

# Spotlight on Health

## Myasthenia Gravis

### A Chronic Immune Disease

Myasthenia gravis (MG) is a chronic autoimmune disease. It causes weakness of skeletal muscles and, sometimes, muscles that control breathing. MG does not affect involuntary muscles, such as the heart muscles. About 60,000 people in the United States have MG.<sup>1</sup> Many doctors think that the prevalence may be higher. MG occurs in all ethnic groups and in both genders. It most commonly develops in women younger than 40 and men older than 60 years of age.<sup>2</sup> But it can strike at any age. MG is not directly inherited but sometimes affects more than one member of the same family. Most people with MG have a normal life expectancy.

### Causes of MG<sup>3</sup>

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.

### 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.<sup>3</sup>

The other form, which affects other muscles too, is called generalized MG. In addition to eye symptoms, a person with generalized MG may have<sup>4</sup>:

- An unstable or waddling gait
- A change in facial expression
- Difficulty in chewing or swallowing
- Difficulty breathing
- Impaired speech
- Weakness in the arms, hands, fingers, legs, and neck



### 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)

Although not a symptom, an abnormal thymus is a sign of MG. This gland is part of the immune system. It's thought to produce the antibodies that occur in MG. About 10% of people with MG develop thymomas, tumors of the thymus; the prevalence increases with age.<sup>3</sup> These thymomas are usually benign but can become malignant.

## Diagnosing MG

Clinical manifestations of MG can vary. Relevant signs, symptoms, and tests are used to diagnose MG. Different antibody tests are used to confirm diagnosis, and help divide MG into subgroups.

## Clinical Tests

The ice pack test can be used for people who have a drooping eyelid. The rest test can be used for people with weakness of the muscles that control eye movement. If neither of these tests is positive, an intravenous edrophonium test can be used.<sup>2</sup> This substance causes brief increases in levels of acetylcholine by inhibiting its breakdown. If a patient's eye-muscle weakness improves, this indicates a positive test result. 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 is negative, the single-fiber electromyography (SFEMG) test can be used. The SFEMG test is more difficult to perform but has greater sensitivity; it is positive in about 96% of MG patients.<sup>5</sup>

## Antibody Tests

About 85% of people with generalized MG have antibodies to the acetylcholine receptor (AChR).<sup>6</sup> The presence of these antibodies is diagnostic of MG. But a negative AChR antibody test does not exclude MG. Other antibody tests are also useful for diagnosing MG. For example, some MG patients have striational antibodies.<sup>2</sup> The presence of some of these antibodies can provide more clinical information and aid in the diagnosis of thymoma.<sup>8</sup> Examples are antibodies to titin and ryanodine receptor.

About 40% of people with MG who don't have AChR antibodies have antibodies to muscle-specific tyrosine kinase (MuSK).<sup>2</sup> 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 an AChR-binding antibody test is negative. It can also be used to monitor disease severity.

Lipoprotein receptor-related protein 4 (LRP4) antibodies are found in up to 50% of patients who are negative for both AChR and MuSK antibodies.<sup>7</sup> People with LRP4 antibodies have a mild form of MG.

## Myasthenic Crises

The muscles that control breathing can become so weak that a person can't get enough oxygen. A 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 medication

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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 also offers tests for MuSK, LRP4, striated muscle, and titin\* antibodies. The importance of these tests in the diagnosis of MG is increasingly being recognized.<sup>4</sup> You can find more information about selection and interpretation of antibody tests for MG from the Quest Diagnostics online white paper, [Myasthenia Gravis and Autoantibodies](#).

\*These tests are available from Athena Diagnostics, a Quest Diagnostics company.

## References

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