

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ



Cholinergic Drugs; **(Parasympathomimetic Drugs)**

By

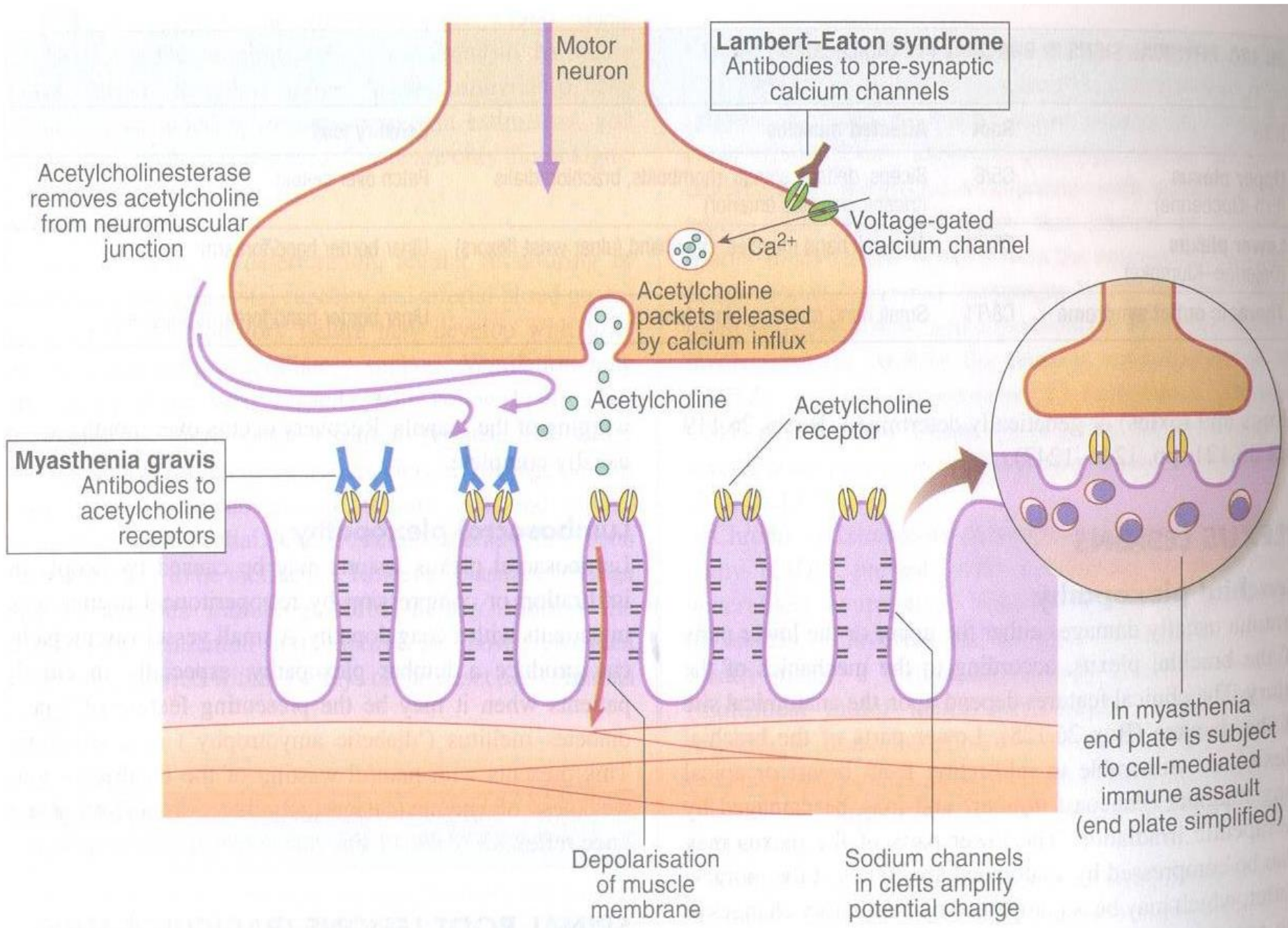
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Clinical uses of Cholinomimetic drugs;

1. Neuromuscular junction;

- Myasthenia gravis.
- Reversal of NM blocking drugs.
- **Myasthenia gravis;** Edrophonium, Pyridostigmine.
 - **An autoimmune process. Weakness and easy fatigueability on repeated activity, with recovery after rest due to loss N_M Receptors.**

- **Diagnosis of Myasthenia gravis;**
 - 1. Ach receptor antibodies. 2. CT scan thorax for thymoma.
 - 3. EMG – repetitive nerve stimulation.
 - 4. Edrophonium test.
 - » Baseline measurement of muscle strength.
 - » Edrophonium 2 mg I/v-----
improvement in muscle strength.
 - » If no reaction occurs after 45 minutes,
an additional 8 mg may be injected.
Myasthenia Gravis --- ↑ muscle
strength.



