Assessment of necropsy findings in sled dogs that died during Iditarod Trail sled dog races: 23 cases (1994–2006)

Michelle M. Dennis, DVM, PhD, DACVP; Stuart N. Nelson, DVM; Glenn H. Cantor, DVM, PhD, DACVP; Derek A. Mosier, DVM, PhD, DACVP; John E. Blake, DVM, MVetSc; Randall J. Basaraba, DVM, PhD, DACVP

Objective—To describe the character and frequency of causes of death and associated lesions in long-distance racing sled dogs.

Design—Retrospective case series.

Animals—23 dogs.

Procedures—Medical records of dogs that died during or soon after competition in the Iditarod Trail sled dog races (1994 through 2006) were examined for findings of gross necropsy and histologic evaluation of tissue samples. From the data, descriptive and comparative statistics were obtained.

Results—Recognized causes of death included aspiration of gastric contents (n = 4), aspiration pneumonia (4), acute blood loss secondary to gastric ulceration (3), and sled dog myopathy (2). A cause of death was not established for 7 dogs. Prevalent lesions among the study population included rhabdomyolysis (n = 15), enteritis (10), gastritis (10), aspiration pneumonia (8), and gastric ulceration (8). All dogs with aspiration pneumonia had concurrent gastric mucosal lesions. Subjective biventricular cardiac hypertrophy was evident in most dogs; other lesions detected frequently included centrilobular hepatic fibrosis, gastric dilatation, and mild cardiac myodegeneration and necrosis.

Conclusions and Clinical Relevance—Unexpected death is a rare event among conditioned sled dogs during competition in endurance races. Potentially life-threatening conditions of dogs that are associated with periods of long-distance physical exertion include aspiration pneumonia, gastric mucosal lesions, and severe rhabdomyolysis. Dogs that develop clinical signs suggestive of these conditions should be excluded from strenuous activities. Epidemiologic investigations are required to clarify the risk for death associated with these lesions in dogs competing in endurance races. (*J Am Vet Med Assoc* 2008;232:564–573)

The Iditarod Trail Sled Dog Race is an approximately 1,770-km (1,100-mile) race from Anchorage to Nome, Alaska. It is held annually starting in the first week of March and involves approximately 1,200 dogs/y. The race is completed by most teams within 9 to 14 days. Cold weather combined with the physical demands of endurance racing necessitates tremendous energy expenditure (> 12,000 kcal/d) by racing dogs.[1] Several measures are taken to safeguard the health of participating dogs, such as intensive prerace health screens that include serum biochemical and ECG evaluations, physical examinations performed by veterinary personnel at > 20 checkpoints throughout the race, and tightly controlled and monitored use of drugs. These measures necessitate a sizable veterinary staff; the Iditarod Trail Committee typically enlists the volunteer efforts of approximately 45 veterinarians and 10 veterinary technicians each year. Throughout the course of the race, approximately 33% to 35% of dogs that start the race are removed from competition. Common reasons for discontinuation of a dog's participation in the race include fatigue, lameness, foot lesions, and diarrhea. Other apparently healthy dogs are withdrawn from the race because they are slower than the rest of their teammates or for strategic reasons. Despite rigorous efforts to protect the health of competing dogs, apparently healthy dogs infrequently die during a race.

Information concerning causes of exercise-associated unexpected death in apparently healthy dogs is sparse. Efforts to understand and prevent the rare

From the Animal Population Health Institute, Department of Clinical Sciences (Dennis) and the Veterinary Diagnostic Laboratory (Dennis), Department of Microbiology, Immunology, and Pathology (Basaraba), College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins, CO 80523; Iditarod Trail Committee, Mile 2.2 Knik Rd, Wasilla, AK 99687 (Nelson); Discovery Toxicology, Bristol-Myers Squibb, Princeton, NJ 08540 (Cantor); the Department of Diagnostic Medicine/Pathobiology, College of Veterinary Medicine, Kansas State University, Manhattan, KS 66506 (Mosier); and the Institute of Arctic Biology, University of Alaska, Fairbanks, AK 99775 (Blake).

