MYASTHENIA GRAVIS

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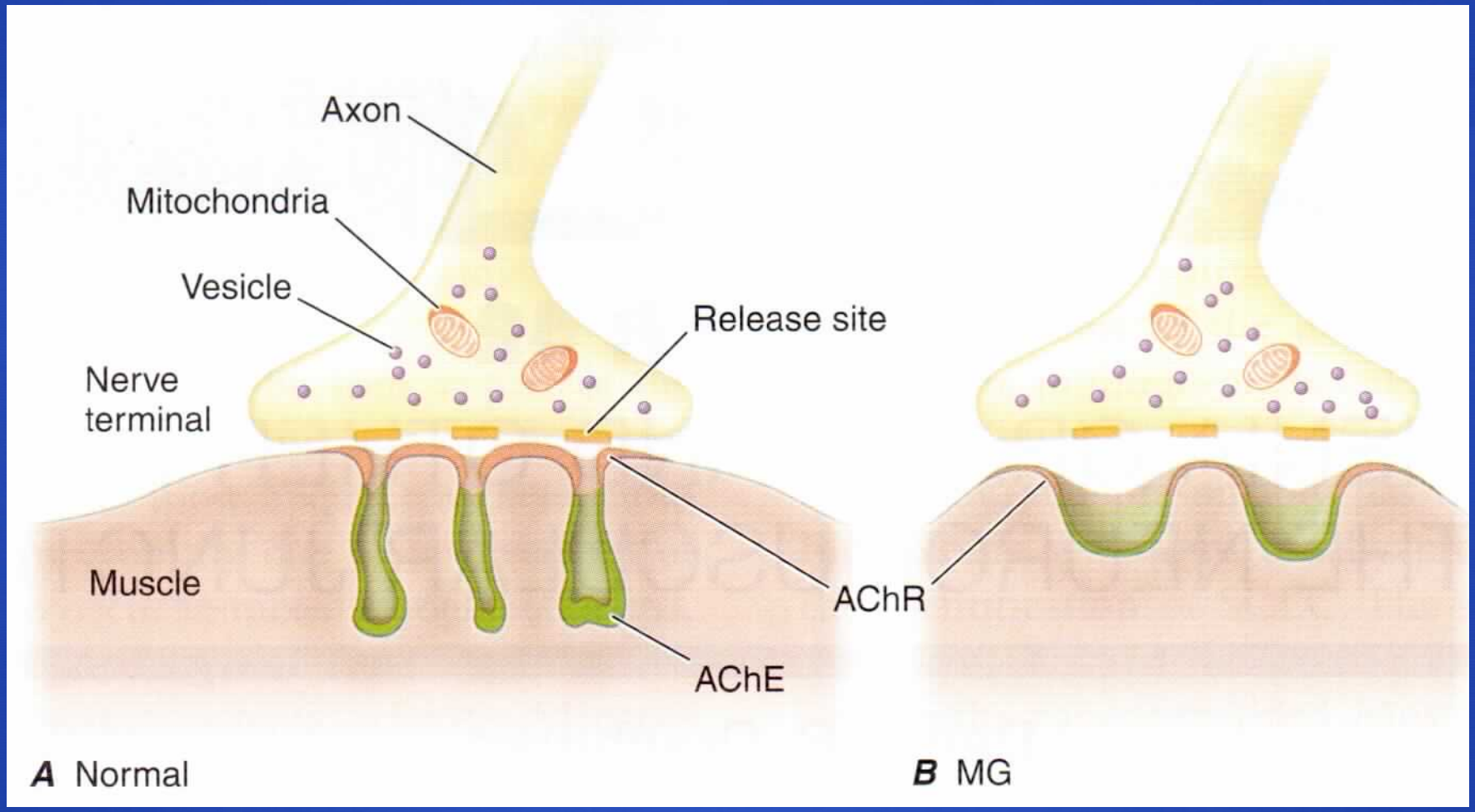
MYASTHENIA GRAVIS:

is an autoimmune disease in which the lymphocytes in the blood produce antibodies that destroy muscle-cell sites for the reception of acetylcholine molecules. Normally, acetylcholine is used in signal transmission between nerves and muscles, its ultimate goal is to provide for muscle contractions. Therefore, in myasthenia gravis, in which acetylcholine receptors are destroyed, muscle contractions cannot be initiated.

