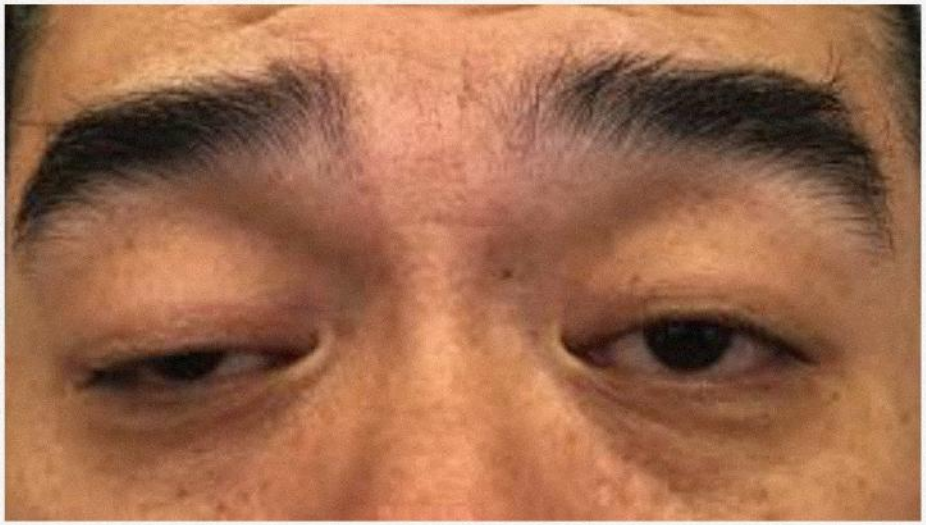
Myasthenia Gravis



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Presentation lay out

- Introduction
- Definition
- Etiology
- Pathophysiology
- Role of thymus gland
- Types
- Classification
- Diagnosis
- Differential diagnosis
- Management

INTRODUCTION

- **A neurological / neuromuscular autoimmune disorder**
- **Error in the transmission of nerve impulses to muscles at the neuromuscular junction—the place where nerve cells connect with the muscles they control**
- Antibodies to the **acetylcholine receptor (AChR)**,nicotinic receptors found in the serum of 85% of patients
- **Affects 1 in 10,000 population**
- **Leads to weakness and fatigability**

Potential Risk Factors for Developing Myasthenia Gravis

Women 20-40 years old and men 50-80 years old

People who have rheumatoid arthritis or lupus

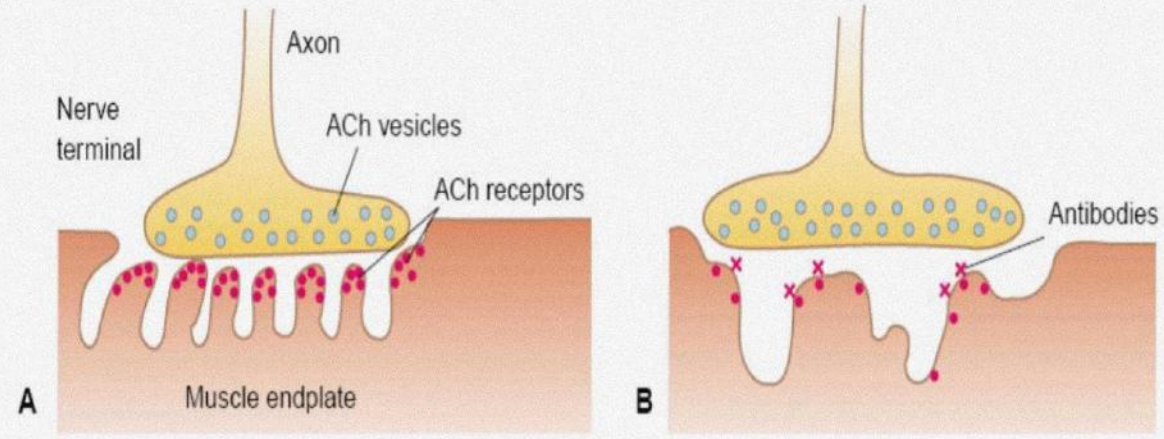
Taking certain medications for malaria, heart arrhythmia, antibiotics and psychiatric drugs

Having undergone extensive surgeries in the past

Issues with the thyroid gland

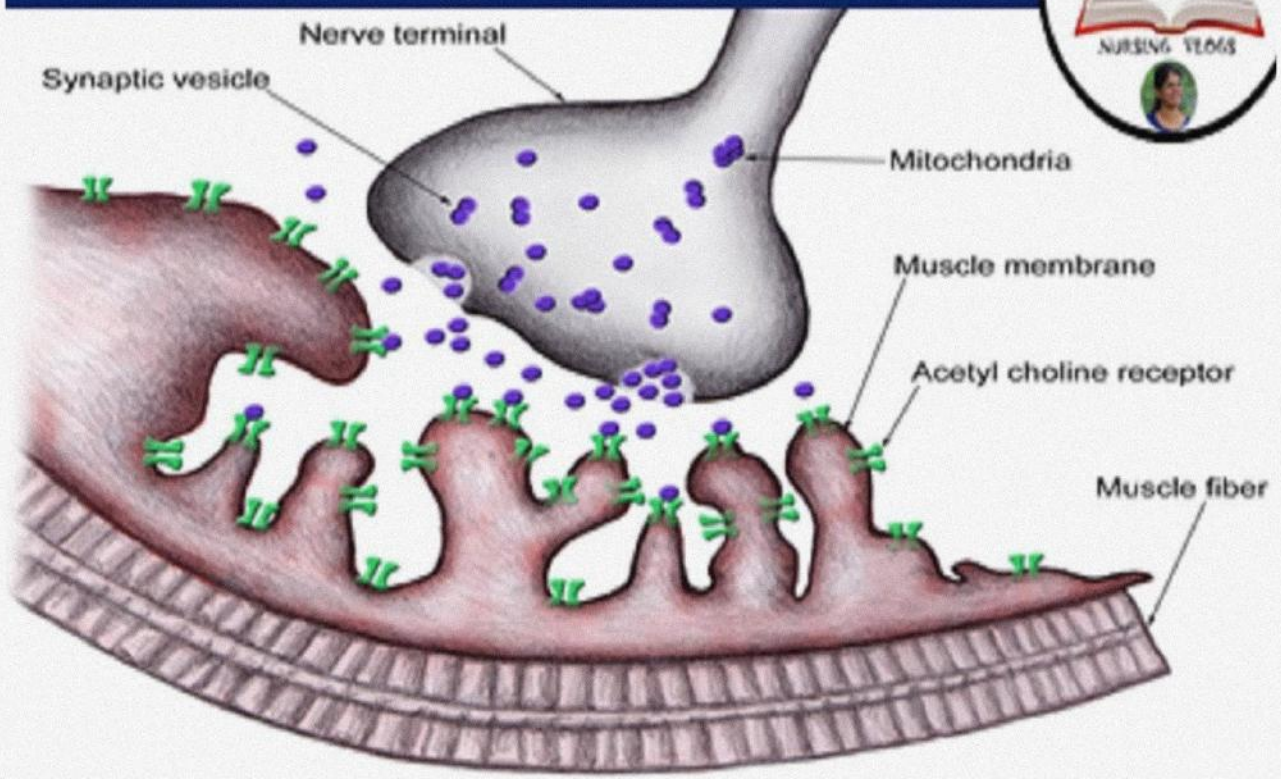
PATHOPHYSIOLOGY

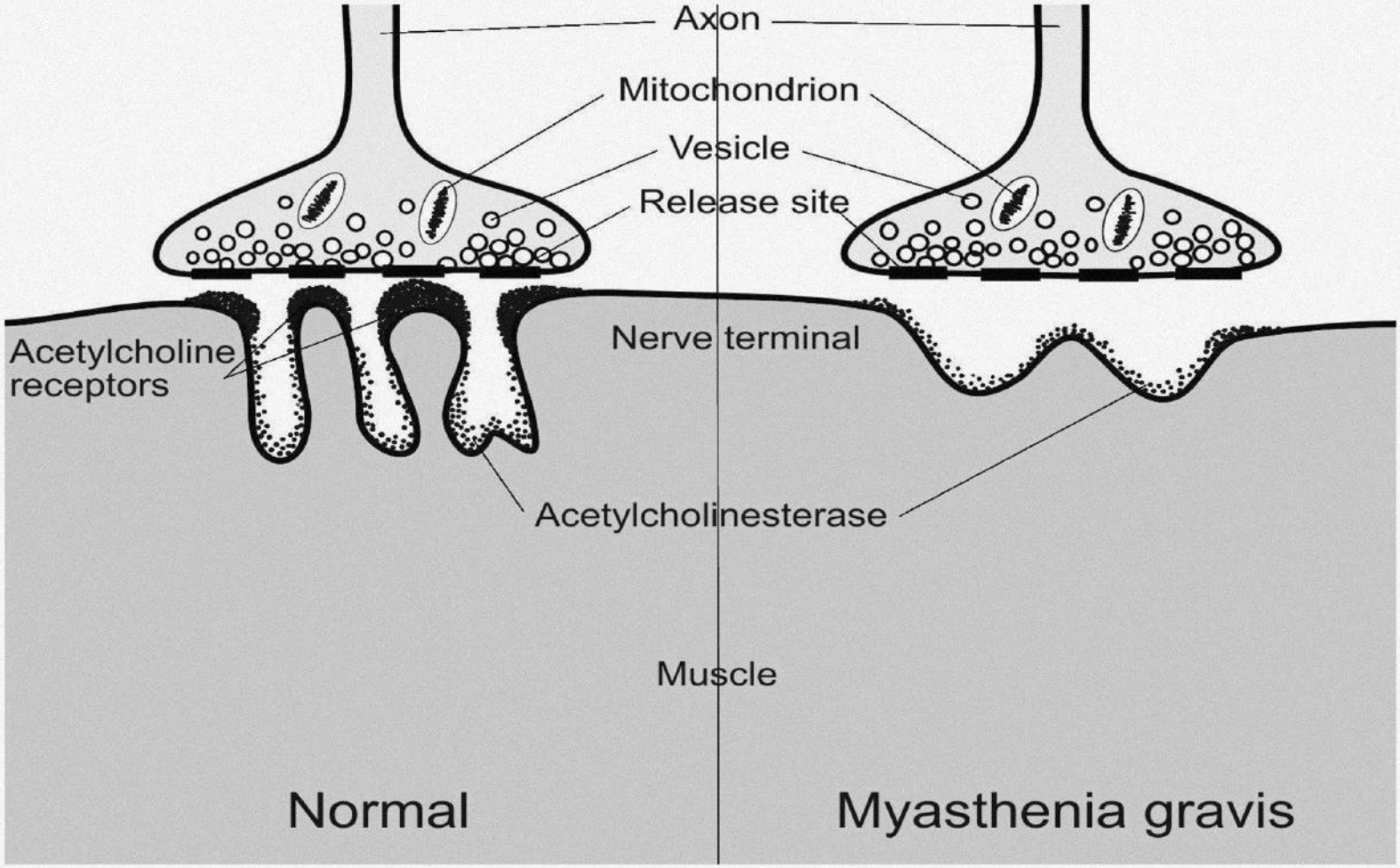
- Normally, a chemical impulse precipitates the release of acetylcholine from vesicles on the nerve terminal at the myoneural junction. The acetylcholine continuously bind to the receptor sites on the motor end plate, for muscle contraction to sustain.

