

PharmPill team

1428-1429

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اللهم طهر قلبي من النفاق وعلمي من الرياء ولساني من الكذب وعيني من الغيابة فأنت تعلم خائنة اللاعبين وما تخفي السرور
اللهم امدني بالحسن الاعمال والاخلاق ..

اخواني الطلاب .. اخواتي الطالبات دفعة 426

نحن فاره بل تيم قمنا بجمع مذكرات البنات مع الأولاد في هذه المذكرة

مع إضافة نوات هذا العام

نسأل الله أن تنفعنا وإياكم ... وتعود بالنفع لغيرنا

ان اصبنا فمن الله وان اخطانا فمننا ومن الشيطان

"أوجه شكر خالص الى الأخت دعاء البلوي دفعة 424"

Team leader : Dr.noop

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باقي الاعضاء:

ابويسرا

Blue eye

Dr.Cool

محمد الرويشد



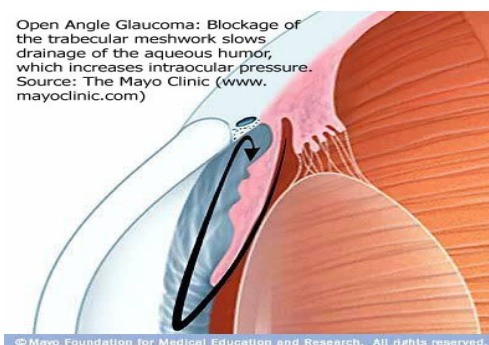
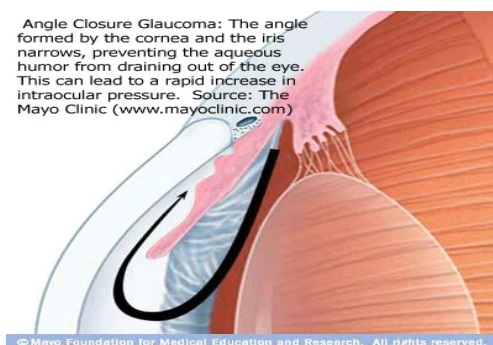
Clinical Uses

1-The Eye:- Glaucoma

- There are two types of **acquired glaucoma**, primary & secondary [caused by trauma, inflammation, surgical procedures]
 - a. **Primary glaucoma** is either angle closure or open angle[chronic not amenable to surgery]
 - b. **Acute angle closure** is a medical emergency, initially treated by drugs, surgery for permanent correction [**iridectomy**]

Note :

- ✓ Acute angle-closure glaucoma : is primary glaucoma in which contact of the iris with the peripheral cornea excludes aqueous humor from the orbicular drainage meshwork .



- Muscarinic stimulants ↓intraocular pressure by facilitating **outflow** of aqueous humour & ↓rate of its **secretion**
- **Direct stimulants**:- methacholine , carbachol, pilocarpine.
- **Indirect**:-physostigmine, ecothiopate



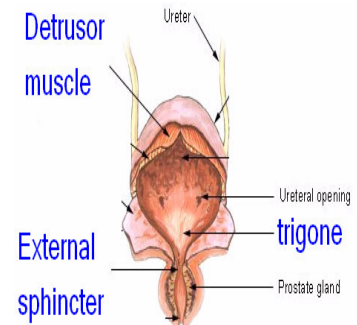
2-GIT & Urinary tract:-In clinical conditions where there is **depression** of smooth muscle activity without obstruction e.g:

a-postoperative ileus “**atony**” or paralysis of the stomach following surgery[limited or absent intestinal passage characterized by nausea ,vomiting ,abdominal distension & constipation]

b- postoperative **urinary retention**.

✓ Bethanechol & neostigmine

In atony of the bladder ,neostigmine increases the tone of the detrusor muscle and decreases the volume of the bladder , coupled with relaxation of the trigone and external sphincter facilitating urination.



3-Neuromuscular junction:- Myasthenia gravis, disease of skeletal muscle,

■ **autoimmune disease** → production of antibodies→ ↓ no. of functioning nicotinic receptors at endplate, → weakness , fatigue affecting muscles of hand ,head, neck , extremities→ ptosis, diplopia, difficulty of speaking & swallowing.

Note : diplopia = double vision .

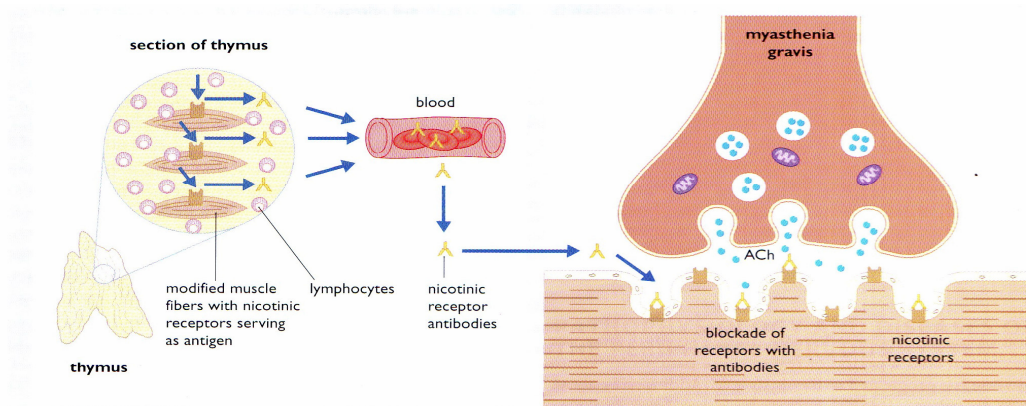


Fig. 14.19 Postulated source of antigen and antibody production in myasthenia gravis. A diagrammatic representation of a section of the thymus gland containing modified muscle cells with nicotinic receptors on the surface. It is suggested that this gland may be the source of the antigen that serves as a template for the production of nicotinic antibodies in myasthenic patients. These antibodies block the nicotinic receptors at the neuromuscular junction and prevent interaction between the neurotransmitter and the nicotinic receptors (see Fig. 14.18). (ACh, acetylcholine)



Explanation :

Thymus (muscle fiber antigen) => antibody => blood => neuromuscular junction

=> bind to nicotinic receptor => preventing the receptor to bind to Ach .

