# Myasthenia gravis

## What is Myasthenia Gravis?

Myasthenia gravis (MG) is a chronic auto-immune neuromuscular disorder that leads to rapid weakness and fatigue of the voluntary muscles of the body. Characteristically individuals with MG experience muscle weakness that increases during periods of activity and improves after periods of rest. The muscles that control eye and eyelid movement, facial expression, chewing, talking and swallowing are most frequently, but not always, involved in the disorder. Muscles of the limbs and those that control breathing and the neck may also be affected.

MG occurs in all genders and ethnic groups. Onset most commonly occurs at 20-40 years of age for women and 60 years and over for men, though it can affect individuals at any age. MG affects approximately 14 in 100,000 people and life expectancy remains normal.

In some cases, the foetus of a pregnant mother with MG may acquire immune antibodies. This is called neonatal myasthenia and is generally temporary, with the child's symptoms often disappearing within a few weeks of birth. Some children may develop MG indistinguishable from adults.

Congenital myasthenia is a rare disorder where babies are born with a genetic defect in neuromuscular transmission similar to MG; however, it is not an auto-immune disorder.

## What are the Features of Myasthenia Gravis?

MG can affect any voluntary muscle and the onset of symptoms may be quite sudden. Involuntary muscles such as the digestive system, heart and brain are not affected. Muscle weakness is not always symmetrical.

In most cases, the first symptoms to appear are weakness and fatigue of the eye muscles. This may cause the eye muscles to droop (ptosis). Individuals may experience double vision or blurred eyesight (diplopia), and there may also be some difficulty in holding a steady gaze.

The degree of muscle weakness experienced in MG varies enormously, ranging from a localised form, for instance limited to eye muscles (ocular myasthenia), to a severe or generalised form in which many other muscles are involved.

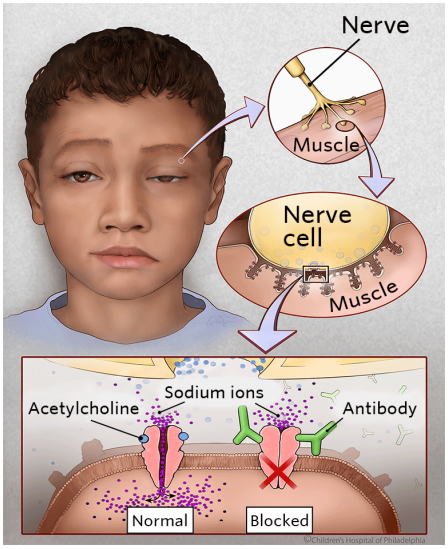



*IMAGE SOURCE: The Childrens' hospital of Philadelphia http://www.chop.edu/conditions-diseases/myasthenia-gravis#.VVKKAl6qqko*

Other muscles that are commonly involved include the oropharyngeal muscles in the throat, which can cause difficulty chewing and swallowing (dysphagia). Inhaling while trying to swallow may result in a tendency to gag or choke, particularly while drinking. Talking difficulties may be experienced (dysarthria) and a speech therapist may be beneficial. Muscles of the face may also be affected and become paralysed, leading to a tendency to drool.

Muscle weakness may progress to the hips, arms, and legs, and may produce an unstable or waddling gait. Individuals may experience difficulty climbing stairs, getting out of chairs and lifting objects. Weakness in the neck can produce a drooping head, which may require support. Weakness in the jaw can also occur and produces a hanging jaw.

Breathing difficulties due to a weakness of the respiratory muscles, can result in inadequate intake of air or an inability to cough effectively, and can have serious consequences. This is called a myasthenic crisis and can be triggered by infection, fever, adverse reaction to medication, or emotional stress. Assisted ventilation may be necessary to sustain life.

Following the onset of the condition symptoms tend to progress (get worse over time) during the first five to seven years and then plateau. The severity of weakness also fluctuates during the day, usually least severe in the morning and worsening as the day progresses, especially after prolonged use of affected muscles.

## What Causes Myasthenia Gravis?

MG is an auto-immune disorder. The immune system primarily protects us from infection and produces antibodies to destroy foreign molecules. In auto-immune disorders, the immune system fails to differentiate between foreign molecules and those of its own body, producing antibodies directed against the destruction of its own body's proteins.