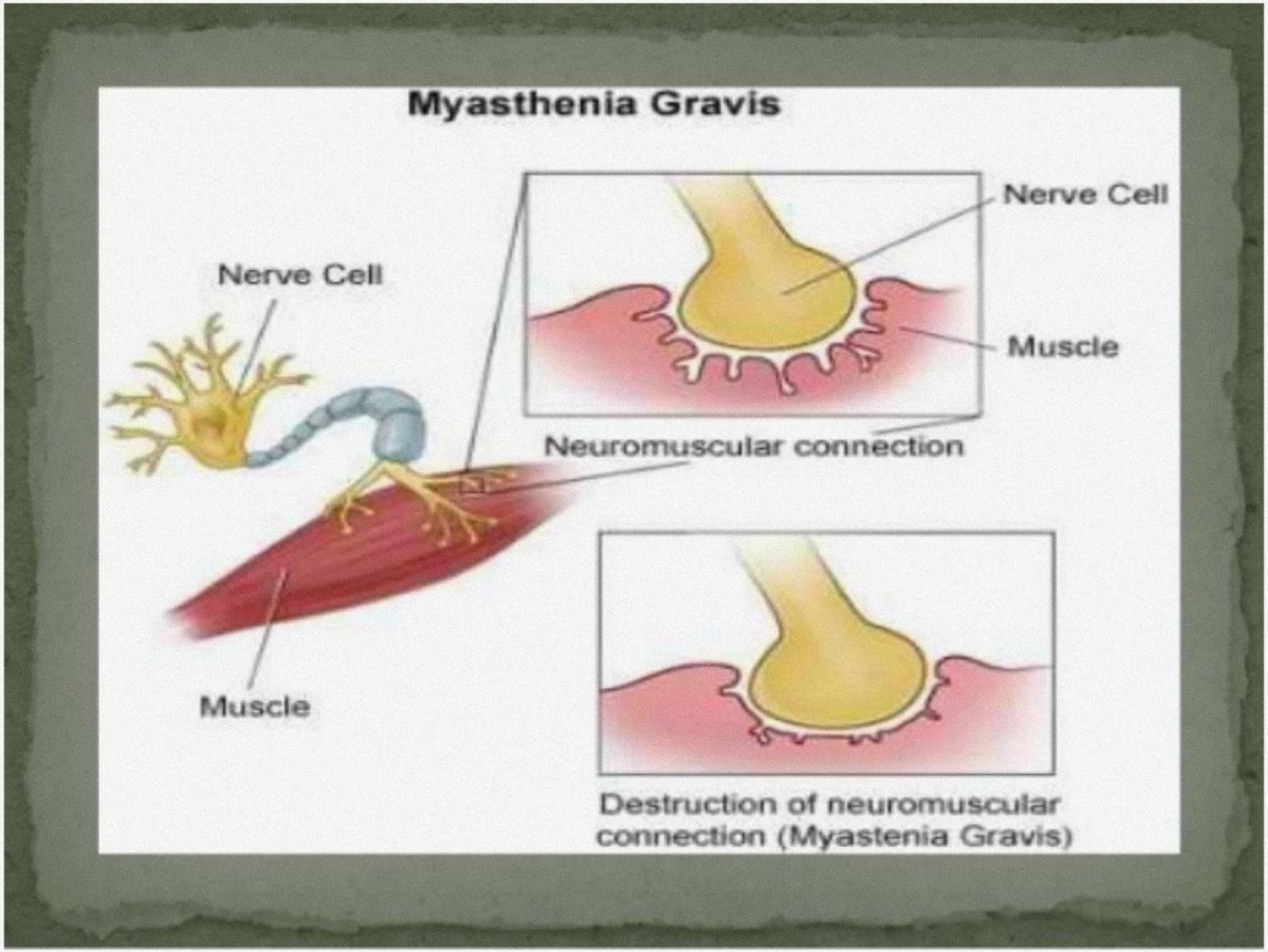


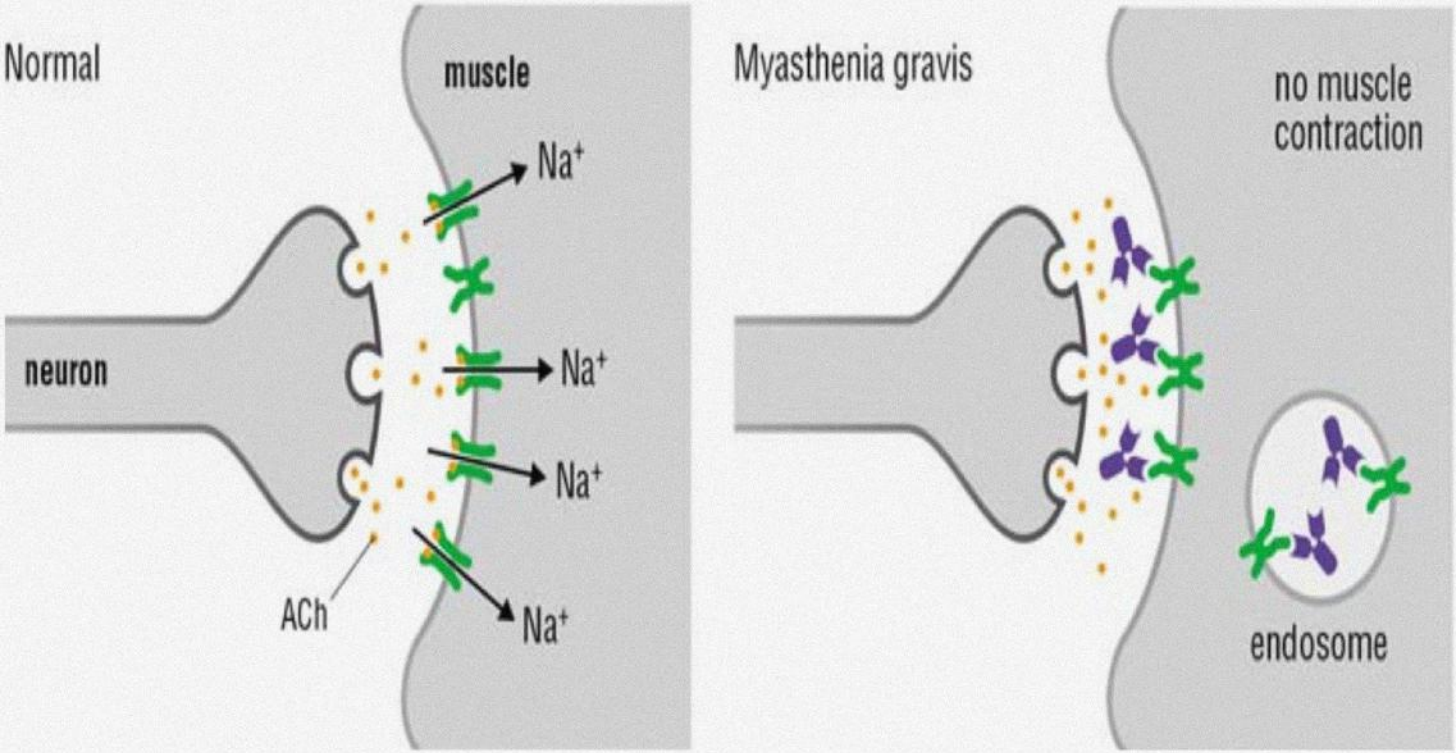
Myasthenia gravis. (A) Normal ACh receptor site. (B) ACh receptor site in myasthenia gravis.