- Treatment with **cholinesterase inhibitors+ immunosuppressants**.
- Chronic long term therapy → Neostigmine, pyridostigmine & ambenonium.
- Muscarinic side effects can be controlled by antimuscarinics.
- **Edrophonium** is used as:

1-**Test for diagnosis** . An improvement in muscle strength last for 5min is noted.

2-It is also used to **assess the adequacy** of treatment with the longer –acting cholinesterase inhibitors.

- Note : endrophonium not used as treatment for myasthenia gravis .

✓ If muscle tone improve so the dose is low => we should increase it.

✓ If muscle tone is weaker so the dose is excessive => we should decrease it.

- In case of excessive amount of cholinesterase inhibitor, patient becomes weak because of **depolarization block** + symptoms of muscarinic stimulation.
- If patient improves with a dose of edrophonium , **↑ in CI is indicated**.
- Severe myasthenia[**myasthenia crisis**], requires mechanical ventilation
- Excess drug therapy[**cholinergic crisis**]

4-To reverse pharmacological paralysis produced in case of anaesthetic adjunct.

5-Heart:- for treatment of supraventricular tachycardia, edrophonium potentiates the effect of Ach at AV node →slow AV conduction & ventricular rate.

6-Antimuscarinic drug intoxication:- atropine over dose is toxic in children → severe muscarinic block ,

- blockade is competitive , overdose can be overcome by ↑ amount of endogenous Ach.
- Physostigmine is used because it crosses the BBB , reverses central & peripheral signs.

7-Alzheimer disease:-Loss of intellectual ability.

- Donepezil is less toxic ,not hepatotoxic.

Note (just for reading) :

- - donepezil , galantamine and rivastigmine are used to treat this disease better than the older drug (tacrine) because they :
- avoid hepatic toxicity .
- more selective acetylcholinesterase inhibitors .



- **8-Sjogren's Syndrome** is an autoimmune disease resulting in inflammation of lacrimal and salivary glands → eye and mouth dryness.
- Cevimeline is **muscarinic agonist**, with particular effect on M3 receptors.
- By activating the M3 receptors cevimeline stimulates secretion by the **salivary glands**, thereby alleviating dry mouth.
- Rapidly absorbed after oral administration and excreted unchanged in urine

Toxicity

A-Directly- acting muscarinic stimulants:

- nausea,
- vomiting ,
- diarrhoea,
- salivation,
- cutaneous vasodilatation ,
- bronchial constriction.

B-Directly- acting nicotinic stimulants:-

1) Acute toxicity:-

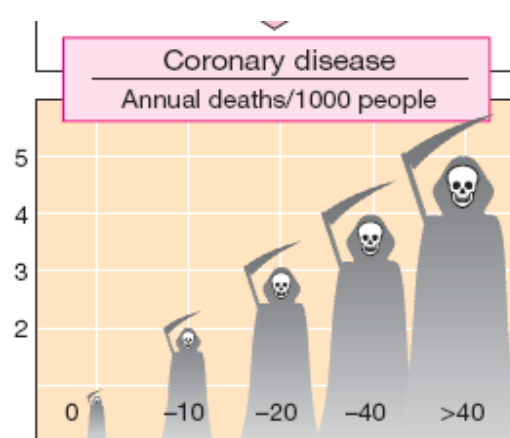
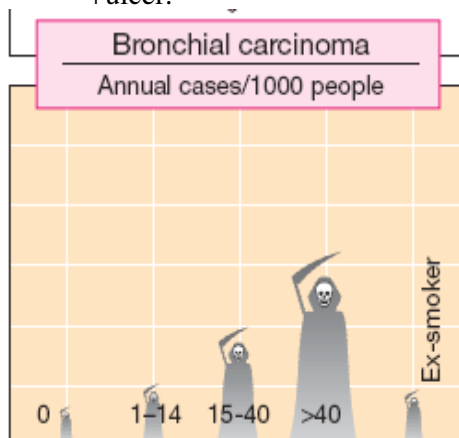
- **A- CNS stimulant action**, convulsions , coma , respiratory arrest
- **B-Skeletal muscle endplate depolarization** → depolarization block & respiratory paralysis.
- **C-Hypertension & cardiac arrhythmias.**

Note :

- treatment is related largely to symptoms .
- nicotine is metabolized and excreted relatively rapidly , so patient who survive the first 4 months from nicotine usually recover completely if hypoxia & brain damage does not occur .

- **ii-Chronic nicotinic toxicity:-**30% of deaths due to cancer & CHD are due to smoking.

- Nicotine contributes to ↑risk of vascular diseases, sudden coronary death, ↑ulcer.





- ✚ Dominant initial signs of muscarinic excess, miosis, salivation, sweating , bronchial constriction, V,D, CNS involvement follows accompanied by peripheral nicotinic effects
- ✚ **Therapy:-** 1- **maintenance of vital signs** , respiration may be impaired
- ✚ 2-**Decontamination** to prevent further absorption, removal of cloth, washing of skin
- ✚ **Parenteral atropine** in large doses. **Pralidoxime[PAM]** often