Myasthenia Gravis

Definition

Myasthenia Gravis (pronounced My-as-theen-ee-a Grav-us) comes from the Greek and Latin words meaning "grave muscular weakness." The most common form of MG is a chronic autoimmune neuromuscular disorder that is characterized by fluctuating weakness of the voluntary muscle groups. The prevalence of MG in the United States is estimated to be about 20/100,000 population. However, MG is probably under diagnosed and the prevalence may be higher. Myasthenia Gravis occurs in all races, both genders, and at any age. MG is not thought to be directly inherited nor is it contagious. It does occasionally occur in more than one member of the same family.

The voluntary muscles of the entire body are controlled by nerve impulses that arise in the brain. These nerve impulses travel down the nerves to the place where the nerves meet the muscle fibers. Nerve fibers do not actually connect with muscle fibers. There is a space between the nerve ending and muscle fiber; this space is called the neuromuscular junction.

When the nerve impulse originating in the brain arrives at the nerve ending, it releases a chemical called acetylcholine. Acetylcholine travels across the space to the muscle fiber side of the neuromuscular junction where it attaches to many receptor sites. The muscle contracts when enough of the receptor sites have been activated by the acetylcholine. In MG, there can be as much as an 80% reduction in the number of these receptor sites. The reduction in the number of receptor sites is caused by an antibody that destroys or blocks the receptor site.

Antibodies are proteins that play an important role in the immune system. They are normally directed at foreign proteins called antigens that attack the body. Such foreign proteins include bacteria and viruses. Antibodies help the body to protect itself from these foreign proteins. For reasons not well understood, the immune system of the person with MG makes antibodies against the receptor sites of the neuromuscular junction. Abnormal antibodies can be measured in the blood of many people with MG. The antibodies destroy the receptor sites more rapidly than the body can replace them. Muscle weakness occurs when acetylcholine cannot activate enough receptor sites at the neuromuscular junction.
Myasthenia Gravis

Common symptoms can include:

A drooping eyelid
Blurred or double vision
Slurred speech
Difficulty chewing and swallowing
Weakness in the arms and legs
Chronic muscle fatigue
Difficulty breathing

Test & Diagnostic methods

In addition to a complete medical and neurological evaluation, a number of tests may be used to establish a diagnosis of MG. A characteristic of MG is that patients have weakness that comes on with activity and improves following rest. To examine for weakness with activity, a clinician might have a patient do a sustained task, such as looking upwards (which induces the eyelids to remain elevated) to see if the eyelids start to droop (referred to clinically as ptosis) when the eyelids are open for several minutes. To test for recovery of strength after rest, a clinician may examine muscle strength and then have the patient suspected to have MG rest or rest a part of the body and then retest muscle strength after rest to see if strength improves. For example if a person who is suspected to have MG has droopy eyelids, the physician might have the patient lay down with his/her eyes closed for several minutes, perhaps with a cool pack over the eyelids, to see if eyelid function improves after rest.

A diagnosis can be confirmed in several ways, including the following:

Acetylcholine Receptor Antibody— a blood test for the abnormal antibodies can be performed to see if they are present. Approximately 85% of MG patients have this antibody and, when detected with an elevated concentration the AChR antibody test is strongly indicative of MG.

Anti-MuSK Antibody testing— a blood test for the remaining 15% of MG patients who have tested negative for the acetylcholine antibody. These patients have seronegative (SN) MG. About 40-70% of patients with SNMG test positive for the anti-MuSK antibody. The remaining patients have unidentified antibodies causing their MG.
Office Tests—Sleep, Ice Pack and Edrophonium tests are examinations performed by specialists to evaluate an improvement in strength that may be consistent with MG.

Electromyography— (EMG) studies can provide support for the diagnosis of MG when characteristic patterns are present. Repetitive Nerve Stimulation is used to check for a pattern of response that is characteristic of MG.

Single Fiber EMG— studies can provide support for the diagnosis of MG when characteristic patterns are present. The single fiber EMG and AChR antibody test are primary tests used to confirm a clinical diagnosis of MG.

Sometimes all of these tests are negative or equivocal in someone whose story and examination still seem to point to a diagnosis of MG. A clinician skilled in recognizing MG and distinguishing MG from other conditions would need to determine if such a patient has MG or another disorder.

**Treatment for MG**

There is no known cure for MG, but there are effective treatments available. Common treatments include medications, thymectomy and plasmapheresis. Spontaneous improvement and even remission may occur without specific therapy.

Medications are most frequently used in treatment. Anticholinesterase agents (e.g., Mestinon®) allow acetylcholine to remain at the neuromuscular junction longer than usual so that more receptor sites can be activated. Corticosteroids (e.g., prednisone) and immunosuppressant agents (e.g., Imuran®) may be used to suppress the abnormal action of the immune system that occurs in MG. Intravenous immunoglobulins (IVIg) are sometimes used to affect the function or production of the abnormal antibodies also.

**Treatment Summary**

No known cure for MG

Effective treatments allow many with MG to lead full lives

Treatment goals are individualized

Thymectomy (surgical removal of the thymus gland) is another treatment used in some patients. The thymus gland lies behind the breastbone and is an important part of the immune system. When there is a tumor of the thymus gland (in 10-15% of patients with MG), it is always removed because of the risk of malignancy. Thymectomy frequently lessens the severity of the
MG weakness after some months. In some people, the weakness may completely disappear. This is called a remission. The degree to which the thymectomy helps varies with each patient.

Plasmapheresis, or plasma exchange, may be useful in the treatment of MG also. This procedure removes the abnormal antibodies from the plasma of the blood. The improvement in muscle strength may be striking, but is usually short-lived, since production of the abnormal antibodies continues. When plasmapheresis is used, it may require repeated exchanges. Plasma exchange may be especially useful during severe MG weakness or prior to surgery.

Treatment decisions are based on knowledge of the natural history of MG in each patient and the predicted response to a specific form of therapy. Treatment goals are individualized according to the severity of the MG weakness, the patient’s age and sex, and the degree of impairment.

**What is the prognosis for those with MG?**

The current treatments for MG are sufficiently effective that the outlook for most patients is bright. Although the treatments will not cure MG, most patients will have improvement in their muscle strength. In some cases, MG may go into remission, during which no treatment is necessary. There is much that can be done, but still much to understand. New drugs to improve treatments are needed. Research plays an important role in finding new answers and treatments for MG.