- **Drug treatment;**
 - **Pyridostigmine -- 30-60 mg TID/ QID (may be ↑ every 2-3 hours)**
The doses are titrated. Sustained release preparations used at night. Neostigmine (every 4 hours) or Ambenonium are alternative.

Treatment – other modalities;

Immunosuppression by **Corticosteroids**, Azathioprine, cyclophosphamide, Cyclosporin. **Thymectomy** & **Plasmapheresis**.





Myasthenic crisis / cholinergic crisis;

- **Myasthenic crisis** ----- Severe myasthenia
- **Cholinergic crisis** ----- paradoxical weakness due to **Excessive drug therapy** (cholinesterase inhibitors) causing **paradoxical weakness** because of **nicotinic depolarizing block of the motor endplate** + Symptoms of excessive stimulation of muscarinic receptors.

- How will you differentiate Myasthenic crisis from cholinergic crisis?
- **Edrophonium test (Tensilon test); Inject Edrophonium (2mg i/v).**
- **Myasthenic crisis ---- Improvement in muscle strength.**
- **Cholinergic crisis ----- Worsening of symptoms.**

- **Reversal of neuromuscular blocking drugs;**
 - Neostigmine & edrophonium I/V or I/ M.
 - **Used postoperatively** to reverse the pharmacological paralysis caused by the **nondepolarizing muscle relaxants such as pancuronium.**

2. Antimuscarinic drug intoxication;

- Atropine intoxication.
- TCA in toxic doses.
 - **Physostigmine** is preferred because **it enters the CNS** and reverses the central as well as peripheral signs of muscarinic blockade.

3. GIT & urinary bladder;

- Bladder & bowel atony --- after surgery or spinal cord injury.
- Postoperative **ileus**, Congenital megacolon.
- **Neurogenic bladder** -- Postoperatively or postpartum, secondary to spinal cord injury or disease.
- It must be ensured that there is no mechanical obstruction to outflow prior to using the Cholinomimetics.
- **GERD** --- To ↑ tone of lower esophageal sphincter.

4. Eye;

– Glaucoma;

- Muscarinic stimulants and cholinesterase inhibitors cause contraction of ciliary muscles. Facilitates the flow of aqueous humor and perhaps also by diminishing the rate of its secretion. Relaxation of suspensory ligaments– bulging of the lens -- Vision fixed for near vision -- Spasm of accommodation
- Direct acting muscarinic agonist;
 - Pilocarpine, Methacholine, Carbachol.
- Cholinesterase inhibitors;
 - Physostigmine, Demecarium, Echothiopate, Isoflurophate.

– Accomodative esotropia;

- strabismus caused by hypermetropic accommodative error in young children --- Esotropia convergent strabismus.

5. Glands;

- To increase salivary secretion;**
 - Pilocarpine – Sjogren syndrome.**
 - Pilocarpine Mouth spray in xerostomia resulting from irradiation.**
- Cevimeline is a direct acting muscarinic used for the treatment of dry mouth of Sjogren syndrome.**

6. Smoking cessation treatment;

- **Nicotine** (patch, chewing gum) replaces rapid onset nicotine (cigarettes) with slow action.
- **Varenicline --- A direct acting nicotinic agonist.**
 - Selective for $\alpha_4 \beta_2$ isoform of N_N receptor.
 - Orally active, half life 14-20 hours.
 - Toxicity nausea, headache and sleep disturbances.

7. Heart;

- Very rare use, **Paroxysmal SVT -- Edrophonium.**
- **Adenosine & Ca⁺⁺ channel blockers (verapamil and diltiazem)** are commonly used.

8. CNS -- Alzheimer disease

- Progressive loss of **memory & cognitive functions** ---- may lead to a completely **vegetative state**.
- Memory loss is the hall mark symptom and has been linked to **progressive loss of cholinergic neurons and cholinergic transmission in the cortex**.
- **Overstimulation of glutamate receptors, of NMDA type, results in excitotoxic effects** on neurons resulting in neurodegeneration.

– Alzheimer disease --- treatment;

- **Drugs provide only palliative and modest short term benefit.**
- **Underlying neurodegenerative process is not altered.**
- **Selective reversible acetylcholinesterase inhibitors;**
 - **Galantamine** is a competitive inhibitors.
 - **Donepezil, Rivastigmine** (not metabolized by P 450) & **Tacrine (hepatotoxicity)** are uncompetitive inhibitors.
- **NMDA(N-methyl-D-aspartate) type of glutamate receptor antagonists;**
 - **Memantine.**

A landscape photograph featuring rolling green hills in the foreground and middle ground. The foreground is dominated by a field of bright yellow wildflowers. The sky is a deep blue, filled with soft, white, wispy clouds. The overall scene is bright and cheerful.

Thank You