PATHOLOGICAL PHYSIOLOGY



Neuromuscular abnormalities in MG are conditioned by an autoimmune response mediated by specific anti-AChR antibodies.

CLINICAL MANIFESTATIONS:

PATHOLOGICAL FATIGABILITY

- General (more expressed in the evening, to the effort)
- Upper eyelid ptosis
- Strabismus (diplopia)
- Dysarthria
- Mastication disorders
- Swallowing disorders

Clinical manifestations. Simpson's test

MYASTHENIC CRISIS:

Progressive weakness despite increasing anticholinesterases is a sign of the onset of a cholinergic or myasthenic crisis.

Patients with progressive respiratory difficulty or handling their secretions and not responding to relatively high doses of anticholinesterases are best treated by tracheal intubation or tracheostomy, support with a ventilator, and intravenous feeding. Refractoriness to drug therapy usually disappears in a few days.

COMPLEMENTARY INVESTIGATIONS:

- *Prozerine* (*Tensilon*) test
- Electroneurograpgic stimulodection examination
- EMG examination with single-fiber electrode (Jitter phenomenon)
- Examination of mediastinum by CT or MRI method (thymoma?)
- Blood analysis on AntiAchR and AntiMusk antibodies

TENSILON (*edrophonium chloride*) test

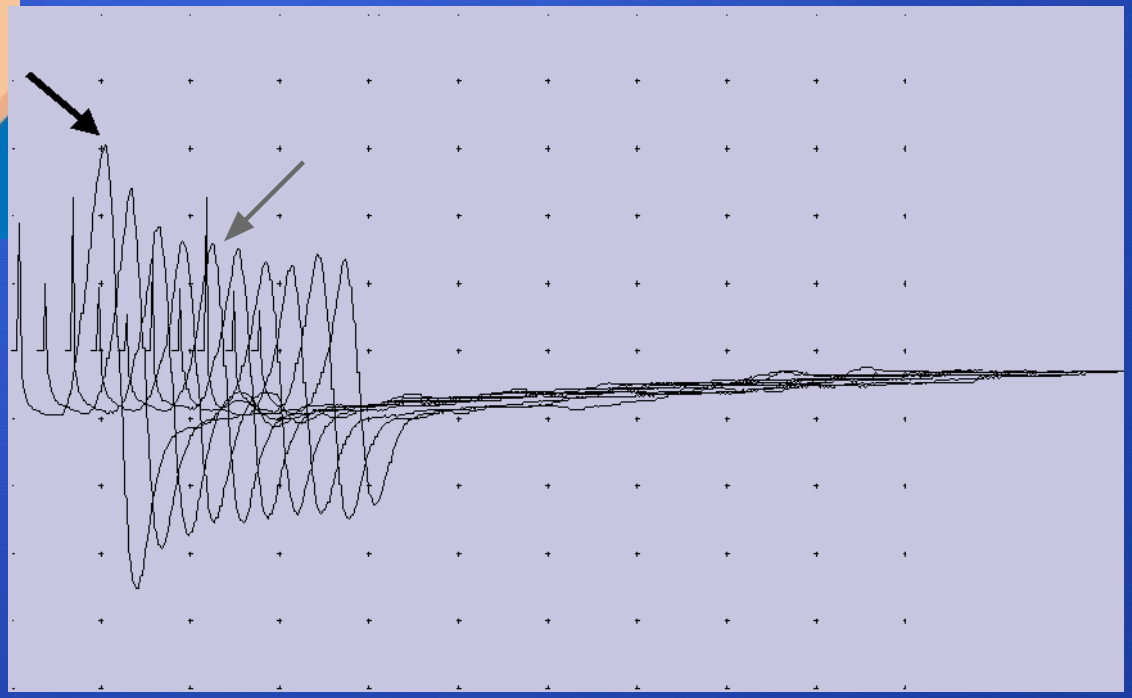
- A *10 mg edrophonium chloride* syringe and a 2 mg atropine syringe are prepared. Atropine is prepared for immediate use in case cholinergic crisis occurs. After a neurologic examination and recording of vital signs, first 2 mg edrophonium is injected intravenously. After waiting 30 seconds and ensuring that no adverse reactions occurred, the remaining 8 mg of edrophonium is also injected. A patient suffering from myasthenia gravis experiences improvement in muscle strength and endurance with repetitive movements, while normal persons do not feel any difference.

