

# Exercise-Induced Collapse of Labrador Retrievers: Survey Results and Preliminary Investigation of Heritability

Completed surveys were obtained from owners of 225 Labrador retrievers affected by the syndrome of exercise-induced collapse. Questions addressed signalment, age of onset, description of collapse episodes, and owner perception of activities and factors associated with collapse. Most dogs were young (mean 12 months) when collapse episodes began. Retrieving was the activity most commonly associated with collapse. Owners felt that excitement (187/225; 83%) and high environmental temperatures (71/225; 31%) increased the likelihood of collapse. Analysis of pedigrees collected from 169 affected dogs was most consistent with an autosomal recessive mode of inheritance. *J Am Anim Hosp Assoc* 2008;44:295-301.

Susan M. Taylor, DVM,  
Diplomate ACVIM (Internal Medicine)

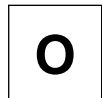
Cindy L. Shmon, DVM, DVSc,  
Diplomate ACVS (Surgery)

G. Diane Shelton, DVM, PhD,  
Diplomate ACVIM (Internal Medicine)

Edward (Ned) E. Patterson, DVM,  
PhD, Diplomate ACVIM  
(Internal Medicine)

Katie Minor, BS

James R. Mickelson, PhD



From the Department of Small Animal  
Clinical Sciences (Taylor, Shmon),  
Western College of Veterinary Medicine,  
University of Saskatchewan, Saskatoon,  
Saskatchewan S7N 5B4 Canada;  
the Comparative Neuromuscular Laboratory  
(Shelton), Department of Pathology,  
School of Medicine,  
University of California-San Diego,  
La Jolla, California 92093-0709;  
and the Departments of Veterinary  
Clinical Sciences (Patterson) and  
Biomedical Sciences (Minor, Mickelson),  
College of Veterinary Medicine,  
University of Minnesota,  
St. Paul, Minnesota 55108.

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## Introduction

A syndrome of exercise intolerance and collapse in young adult Labrador retrievers was first described in the veterinary literature in 1993.<sup>1</sup> Elevated rectal temperatures and increased plasma lactate concentrations after exercise, and normal findings on examination of muscle biopsies were documented in a few affected dogs.<sup>1</sup> Recently this syndrome has been shown to be an important cause of exercise intolerance, interfering with performance in otherwise healthy, young adult, competitive field trial and hunting Labrador retrievers.<sup>2-4</sup> Veterinarians evaluating affected dogs have attributed collapse to heat intolerance, hypoglycemia, a cardiac rhythm disturbance, or a possible metabolic myopathy, but no consistent abnormalities have been identified in affected dogs.<sup>1-4</sup> The syndrome has come to be called exercise-induced collapse (EIC) of Labrador retrievers.<sup>4,5</sup> Affected dogs sometimes develop an abnormal gait or collapse when subjected to strenuous exercise, but factors important in inducing episodes of collapse have not been well established.

This study reports results of surveys completed by owners of 225 Labrador retrievers with presumed EIC. Also presented are preliminary results of an investigation into the heritability of this condition. This is the first large-scale descriptive study of EIC, providing veterinarians with the information needed to recognize the syndrome and make informed decisions regarding management and prognosis of affected dogs.

## Materials and Methods

### *Descriptive Study*

A survey was developed to obtain demographic and descriptive clinical histories on dogs with presumed EIC [see Appendix]. The survey was distributed to owners of Labrador retrievers with a collapse syndrome determined by their veterinarian to most likely be EIC. Owners were identified when they contacted investigators after learning about the study through their veterinarian or magazine articles targeting owners of working retrievers.<sup>2,3</sup> Between the years of 2000 and 2006, 361 owner-completed surveys were received.

In order to be included in the descriptive study, dogs had to meet three criteria: (1) be a purebred Labrador retriever registered with the Canadian Kennel Club (CKC) or American Kennel Club (AKC); (2)

have experienced at least three observed episodes of exercise-induced collapse; and (3) veterinary evaluation must have ruled out commonly recognized systemic and cardiac causes of collapse. Minimum requirements for veterinary evaluation included physical and neurological examinations, complete blood count and serum biochemical profile, and thoracic radiographs. Normal results were reported for some dogs on additional tests including electrocardiograms, cardiac echocardiography, adrenocorticotropic hormone stimulation tests, and muscle biopsies. Completed surveys were obtained from 223 owners describing 225 dogs meeting all of these criteria, and those results were tabulated and analyzed. Descriptive statistics were calculated and are reported as median and minimum and maximum values for all data.

