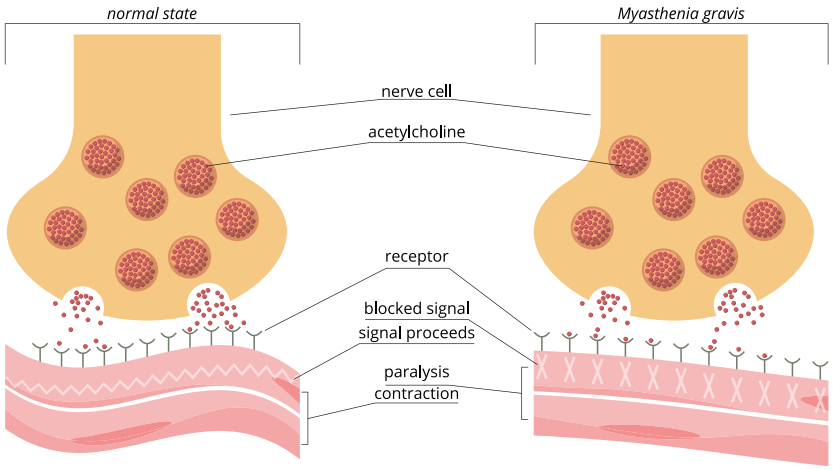
AUSTIN NEUROMUSCULAR CENTER

A Guide to Understanding and Treating Myasthenia Gravis (MG)

WHAT IS MYASTHENIA GRAVIS?

Myasthenia gravis (MG) is a chronic autoimmune disease that causes the immune system to attack the connection between nerves and muscles, known as the neuromuscular junction (NMJ). This interrupts their communication and causes weakness in muscles responsible for movement and breathing.



Myasthenia Gravis affects about 1 in 5,000 people. It is more commonly found in women under 40 and men over 60, but it can be seen across all age, racial, and ethnic groups. MG is not inherited and is not contagious, but there are cases where the disease is found in more than one family member.

There is also evidence that the thymus could be related to the diagnosis. 10–15% of people with MG are found to have a thymoma, a thymic tumor. Another 65% of people have overactive thymic cells, a condition known as thymic hyperplasia.

Lab tests including blood work can be utilized to formally diagnose MG. Most people with the disease are *seropositive*, meaning they produce antibodies that attack different proteins in the NMJ. About 80% of people with generalized MG are found to have antibodies that attack the acetylcholine receptor (AChR) on the NMJ. About 10% have muscle specific kinase (MuSK) antibodies in their blood, and even fewer have lipoprotein-related protein 4 (LRP4) antibodies. Those without any of these antibodies are known to have *seronegative MG*.[1]

WHAT ARE SIGNS AND SYMPTOMS OF MYASTHENIA GRAVIS?

	Weakness in muscles that control the eyes, face, neck, and limbs
	Partial paralysis of eye movements, double vision, blurry vision, drooping of one or both eyelids
	Shortness of breath
	Fatigue in the neck and jaws, causing difficulty in speech, chewing, swallowing, and holding up the head

The onset of MG can be sudden and symptoms may not be immediately identified as being caused by the disease. In the early stages, eye muscles are usually affected first, with drooping eyelids, double vision, and partial paralysis of eye movements being common initial indications. Other common early symptoms include weakness and fatigue in the jaw and neck, causing difficulty talking, chewing, swallowing, and holding the head up.

There is a large variation in the degree of weakness found in individuals, ranging from being localized in the eye muscles (ocular myasthenia) to affecting the entire body (generalized myasthenia). This weakness tends to spread from the face down the body to the neck, upper limbs, hands, and then the lower limbs. It can also fluctuate from day-to-day as well as throughout the day. People with MG tend to feel the strongest in the morning and weaker in the evening.

In some people, this weakness can spread to the muscles that control breathing. In severe cases, this may cause respiratory failure, which will necessitate a ventilator and immediate emergency medical care. About 10–20% of people with MG will experience at least one of these myasthenic crises, which may be triggered by infections, stress, surgery, or adverse reactions to medication.

Over time, these symptoms usually progress and will often reach their maximum severity one to three years after onset. It is uncommon for the disease to cause weakness drastic enough to require a wheelchair. If properly treated, most people can continue to be physically active.

20% of people with MG experience short- and long-term remission, usually lasting five years on average, but there have been cases of it lasting over 20 years. There have also been several individuals who have experienced multiple remissions.[2]

HOW IS MYASTHENIA GRAVIS TREATED?