MYASTHENIA GRAVIS



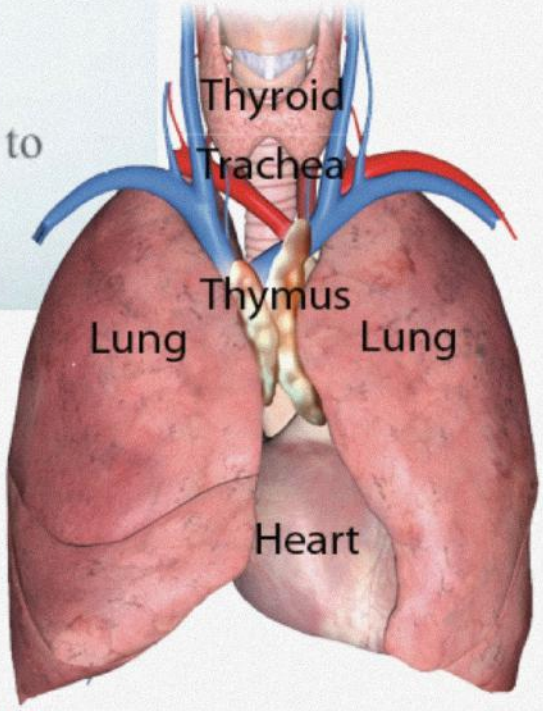


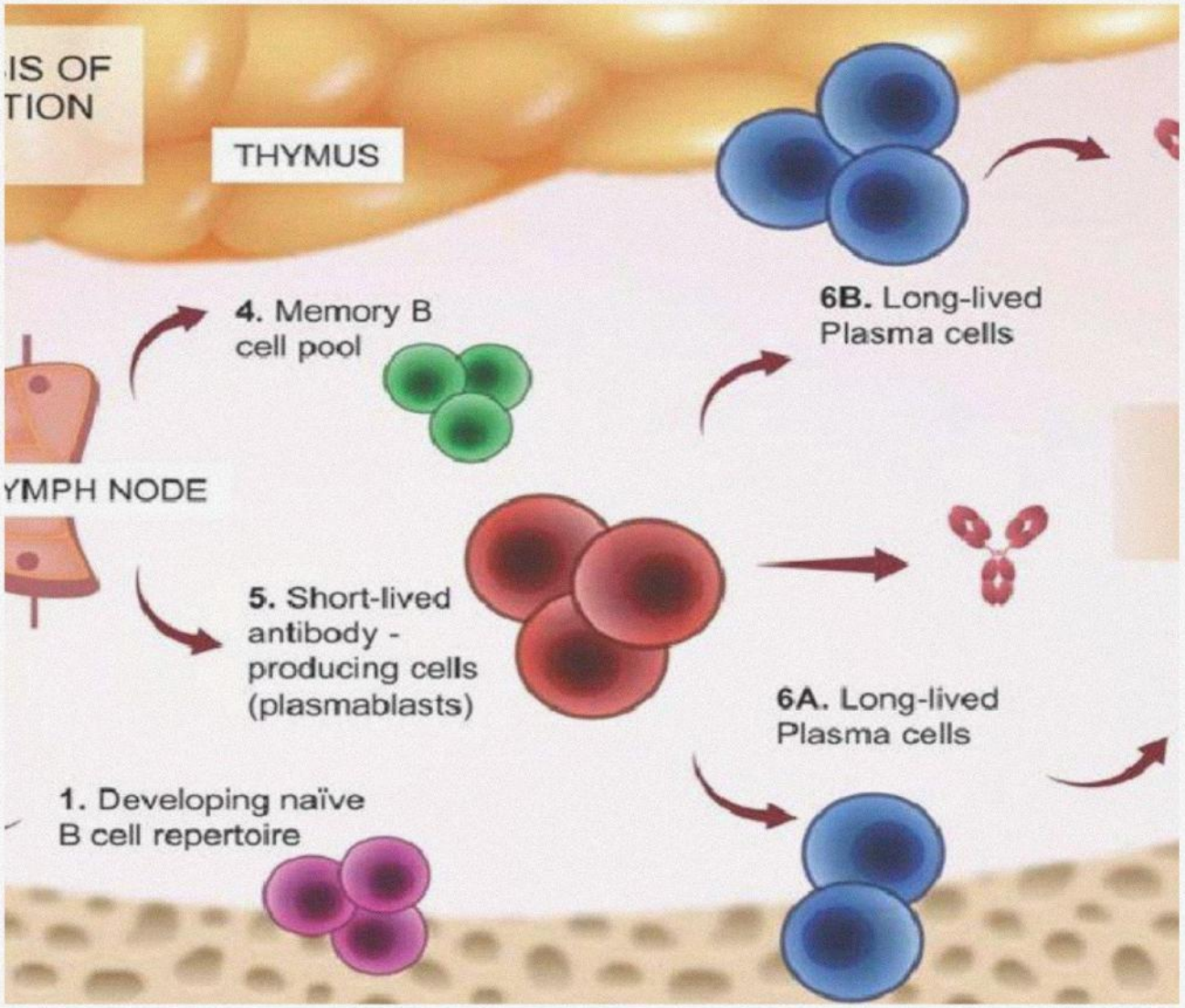

Myasthenia Gravis
Nerve Cell
Nerve Cell
Muscle
Neuromuscular connection
Muscle
Destruction of neuromuscular connection (Myastenia Gravis)



ROLE OF THYMUS GLAND

- The factors that trigger the autoimmune process are not known, but the thymus gland is involved.
- The thymus lies behind the sternum and may extend down to the diaphragm or up to the neck.
- This gland plays a role in the responsiveness of T cells to foreign antigens.




IS OF
TION
THYMUS
4. Memory B
cell pool
6B. Long-lived
Plasma cells
YMPH NODE
5. Short-lived
antibody -
producing cells
(plasmablasts)
6A. Long-lived
Plasma cells
1. Developing naïve
B cell repertoire

Pathophysiology:-

- Due to etiological factors

↓

- Lymphocyte produce acetylcholine receptor antibodies that attack the post synaptic muscle membrane

↓

- Depletion of acetylcholine receptor of the neuromuscular junction

↓

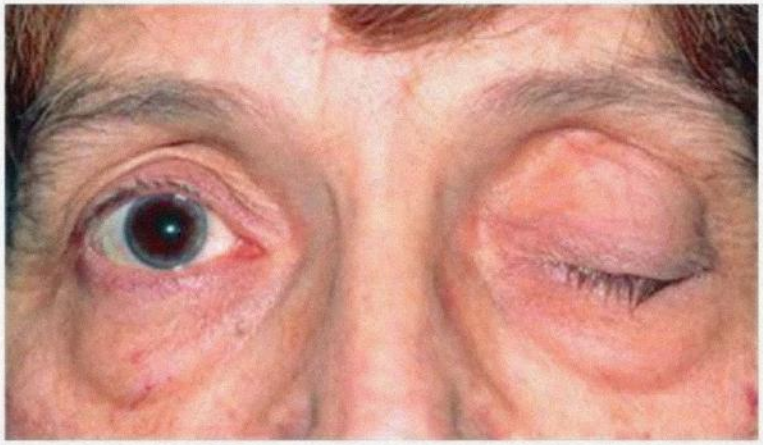
Defect in the transmission of impulse from nerve to muscle cell

↓

- Myasthenia gravis

Clinical Manifestations

- Muscle weakness
- Double vision (diplopia)
- weak eyelids (unilateral ptosis)
- Difficulty speaking or smiling
- Difficulty chewing and swallowing



TYPES OF MG

- **OCULAR/BULBAR/GENERALIZED**

OCULAR

- Diplopia
- Ptosis
- Ophthalmoplegia

RESPIRATORY

- Breathlessness
- Weak breathing
- Respiratory failure

BULBAR

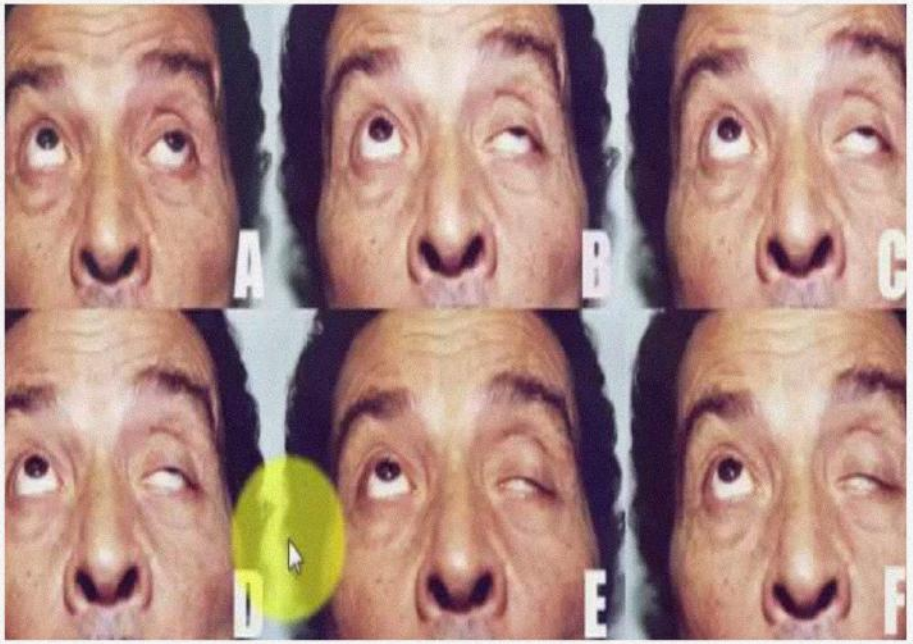
- Fatiguable chewing
- Dysarthria
- Dysphagia

LIMBS, NECK

- Dropped head
- Proximal > distal
- Arms > legs

OCULAR MYASTHENIA

- **Ocular myasthenia gravis (OMG) can mimic isolated cranial nerve palsies, gaze palsies, internuclear ophthalmoplegia, blepharospasm, and even a stroke**



Strabismus types	Number of patients (%)
Vertical deviation	6 (28.6)
Exotropia and vertical deviation	5 (23.8)
Esotropia	4 (19.0)
Esotropia and vertical deviation	3 (14.3)
Exotropia	3 (14.3)
Total	21 (100.0)

Classification

- Class I: Eye muscle weakness only
- Class II: Eye muscle weakness
  + mild weakness of other muscles
- Class III: Eye muscle weakness
  + moderate weakness of other muscles
- Class IV: Eye muscle weakness
  + severe weakness of other muscles

  OR need for nasogastric feeding
- Class V: Intubation needed to maintain airway

Diagnosis: CLINCAL, SEROLOGIC AND EMG FINDINGS

1.Clinical DX:

-Bedside: ice pack test/ Edrophonium test

- Cogan sign
- Peek sign

Imaging:

CT CHEST: Evaluate for thymoma

2.Electrophysiologic confirmation:

-Repetitive nerve stimulation

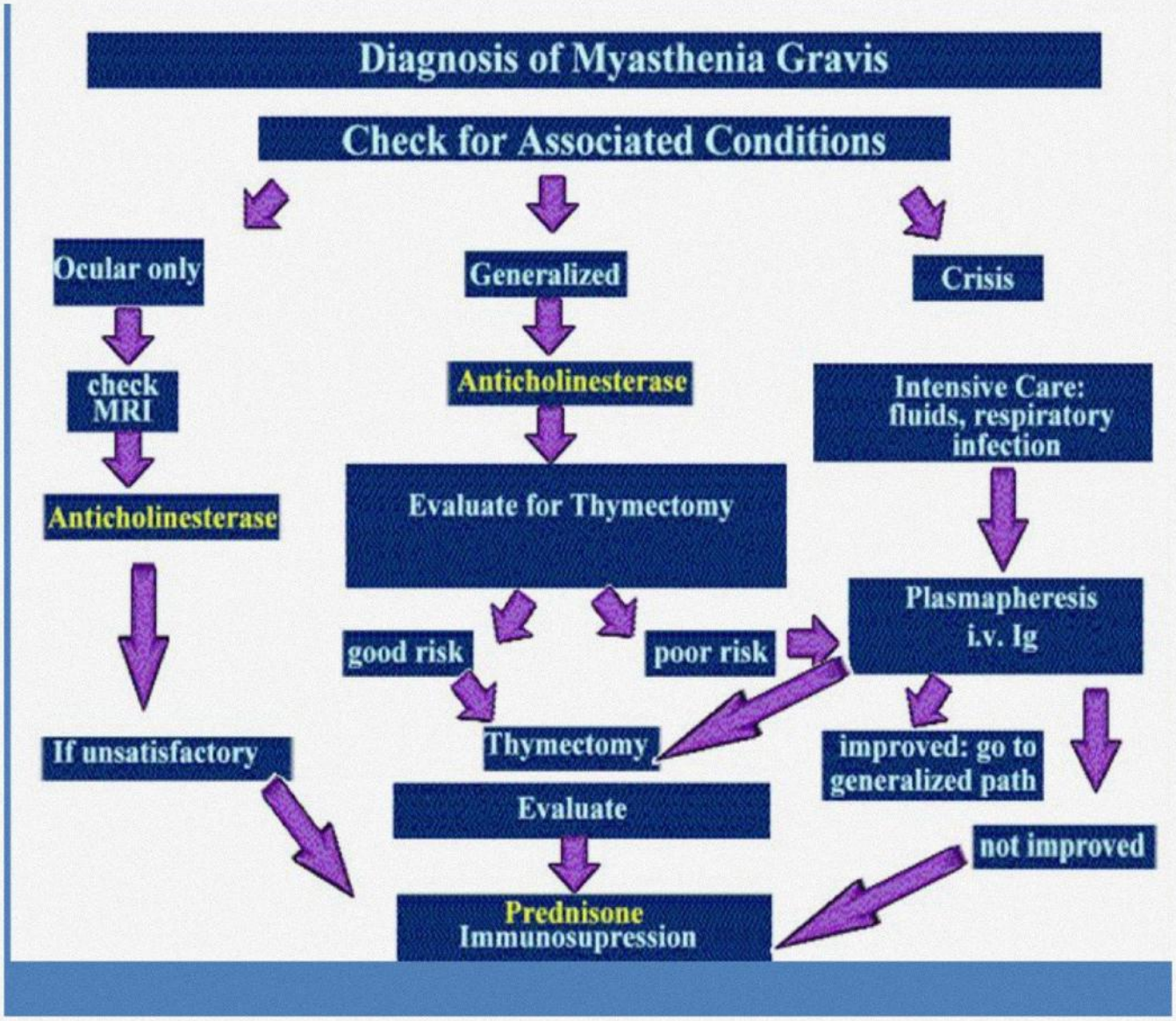
-Single fiber electromyography

3.Labs:

