

What is...

Myasthenia Gravis



Myasthenia gravis (MG) is a **chronic autoimmune disease** — a disease that occurs when the immune system mistakenly attacks the body's own tissues.

In MG, the immune system attacks and interrupts the connection between nerve and muscle, called the **neuromuscular junction (NMJ)**. This causes weakness in the skeletal muscles, which are responsible for breathing and moving parts of the body.

In most cases of MG, the immune system targets the **acetylcholine receptor** — a protein on muscle cells that is required for muscle contraction.

About 85 percent of people with MG have **antibodies against** the acetylcholine receptor in their blood. The antibodies target and destroy many of the acetylcholine receptors on muscle. Consequently, the muscle's response to repeated nerve signals declines with time, and the muscles become weak and tired.

About 15 percent of individuals with MG are **seronegative for antibodies** to the acetylcholine receptor, meaning the antibodies aren't detectable in their blood (serum). It's been discovered that a large fraction of these individuals have antibodies to **muscle-specific kinase (MuSK)**, a protein that helps organize acetylcholine receptors on the muscle cell surface.

There's also evidence that an immune system gland called the **thymus** plays a role in MG. About 10-15 percent of people with MG have a thymic tumor, called a **thymoma**, and another 65 percent have overactive thymic cells, a condition called **thymic hyperplasia**. When the thymus doesn't work properly, the immune system may lose some of its ability to distinguish self from non-self, making it more likely to attack the body's own cells.

MG affects both men and women and occurs across **all racial and ethnic groups**. It most commonly impacts young adult women (younger than 40) and older men (older than 60), but it **can occur at any age**, including during childhood.

MG is **not inherited, and it is not contagious**. Although MG is not hereditary, **genetic susceptibility** appears to play a role in it. Occasionally, the disease may occur in more than one member of the same family.

MG causes **weakness** in muscles that control the eyes, face, neck, and limbs. Symptoms include partial paralysis of eye movements, double vision, and droopy eyelids, as well as weakness and **fatigue** in neck and jaws with problems in chewing, swallowing, and holding up the head.

Muscle weakness in MG gets **worse with exertion** and **improves with rest**.

Approximately **10-20 percent** of people with MG experience at least one myasthenic crisis, an emergency in which the muscles that control breathing weaken to the point where the individual requires a ventilator to help them breathe. This condition may be triggered by infection, stress, surgery, or an adverse reaction to medication, and usually requires immediate medical attention.

There is no known cure for MG, but there are treatments that can control symptoms and allow people with MG to have a relatively high quality of life. Most individuals with the condition have a normal life expectancy.

Most people with MG are able to manage their symptoms and lead active lives, and a few experience remission lasting many years.



What are the signs and symptoms of MG?

Myasthenia gravis weakens and fatigues the body's voluntary muscles (those we can move at will). It doesn't damage the musculature of the heart or the gastrointestinal tract.

Skeleton and muscle

- Muscle weakness
- Partial paralysis of eye movements
- Drooping of one or both eyelids
- Blurred vision
- Double vision
- Change in facial expression
- Difficulty chewing or swallowing
- Impaired speech



Lungs

- Shortness of breath

What should I know about MG?

- 1 The onset of myasthenia gravis may be sudden, and symptoms sometimes may not be immediately identified as being caused by MG.
- 2 Early in its course, MG tends to affect the muscles that control movement of the eyes and eyelids, causing ocular weakness. Consequently, a partial paralysis of eye movements, double vision, and droopy eyelids are usually among the first symptoms of MG.
- 3 Weakness and fatigue in the neck and jaw also can occur early in MG. This bulbar weakness — named for the nerves that originate from the bulblike part of the brainstem — can make it difficult to talk, chew, swallow, and hold up the head.
- 4 The degree of muscle weakness involved in MG varies greatly among individuals, ranging from a localized form limited to eye muscles (ocular myasthenia), to a severe or generalized form in which many muscles — sometimes including those that control breathing — are affected.
- 5 In generalized MG, weakness tends to spread sequentially from the face and neck to the upper limbs, the hands, and then the lower limbs. It may become difficult to lift the arms over the head, rise from a sitting position, walk long distances, climb stairs, or grip heavy objects. In some cases, weakness may spread to muscles in the chest that control breathing.
- 6 Sometimes the severe weakness of MG may cause respiratory failure, which requires immediate emergency medical care.
- 7 Many prescription drugs can unmask or worsen symptoms of MG. These include: muscle relaxants used during surgery, aminoglycoside and quinolone antibiotics, cardiac anti-arrhythmics, local anesthetics, and magnesium salts (including milk of magnesia).
- 8 Overexertion, emotional stress, infections (anything from tooth abscesses to the flu), menstruation, and pregnancy also might lead to increased weakness in MG.
- 9 Weakness and fatigue in MG tend to fluctuate from day to day, and even during a single day. People with the disease are often strongest in the morning after a full night's sleep, and weakest in the evening.
- 10 Over a longer term, the symptoms of MG usually progress, reaching maximum or near-maximum severity within one to three years of onset in most people.
- 11 Weakness serious enough to require full-time wheelchair use is not common in MG. Most people, when properly treated, find they can remain physically active.
- 12 Remission, a reversal of some or all symptoms, occurs in about 20 percent of people with MG. Usually, the remissions are temporary, with an average duration of five years, but some experience more than one remission during their lifetime. A few individuals have experienced apparently permanent remissions lasting more than 20 years.

