



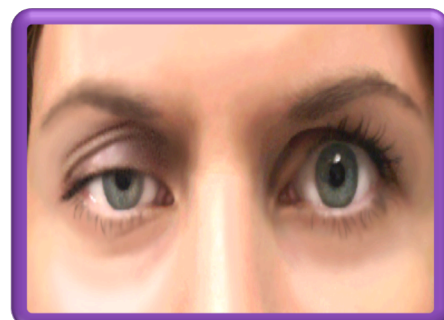
Second case

I need to rest every few minutes

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Key points from the Scenario:

- 30 years old; librarian-assistant.
- She works in hospital library and she's responsible for placing books back to the bookshelves.
- She feels tired, particularly after midday.
- Recently, she noticed that she is unable to continue putting books, and she has to take rest every few minutes.
- She noticed **drooping** of her eyelid usually near the end of the end of her work shift.
- She said "my arms seem to become weak after placing few books".
- Also, she said "in the morning I am much better, but I feel they are weak when I need to raise my arms".
- She has difficult to climb the stairs.
- These changes made her feel down and **Frustrated**.
- She does not have shortness of breath or pain; also she does not have problems with swallowing and does not have **tingling** or **numbness**.

Eye examination:

- She has ptosis of her right eyelid.

Neurological examination :

- No **muscle wasting** or **hypertrophy**.
- Muscle tone, reflexes and sensation are normal.
- Weakness mainly affecting her **proximal muscles**.

Investigations → results

- | | | |
|-------------------------------|---|---|
| - Blood test | → | Serum anti-Acetylcholine Receptor Antibodies is raised . |
| - <u>Electromyogram (EMG)</u> | → | Shows decremental response . (long thoracic nerve) |
| - <u>Tensilon test</u> | → | Substantial improvement in weakness. |

Diagnosis:

Myasthenia Gravis. (**neuromuscular junction**)

Management:

The doctor commences on **pyridostigmine** (60 mg tablets) every 4 hours.

To know other drugs can treat myasthenia gravis: see lecture (Indirect acting cholinergic)

MYASTHENIA GRAVIS :

is an autoimmune disease in which acetylcholine-receptor autoantibodies bind to cholinergic receptors on muscle cells, which impairs the ability of the neurotransmitter acetylcholine to induce muscular contraction.

Physiological changes could lead to muscle fatigue in prolonged exercises:

1. Accumulation of metabolites within muscle fiber.
2. Decrease Oxygen supply to muscles.
3. Decrease Energy to fuel contraction.
4. Decrease ATP, glycogen, and creatine phosphate.
5. Increase Intracellular ADP, reactive oxygen species, and magnesium.
6. Increase Intracellular sodium.
7. Change in intracellular pH (accumulation of lactic acid)

Anatomical structure and functions we need for normal skeletal muscle function:

- **Normal nerve fibers.**
- **Normal skeletal muscles**
(actin, myosin, troponin, tropomyosin molecules, normal Ca^{+2} concentration, normal ATP, glycogen, creatine phosphate)
- **Normal neuromuscular junction**
(normal vesicles, chemical transmitters, normal receptors, availability of normal receptors)
- **Normal muscle origin, insertion, bones, ligaments, joint, arterial, venous supply.**

Problems with these structures produce problems with muscle contraction:

- **Normal nerve fibers** → inflammation, injury.
- **Normal skeletal muscles** → injury, tear and inflammation :
 - Actin, myosin, troponin, tropomyosin molecules
→ decrease sensitivity to Ca^{+2} , malstructure /function.
 - Ca^{+2} (ion concentration)
→ interferes with the release of Ca^{+2} , lack of sensitivity to released calcium.
 - ATP, glycogen, creatine phosphophate
 - → exhausted, decreased.
- **Normal neuromuscular junction:**
 - Vesicles and chemical transmitters
→ damaged vesicles, lack of chemical transmitter, rapidly destroyed.
 - Receptor/availability of normal receptor
→ lost receptor/damaged, occupied by other substances or antibodies.
- **Muscle origin, insertion, bones, ligaments, joint, arterial/venous supply**
→ Pathological problem (fracture, anomaly, tear, injury, blocked arteries).

Questions:

What is Electromyogram (EMG)?

Is a technique for evaluating and recording the electrical activity produced by skeletal muscles. (To know where is the problem “ muscles or nerves).

How the Edrophonium (Tensilon) test will help the diagnosis?

a medicine called Tensilon (also called edrophonium) is given intravenously (2 mg) during this test, followed gradually by 8 mg (a total of 10 mg) then check whether the Tensilon improves the muscle strength if there is weakness of the eye or face muscles. The test may be repeated and may have other Tensilon tests to help tell the difference between myasthenia gravis and other conditions

what does Decremental response mean?

The activity is decreasing or becoming gradually less.

New terms you should know:

- **Drooping:** to hang downward, pulled down from its normal place.
- **Tingling:** to have a sensation of slight prickles, stings, as from cold, a sharp blow or excitement.
- **Proximal muscle:** Muscles closest to the center of the body (trunk) in anatomical position.
- **Numbness:** loss of physical sensation.
- **Frustrated:** disappointed.
- **Muscle wasting:** loss of muscle mass.
- **Muscle hypertrophy:** an increase in muscle size due to increased muscle cell (fibers), rather than by cell **multiplication**, it can be physiological (e.g. exercises) or pathological.
- **Muscle tone:** a continues, passive, and partial contraction of skeletal muscles. in other words it is the muscle's resistance to passive stretch during resting state. It helps maintaining body posture.
- **Ptoisis:** is a drooping or falling of the eyelid.
- **Serum anti-Acetylcholine Receptor (AChR) Antibodies:**
Antibodies bind to AChR and prevent acetylcholine from doing its function which is stimulating the muscle contraction.
- **Cholinesterase inhibitors: (AntiCholinesterase)**
is a chemical that inhibits the acetylcholinesterase enzyme from breaking down acetylcholine and increasing the level and duration of action of the neurotransmitter acetylcholine.