### Heritability

Pedigrees and whole blood were collected from 169 affected Labradors and 157 unaffected, related dogs. Affected dogs were determined by their veterinarians to have EIC based on at least two episodes of collapse or incoordination typical of EIC and failure to identify a systemic, cardiac, or neurological reason for the collapse. Many of these affected dogs had at least three episodes of collapse, so they qualified for and participated in the descriptive study as well. Dogs were considered unaffected if they had never experienced weakness or collapse in spite of rigorous field training. Pedigrees were assembled for analysis using Pedigraph software,<sup>3</sup> and they were examined for evidence of heritability.<sup>6,7</sup>

## Results

### Descriptive Study

Completed surveys were obtained from the owners of 225 Labrador retrievers that met the study criteria [see Appendix]. Male (53.8%) and female (46.7%) dogs were approximately equally represented, and all of the dogs were sexually intact when their episodes of collapse began. Black (53.8%), yellow (36.9%), and chocolate (9.3%) dogs were affected. Age at the first episode of collapse ranged from 5 to 60 months (median 12 months). When asked to comment on their dog's body condition, level of fitness, and temperament, all owners reported that their dogs were in good physical condition; dogs were commonly described as extremely fit, muscular, and excitable.

Dogs had experienced from three to 34 (a median of five) observed episodes of collapse at the time the survey was completed. Twenty-two (10%) dogs had experienced >25 episodes. Seven (3%) of the dogs for which surveys were completed had died during their last episode of collapse; these dogs had experienced three to 10 (a median of four) previous episodes of collapse. Three of the seven dogs that died during collapse were observed to experience what the owners reported as a short, generalized seizure just before death.

Owners described in their own words the clinical findings during each collapse episode, and they completed

checklists [Table 1]. Most (78%) owners reported that their dog's rear legs were floppy and unable to support weight during episodes and that many continued to run while dragging their rear legs. A wobbly, incoordinated, base-wide or "loose" gait was described in 135 (60%) dogs. Although rear limbs alone were most often affected, all four limbs were abnormal during at least one episode of collapse in 18% of dogs. Staggering and falling to the side or difficulty maintaining balance was reported in 68% of the dogs during at least one episode, but no head tilt or nystagmus was noted.

When dogs were recumbent during an episode, 18% of owners noticed forelimb extensor rigidity. Most (77%) dogs were reported by their owners to be mentally normal during every episode, but 52 (23%) dogs had experienced one or more episodes where the owners felt they lost concentration or appeared dazed or confused. Excessive or loud panting was noted during at least one episode in 43 (19%) dogs, and an abnormally enlarged tongue and ropey saliva were reported in 18 (8%) dogs. Seven (3%) dogs experienced a short, generalized seizure during a single episode of collapse, and three of these dogs died. Body temperature was measured during at least one episode of collapse in 82 dogs and ranged from 39.4°C to 42.8°C (median 41.1°C). Owners described recoveries from episodes as gradual, with the time required for return to a normal gait estimated at 5 to 45 minutes (median 10 minutes).

Activities most often associated with collapse are presented in Table 2. Not all dogs participated in all activities listed, making it impossible to assess the comparative risk associated with each activity. Commonly cited trigger activities included hand-thrown "fun" retrieves of balls, toys, or

**Table 1**

**Owner Description of Collapse Episodes in 225 Labrador Retrievers With Exercise-Induced Collapse**

Description	% of Dogs
Rear limbs floppy/dragged	78
Wobbly, incoordinated	60
Falling to side/balance problem $\geq 1$ episode	68
Rear limbs only affected	82
All four limbs affected $\geq 1$ episode	18
Forelimb rigidity $\geq 1$ episode	18
Dazed/disoriented $\geq 1$ episode	23
Loud/excessive panting $\geq 1$ episode	19
Generalized seizure during 1 episode	3

