

Myasthenia Gravis

Making a Difference Today

Myasthenia gravis (MG) is an autoimmune disease that occurs when the immune system attacks a specific part of the body's own muscles. The disease interrupts messages relayed at the neuromuscular junction, the area between the end of a nerve that originates in the spinal cord and a muscle fiber. Voluntary muscles—those that can be moved at will—that control the eyes, face, neck, and limbs are commonly affected, becoming weak and fatigued.

If untreated, MG can lead to difficulty in swallowing, impaired speech, blurred vision, unstable gait, and, in some severe cases, respiratory failure.

It has been estimated that over 100,000 people in the United States are affected by MG.

Research Leads to Understanding

Fortunately, thanks to continued research, scientists have learned more about what causes MG and what goes wrong at the neuromuscular junction and how to treat it.

In the 1970s, researchers showed that people with the disease have a reduced number of receptors—specialized proteins located on the surface of muscle cells—where the nerve chemical acetylcholine (ACh) binds and causes muscle contractions and voluntary movement.

Through animal and human research funded by the National Institutes of Health (NIH), scientists later discovered that antibodies—chemicals that the immune system normally uses to attack bacteria and viruses—target and damage or block many of the ACh receptors on the muscle, preventing ACh from binding to the receptors and acting on the muscle. Impaired signaling between the muscles and the nerves causes muscle weakness.

Another antibody recently detected targets muscle-specific tyrosine kinase (MuSK), a protein that helps organize ACh receptors on the muscle cell. This antibody is responsible for MG in a smaller group of people. Scientists have recently developed a commercial blood test for MuSK-related MG that helps to distinguish it from other types of the disorder.

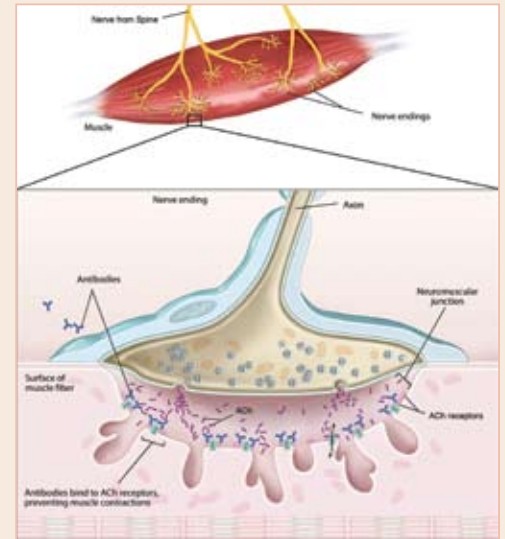
Research Leads to Treatments

Thanks to increased understanding of the mechanism behind MG from over 40 years of research, effective treatments now are available for patients.

Medications known as cholinesterase inhibitors can provide relief from symptoms in minutes, by blocking the action of an enzyme that breaks down ACh, thus increasing the amount of ACh that can act at the neuromuscular junction. Through research funded by the NIH, drugs that suppress the immune system, including corticosteroids that decrease inflammation, also were developed to keep antibodies from attacking the ACh receptors or the MuSK proteins.

More recent research has led to new treatments. In plasma exchange, antibodies that attack the ACh receptors or MuSK proteins are removed from the blood. IVIg therapy is an injection of a nonspecific collection of antibodies pooled from human donors that scientists think might work by decreasing the immune system's production of its own antibodies. These treatments usually are used only until other interventions begin to have an effect, because their therapeutic effects are short-lived.

Although understanding of MG and treatments for the disease has advanced, more research still is needed to improve understanding of the disease processes in MG and to develop more targeted medications with fewer side effects, such as gastrointestinal problems.



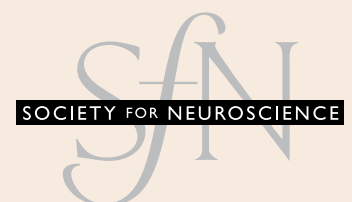
Myasthenia gravis is a disease of the neuromuscular junction, the area between the ending of a nerve that originates in the spinal cord and a muscle fiber. The disease can occur when the immune system makes antibodies that target and damage or block many of the muscle's acetylcholine receptors, specialized proteins located on the surface of muscle cells where the nerve chemical acetylcholine (ACh) binds and causes muscle contractions. This prohibits ACh to bind to the damaged receptors and act on the muscle, which reduces muscle contractions, leading to weakness and fatigue of muscles.

