MYASTHENIA GRAVIS

[Grave Muscle Disease]

DR JANET LALONDE DVM

SUNSHINE A TWO YEAR OLD Saluki bitch raced to the finish catching the lure. She happily shook the prize claiming it as her own. Sunshine had been awarded four Best in Field titles while competing in seven events during the year. As a two year old, she was promising on the coursing field and equally exciting in the conformation ring. Sunshine loved to run. There was no need for prompting or encouragement to follow the lure. Sunshine would lunge at the end of her lead, bark and cry frantically at the whine of the cord dragging the lure. When released from the post her grace, symmetry and speed mesmorised the audience. She truly portrayed her heritage; a swift desert hound used by the Bedouin to hunt gazelle and hare as food for the tribe.

2 Shortly after the trial Sunshine missed two months of events caused by the onset of her heat cycle and at the same time also lost her voice. Her voice later returned however a *'hoarse'* bark and an occasional gagging cough that was unresponsive to medical therapy persisted. Sunshine was entered in a trial in October. She ran the course well but after the race when walking back to her owner's trailer something appeared to be wrong. She began to stagger and tremble. Electrolyte and blood sugar imbalance subsequent to the race was suspected and she was given oral electrolytes. She appeared to make a full recovery. She was pulled from the next day's race but was taken for a 20 minute walk. The same symptoms returned including a generalised *'fatigue.'*

3 Sunshine returned home and went through extensive testing including blood chemistry profiles, ECGs and X-Rays. All test results were normal. There was no apparent reason for Sunshine's symptoms. Over the next few months Sunshine rested, ate normally and did not show any of the symptoms seen at the trial until early February of the following year. Signs of trembling, general discomfort, tensing of the abdomen and poor eating habits began to emerge.

4 Sunshine maintained a cough and when encouraged to run up and down the driveway for a five minute period would lapse into a stilted goose stepping gait. Stiffness was exhibited in the front legs and she was in respiratory distress. She then collapsed. The diagnostic tests were repeated and again found to be normal. After a sufficient rest period Sunshine was injected with Neostigmine and put through her paces again. This time there were no signs of fatigue or collapse. Sunshine was diagnosed to be suffering from acquired Myasthenia Gravis, a skeletal muscle disorder.

Acquired Myasthenia

5 Acquired Myasthenia Gravis is an immune mediated disorder. Antibodies are produced and directed against acetylcholine receptors of the neuromuscular junction. This in turn results in a deficiency of functional acetylcholine receptors which receive the chemical stimulant [acetylcholine] for muscle contraction. The cause of the immune disturbance is unknown.

Anatomy

6 Skeletal muscle is comprised of bundles of *muscle fibres*. The muscle fibres consist of muscle cells known as *myofibrils*. The nerve together with the muscle fibres that it innervates are called a *motor unit*. There is a specialised region at the junction of the nerve onto skeletal muscle fibres which is called the *motor end plate*. The nerve branches allowing the branches to occupy recesses in the surface of the muscle fibre called *synaptic troughs*. Within the nerve endplates there are vesicles which store a neurotransmitter substance called acetylcholine. The receiving muscle fibre endplate has receptors which accept the *acetylcholine* and vesicles which store an enzyme [*acetylcholinesterase*].

Physiology

7 The voluntary contraction of skeletal muscle must follow a series of nerve and muscle pathways. The brain sends a message via the spinal cord to a nerve trunk which splits off from the cord as a rootlet known as a *spinal nerve*. The spinal nerve relays the message to the limb as part of a specific *peripheral nerve*, which is distributed to a specific group of muscles.

8 The peripheral nerve branches once it reaches the muscle cells allowing the axonal branches to end on a muscle cell at a motor end plate. The axonal nerve ending processes the message so that acetylcholine is released from the vesicles. This chemical traverses the synaptic trough and is received by specialised receptors on the muscle cell. The receptors upon receiving acetylcholine trigger an electric change which causes the muscle fibre to contract. The enzyme acetylcholinesterase is then released to digest the acetylcholine removing the stimulus which causes the contraction.

Dr Janet Lalonde

Pathophysiology

9 Acquired Myasthenia Gravis is a disorder where there is an interruption in the neuromuscular transmission. Proteins in the form of antibodies, specifically IgG are produced and directed against acetylcholine receptors on the muscle cell. The coating of these receptors makes them non-functional as they are unable to receive the acetylcholine released by the nerve axon. Clinical symptoms in dogs are muscle weakness that is exacerbated by exercise, varying degrees of lameness, collapse, tremors, regurgitation, drooling and megaesophagus.