**Table 2**

Owner-Reported Activities Associated With Collapse in 225 Labrador Retrievers With Exercise-Induced Collapse

Activity	% of Dogs
Fun retrieves	46
Training retrieves on land	43
Upland hunting (pheasant, dove, quail)	25
Excited play with other dogs	22
Training retrieves in water	12
Waterfowl hunting	2

bumpers (a soft, plastic tube or retrieving dummy), especially in competition with other dogs; retrieving bumpers or birds on land as part of a training exercise or field trial; excited play with other dogs; and hunting on land for pheasant, dove, or quail (upland hunting). Collapse during trained swimming retrieves or waterfowl hunting were less common, and many owners commented that collapse was less likely to occur when the dog was swimming. Individual collapse episodes were also reported in dogs chasing horses (one dog), deer (three dogs), and rabbits (two dogs).

Owners were asked to speculate on possible factors contributing to collapse in their dog [Table 3]. Excitement associated with a trigger activity was the most commonly reported factor (187 dogs, 83%). Some owners reported

**Table 3**

Factors Reported by Owners as Contributing to Collapse in 225 Labrador Retrievers With Exercise-Induced Collapse

Factor	% of Dogs
Excitement	83
Heat and humidity	31
Live birds in training or hunting	25
Stress during training	13
Competition with other dogs	9

they “could tell” that their dog was going to have an episode, because the dog would bark or be excessively excited when starting the trigger activity. The use of live birds in retriever training, chasing crippled birds during hunting, and stress during formal retriever training (e.g., difficulty finding a marked retrieve, electronic collar correction, repeating an unsuccessful marked retrieve) were all cited as factors leading to collapse.

Competition with other dogs during play or retrieving was also considered to be a factor increasing the level of excitement and likelihood of collapse. All owners reported that they believed their dogs could engage indefinitely in moderately strenuous activity not associated with excitement, such as jogging or running alongside a bicycle, without exhibiting signs of collapse.

Some owners (71 dogs, 31%) felt that excessive environmental heat and humidity increased the likelihood of collapse in their dogs. Owners were asked to report the environmental conditions during observed episodes of collapse, and their estimates of ambient temperature were categorized as hot (>21°C), moderate or cool (5°C to 21°C), or cold (-20°C to 5°C). Ambient temperatures were estimated for 834 episodes of collapse in the 225 dogs. Forty-two percent of the individual collapse episodes were reported to occur in hot weather; 55% were reported to occur in moderate or cool weather; and 3% were reported to occur in cold weather.

Most owners were unable to state with certainty whether other dogs related to theirs were affected with EIC, but 29 (13%) dogs were known to have one or multiple littermates affected with a collapse syndrome. Occasional observations were reported of other closely related dogs being affected and a few instances of sudden exercise- or heat-associated death in related dogs.

Owners were asked to assess the impact that EIC had on their dog's life and to describe the responses to treatments they had tried. Seven (3%) dogs had died during an episode of collapse. Twenty (9%) dogs were euthanized or placed in a pet home because they could no longer be bred or intensively trained for field competition. The response to treatment or management was difficult to determine from the questionnaires. Most owners who had tried restricting their dog's participation in trigger activities (135/138) reported either a dramatic decrease in the number of collapse episodes or a complete resolution of the clinical syndrome. Five owners commented that if they observed their dog carefully and stopped exercise at the first sign of an abnormal gait, they could prevent collapse. Owners of 10 dogs (eight males, two females) concluded that neutering had resulted in clinical improvement; they reported no further episodes of collapse with moderately restricted exercise. Four competitive field trial dogs treated with phenobarbital (2 mg/kg once or twice a day) had a dramatic decrease in episodes or complete resolution of the syndrome, despite continued participation in training and field trial competition. None of the dogs with EIC developed unusual sys-

temic or neurological abnormalities during the follow-up period of 3 months to 13 years (median 1.5 years) between the first collapse episode and completion of the survey.

