



Myasthenia Gravis

Myasthenia gravis (MG) is a disorder characterized by weakness. The weakness can involve the leg muscles and swallow tube (esophagus) of the body **generalized form** or selectively involve the muscles of the face and swallow tube in the **regional form** of the disease. MG may be present at birth, **congenital**, or develop after birth in the **acquired** form of the disease.

Muscles function by contracting when stimulated by nerves, resulting in the movement of bones they are attached to. Individual muscle cells, **myofibers**, are dependent upon the nerves to stimulate them to contract. Nerves supply this stimulation by converting their electrical impulses into chemical transmission. A specialized gap, or junction (**neuromuscular junction**) separates the nerve ending from the muscle membrane. To allow electrical transmission to reach the muscle membrane, a small amino acid complex, **neurotransmitter**, produced in the nerve ending is released and acts as a **messenger** in transmitting the stimulating impulse from the nerve to the muscle. The neurotransmitter called **acetylcholine**, binds to specialized regions of the muscle membrane called **acetylcholine receptors** (Ach-R). If enough Ach-R bindings occur, the muscle will depolarize and the muscle will contract causing movement.

Etiology

Congenital MG is a genetic condition characterized by a lack of Ach-R. Acquired MG is an autoimmune disease where defense products (**antibodies**) are produced against the acetylcholine receptors of the muscle after birth, resulting in destruction and loss of many of the Ach-receptors. The end result with both forms of this disease is a lack of Ach-R for Ach to bind to, and muscle weakness.

Clinical Signs

The clinical signs your pet can experience with the generalized form of MG may include muscle stiffness when trying to walk, leg weakness characterized by shortening of the steps, buckling of the limbs, followed by collapse. Facial expression change (droopy lips) or weakness of the swallow tube (regurgitation of food or water) may be present, with or without leg weakness in the regional form of myasthenia gravis. Because the esophagus in dogs and cats is made up of the same type of muscle and requires the same neurotransmitter, Ach, weakness of the swallow tube can result in progressive hypomotility and enlargement of the esophagus (megaesophagus) and regurgitation (passive flow of ingested food and water from the esophagus).

While the signs of Myasthenia gravis are characterized by weakness, which is associated with exercise and resolves with rest, **Myasthenic crisis** is a form of MG where acute, generalized muscle failure results in collapse, and which does not improve with rest. While this form of the disease is unusual, it represents a life threatening neurologic emergency because it can result in respiratory failure and death if not treated immediately.

Diagnosis

The diagnosis of myasthenia gravis may involve a combination of test procedures, dependent upon the clinical picture and history your dog or cat provides. The diagnosis of congenital myasthenia gravis is based upon proving your pet has insufficient Ach-receptors to receive the neurotransmitter. Special stains are used to demonstrate the Ach-R for quantification in biopsied intercostal (between the ribs) muscle. Identification of the antibody toward the Ach-R in your pet's serum (blood component) is felt to be gold standard in diagnosing the acquired form of MG at this time. It is positive in over 98% of the acquired cases. While this is good, it leaves 2% of the acquired cases, congenital and regional MG patients without a simple diagnostic means.

Edrophonium hydrochloride is a pharmaceutical compound that inhibits the action of the enzyme **acetyl cholinesterase**, responsible for the digestion of the neurotransmitter Ach. When given intravenously, the bound Ach neurotransmitter is able to remain bound to the reduced number of Ach-receptors and maintain muscle strength and function for 3-5 minutes. The pet that is unable to walk when fatigued will immediately stand and walk without weakness. While this test is less specific (there are false positive results) than the Ach-R antibody test, rapid diagnosis and therapeutic intervention may mean the difference in success in the treatment of this disorder.

Electrodiagnostic testing using repetitive nerve stimulation, single fiber electromyography and muscle/nerve biopsy may be employed in certain cases based upon the neurologist's decision. This will be discussed with you if our neurologists feel it is necessary in the diagnosis and treatment of your pet.

Treatment

Therapy of MG is dependent upon prolonging the actions of the neurotransmitter Ach and reducing or stopping the production of antibody against the Ach-receptor. Pyridostigmine hydrochloride (Mestinon) is the most common medication used to prolong the actions of Ach. It is utilized on a two to three times a day schedule. Side effects can include salivation, diarrhea, slow heart rate, trembling and rarely weakness. If these signs are seen, the neurologist should be contacted immediately.

Immunosuppressive agents are utilized to stop the production of Ach-R antibodies by the bodies defense system in the acquired form of MG. This will allow the Ach-R numbers to increase and maintain strength and function. Prednisone and Dexamethasone are glucocorticoids that are often used alone, or in conjunction with Azathioprine and Cyclosporine for long-term control of the immune production of antibodies.

It is essential to work with your neurologist and family veterinarian in the management of your pet's condition. Evidence of weakness, coughing, difficulty breathing and regurgitation are reasons for concern. Please do not delay medical assistance if needed.