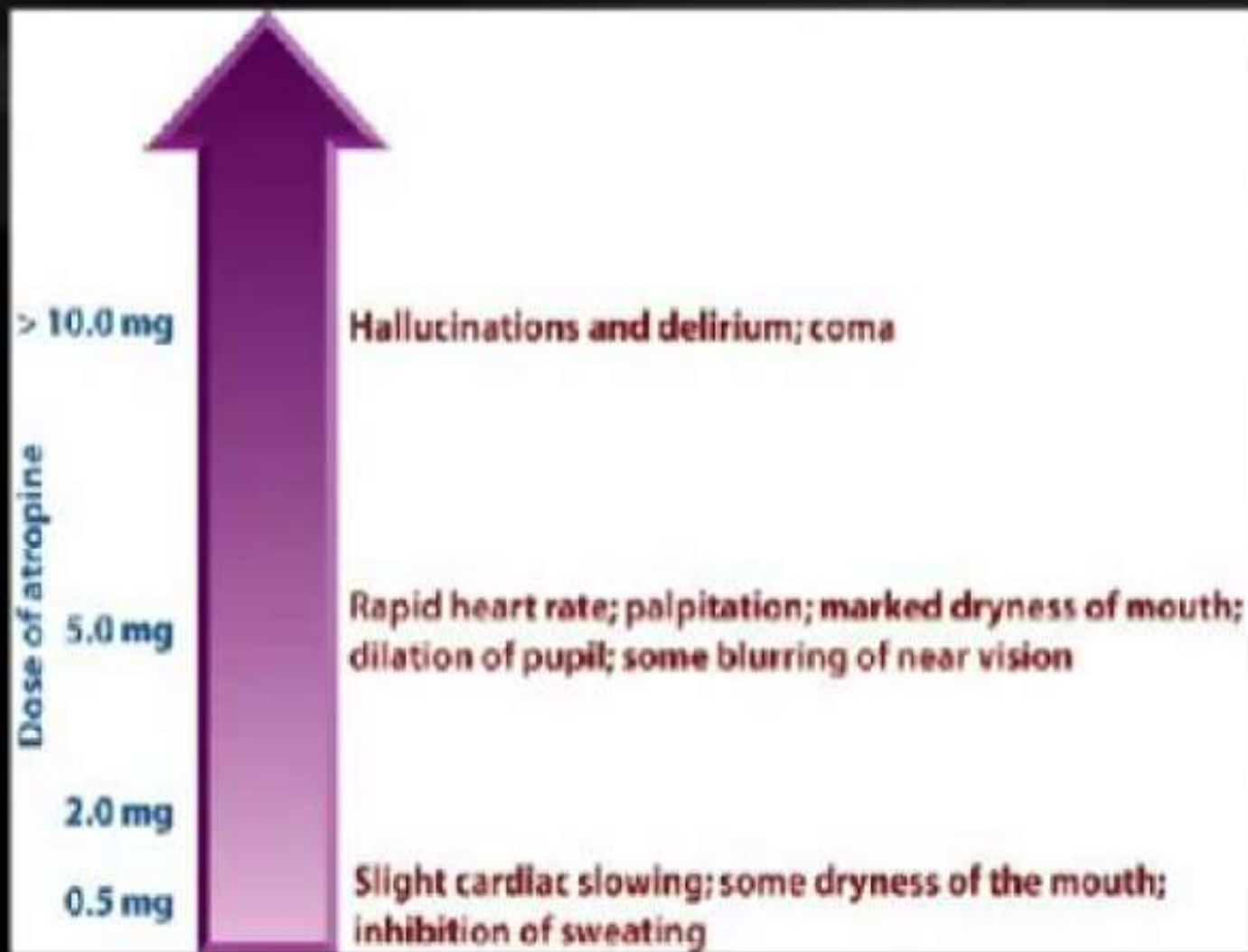
Tachycardia

Sedation

Urinary retention and constipation

Behavioral excitation and hallucinations

Dose-Dependent Effects of Atropine



Anti-ACh

- **Atropine** – Mydriasis w/Cyclopegia, Management of Anti-AChE “poisoning”
- **Benztropine/Trihexyphenidyl** – Lipid Soluble (CNS Entry) for Parkinson's, and EPS Symptoms due to antipsychotics
- **Ipratropium** – Safe to use in Asthma and COPD
- **Glycopyrrulate, Oxybutinin** – Reduce urgency in mild cystitis and reduce bladder spasms
- **Scopolamine** – Motion Sickness

A close-up photograph of a quill pen resting in a dark glass inkwell. The inkwell is placed on an open book, with the pages visible in the background. The lighting is soft, highlighting the texture of the quill and the glass of the inkwell.

”مخيفة هي الكتابة دائماً.
لأنها تأخذ لنا موعداً مع كلِّ الأشياء
التي نخاف أن نواجهها أو نتعمَّق في فهمها“.

فوضى الحواس - أحلام مستغاني