### Heritability

Examination of the pedigrees established that many affected dogs were closely related. All EIC dogs for which the authors had a sufficient amount of generational information could be assembled into one large kindred, indicating a familial basis for the condition. Eight more manageable pedigrees containing three to 49 affected individuals were assembled for analysis. Within these eight pedigrees, 16 matings resulted in two or more affected offspring. Males and females were equally represented (51%:49%), excluding an X-linked mode of inheritance. In the authors' sample set of 326 dogs, only nine of 169 affected dogs were known to have an affected parent. Six known affected parents appear in these pedigrees. From these affected parents, one family with full phenotypic information (in which one affected parent mated to an unaffected parent) produced two affected and two unaffected offspring. In three families, an affected dog produced multiple (in one case 15) affected second- and third-generation offspring. The pedigree analysis was most consistent with an autosomal recessive mode of inheritance, although a dominant disorder with partial penetrance or a polygenic disorder could not be excluded.

### Discussion

The syndrome of EIC is a relatively common cause of exercise intolerance, limiting performance in working Labrador retrievers; but detailed descriptions of the syndrome are not available in the veterinary literature. No test for EIC currently exists, so presumptive diagnosis requires recognition of the syndrome and elimination of other causes of exercise intolerance and collapse. This report describes owner survey responses of the demographic and clinical features of EIC as well as the types of activities most likely to lead to collapse in affected dogs.

Dogs with EIC often continued to run while dragging their crouched rear legs during episodes of collapse. Incoordination was noted in the rear legs or, occasionally, in all four legs; falling to the side suggested a problem with balance in >50% of the dogs. These findings are more suggestive of a neurological disorder than a condition affecting skeletal muscle.<sup>8-10</sup> Dogs with weakness due to an abnormality of muscle, peripheral nerve, or the neuromuscular junction are normally reluctant to continue exercising. They typically develop a short-strided, stiff gait rather than the "wobbly," base-wide, or incoordinated gait described in these dogs.<sup>10-13</sup> Dogs with EIC, upon recovery, exhibited no evidence of muscle pain or stiffness suggesting overexertion.

Some owners reported that once they learned to recognize early signs of incoordination in their dog, they could prevent collapse by halting activity. Recovery after collapse was gradual, occurring over 5 to 45 minutes. The progressive nature of the collapse and the gradual recovery make it

unlikely that EIC is a manifestation of a paroxysmal disorder like epilepsy or cataplexy.<sup>14,15</sup>

Most affected dogs were mentally normal during EIC episodes, but 23% were reported to be dazed or confused during at least one episode. Seven dogs died during collapse; in three of these seven, a short, generalized seizure was observed terminally. Veterinarians must recognize that EIC can be fatal, and owners and trainers must be counseled to halt activity in their dog when signs of incoordination or gait abnormality first become apparent. The authors know of several instances where dogs with EIC have died during an episode of collapse induced for the purpose of veterinary evaluation.

Exercise-induced collapse has been speculated to be a heat-related disease.<sup>9,12,16</sup> Body temperature recorded during collapse was extremely elevated in some dogs of this study; body temperature may have been underestimated if it was measured as dogs were recovering rather than at the onset of collapse. Body temperatures have, however, been shown to be similarly increased in normal exercise-tolerant Labrador retrievers immediately after 10 minutes of intensive retrieving exercise (mean 41.8°C) and following completion of a 3.5-minute land retrieve test (mean 40.8°C) during an AKC retriever field trial.<sup>17,18</sup> Other breeds of dogs engaging in less intensive or shorter-duration exercise have been reported to experience body temperatures between 40.1°C and 42°C.<sup>19-22</sup> Owners of dogs with EIC commonly reported that excessive environmental heat and humidity increased the likelihood of collapse, and many individual collapse episodes occurred in hot weather. It was apparent, however, that extreme heat was not absolutely necessary for collapse to occur, as the majority of the collapse episodes for which ambient temperature was reported occurred during moderate or cool weather ( $\leq 21^\circ\text{C}$ ), and occasional episodes of collapse occurred in snow or while dogs were swimming in cold water or breaking through ice. Nonetheless, recommendations are that dogs with EIC should avoid trigger activities and intensive exercise, especially when the ambient temperature is hot.

