

Exercise Induced Collapse

A syndrome of exercise intolerance and collapse (EIC) has been recognized in young adult Labrador Retrievers.

A comprehensive study of this condition is underway involving collaborators from the Western College of Veterinary Medicine (WCVM) of the University of Saskatchewan, the College of Veterinary Medicine at the University of Minnesota and the Comparative Neuromuscular Unit at the University of California. The objectives of this study are to (1) describe the syndrome so that it can be recognized by dog owners, veterinarians and trainers, (2) to thoroughly evaluate affected dogs to try to establish an efficient means of diagnosis and to gain some insight into the cause of the collapse and (3) to determine the genetic basis for the collapse syndrome. This research is being supported by generous grants from the Morris Animal Foundation and the WCVM's Companion Animal Health Fund.

The following is a summary of some of what we have learned in the last 5 years about the syndrome of Exercise Induced Collapse in Labrador Retrievers:

WHO GETS IT?

The syndrome of exercise intolerance and collapse (EIC) is being observed with increasing frequency in young adult Labrador Retrievers. Most, but not all, affected dogs have been from field-trial breedings. Black, yellow and chocolate Labradors of both sexes are affected, with the distribution of colors and sexes closely reflecting the typical distribution in field trials (black males most common). Signs become apparent in young dogs as they encounter heavy training or strenuous activity - usually between 5 months and 3 years of age (average 14 months). In dogs used for field trials, this usually coincides with the age at which they enter heavy training. Littermates and other related dogs are commonly affected but depending on their temperament and lifestyle may or may not manifest symptoms. Affected dogs exhibiting symptoms of collapse are usually described as being extremely fit, muscular, prime athletic specimens of their breed with an excitable temperament and lots of drive.

DESCRIPTION OF COLLAPSE

Affected dogs can tolerate mild to moderate exercise, but 5 to 20 minutes of strenuous exercise with excitement induces weakness and then collapse. Severely affected dogs may collapse whenever they are exercised to this extent - other dogs only exhibit collapse sporadically and all of the factors important in inducing an episode have not yet been well established.

The first thing noted is usually a rocking or forced gait. The rear limbs then become weak and unable to support weight. Many affected dogs will continue to run while dragging their back legs. Some of the dogs appear to be uncoordinated, especially in the rear limbs, with a wide-based, long stride rather than the short, stiff strides typically associated with muscle weakness. In some dogs the rear limb collapse progresses to forelimb weakness and occasionally to a total inability to move. Some dogs appear to have

a loss of balance and may fall over, particularly as they recover from collapse. Most collapsed dogs are totally conscious and alert, still trying to run and retrieve but as many as 25% of affected dogs will appear stunned or disoriented during the episode.

It is common for the symptoms to worsen for 3 to 5 minutes even after exercise has been terminated. NOTE: A few affected dogs have died during exercise or while resting immediately after an episode of exercise-induced collapse so an affected dog's exercise should ALWAYS be stopped at the first hint of incoordination or wobbliness

Most dogs recover quickly and are usually normal within 5 to 25 minutes with no residual weakness or stiffness. Dogs are not painful during the collapse or after recovery. Massage of the muscles or palpation of the joints or spine is not uncomfortable. Affected dogs are not stiff or sore or limping upon recovery.

Body Temperature

Body temperature is normal at rest in dogs with EIC but is almost always dramatically increased at the time of collapse (temperature >41.5 C, >107.6F). We have shown experimentally, however, that clinically normal Labrador Retrievers doing this type of exercise for 10 minutes routinely had similar dramatic elevations in body temperature yet exhibited no signs of weakness, collapse or disorientation. Dogs with EIC will pant hard during the time of collapse, in an attempt to cool off, but this is similar to normal dogs exercised in the same manner. The time it takes for dogs with EIC to return to their resting temperature after exercise is not different from normal dogs. Although temperature may play some role in EIC, and may contribute to the death of some affected dogs, inability to properly regulate temperature does not appear to be the underlying problem in dogs with EIC.

FACTORS CONTRIBUTING TO COLLAPSE IN DOGS WITH EIC

Ambient Temperature. Actual ambient temperature does not seem to be a critical factor contributing to collapse, but if the temperature is much warmer or the humidity is much higher than what the dog is accustomed to, collapse may be more likely. Affected dogs are less likely to collapse while swimming than when being exercised on land. There are dogs, however, who have exhibited collapse while breaking ice retrieving waterfowl in frigid temperatures and there are dogs who have drowned when experiencing EIC-related collapse in the water.