How is MG treated?

MEDICATIONS

Medications to treat MG include anticholinesterase agents, also called cholinesterase inhibitors, such as **mestinon** or **pyridostigmine**, which slow the breakdown of **acetylcholine** at the **neuromuscular junction** and thereby **improve neuromuscular transmission** and **increase muscle strength**.

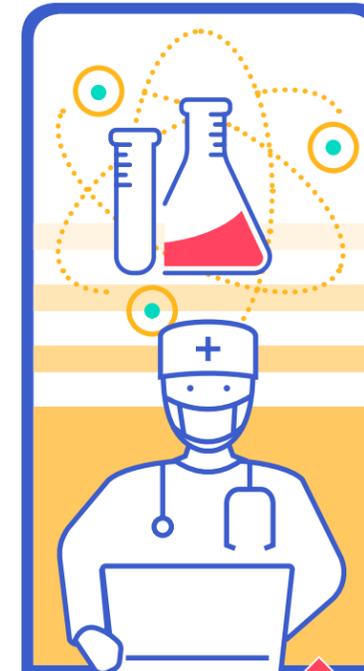


Immunosuppressive drugs improve muscle strength by suppressing the production of abnormal antibodies. They include prednisone, azathioprine, mycophenolate mofetil, tacrolimus, and rituximab.

The US Food and Drug Administration (FDA) has approved eculizumab (brand name Soliris), a type of complement inhibitor, as a treatment for adults with generalized MG who are anti-acetylcholine receptor antibody-positive. Soliris

is a terminal complement inhibitor that targets a part of the immune system called the complement system, which is responsible for helping antibodies clear damaged cells and potentially toxic microbes that could cause infections. In MG, antibodies whose job it is to target these toxic pathogens instead inappropriately recruit the complement system and target the NMJ. Soliris is thought to work in MG by inhibiting the complement pathway to prevent destruction of the NMJ. Treatment with Soliris will not cure generalized MG, but it may improve disease symptoms, the ability to carry out activities of daily living, and quality of life.

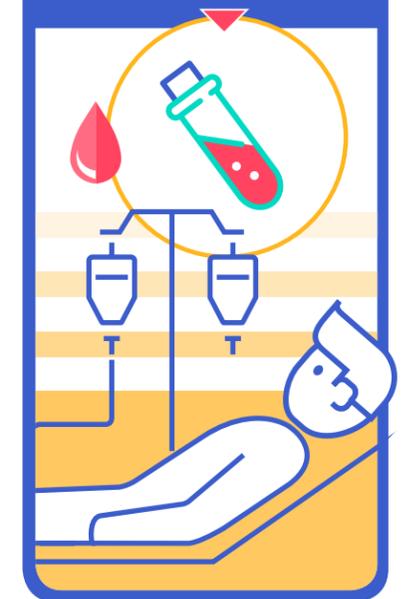
SURGERY



Thymectomy, an operation to remove the thymus gland, is required in MG patients with a thymic tumor and, in other cases, may lessen the severity of MG symptoms. It may also reduce the patient's need for the use of additional drugs to control MG symptoms.

INTRAVENOUS THERAPY

Plasmapheresis and intravenous immunoglobulin are other therapies that may be options in severe cases of myasthenia gravis. Individuals can have antibodies in their plasma (a liquid component in blood) that attack the NMJ. These treatments remove the destructive antibodies, although their effectiveness usually lasts only for a few weeks to months.



- **Plasmapheresis** is a procedure in which a machine is used to remove harmful antibodies in plasma and replace them with good plasma or a plasma substitute.
- **Intravenous immunoglobulin** is a highly concentrated injection of antibodies pooled from many healthy donors that temporarily changes the way the immune system operates. It works by binding to the antibodies that cause MG and removing them from circulation.

Please talk to your medical provider to obtain more information about potential treatments for MG.



MDA Glossary

Autoimmune disease

A disease characterized by an inappropriate attack of the immune system on the body's own tissues

Diplopia

Double vision

Dysarthria

Difficulty speaking or forming words

Dysphagia

Difficulty swallowing

Dyspnea

Difficulty breathing

Genetic susceptibility

An increased likelihood of developing a particular disease based on a person's genetic makeup

Myasthenic crisis

A medical emergency that occurs when the muscles that control breathing weaken to the point where individuals require a ventilator to help them breathe

Neuromuscular junction

The place where nerve cells connect with the muscles they control

Neuromuscular junction disorder

A condition that is a result of the destruction, malfunction, or absence of one or more key proteins involved in the transmission of signals between muscles and nerves

Neurotransmitter

Chemicals that neurons, or brain cells, use to communicate information

Ophthalmoparesis

Partial paralysis of eye movements

Ptosis

Drooping of one or both eyelids

Thymus

A gland, located in the chest behind the breast bone, that controls immune function and may be associated with myasthenia gravis

To learn more about MG, visit mda.org or contact the MDA National Resource Center at 833-ASK-MDA1 (275-6321).



Designated a Top-Rated Charity by the American Institute of Philanthropy, MDA is the first nonprofit to receive a Lifetime Achievement Award from the American Medical Association for "significant and lasting contributions to the health and welfare of humanity."



Muscular Dystrophy Association

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