TENSILON (*edrophonium chloride*) test

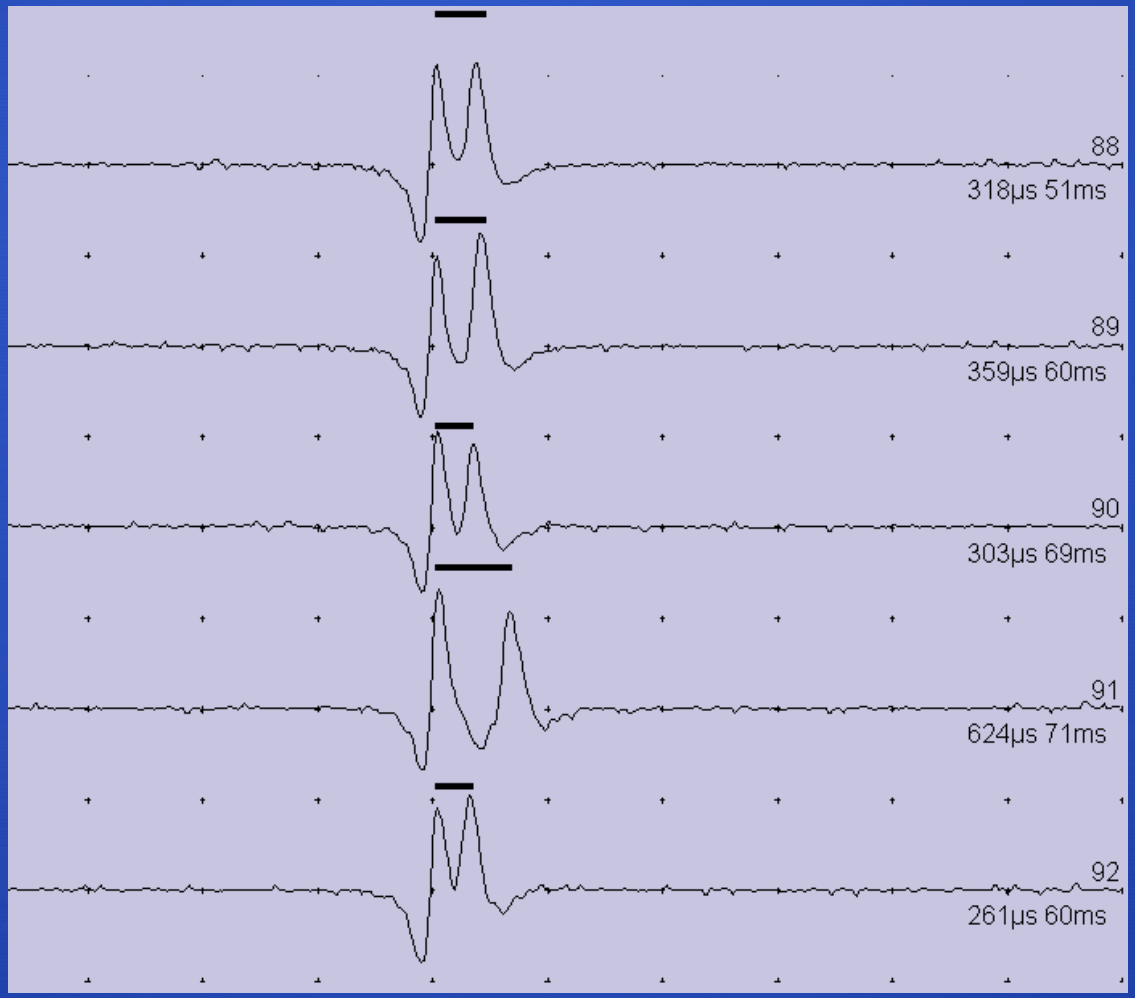
Tensilon test: Before (left); After (right)

Stimulus detection test (ENG)

