MG—a chronic immune disease

Myasthenia gravis (MG) is a chronic autoimmune disease. It causes weakness of skeletal muscles and, sometimes, muscles that control our breathing. MG does not affect involuntary muscles, like the heart muscles.

About 36,000 to 60,000 people in the United States have MG. Many doctors think the prevalence may be higher. MG occurs in all ethnic groups and in both genders. It most commonly develops in young women (under 40 years of age) and older men (over 60 years of age). But it can strike at any age.

Causes of MG

MG is caused by faulty transmission of nerve impulses to muscles. Normally, a nerve impulse travels along a nerve cell to a muscle cell. There the nerve ending releases acetylcholine, which binds to receptors on the muscle cell. This causes the muscle fiber to contract. But in MG, antibodies prevent acetylcholine from binding to its receptor. This prevents some muscle fibers from contracting. The result is that only some of the muscle fibers contract when a muscle is functioning. So the muscle gets tired more easily than it should.

Scientists don’t yet understand why some people get MG. It’s not directly inherited but sometimes affects more than one member of the same family.

Symptoms of MG

The hallmark of MG is muscles that become weaker with activity and then improve after rest. In most cases, the first noticeable symptom is weakness of the eye muscles. This manifests as drooping of one or both eyelids and double or blurred vision. Eye symptoms may be intermittent. When eye muscles are the only muscles affected, the condition is called ocular MG. This form accounts for about 15% of people with MG.

The other form, which affects other muscles too, is called generalized MG. In addition to eye symptoms, a person with generalized MG may have:

- An unstable or waddling gait
- A change in facial expression
- Difficulty in chewing or swallowing
- Difficulty breathing

Factors that can worsen MG

These factors can trigger MG symptoms or make them worse:

- Emotional stress
- Illness
- Fatigue
- High fever
- Surgery
- Immunization
- Menstruation
- Some medications (eg, aminoglycosides, ciprofloxacin, chloroquine, procaine, lithium, phenytoin, beta-blockers, procainamide, statins)

Myasthenic crises

The muscles that control breathing can become so weak that a person can’t get enough oxygen. This myasthenic crisis is a medical emergency. A respirator is needed to help the person breathe. These crises can be triggered in people with weak respiratory muscles. Triggers include:

- Infection
- Fever
- Adverse reaction to a medication
• Impaired speech
• Weakness in the arms, hands, fingers, legs, and neck

Although not a symptom, an abnormal thymus is a sign of MG. It is abnormal in 80% to 90% of people with MG. This gland is part of the immune system. It’s thought to produce the antibodies that occur in MG. About 20% of people with MG develop thymomas, tumors of the thymus. These are usually benign, but they can become malignant.

Most people with MG have a normal life expectancy.

Diagnosing MG
Several kinds of tests are used to diagnose MG.

Clinical tests
The ice pack test can be used in people who have a drooping eyelid. In people with weakness of muscles that control eye movement, the rest test can be used. If neither of these tests is positive, an intravenous edrophonium test can be used. This substance inhibits the breakdown of acetylcholine. So it briefly increases its level. This in turn can cause a temporary relief of eye muscle weakness. If any of these tests are positive, nerve conduction and/or antibody tests are needed to confirm a diagnosis.

Nerve conduction tests
Two nerve conduction tests are used. The repetitive nerve stimulation test is used most often. If it’s negative, the single-fiber electromyography (SFEMG) test can be used. It’s more difficult to perform but has greater sensitivity. It’s positive in about 96% of MG cases.

Antibody tests
About 85% of people with generalized MG have antibodies to the acetylcholine receptor (AChR). The presence of these antibodies is diagnostic of MG. But a negative AChR antibody test does not exclude MG. Three kinds of AChR antibodies have been described. They are called binding, blocking, and modulating antibodies. An AChR binding antibody test is used for initial screening. If this test is negative, an AChR modulating antibody test may be helpful to confirm a diagnosis.

Other antibody tests are also useful for diagnosing MG. For example, some MG patients have striational antibodies. They bind to different types of muscle proteins. Some of these antibodies can provide more clinical information and aid in the diagnosis of thymoma. Examples are antibodies to titin and ryanodine receptor.

Other myasthenic syndromes
• Congenital myasthenia is a genetic disease. It begins in childhood and it’s caused by abnormal receptors on muscle cells.
• Neonatal myasthenia affects about 10% to 20% of infants born to women with MG. It’s caused by the mother’s antibodies that cross the placenta. It usually resolves in weeks or months after birth.
• Lambert-Eaton myasthenic syndrome is another autoimmune disease. It’s also caused by antibodies to a molecule at the junction of nerve and muscle cells. 50% to 60% of people with this disease have small-cell-lung carcinoma.
About 40% of people with MG who don’t have AChR antibodies have antibodies to muscle-specific tyrosine kinase (MuSK). People with antibodies to MuSK are much less likely to have a thymoma. A test for MuSK antibody can be used to:

• Help confirm a diagnosis when AChR binding antibody test is negative
• Monitor disease severity

People with similar MG symptoms can have very different AChR antibody levels. So the results of antibody tests for different people with MG can’t be compared. But changes in antibody levels in one person can be meaningful. So these antibody tests are sometimes used to assess disease progression and the response to treatment.

How the laboratory can help
Quest Diagnostics offers tests for binding, blocking, and modulating AChR antibodies. Quest Diagnostics also offers tests for MuSK, striated muscle, and titin* antibodies. The importance of these tests in the diagnosis of MG is increasingly being recognized.

You can find more information about selection and interpretation of antibody tests for MG from the Quest Diagnostics online White Paper.

*Available from Athena Diagnostics, a Quest Diagnostics company.