While there is no cure for this disease, the best way to treat it is to reduce symptoms and minimize possible side effects of medications. There are several options to help with this:

MEDICATIONS

Cholinesterase inhibitors

These help to slow the breakdown of the NMJ, improving strength.

- Mestinon (Pyridostigmine)
  - This is not as effective for individuals with MuSK-positive MG.

Immunosuppressive drugs

These drugs suppress the production of abnormal antibodies to help improve strength.

- Prednisone, Azathioprine (Imuran), Mycophenolate mofetil (CellCept), Tacrolimus, and Rituximab (Rituxan)
  - These are used if Pyridostigmine is not fully controlling symptoms.
  - It is common to start prednisone and then taper off long term if effective.
  - If prednisone does not help after tapering or is completely ineffective, other medications may be started.

- Eculizumab (Soliris), Ravulizumab (Ultomiris), and Efgartigimod (Vyvgart) are infusion/injection medications meant to reduce antibody production or alter certain pathways in the pathophysiology of MG. These are used if the above measures fail.

ACUTE INTRAVENOUS THERAPY

Plasmapheresis

Plasmapheresis is a procedure where a machine is used to remove harmful antibodies in plasma and replace them with good plasma or a plasma substitute.

Intravenous immunoglobulin

Intravenous immunoglobulin is a highly concentrated injection of antibodies from donors that can temporarily change the way the immune system works.

These treatments are used for more moderate to severe MG, those resistant to other immunomodulating agents, or for MG crises.

SURGERY

Thymectomy

- A thymectomy is an operation to remove the thymus.
- Removal of the thymus can lessen the severity of MG symptoms and may also reduce the need for other medications in the future.

- ANESTHESIA GUIDELINES
  - Try to avoid surgery when MG symptoms are not controlled.
  - Avoid use of nondepolarizing agents, mainly neuromuscular blockers (NMBs).
  - If possible, use local or regional anesthesia. IV anesthetics (propofol) can be safely used because they are short acting and have rapid onset.
  - You may need extra respiratory monitoring overnight after surgery and neurology should be consulted.
  - Pre/postop antibiotics that are safe are penicillin, cephalosporins, metronidazole, sulfa drugs.

MEDICATIONS TO AVOID

DRUGS THAT MAY UNMASK OR WORSEN MYASTHENIA GRAVIS:[3, 4]

Anesthetic agents

- Neuromuscular blocking agents

Antibiotics

- Aminoglycosides (e.g., gentamicin, neomycin, tobramycin)
- Fluoroquinolones (e.g., ciprofloxacin, levofloxacin, norfloxacin)
- Ketolides (e.g., telithromycin)
- Macrolides (e.g., azithromycin, clarithromycin, erythromycin)

Cardiovascular drugs

- Beta blockers (e.g., atenolol, labetalol, metoprolol, propranolol)
- Procainamide
- Quinidine

Other drugs

- Anti-PD-1 monoclonal antibodies (e.g., nivolumab and pembrolizumab)
- Botox
- Chloroquine
- Hydroxychloroquine
- Magnesium
- D-Penicillamine
- Quinine
- Desferrioxamine

DRUGS THAT MAY BE ASSOCIATED WITH EXACERBATION OF MYASTHENIA GRAVIS

Anesthetic agents

- Inhalation anesthetics (e.g., isoflurane, halothane)
- Local anesthetics (e.g., lidocaine, procaine)

Antibiotics and antiviral agents

- Antiretroviral agents (e.g., ritonavir)
- Clindamycin
- Metronidazole
- Nitrofurantoin
- Tetracyclines (e.g., doxycycline, tetracycline)
- Vancomycin

Anticonvulsants

- Carbamazepine
- Ethosuximide
- Gabapentin
- Phenobarbital
- Phenytoin

Antipsychotics and other psychiatric drugs

- Butyrophenones (e.g., haloperidol)
- Lithium
- Phenothiazines (e.g., chlorpromazine, prochlorperazine)

More resources are available on www.myasthenia.org

REFERENCES

[1, 2] MDA: Myasthenia gravis (MG) Fact Sheet

[3] UpToDate: Overview of the treatment of myasthenia gravis

[4] Myasthenia.org: Cautionary Drugs For MG Patients

AUSTIN NEUROMUSCULAR CENTER

4705 Spicewood Springs Road | Austin, TX 78759 | Phone (512) 920-0140 | Fax (512) 920-0142 | www.austinneuromuscle.com