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# MYASTHENIA GRAVIS

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**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 SHOULD I KNOW ABOUT MG?

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- 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, certain classes of antibiotics, cardiac antiarrhythmics statins, 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.



# MEDICATIONS

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The goals of therapy for Myasthenia Gravis are to reduce symptoms and minimize side effects of medications. Several therapies are available to help individuals reduce muscle weakness.

**Medications to treat MG act in different ways to counteract or interrupt damage to the neuromuscular junction (NMJ) caused by the immune system. These therapies include cholinesterase inhibitors, immunosuppressants, and complement inhibitors.**

**Cholinesterase inhibitors** slow the breakdown of acetylcholine at the NMJ, helping to improve communication between muscle and nerve and thereby improve muscle strength. These include mestinon (brand name Pyridostigmine) and neostigmine.

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

**Complement inhibitors** target a part of the immune system called the complement pathway, which helps trigger an effective immune response to potential invaders. In MG, the complement system is inappropriately recruited by antibodies to target the NMJ. The US Food and Drug Administration (FDA) has approved the complement-inhibitor eculizumab (brand name Soliris) on October 2017, efgartigomod (brand name Vyvgart) on December 2021 and ravulizumab (brand name Ultomiris) on April 2022 as a treatment for adults with generalized MG who are anti-acetylcholine receptor antibody-positive. Soliris is thought to work in MG by inhibiting the complement pathway to prevent destruction of the NMJ. Vyvgart is

designed to reduce the number of antibodies in the body, including the autoreactive antibodies that cause gMG. Ultomiris is designed to target a component of the immune system (known as complement), which underlies many autoimmune disorders including gMG. Treatment with Soliris, Vyvgart, , and Ultomiris 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.

## Antibody Therapy

Individuals with MG 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.

- **RYSTIGGO®** (rozanolixizumab-noli) is administered as an injection for subcutaneous infusion. It is the only FDA-approved treatment for adults with MG who are anti-acetylcholine receptor (AChR) or anti-muscle-specific tyrosine kinase (MuSK) antibody positive. It has been designed to block the interaction of FcRn and IgG, accelerating the catabolism of antibodies and reducing the concentration of pathogenic IgG autoantibodies.
- **SOLIRIS®** (eculizumab) is an FDA-approved intravenous infusion treatment for adults with gMG who are AChR antibody positive. Soliris is thought to work in MG by inhibiting the complement pathway to prevent destruction of the NMJ. It can improve activities of daily living and reduce disease severity.
- **ULTOMIRIS®** (ravulizumab-cwvz) is an FDA-approved intravenous infusion for adults with AChR antibody positive gMG. There is an initial loading dose followed by maintenance doses every eight weeks. Ultomiris is designed to target a component of the immune system (known as complement), which underlies many autoimmune disorders including gMG.
- **VYVGART HYTRULO®** (efgartigimod alfa and hyaluronidase-qvfc) is an FDA-approved subcutaneous injection treatment for adult patients who are anti-acetylcholine receptor (AChR) antibody positive. It is recommended that a dose of Vyvgart Hytrulo administered subcutaneously by a medical professional in treatment cycles of once-weekly injections for 4 weeks. Vyvgart Hytrulo works by attaching to and blocking a protein called neonatal Fc receptor (FcRn) which is involved in regulating levels of autoantibodies.

Treatment with RYSTIGGO®, SOLIRIS®, ULTOMIRIS®, VYVGART® or VYVGART HYTRULO® will not cure generalized MG, but they may improve disease symptoms, the ability to carry out activities of daily living, and quality of life. Please talk to your medical provider to obtain more information about potential treatments for MG.

### FcRn Antagonist

- **VYVGART®** (efgartigimod alfa-fcab) is the first FDA-approved treatment that uses a fragment of an IgG antibody to treat adults with anti-AChR antibody positive gMG. It is an infusion that is given in cycles of four doses over four weeks. It binds to a protein (FcRn) and prevents the recycling of the antibodies that cause MG which improves activities of daily living and reduces muscle weakness.



# WHAT ARE THE SIGNS AND SYMPTOMS OF MG?

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## 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

To learn more about MG, visit [mda.org](https://mda.org) or contact the MDA Resource Center at [resourcecenter@mdausa.org](mailto:resourcecenter@mdausa.org) or 1-833-ASK-MDA1.



# MDA GLOSSARY

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## 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

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