Excitement. Dogs that exhibit the symptoms of EIC are most likely to have intense, excitable personalities, and it is apparent that their level of excitement plays a role in inducing the collapse. There are some severely affected dogs who, if they are very excited, do not require much exercise to induce the collapse. Dogs with EIC are most likely to collapse when engaging in activities that they find very exciting or stressful. This can include retrieving of live birds, participation in field trials, training drills with electric collar pressure and quartering for upland game.

Type of Exercise. Routine exercise like jogging, hiking, swimming, most waterfowl hunting and even

agility or flyball training are not very likely to induce an episode in dogs with EIC. Activities with continuous intense exercise, particularly if accompanied by a high level of excitement or anxiety most commonly cause collapse. Activities commonly implicated include grouse or pheasant hunting, repetitive "happy retrieves", retrieving drills or repetition of difficult marks or blinds where the dog is being repeatedly corrected or is anticipating collar correction, and running alongside an ATV.

VETERINARY EVALUATION OF AFFECTED DOGS/DIAGNOSIS

Twenty affected dogs have undergone extensive testing before and after exercise at the WCVU. Nervous system, cardiovascular and musculoskeletal examinations are unremarkable in dogs with EIC as is routine blood analysis at rest and during an episode of collapse. These dogs do not experience heart rhythm abnormalities, low blood sugar, electrolyte disturbances or respiratory difficulty that could explain their collapse. Body temperature is remarkably elevated during collapse (average 107.1F, many up to 108F), but this has been found in normal exercise-tolerant Labradors as well. Affected dogs hyperventilate and experience dramatic alterations in their blood carbon dioxide concentration (decreased) and their blood pH (increased) but these changes were also observed in the normal exercising dogs. Testing for the neuromuscular disorder myasthenia gravis is negative. Thyroid gland function and adrenal gland cortisol production appear to be normal. Affected dogs are negative for the genetic mutation known to cause malignant hyperthermia in dogs (a different muscle disorder). Metabolic testing of blood and muscle from affected dogs before and after exercise suggests that these dogs may have a defect in the chemical reactions necessary for energy production in their muscles and in their brain. The precise defect has not been identified and the changes are mild and not conclusive. Further investigation is ongoing.

At this time (until we develop a genetic test) EIC can only be diagnosed by ruling out all other muscle disorders and by observing characteristic clinical features, history and laboratory test results in affected dogs. Any dog with exercise intolerance should always have a complete veterinary evaluation to rule-out joint diseases, heart failure, anemia, heart rhythm disturbances, respiratory problems, low blood sugar, myasthenia gravis, hypoadrenocorticism (low cortisol), other muscle diseases and other systemic disorders.

LONG TERM OUTLOOK

Symptomatic dogs are rarely able to continue training or competition. It seems that if affected dogs are removed from training and not exercised excessively the condition will not progress and they will be fine as pets. They are able to continue to live pretty normal lives, if owners limit their intense exercise and excitement. Many dogs will seem to "get better" as they age and slow down their activity and their excitement level. It is important that owners of dogs with EIC be made aware that the dog's exercise should be stopped at the first hint of incoordination or wobbliness as some affected dogs have died during collapse when their owners allowed or encouraged continuing exercise. Not all of the EIC deaths have occurred in dogs rated as severely affected based on their number of episodes of collapse or the amount of activity required to induce an episode.

TREATMENT

As the actual biochemical defect underlying EIC is still unknown, it is difficult to recommend an effective treatment. Owners of some affected dogs have reported that if they feed their dogs a higher fat diet and/or keep more weight on their dog, that the episodes may be more difficult to induce. The best treatment in most dogs consists of avoiding intensive exercise in conjunction with extreme excitement and ending exercise at the first sign of weakness/wobbliness. A few dogs have, however, responded to medical treatment to the degree that they can re-enter training and competition at a high level. Each of the treatments listed below has been effective in a few dogs, but none of them has been 100% effective in all dogs.