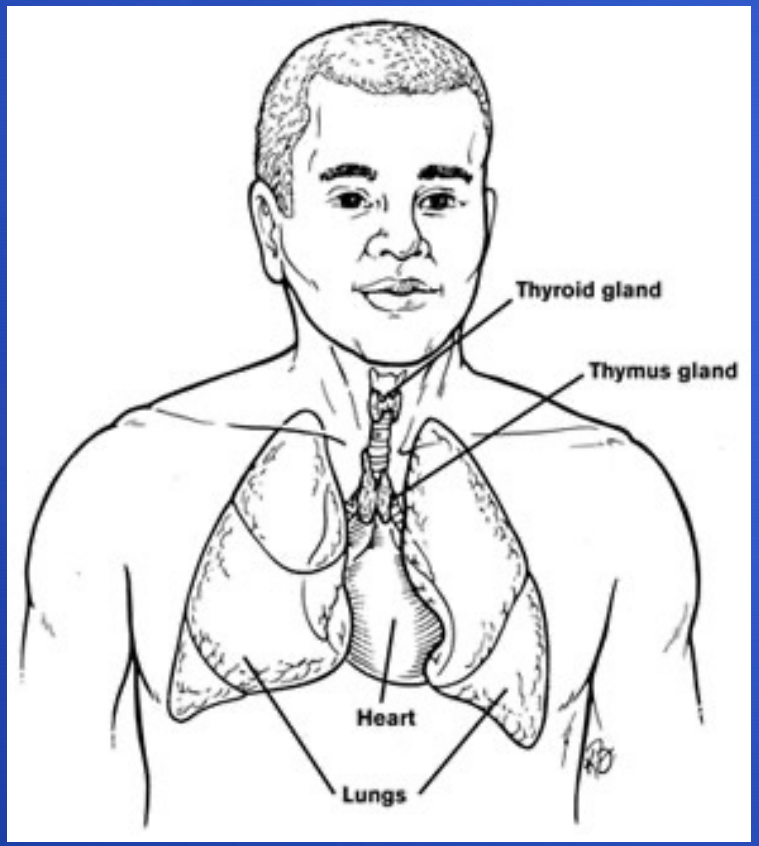
Decrement A1/A4 >12% means +



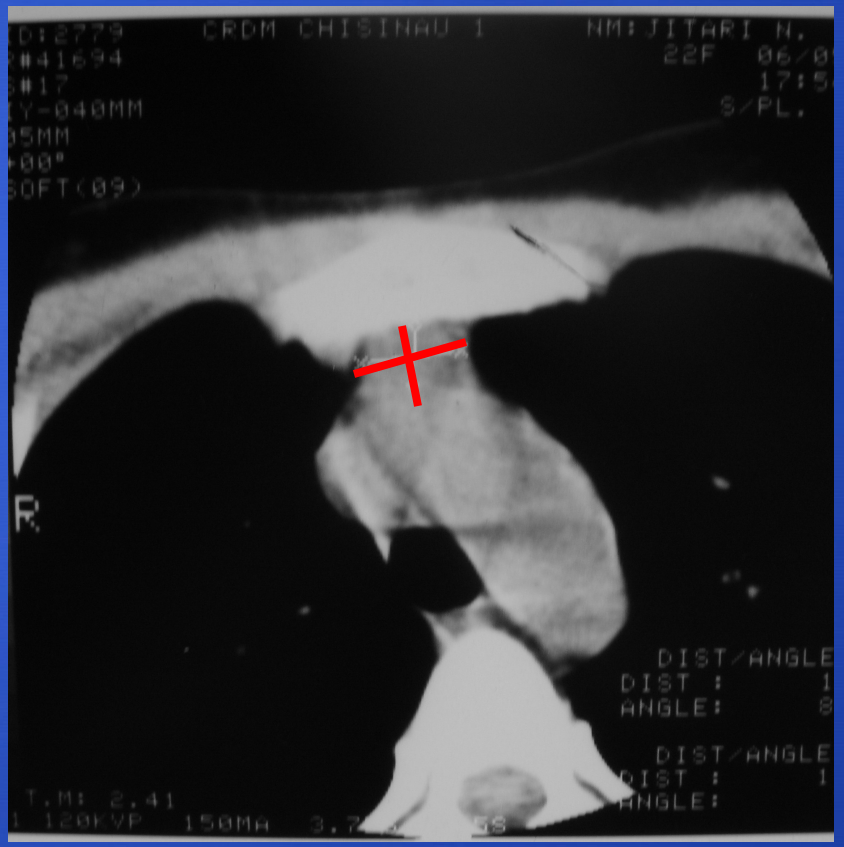
Single fiber EMG („jitter")



THYMOMA?
CT or MRI examination of mediastinum



Thymoma is found in 20% of patients with MG.



CT

Why Thymoma and MG ?

?

Thymoma → thymic follicular hyperplasia

↓

ectopic germinal centers

↓

AChR antibody!