AchR antibodies- first step in immunologic assay

MuSK antibodies

LRP4 antibodies

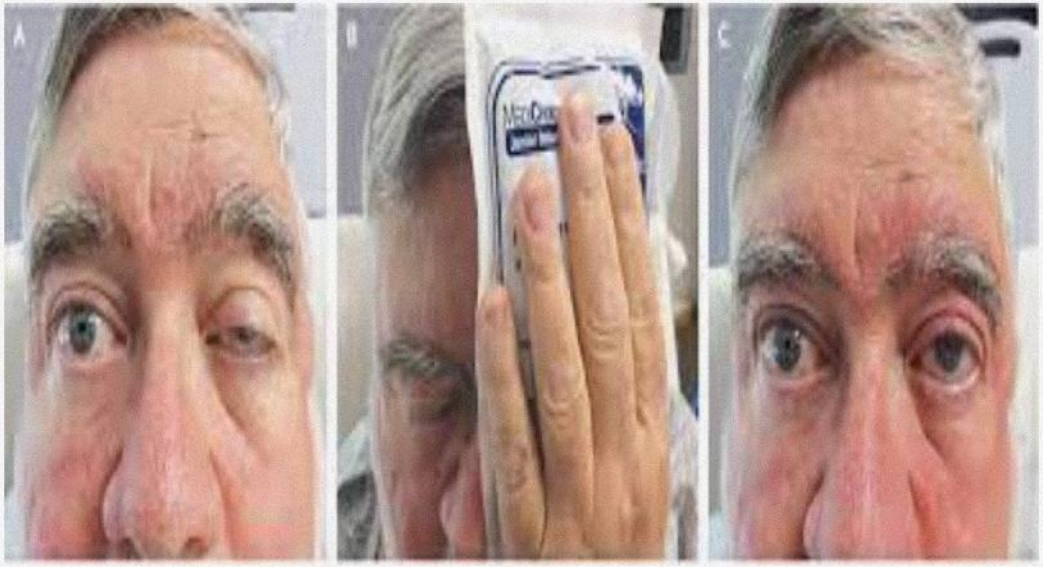


Test	Positive Result
Fatigue test	Worsening of symptoms after prolonged use
Ice test or sleep test	Improvement of ptosis after ice pack application or period of rest
Edrophonium (Tensilon or Enlon)	Improvement in symptoms within 30-60 seconds
Serologic screening	Identification of circulating AchR, MuSK or LRP4 antibodies
Electrophysiologic testing (RNS, SFEMG)	Decrease in action potential of stimulated nerves
Thyroid panel, thoracic imaging	Used to identify coexisting conditions

RNS = repetitive nerve stimulation; SFEMG = single-fiber electromyography

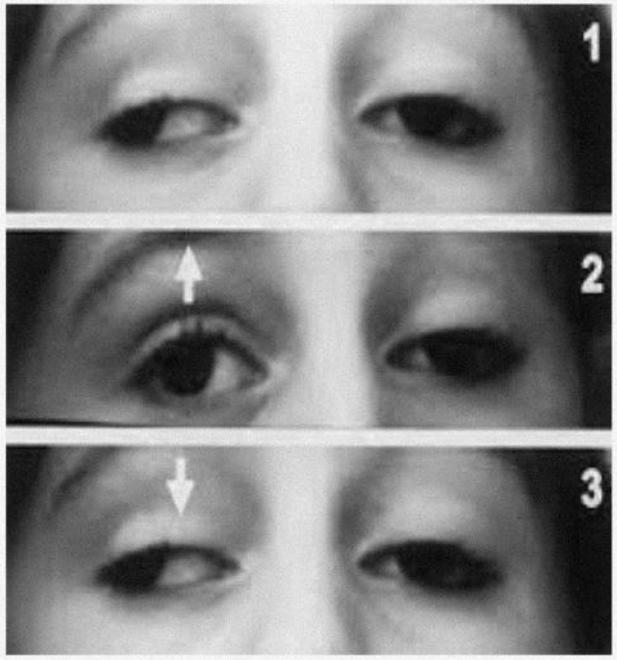
ICE PACK TEST

- Apply ice pack for 3 to 5 minutes
- Bed side test
- **Cold improves neuromuscular transmission**
- **Sensitivity of 85%**

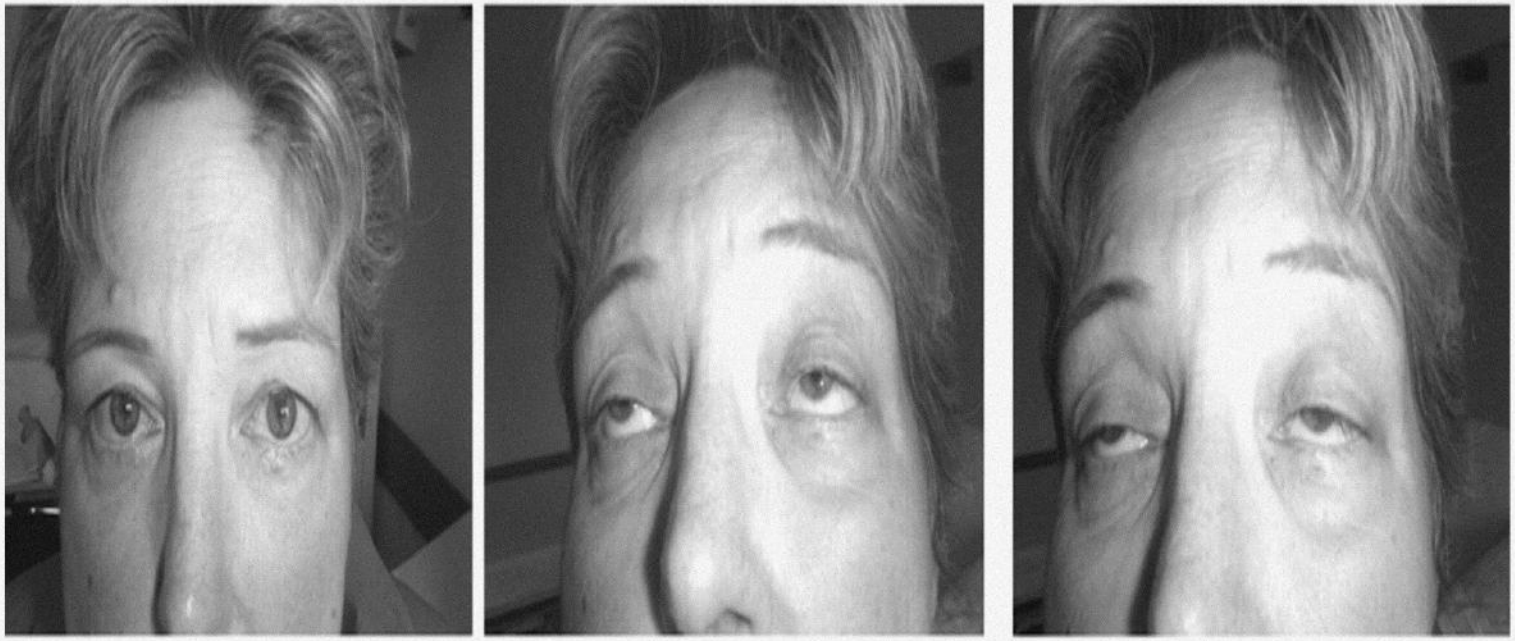


Cogan's sign

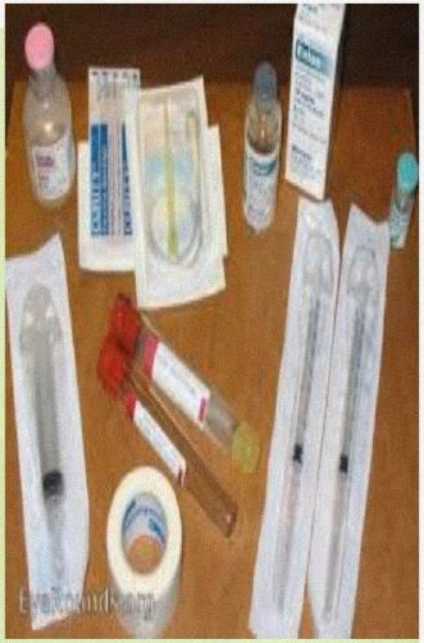
- Ask the patient to gaze downward for 10–15 seconds and then returning to primary gaze
- Cogan's sign is present **when the affected lid briefly "twitches" upward on returning to primary gaze**