Dogs with EIC seem to tolerate mild to moderate exercise and can engage normally in activities such as jogging, hiking, or swimming. Activities with continuous, intense exercise accompanied by a high level of excitement or anxiety most commonly caused collapse. Competition with other dogs, hunting for live birds, and the stress of formal training were all cited as factors contributing to collapse in these dogs. Genetically affected dogs not being trained for hunting or retriever competition may go unrecognized if they never experience the necessary combination of activity and excitement to induce an episode of collapse.

The consequences of a dog having EIC were variable in this population of dogs and largely related to owner expectations. Dogs with EIC were rarely able to continue training or competition without some restrictions, and some of the dogs in this study were euthanized if their primary purpose was for competition or for breeding. Limiting trigger activities and excitement allowed some dogs to continue as

working dogs or pets. Exercise-induced collapse does not seem to be a progressive disorder, and most affected dogs are able to live a normal life if trigger activities are avoided. Although some owners reported that neutering or the administration of phenobarbital may decrease the likelihood of episodes of collapse and allow some dogs to participate in trigger activities, further investigation into potential treatments for EIC is necessary.

The occurrence of EIC in littermates and the established tendency for dogs from specific pedigree lines to be affected strongly suggest that EIC is hereditary, but the precise mode of inheritance has not been determined. Pedigree analysis was most consistent with an autosomal recessive mode of inheritance.<sup>7</sup> Thus, owners and breeders must be aware that mating apparently unaffected dogs that are carriers of an EIC susceptibility gene can produce affected puppies. By using pedigrees and deoxyribonucleic acid collected from affected dogs in this study, investigators recently have identified multiple genetic markers linking EIC to a particular chromosomal locus and have identified a genetic mutation that is highly associated with EIC susceptibility.<sup>b</sup>

## Conclusion

At the present time, EIC is a presumptive diagnosis made by ruling out other disorders causing exercise intolerance and by observing characteristic clinical features in affected Labrador retrievers. This descriptive study of EIC should help practicing veterinarians recognize the syndrome and counsel owners of affected dogs regarding management strategies and prognosis.

## Footnotes

<sup>a</sup> Pedigraph software; University of Minnesota, St. Paul, MN 55108

<sup>b</sup> Mickelson, personal communication, 2008

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**Appendix****Survey Completed by Owners of Labrador Retrievers With Exercise-Induced Collapse**

Dog name:

Color:

Sex:

1. What is the birth date of your dog? \_\_\_\_\_
2. Has your dog ever had any medical problems except for collapse episodes?
3. Is your dog on any medications?
4. When was the first collapse noted?
  - What was the dog doing at the time?
  - What was the weather like?
  - What did you see first?
  - What did you do and what happened next?
  - How long did the collapse last?
  - Could your dog walk?
  - How long until your dog was normal?
5. How many episodes has your dog had?
6. Have all episodes been the same as the first, or were there differences?
7. What have been the circumstances (activity and weather) for each collapse?
8. Has there been anything abnormal that you note before, during, or after an episode?
9. Has there been anything that you think seems to make your dog more or less likely to have an episode on a given day?
10. Does it seem to you that it has gotten easier to induce an episode, or is it harder to induce or unchanged?
11. Have you tried any treatments or changed management? If so, do you think this has helped?
12. Is your dog always completely conscious and aware during the collapse?
13. Are just rear legs affected, or all four legs?
14. During collapse and recovery, which of the following best describes your dog:  
(circle all that apply)
  - a. Legs seem floppier than normal, don't seem to be able to hold up my dog's weight
  - b. My dog seems to have trouble maintaining balance and will fall over to the side
  - c. Legs seem to be stiffer than normal, and held straight
15. Have you taken your dog's temperature during an episode of collapse? What was it?

**(Continued on next page)**

**Appendix (cont'd)**Survey Completed by Owners of Labrador Retrievers With Exercise-Induced Collapse

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16. Do you know of any other related dogs that are affected?
17. Have other dogs from this dog's litter been used for competitive retrieving events?
18. What do you feed your dog?
19. When was the last time you observed an episode of collapse?
20. How would you judge your dog's body condition right now?
  - a. Fat, out of shape
  - b. A little heavy, but in good shape
  - c. In perfect condition
  - d. Very thin