Blood analysis on AntiAchR

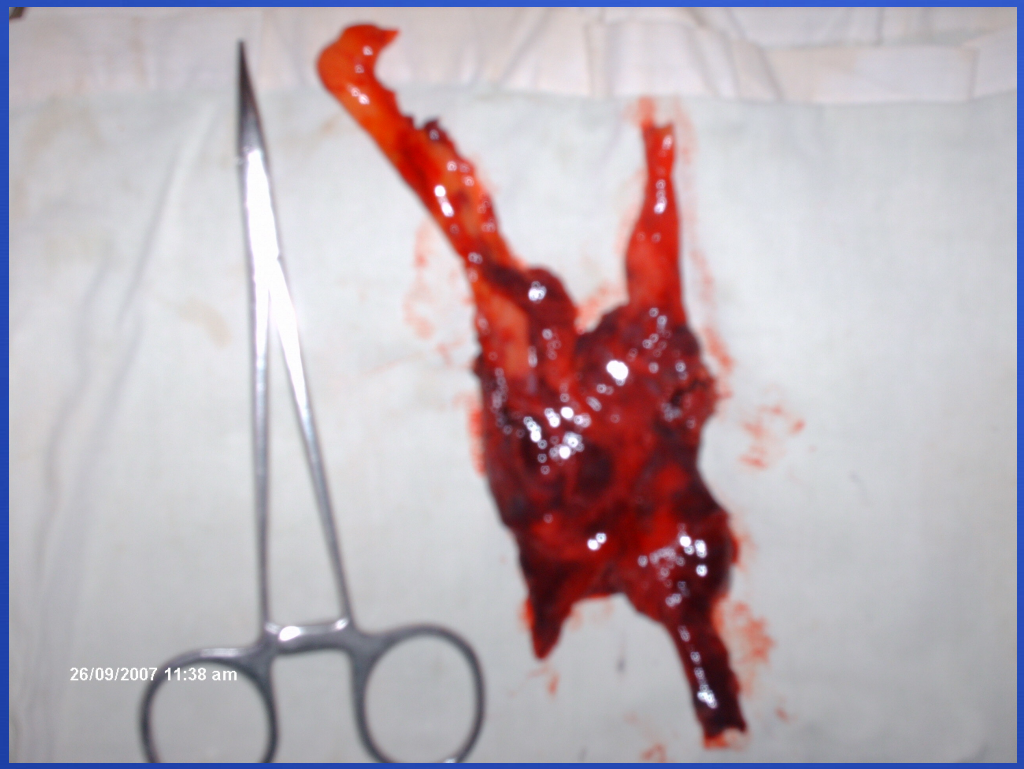
- test is for antibodies against the acetylcholine receptor; the test has a reasonable sensitivity of 80–96%, but in ocular manifestations, the sensitivity falls to 50%.

THERAPY OF MYASTHENIC CRISIS:

1. Removal of the thymus.
2. Anticholinesterase drugs
3. Immunosuppression therapy
4. Plasmapheresis.
5. Intravenous immunoglobulin therapy

THYMECTOMY :

Increases the remission rate and also improves the clinical course of the disease. Controlled studies of thymectomy according to age, sex, severity and duration of disease have never been carried out. However, there is general agreement that the best response is in young women with a hyperplastic thymus gland and a high antibody titer.



ANTICHOLINESTERASE DRUGS

Pyridostigmine bromide (Mestinon, Kalymine) (60 mg tablets) acts for 3 to 4 hours. Neostigmine bromide (Nivalin) (15 mg tablets) acts for only for 2 to 3 hours and has more muscarinic side effects than pyridostigmine bromide.

In critically ill patients or postoperatively intramuscularly injectable pyridostigmine bromide (the dose is one thirtieth of the oral dose) or neostigmine methylsulfate (the dose is one fifteenth of the oral dose) can be used.

IMMUNOSUPRESSION

THERAPY

Alternate-day **prednisone therapy**.

Alternate day prednisone therapy significantly improves the disease in more than half the patients, but initially the drug may worsen the disease. The safest treatment schedule begins with 25 mg on alternate days; this is raised in 12.5 mg steps every 6 days until either 100 mg or maximum benefit is reached (Seybold and Drachman 1974). In a careful study, the average time for significant improvement was 5 months and the average dose 68 mg on alternate days (Tindall 1980).