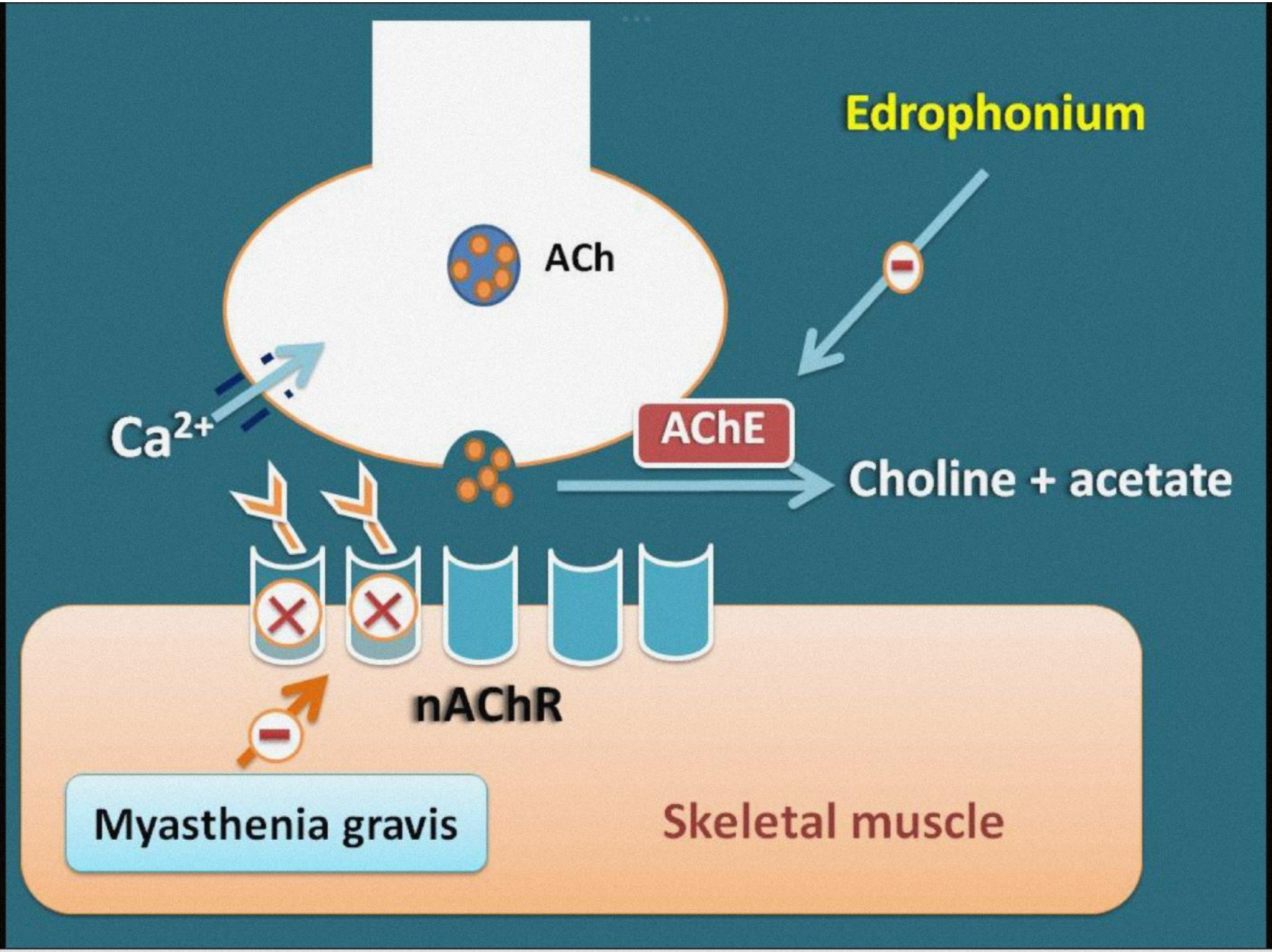
FATIGUIBILITY TEST



Tensilon Test



- Edrophonium chloride
  - Inhibits acetylcholinesterase
- Onset 30 seconds; duration 5-10 min
- NEED A CLEAR OBJECTIVE ENDPOINT
  - Works best with complete ptosis
- Compare to placebo (saline)
- Prepare atropine
- Give test dose 1-2 mg then up to 10 mg total
- SFX:
  - salivation, sweating, nausea, abdo cramping, fasciculations; hypotension & bradycardia are rare (may be as low as 0.16%)
- Sensitivity 71.5- 95%
- Specificity: not clear but can be positive in many other conditions (even ALS or normal controls)
- Not availible



How it is given?