Treatment as a metabolic myopathy

There is some biochemical evidence that EIC may be caused by a defect in oxidative metabolism within the brain and muscle. This means that dogs with EIC could be deficient in a substance needed for normal energy production in these tissues. Carnitine is a compound normally found in high concentrations in muscle and brain that is necessary for transport of fatty acids into the mitochondria for energy production in these tissues. We have found that approximately 30% of dogs with EIC have lower than normal levels of muscle carnitine. A few affected dogs have had a positive clinical response to oral supplementation with carnitine (50mg/kg 2X/day), CoEnzyme Q10 (100mg/day) and Riboflavin (100 mg/day) - a standard cocktail for metabolic myopathies/neuropathies.

Treatment with 7-KETO

There is anecdotal evidence that a number of severely affected dogs have responded positively to a nutraceutical called 7-KETO. This is a breakdown product of the hormone dehydroepiandrosterone (DHEA), a steroid made by the adrenal glands and brain. The dosage used has been 100 mg twice each day. The precise mechanism of action of 7-KETO in affected dogs is unknown, but it has demonstrated positive effects on energy production in the muscle and brain as well as acting as a neuroactive steroid, with effects on several neurotransmitter receptors in the brain.

Treatment with Phenobarbital

There are now numerous reports of quite a few severely affected dogs improving when they were treated with Phenobarbital (2 mg/kg every 12 hours). This drug is an anti-seizure medication commonly used to treat dogs with epilepsy. Phenobarbital decreases the intrinsic excitability of brain cells and decreases the spread of abnormal electrical discharges in the brain. The mechanism underlying its effectiveness in dogs with EIC is uncertain but is under investigation.

HEREDITY

Littermates and other related dogs are commonly affected, suggesting that EIC is hereditary. Clinically unaffected dams and sires commonly produce litters with more than one affected dog, suggesting either an autosomal recessive mode of inheritance (must be inherited from both parents) or inheritance as a dominant trait with incomplete penetrance (can be inherited from just one parent). A few clinically unaffected males have sired many puppies with EIC when bred to different bitches. Pedigree analysis of greater than 150 affected dogs is underway in an attempt to more precisely determine the mode of inheritance.

Major difficulty currently exists in classifying individual dogs as definitively affected or unaffected by EIC. Some dogs may have the genetic makeup and metabolic abnormalities underlying EIC, yet they never collapse because they are not asked to perform strenuous exercise or they may perform the exercise without the mix of enthusiasm and excitement necessary to induce collapse. We will not be able to identify these dogs as being affected by EIC until there is a simple, specific test genetic for the condition.

DNA harvested from the blood of affected dogs and their relatives is currently being used to perform a full genome scan at the University of Minnesota in order to identify a genetic marker for EIC, and find the genetic mutation causing EIC. This is a slow and tedious process. Once the affected gene is identified, we will be able to use DNA testing to identify dogs that carry this gene as well as to identify dogs that are affected before they start to show clinical signs. A genetic test would allow veterinarians to definitively diagnose the condition using a simple blood test. As well, breeders could test their breeding stock to identify affected dogs and carriers. The test could also be used to test litters of puppies - obviously affected dogs should not be sold into working homes and known carriers should not be bred.

In order for the genome scan to be successful, large numbers of samples must be collected from affected dogs and their affected and unaffected relatives. The most useful families for molecular genetic analysis are those for which we have DNA samples from multiple closely related affected dogs (siblings or half-siblings) and their parents. Many more samples are needed to ensure the success of this study.

HOW CAN YOU HELP?

We have completed our experimental part of this research study and we are currently in the data analysis stage and we are preparing the results for scientific publication. We are, however, still very interested in obtaining pedigrees and blood samples (to help us with our DNA analysis) from affected dogs and their relatives (whether the relatives are affected or unaffected).

Dogs enrolled in this portion of the study should have had at least 3 episodes of collapse with exercise/excitement. It is very important that we not include in this portion of the study dogs that do not really have EIC (ie they have some other reason for the collapse). All dogs enrolled in this portion of the study should therefore have had a full veterinary evaluation to rule out other causes of collapse. This should include:

Physical examination: normal (no muscle atrophy or pain in back, joints or muscles)

Neurologic examination: normal (normal gait and reflexes)

Cardiovascular auscultation, ECG, thoracic radiographs and cardiac ultrasound: normal

Hematologic and biochemical evaluation of blood : normal

ACTH Stimulation test (to rule out hypoadrenocorticism): normal

If you have a dog who meets these criteria and appears to have collapse with exercise/excitement that fits the description of EIC, please contact:

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