Diagnosis

10 Diagnosis is based on clinical signs, serologic blood testing for autoantibodies and dramatic improvement of clinical symptoms following the injection of a short actina anticholinesterase such as neostigmine methylsulphate [Neostigmine] or edrophonium hydrochloride [Tensilon]. These drugs are short acting and inhibit the enzyme cholinesterase at the neuromuscular junction. Neurologic examination of dogs with Myasthenia Gravis is usually normal.

Treatment

11 The prognosis for successful and long term treatment is guarded. Medical therapy usually entails a trial and error approach. Long-acting anticholinesterase drugs such as pyridostigmine bromide [Mestinon] are used to minimise muscular weakness. This drug only provides symptomatic relief of the symptoms and has no effect on the underlying immunologic dysfunction. Mestinon acts primarily by inhibiting the effects of cholinesterase and its duration of effect is much longer than Tensilon or Neostigmine. Immunosuppressive therapy involving the use of corticosteroids is often combined with Mestinon to control the disorder.

5 Acquired Myasthenia Gravis is an immune mediated disorder. Antibodies are produced and directed against acetylcholine receptors of the neuromuscular junction. This in turn results in a deficiency of functional acetylcholine receptors which receive the chemical stimulant [*acetylcholine*] for muscle contraction. The cause of the immune disturbance is unknown.

Anatomy

6 Skeletal muscle is comprised of bundles of *muscle fibres*. The muscle fibres consist of muscle cells known as *myofibrils*. The nerve together with the muscle fibres that it innervates are called a *motor unit*. There is a specialised region at the junction of the nerve onto skeletal muscle fibres which is called the *motor end plate*. The nerve branches allowing the branches to occupy recesses in the surface of the muscle fibre called *synaptic troughs*. Within the nerve endplates there are vesicles which store a neurotransmitter substance called acetylcholine. The receiving muscle fibre endplate has receptors which accept the *acetylcholine* and vesicles which store an enzyme [*acetylcholinesterase*].

Physiology

7 The voluntary contraction of skeletal muscle must follow a series of nerve and muscle pathways. The brain sends a message via the spinal cord to a nerve trunk which splits off from the cord as a rootlet known as a *spinal nerve*. The spinal nerve relays the message to the limb as part of a specific *peripheral nerve*, which is distributed to a specific group of muscles.

8 The peripheral nerve branches once it reaches the muscle cells allowing the axonal branches to end on a muscle cell at a motor end plate. The axonal nerve ending processes the message so that acetylcholine is released from the vesicles. This chemical traverses the synaptic trough and is received by specialised receptors on the muscle cell. The receptors upon receiving acetylcholine trigger an electric change which causes the muscle fibre to contract. The enzyme acetylcholinesterase is then released to digest the acetylcholine removing the stimulus which causes the contraction.

Dr Janet Lalonde

Pathophysiology

9 Acquired Myasthenia Gravis is a disorder where there is an interruption in the neuromuscular transmission. Proteins in the form of antibodies, specifically IgG are produced and directed against acetylcholine receptors on the muscle cell. The coating of these receptors makes them non-functional as they are unable to receive the acetylcholine released by the nerve axon. Clinical symptoms in dogs are muscle weakness that is exacerbated by exercise, varying degrees of lameness, collapse, tremors, regurgitation, drooling and megaesophagus.

Diagnosis

10 Diagnosis is based on clinical signs, serologic blood testing for autoantibodies and dramatic improvement of clinical symptoms following the injection of a short actina anticholinesterase such as neostigmine methylsulphate [Neostigmine] or edrophonium hydrochloride [Tensilon]. These drugs are short acting and inhibit the enzyme cholinesterase at the neuromuscular junction. Neurologic examination of dogs with Myasthenia Gravis is usually normal.

Treatment

11 The prognosis for successful and long term treatment is guarded. Medical therapy usually entails a trial and error approach. Long-acting anticholinesterase drugs such as pyridostigmine bromide [Mestinon] are used to minimise muscular weakness. This drug only provides symptomatic relief of the symptoms and has no effect on the underlying immunologic dysfunction. Mestinon acts primarily by inhibiting the effects of cholinesterase and its duration of effect is much longer than Tensilon or Neostigmine. Immunosuppressive therapy involving the use of corticosteroids is often combined with Mestinon to control the disorder.