Initial safety check

Edrophonium

2 mg by IV

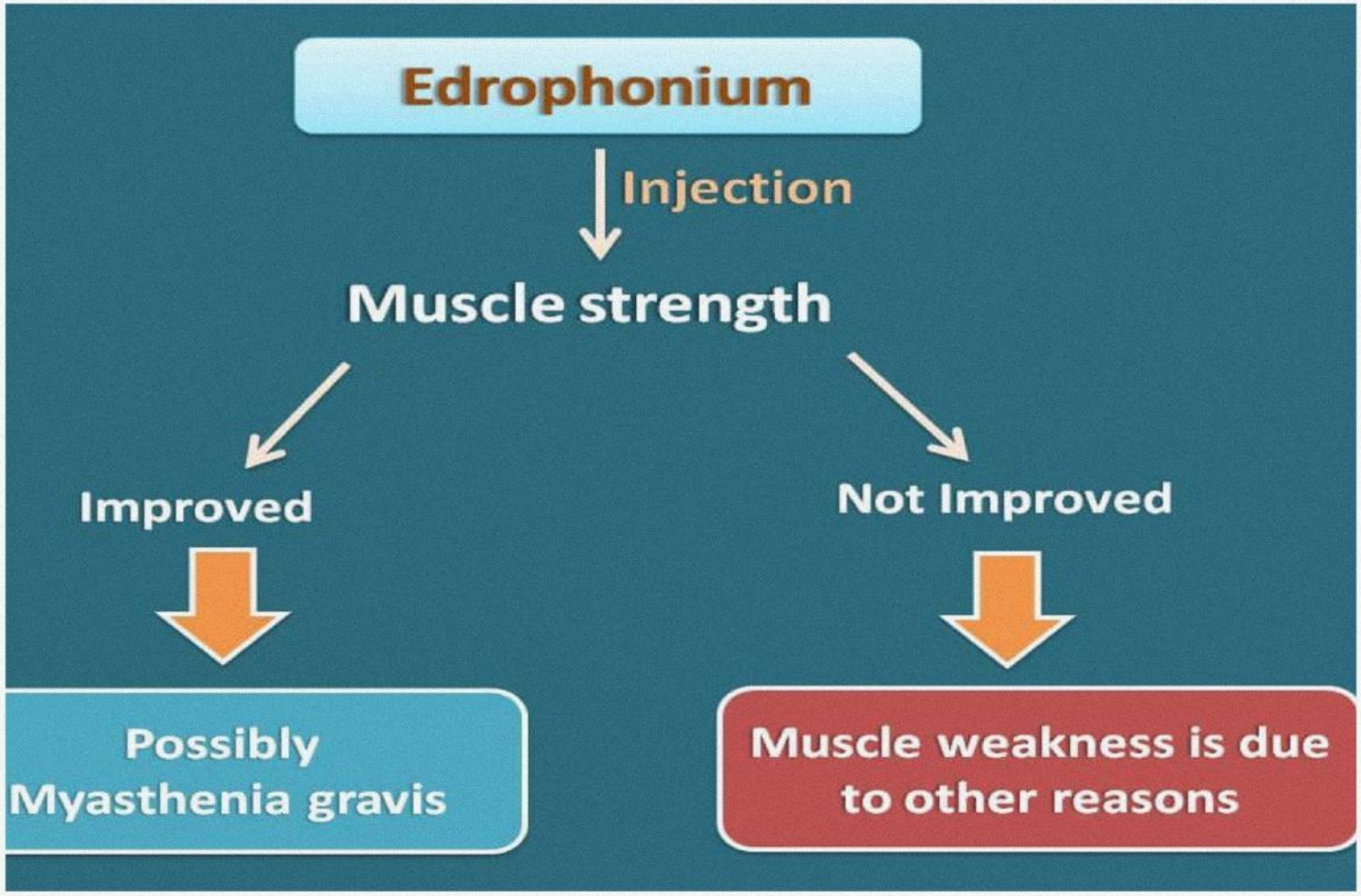
Check for any side effects

Diagnosis step

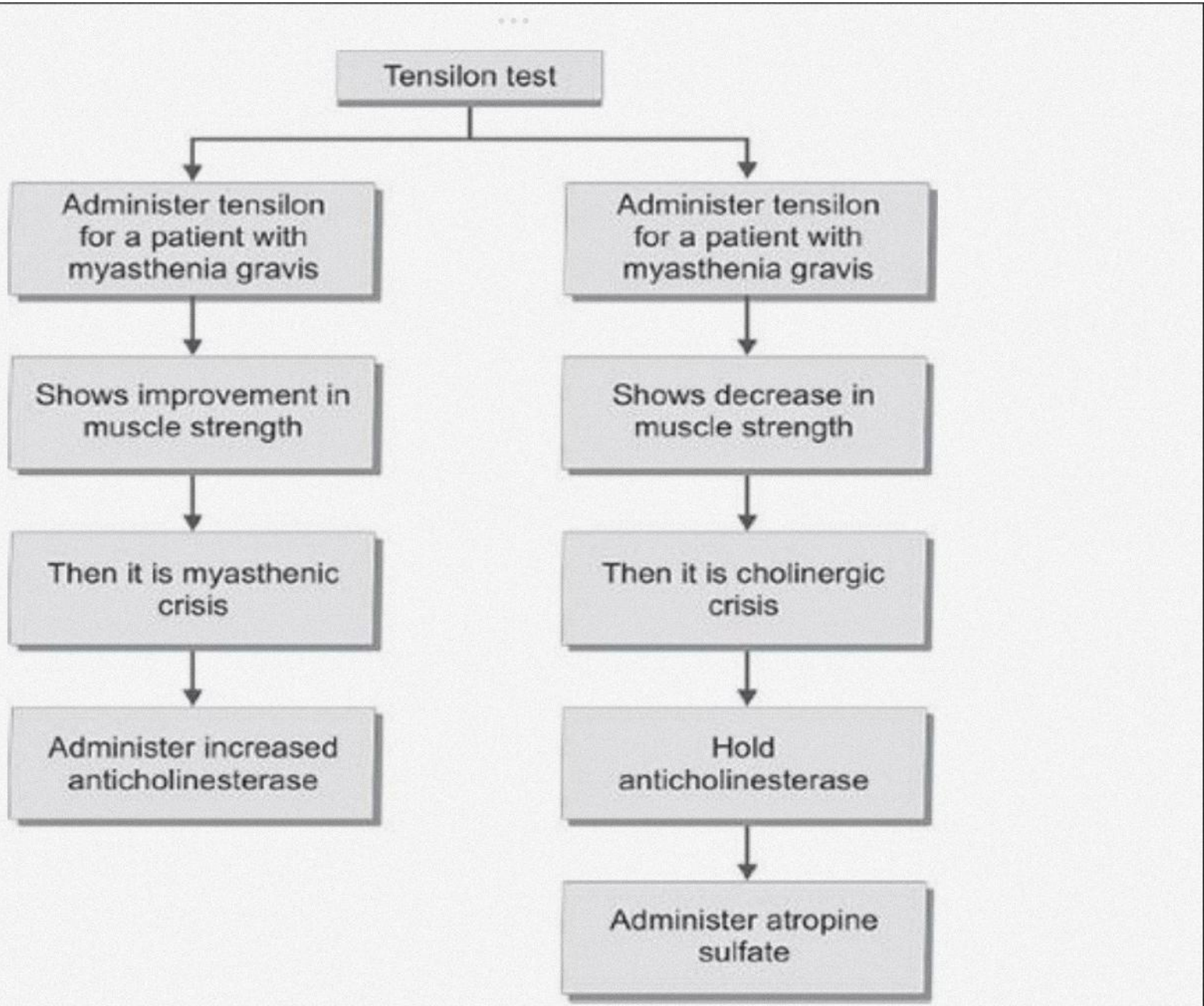
Edrophonium

8 mg by IV

Check for improvement in muscle strength



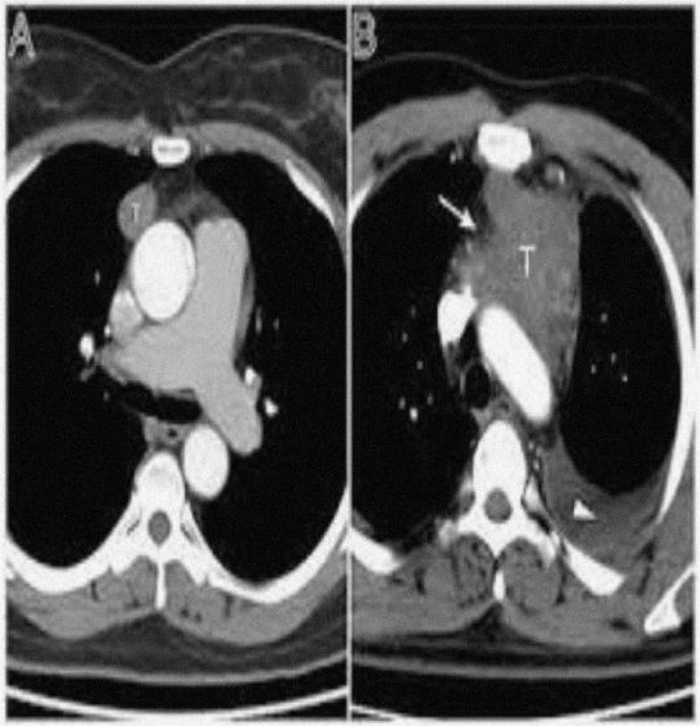
Tensilon test

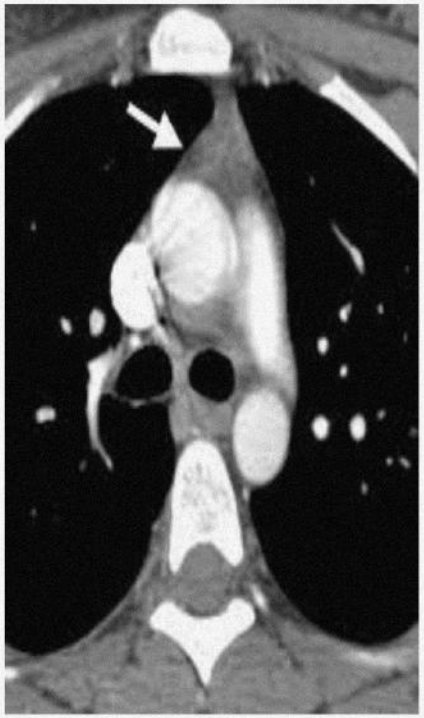


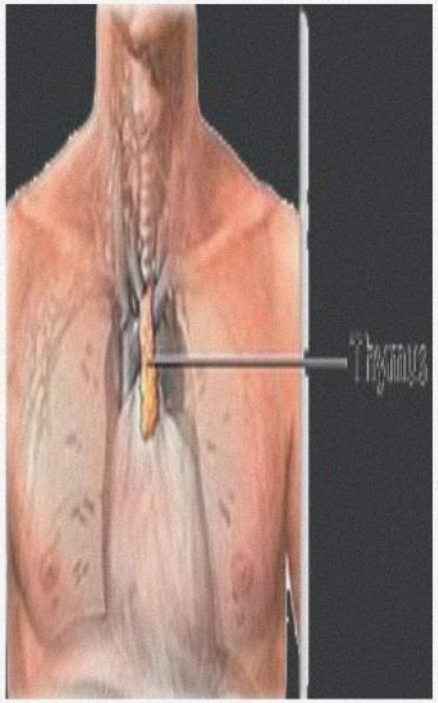
Myasthenic Crisis vs. Cholinergic Crisis

- Mysathenic Crisis
  - Serious complication where patients are unable to breathe adequately and possibly develop respiratory failure
  - Impaired swallowing and managing of secretions leading to aspiration
  - Monitory NIF, vital capacity, tidal volume
- Cholinergic Crisis
  - Due to and excess of acetylcholine at the NMJ as seen in organophosphate poisoning
  - Fasiculations, sweating, myosis, abdominal pain, bradycardia
  - Flaccid paralysis and respiratory failure
- Differentiate with edrophonium test

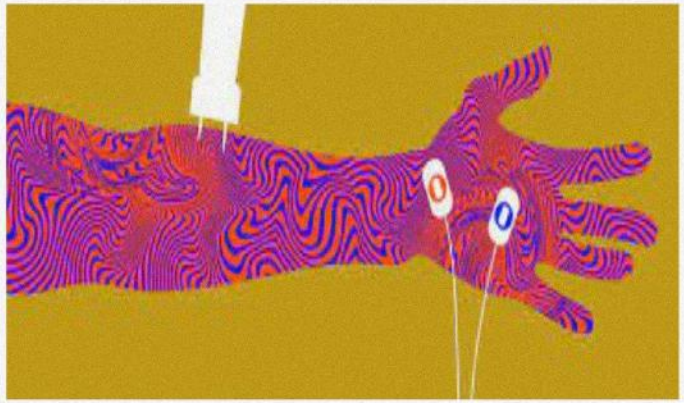
THYMOMA RADIOLOGY

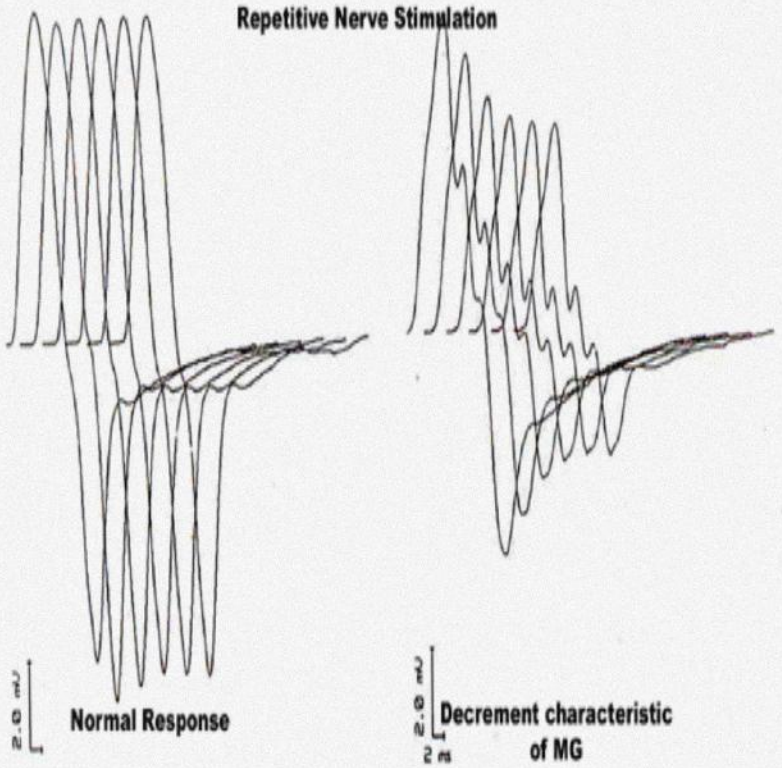




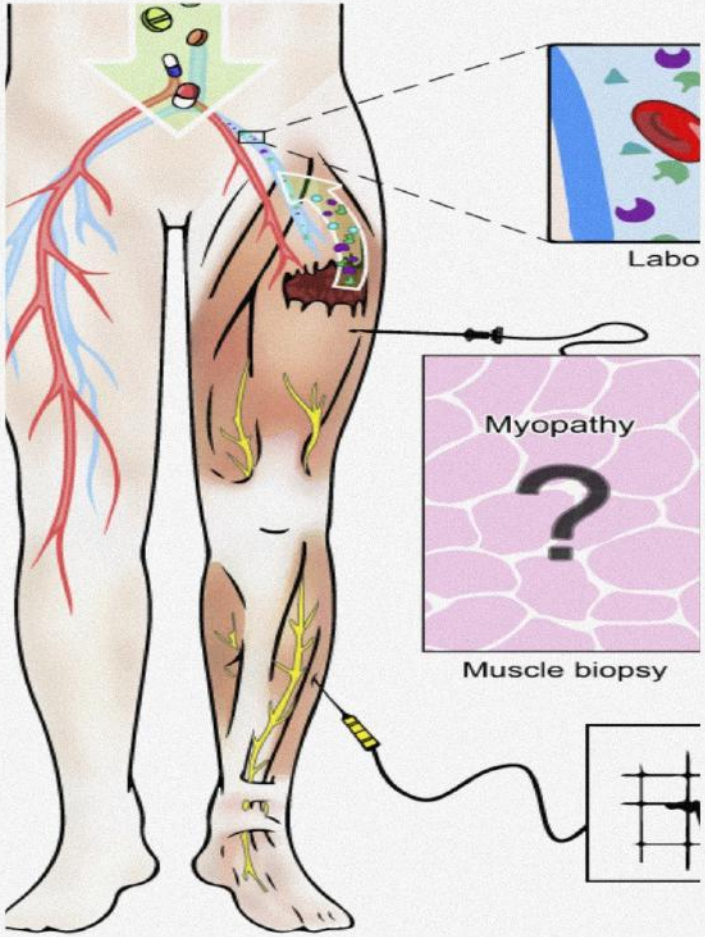


ELEECTROMYOGRAPHY
EMG Studies





MUSCLE BIOPSY



DIFFERENTIAL DIAGNOSIS

Thyroid opthalmopathy
Kearns-Sayre syndrome
Myotonic dystrophy
Brain stem/ Cranial nerve pathology
Generalized fatigue
ALS
Lambert Eaton myasthenia syndrome
Miller Fischer and PCB variants of GBS
Botulism
Penicillamine induced myastheniay

Lambert Eaton myasthenic syndrome:

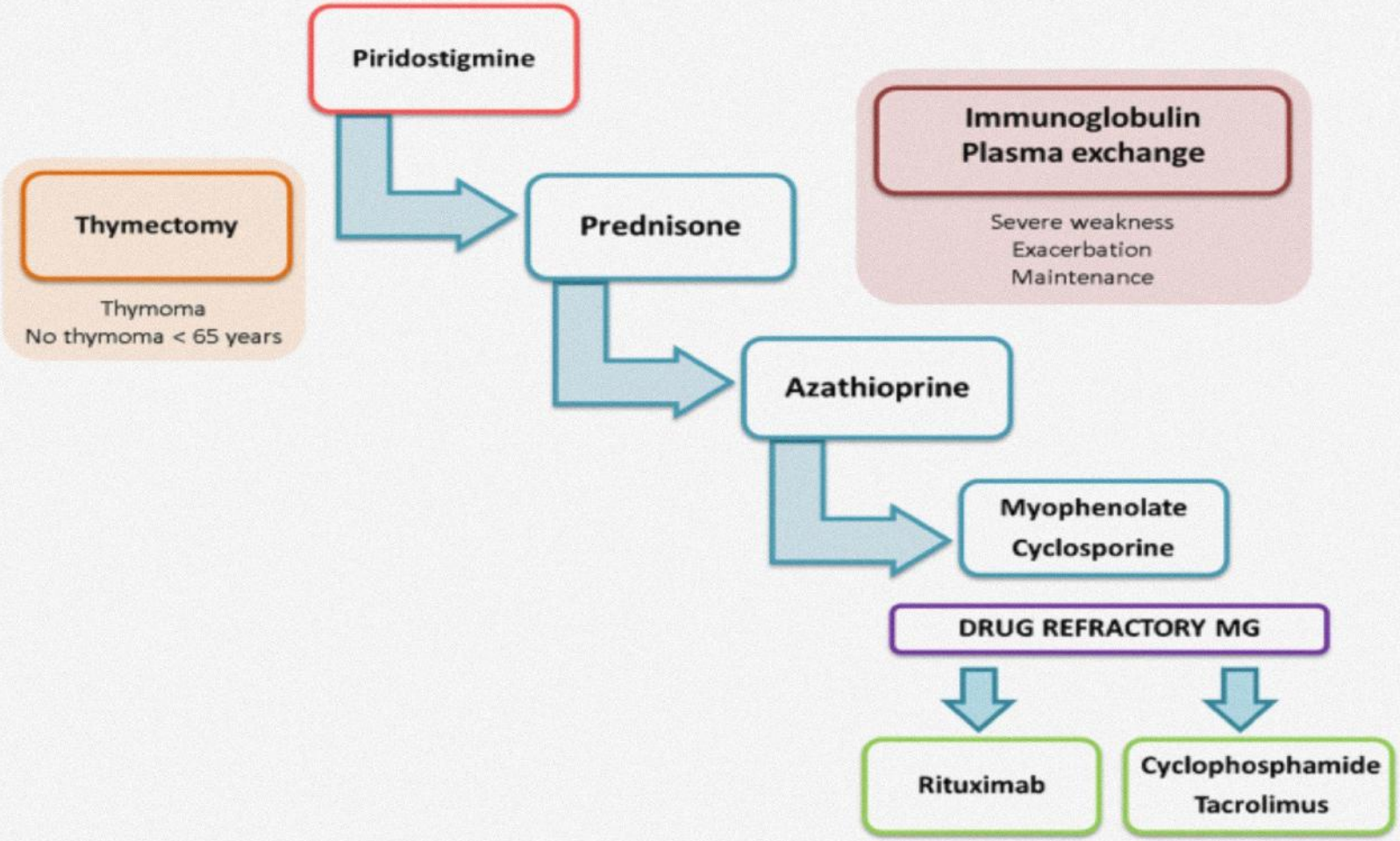
- Rare autoimmune disorder
- The immune system attacks channels that regulate calcium levels in the blood
- This causes insufficient acetylcholine to be released, leading to muscle weakness, fatigue, and other symptoms

Myasthenia gravis	Lambert Eaton syndrome
Antibody against AchR antibody	Antibody against voltage gated calcium channel
Associated with Thymic tumor	Associated with Small cell lung cancer
Weakness worsen on prolonged exercise	Weakness improves on prolonged exercise
Normal Deep tendon reflex	Decreased or absent deep tendon reflex
Autonomic dysfunction is absent	Autonomic dysfunction is present
On repeated nerve stimulation, there is decremental response	On repeated nerve stimulation, there is incremental response

Management plan

- Drug therapy
- Immunomodulation
- Surgical therapy
- Supportive therapy
- Life style modification

MANAGEMENT


Piridostigmine
Thymectomy
Thymoma
No thymoma < 65 years
Prednisone
Immunoglobulin
Plasma exchange
Severe weakness
Exacerbation
Maintenance
Azathioprine
Myophenolate
Cyclosporine
DRUG REFRACTORY MG
Rituximab
Cyclophosphamide
Tacrolimus

DRUGS USED IN MYASTHENIA GRAVIS

1) AChE inhibitors:

- Anticholinesterase inhibit Acetylcholinesterase (AchE), allowing the same Ach molecules to repeatedly interact with the available nicotinic receptors (NRs); frequency of Ach-NR interaction is increased.
- **Drugs:**
  1) Pyridostigmine bromide
  2) Prostigmine

2) Immunosuppressant medicines:

- They inhibit the immunity system, and limiting antibody production.
- **Drug:** Azothiaprine in addition to steroid medication (Prednisolone)

- **Pyridostigmine**
  Anticholinesterase with symptomatic relief

- **Rituximab (Rituxan) and eculizumab (Soliris)** are intravenous medications usually used for those who don't respond to other treatment

- **zilucoplan**, a peptide inhibitor of complement component 5 (C5 inhibitor), for the treatment of generalized myasthenia gravis in adult patients who are acetylcholine receptor antibody positive

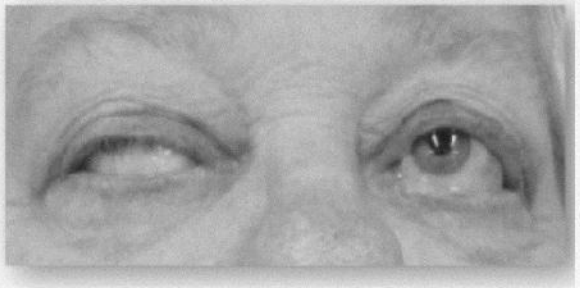
Effects of cholinergic drugs

- CNS – enhance cognitive functions such as arousal, attention, & memory encoding – treatment for Alzheimer's disease & dementia
- Eye – pupil constriction – for surgery & treatment of glaucoma
- GI – smooth muscle stimulant – for post-op abdominal distention or paralytic ileus
- GU – urinary bladder stimulant – for post-op or postpartum urinary retention
- Musculoskeletal (indirect acting cholinergic drugs) – improve muscle tone & strength – for myasthenia gravis

Drugs that can Exacerbate Myasthenia Gravis

Mnemonic - *EXACERBATE*

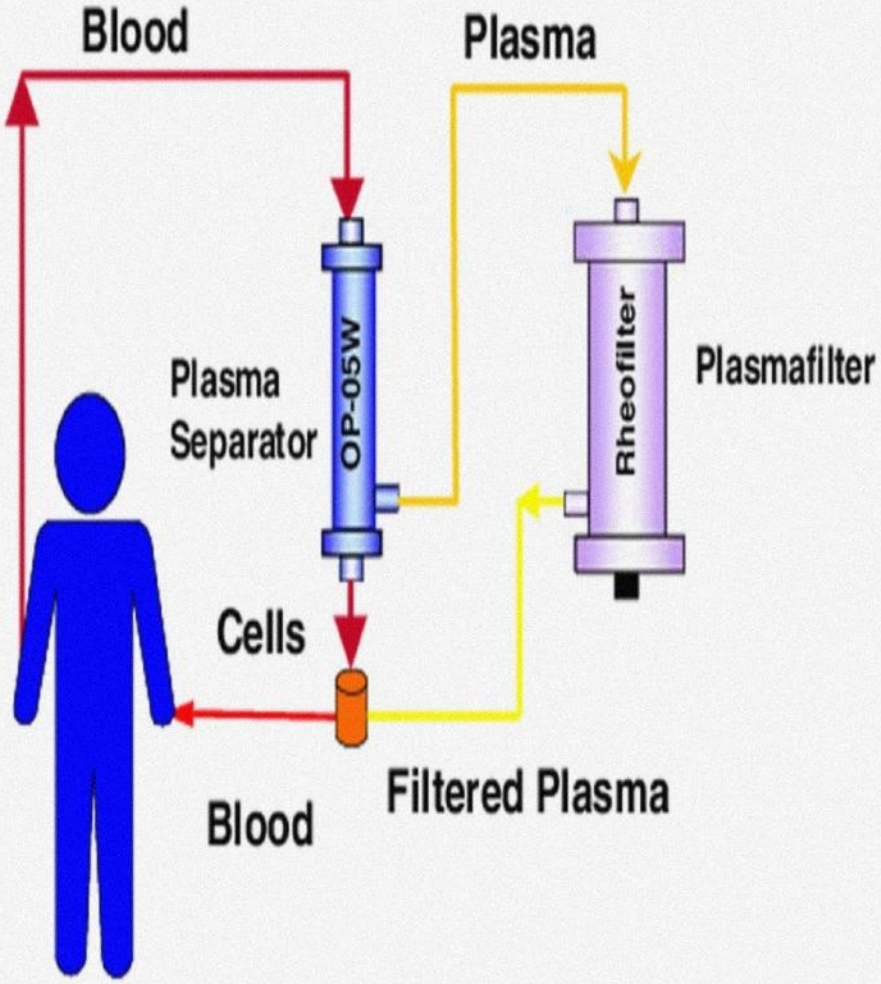
- **E**rythromycin (Macrolides)
- **X**ylocaine (Lignocaine)
- **A**minoglycosides
- **C**iproflox (Quinolones)
- **E**lectrolyte (Mg)
- **R**elaxant (Skeletal Muscle Relaxants)
- **B**otox & Beta Blocker
- **A**nti malarial (Quinine)
- **T**imolol (Eye Drops)
- **E**chothiophate (Eye Drops)

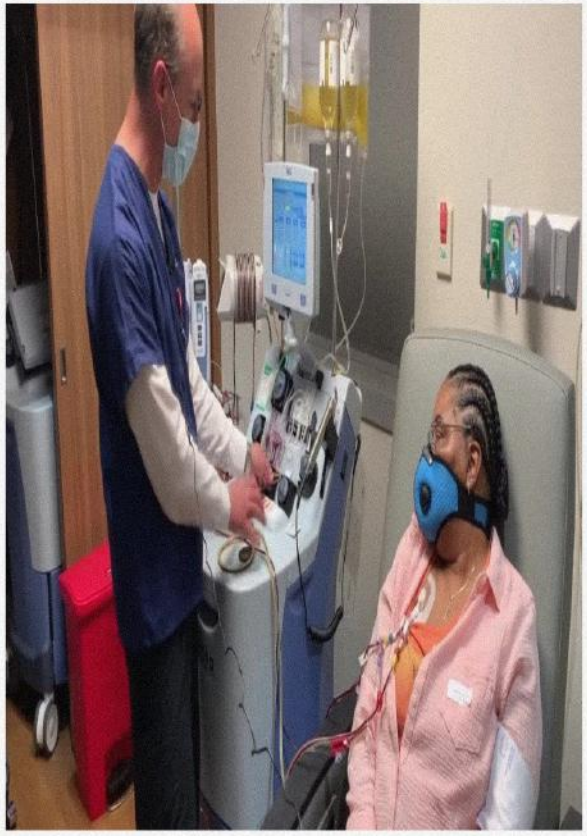


PLASMAPHERESIS

- *A method of removing blood plasma from the body by withdrawing blood, separating it into plasma and cells, and transfusing the cells back into the bloodstream*