IMMUNOSPPRESSION THERAPY

Azathioprine in doses of 2 to 3 mg/kg per day results in improvement in up to 90% of patients. The minimum time for improvement is 3 months, and about half the patients relapse when the medication is withdrawn (Mantegazza et al 1988). The side effects include hematological reactions (18%), serious infection (7%), gastrointestinal irritation (8%), hepatotoxicity (6%) (Mertens et al 1981; Hohlfeld et al 1988; Mantegazza et al 1988).

IMMUNOSPPRESSION THERAPY

Cyclophosphamide and **cyclosporine** have also been used in myasthenia gravis, but their therapeutic effects have not been shown to be superior to that of azathioprine.

RECECENT CHANGES IN THE TREATMENT OF MG

ECULIZUMAB

RITUXIUMAB

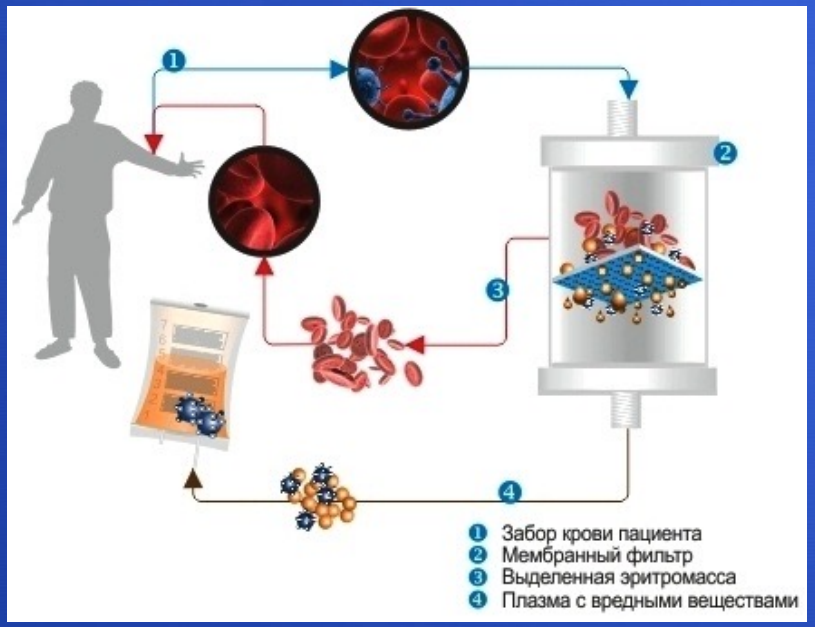
ROZANOLIXIZUMAB

EFGARTIGIMOD

MONARSEN

PLASMAPHERESIS : Plasmapheresis is indicated in severe generalized or fulminating myasthenia gravis refractory to other forms of treatment.

Daily exchanges of 2 liters of plasma result in improvement in a few days. Plasmapheresis alone does not confer greater long-term protection than immunosuppressants alone (Hawkey et al 1981).



INTRAVENOUS IMMUNOGLOBULIN THERAPY:

A dose of 400 mg/kg for 5 consecutive days or 1 g/kg on 2 consecutive days may improve severe myasthenia gravis within 2 to 3 weeks from the start of therapy. The mean duration of the response is 9 weeks in patients also treated with corticosteroids and 5 weeks in those who are not treated (Arsura 1989).

LOW-DOSE TOTAL BODY IRRADIATION :

administered over several weeks has resulted in improvement lasting longer than 2 years in 5 of 12 patients with chronic generalized severe myasthenia gravis (Durelli et al 1993). The long term risks of this form of therapy remain unknown.

DRUGS WITH UNDESIRED EFFECTS INCLUDE：

aminoglycoside antibiotics (eg, streptomycin, polymyxin, colistin, kanamycin, gentamicin), quinine, quinidine, and procainamide. These agents reduce the safety margin of neuromuscular transmission and should be avoided or used with great caution. Ampicillin, erythromycin, chlorpromazine, morphine and b-adrenergic blockers can also worsen defects of neuromuscular transmission and should be used with caution. The contrast agent for magnetic resonance imaging, gadolinium diethyline-triamine-pentaacetic acid can also worsen myasthenia gravis (Engel 1994a).

ALSO TAKE INTO ACCOUNT:

PHYSICAL EFFORT

PSYCHO-EMOTIONAL STRESS

FOOD

LIFESTYLE

GUSTAV KLIMMT

The Kiss