Continued funding for research could lead to:

- A better understanding of what triggers the body's abnormal immune system response in myasthenia gravis and what happens at the neuromuscular junction.
- Increased knowledge of the different causes of myasthenia gravis and of other closely related diseases, such as Lambert-Eaton myasthenic syndrome and congenital myasthenic syndromes.
- More targeted treatments that will aid more people with myasthenia gravis with fewer side effects and without suppressing the rest of the immune system.

For more information please email brss@sfn.org.

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Myasthenia Gravis

Making a Difference Tomorrow

Thanks to years of research, scientists now know more about myasthenia gravis (MG) and how to treat it. However, these treatments may not help everyone, and many of them come with potential serious side effects, such as increased risk of infection and bone weakening.

Did you know that:

- MG weakens and fatigues voluntary muscles—those that can be moved at will—including those that control the eyes, face, neck, and limbs.
- If untreated, MG can lead to difficulty in swallowing, impaired speech, blurred vision, unstable gait, and, in some severe cases, respiratory failure.
- It has been estimated that over 100,000 people in the United States are affected by MG.

Research Leads to Improved Treatments

Research funded by the National Institutes of Health (NIH) seeks to understand the molecular basis of cell-to-cell communication in the nervous system and to apply this knowledge to the treatment of MG.

A relatively new immunosuppressant medication is now in wide use after showing promising results against MG in clinical trials. Recent studies have shown that nearly 75 percent of patients treated with this medication show improvement, with only occasional non-serious side effects.

Researchers funded by NIH are working on therapies that will target only the errant immune cells that cause the disease rather than target the body's entire immune system. These include animal studies of a vaccine-like medication that mimics proteins or antibodies reactive to the ACh receptor and a "guided missile strategy" that uses the body's own immune cells to target and destroy the abnormal antibodies that attack the body's healthy cells.

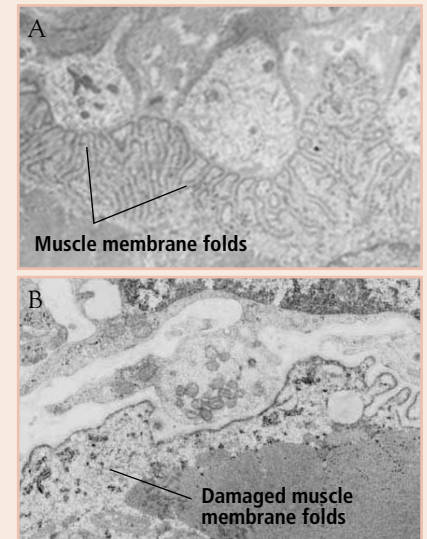
Researchers also are investigating the difference between MG caused by ACh receptor antibodies and MG caused by MuSK antibodies. Preliminary findings show that certain treatments—such as removing the thymus, an immune system gland—might have lower chances of success in MuSK-related MG.

Hope For Other Diseases

Understanding the mechanisms of MG can aid diagnosis and treatment of similar disorders as well. For example, Lambert-Eaton myasthenic syndrome (LEMS) is a rare autoimmune disease that interferes with ACh release from nerve cells, as opposed to ACh receptors on muscle cells as in MG. Another group of disorders called congenital myasthenic syndromes (CMS) is inherited—while MG is an acquired autoimmune disease—caused by defective genes that interfere with the normal production of the ACh receptor or other components of the neuromuscular junction.

Uncovering the specific causes and processes of MG can help to distinguish it from other diseases like LEMS and CMS, which can aid in providing treatments targeted to the underlying causes of each separate disorder.

Scientists have made great strides in advancing the understanding of and treatments for MG, but more research is needed. Only continued funding for MG will bring greater knowledge of the disorder and better, more targeted treatments.



Using electron microscopy, scientists were able to compare healthy neuromuscular junctions to those of patients with myasthenia gravis caused by acetylcholine receptor antibodies. Slide A shows a healthy neuromuscular junction with a well-preserved muscle surface membrane and deep folds. Slide B, however, shows a neuromuscular junction affected by myasthenia gravis where the membrane and folds have been damaged and simplified, caused by the acetylcholine receptor antibodies attacking the area. Overall, the area on the myasthenia gravis muscle surface and the acetylcholine receptor density have been decreased. These changes lead to less of the nerve chemical acetylcholine binding to muscle receptors, which causes muscle fatigue and weakness.

Already research has led to:

- Advanced understanding of the muscle receptor for the nerve chemical acetylcholine and how it is affected in myasthenia gravis.
- The discovery that two antibodies—the acetylcholine receptor and the muscle-specific tyrosine kinase protein antibodies—can cause myasthenia gravis when they attack the acetylcholine muscle receptors.
- More treatment options, such as cholinesterase inhibitors and immunosuppressant drugs, that help many people cope with myasthenia gravis.

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