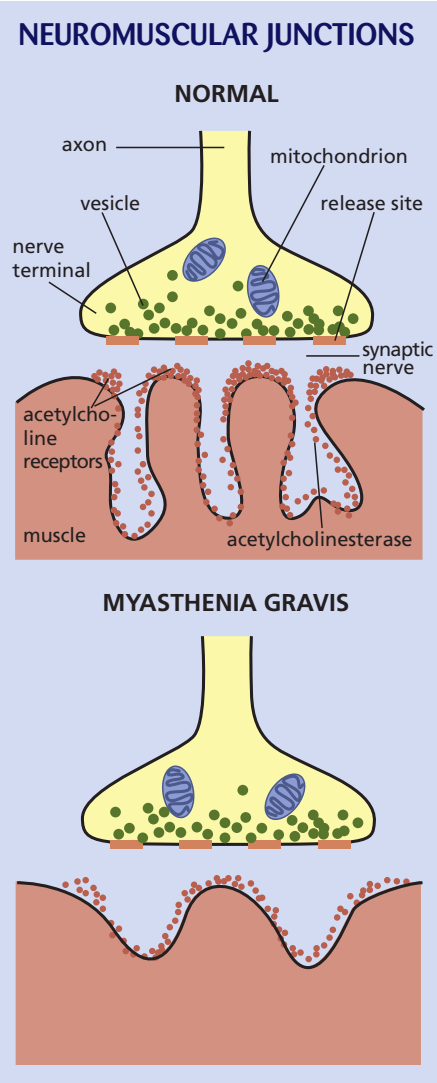
Normally, in muscle contractions, impulses are sent down a nerve and the nerve ending releases a substance (a neurotransmitter) called acetylcholine. This crosses the neuromuscular junction – a place where nerves connect to the muscles they control – and activates acetylcholine receptors on the muscle membrane, generating a muscle contraction. In MG, these receptors are mistakenly blocked, altered or destroyed by faulty antibodies, and fail to respond to the release of acetylcholine, preventing the muscle contraction from occurring. This results in the characteristic muscle weakness and susceptibility to fatigue experienced by people who have MG.

A recently recognised secondary cause of MG is the production of antibodies against a receptor called Muscle Specific Kinase (MuSK), which is required for the formation of the neuromuscular junction. Antibodies prevent the signaling of MuSK, resulting in increased

# Myasthenia gravis

obstruction of the neuromuscular junction and the consequent symptoms of MG.

MG is not directly inherited nor is it a contagious disorder. On some occasions the disorder may occur in more than one member of the same family.




*This image shows the reduction in the number of receptors, which means the muscles are unable to respond normally, leading to muscles being weak and fatiguing. Sourced from: http://medlibes.com/entry/myasthenia-gravis*

## Diagnosis of Myasthenia Gravis

Diagnosis usually commences after identifying key early symptoms of MG:

- Blood Testing – identifies the presence of acetylcholine receptor or MuSK antibodies
- Single-Fibre Electromyography (EMG) – measures the firing pattern ("jitter") of two single muscle fibres
- Repetitive Nerve Stimulation – repeatedly stimulating nerves with electrical impulses to measure the fatigability of the muscle
- Edrophonium Test – administration of edrophonium chloride (Tensilon®), which temporarily increases levels of acetylcholine at the neuromuscular junction, will briefly relieve muscle weakness in individuals with MG
- Chest X-Rays, CT (computed tomography) or MRI (magnetic resonance imaging) Scans – investigate the thymus gland, which is larger and easier to detect in cases of MG

## Management of Myasthenia Gravis

There is currently no known cure for MG, however can be controlled with several available therapies. These can have one of two functions: directly improve the muscle weakness or reduce the auto-immune process.

Cholinesterase inhibitors, such as neostigmine and pyridostigmine, aim to directly improve muscle weakness. This is achieved by slowing the natural enzyme cholinesterase, which normally degrades acetylcholine at the neuromuscular junction. By doing so, acetylcholine is present for longer and therefore enhances neuromuscular transmissions and consequently, muscular contractions.

Immunosuppressive drugs such as prednisone, cyclosporine, and azathioprine may also be used. These improve muscle strength by suppressing the production of abnormal antibodies. Use of these must be monitored closely, as they can have major side effects.

In cases of myasthenia crises, a process known as plasmapheresis in which the abnormal antibodies are removed from the blood. Also, high dose intravenous immune globulin (IVIG) is an alternative therapy which can suppress the immune system to down-regulate antibodies that target the acetylcholine receptor and provide the body with normal antibodies from donated blood. These therapies both have short-lived benefits that can typically be measured in weeks.

Thymectomy, the surgical removal of the thymus gland, has been shown to reduce symptoms in 70% of individuals with MG who do not possess a thymoma, and can cure some individuals – perhaps by rebalancing the immune system. Positive effects can take from weeks to years.

With treatment, most individuals with MG can lead normal lives. Some cases go into remission temporarily. Some individuals will find their muscle weakness disappearing completely and no longer needing to continue medication. As MG comes to be better understood, there is greater hope for better treatment outcomes.

## Research into Myasthenia Gravis

In recent years there have been great advances in technology that allow faster and more accurate diagnosis, and new and improved therapies have improved the management of MG, as knowledge about the structures and processes of the disorder has been enhanced. However research is still being carried out to learn what causes the auto-immune response and to gain greater understanding of the relationship between the thymus gland and MG.

As research makes more discoveries about the underlying causes of MG, it will be possible to develop treatments aimed more directly at these causes, rather than towards the management of its symptoms.

A vaccine has been created that works in mice but more trials are needed before it is known if this will work in humans.

## Support for People with Myasthenia Gravis

Support is available from the MDA, which can offer information, support, advocacy and referrals to other providers. There is also a nationwide Support Network for those interested in meeting with others.

There is no reason why individuals with MG should be disadvantaged in terms of receiving full education. For more information, request the Education Pack available from the MDA.

**Information in this fact sheet was primarily sourced from:**

National Institute of Neurological Disorders and Stroke (2006) Myasthenia Gravis Fact Sheet. www.ninds.nih.gov

Myasthenia Gravis Foundation of America (1997) Myasthenia Gravis. www.myasthenia.org