Myasthenia gravis

Myasthenia gravis is an auto-immune disorder meaning our immune system mistakes our own cells for foreign molecules and produces antibodies directed against the body's own proteins.

Myasthenia gravis (MG) is a chronic auto-immune neuromuscular disorder that leads to rapid weakness and fatigue of the voluntary muscles of the body.

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 one in 100,000 New Zealanders (or one-20 in 100,000 people worldwide – depending on the statistics in the country they are from), 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.

Features of myasthenia gravis

Characteristically, people with MG experience muscle weakness that increases during periods of activity and may improve 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. Limb muscles and those that control breathing and the neck may also be affected.

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). People 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 varies enormously, ranging from localised symptoms, e.g. limited to eye muscles (ocular myasthenia), to more severe or generalised forms in which many muscles are involved.

The severity of muscle weakness can often fluctuate during the day, usually least severe in the morning and worsening as the day progresses, especially after prolonged use of affected muscles.

Other muscles that are commonly involved include the muscles in the throat which may 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 to identify strategies to improve speech and assist swallowing.

Muscles of the face may also be affected and muscle weakness may progress to the hips, arms, and legs, and may result in a person experiencing an unstable or waddling gait, having difficulty climbing stairs, getting out of chairs, or lifting objects. Weakness in the neck can produce a drooping head which may benefit from support.

MG can affect the respiratory muscles which can result in breathing difficulties, snoring and sleep apnoea overnight, and/or or a weak and ineffective cough. A respiratory/sleep physician should be involved at the earliest hint of breathlessness, snoring, or difficulty with coughing.

Sometimes, a 'flare-up' of the condition (called a myasthenic crisis) can occur. These are often triggered by infections, fever, adverse reaction to medications, or emotional stress.

Causes of 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 mistakes our own cells for foreign molecules and produces antibodies directed against the body's own 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 the antibodies, and fail to respond to the release of acetylcholine, preventing the muscle contraction from occurring. This results in the muscle weakness and susceptibility to fatigue experienced by people who have MG.

A 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 signalling of MuSK, resulting in increased 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.

Diagnostic testing may include:

- 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 MG

There is currently no known cure for MG, however symptoms can be controlled with several available therapies. Treatments primarily focus on two purposes: directly improving the muscle weakness, or reducing 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 important side effects. Mycophenolate mofetil, rituximab and methotrexate are also possible treatments.

In cases of myasthenia crises, plasmapheresis in which the abnormal antibodies are mechanically filtered out from the blood can be used. 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-term benefits that can typically be measured in weeks.

Thymectomy, the surgical removal of the thymus gland, has been shown to reduce symptoms in 70 percent 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 and appropriate support, people with MG can lead normal and fulfilling lives. As MG comes to be better understood, there is greater hope for better treatment outcomes. ℞

Support for MG

The Myasthenia Gravis Support Group NZ offers information and education to people with MG, their friends, family and carers.

The group ensures people with MG can connect, however possible, to support and eliminate isolation with people who understand; focusing on positive and practical support.

The group aims to connect members either virtually or face-to-face, as well as raise awareness about MG.

For more information go to www.myastheniagravisnz.wordpress.com, call Talitha Vial on 027 220 3138, email talitha.leafy@gmail.com or join them on Facebook – search Myasthenia Gravis Support group, New Zealand. ℞