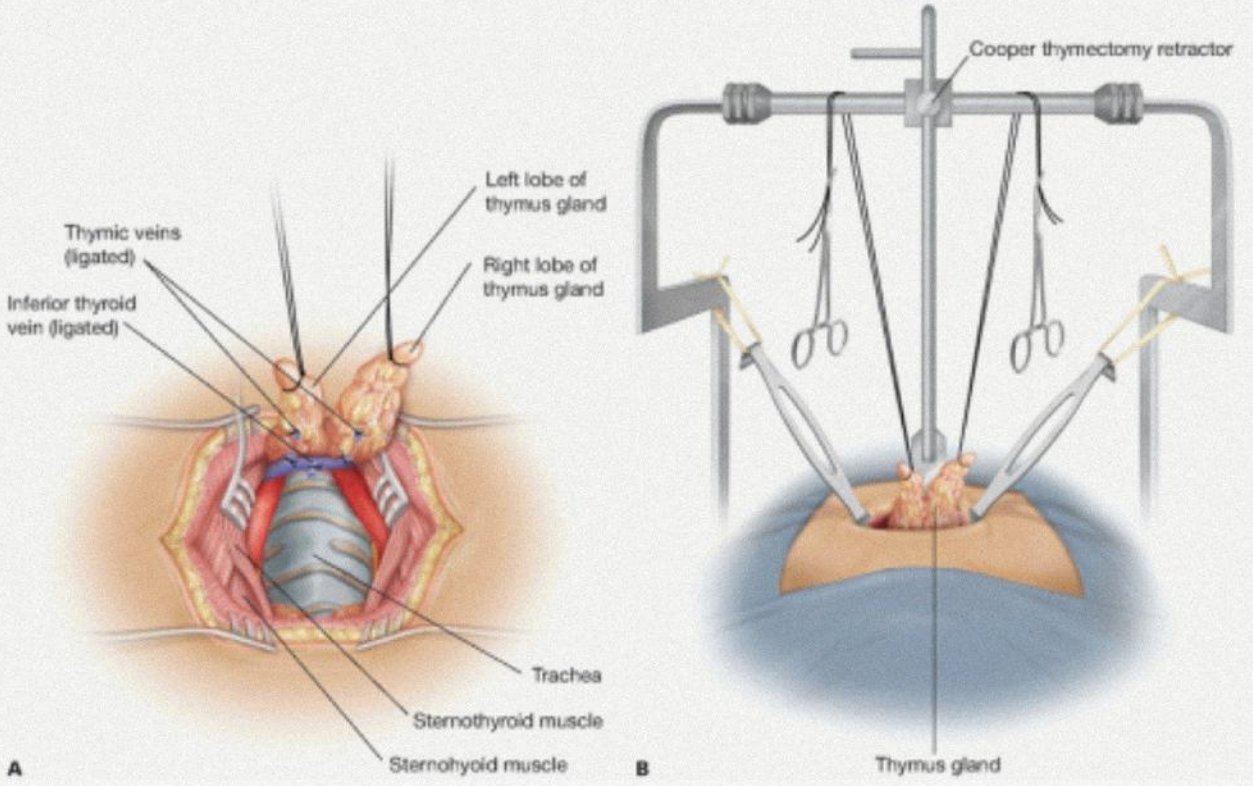
- *It is performed especially to remove antibodies in treating autoimmune condition*


Blood
Plasma
Plasma
Separator
OP-05W
Rheofilter
Plasmafilter
Cells
Filtered Plasma
Blood

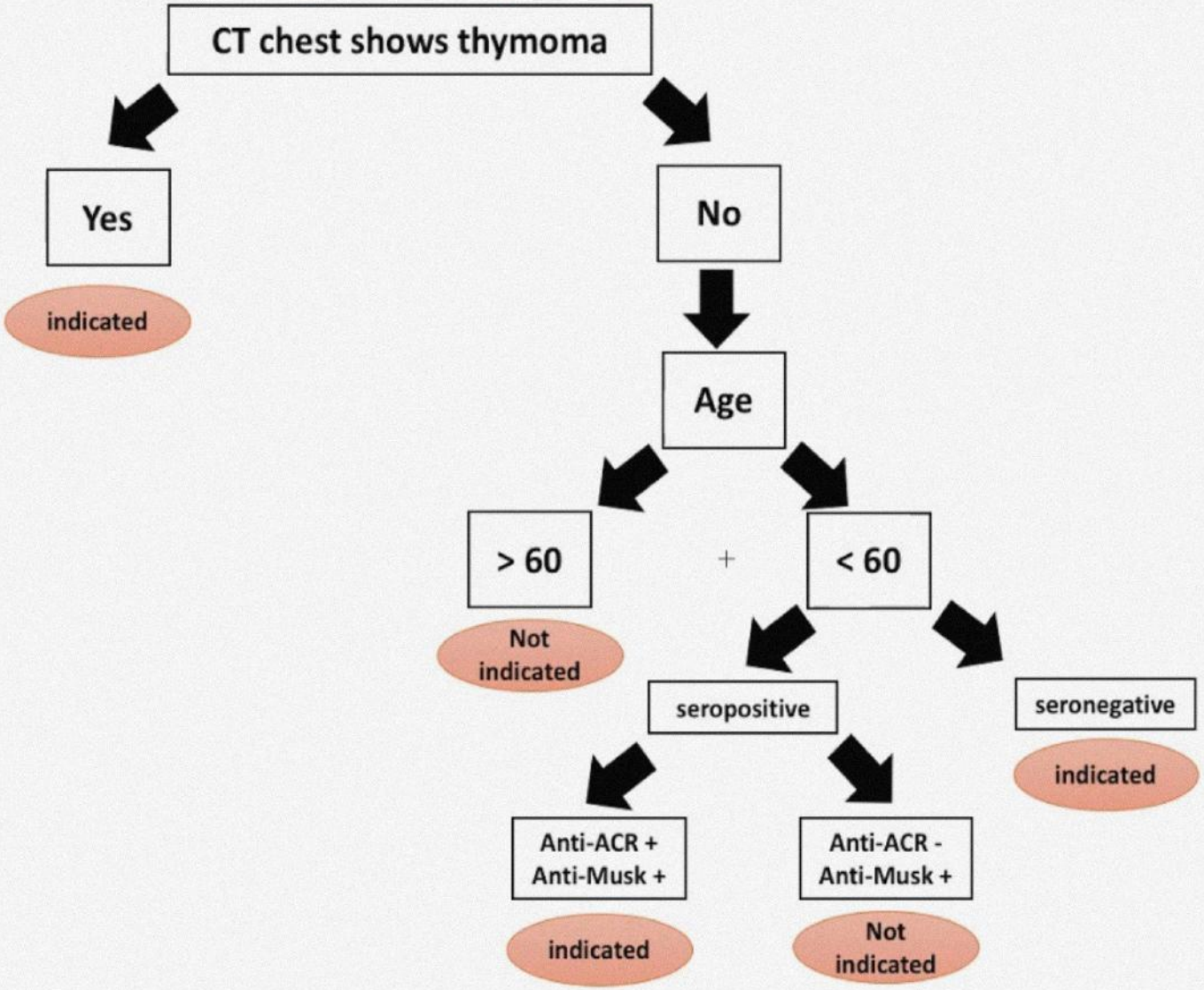


Thymectomy

- The goal is to cause remission of the disease
- To allow dose reduction of harmful immunosuppressive medications



Indications of thymectomy in Myasthenia Gravis



Life style modification

- Avoid physical exertion
- Take Plenty of Rest
- Avoid emotional stress
- Avoid exposure to extreme temperatures
- Continuous positive airway pressure therapy
- If diplopia bothers then occlusion
- Avoid medications such as muscle relaxants
- Avoid pneumonia/respiratory illness
- Avoid Low levels of potassium (diuretics and vomiting)

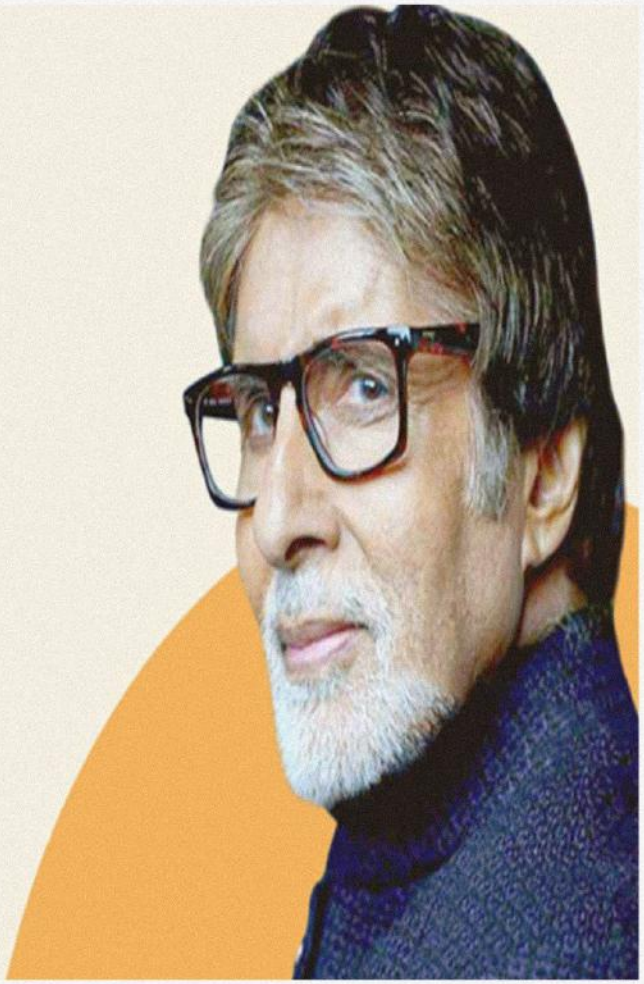
Do you know?

AMITABH BACHCHAN

is suffering from

MYASTHENIA GRAVIS

for the past 30 years!



June is....

Myasthenia Gravis Awareness Month

Many MG patients experience drastic changes in their physical appearance. For some, they may only experience changes in relation to symptoms of the MG (ex. dropping eyelids); however, others may experience changes as a side effect of medications and treatments for controlling the MG (ex. Prednisone leading to weight gain or 'moon face')