Presented at the 49th Annual Conference of the American Association of Veterinary Laboratory Diagnosticians, Minneapolis, October 2006.

The authors thank Drs. Karin Schmidt, Saroja Bharati, Beth Valentine, John King, Brian Summers, Barry Cooper, A. Morris Craig, Deny Albert, Scott Dolginaw, Patricia Talcott, Kathy Burek, Jerome Vanek, Robert Sept, Michelle Fleetwood, Ken Hinchcliff, Jean Dieden, and Alexander deLahunta for technical support.

Address correspondence to Dr. Basaraba.

occurences of sudden death in racing dogs rely on identification of fatality-associated lesions. Such information may facilitate early recognition of dogs affected with race-related, life-threatening conditions. Knowledge of disease processes in canine endurance athletes is also beneficial for understanding the effects of strenuous exercise in animals and humans. The purpose of the study reported here was to describe the character and frequency of causes of death and associated lesions in long-distance racing sled dogs that die during competition.

Materials and Methods

Case selection—Cases for inclusion in the study were identified through cooperation with the Iditarod Trail Committee; these cases occurred over a 13-year period from 1994 to 2006. Only dogs that died during competition or following competition while remaining in the care of the Iditarod Trail veterinary team were included in the study. Dogs that discontinued the race but died later while no longer in the custody of the musher (ie, the primary caregiver for and driver of the dog team) or Iditarod Trail staff were excluded from the study because of the difficulty of obtaining complete follow-up information and inconsistent access to cadavers for complete necropsy examination.

Medical records review—Records of dogs that met the inclusion criteria were examined for information regarding signalment, age, approximate race distance completed, events that preceded death, necropsy findings (gross and microscopic), hepatic vitamin E and selenium concentrations, and presumptive cause of death.

Procedures—In 1994, the Iditarod Trail Committee veterinary staff initiated a program requiring intensive evaluation (by use of a uniform standard procedure) of all dogs that died during an Iditarod Trail race.[2] For each of those dogs, a complete necropsy was commenced as soon after death as possible (within 24 hours in almost all instances). Mushers and Iditarod staff were advised on methods to avoid freezing of the bodies during transport. Samples of the lungs; heart; trachea; liver; spleen; pancreas; brain; stomach; duodenum, jejunum, and ileum; large intestine; mesenteric lymph node; kidneys; thyroid and adrenal glands; urinary bladder; triceps and biceps brachii, epaxial, psoas, quadriceps femoris, cranial tibial, gastrocnemius, and fore- and hind limb superficial and deep digital flexor muscles; and any grossly abnormal tissues were collected and immersed in neutral-buffered 10% formalin. For dogs that died prior to 1997, hearts were relinquished to the International Sled Dog Veterinary Medical Association for in-depth cardiopathologic evaluation.[3] Formalin-fixed, paraffin-embedded tissue samples were sectioned at 3 to 5 µm; sections were stained with H&E for histologic evaluation. Ancillary diagnostic tests were pursued in a case-dependent manner at the discretion of the attending pathologist. Hepatic tissue vitamin E and selenium concentrations were assessed in 8 dogs; the analyses for each dog were conducted at 1 of 3 laboratories. For each dog, gross and microscopic findings and diagnoses were reported by the examining pathologist. Cause of death for each dog was ascribed to the primary lesion or condition for which the severity or estimated clinical importance was sufficient to account for death.

Descriptive and comparative statistics were computed by use of commercially available software.[a] The median race distances completed prior to death in subgroups of dogs with and without certain conditions were compared by use of a Mann-Whitney *U* test. A value of $P \leq 0.10$ was considered significant.

Results

Twenty-three dogs (14 males and 9 females; designated as dog 1 through 23) that died during competition or following competition while remaining in the care of the Iditarod Trail veterinary team were included in the study (**Table 1**). The study population represented 0.15% of approximately 15,600 competing dogs. The mean ± SD age of dogs in the study population was 4.0 ± 1.5 years (range, 1 to 8 years). For many deaths (10/22 dogs with known history), dogs unexpectedly collapsed during the race competition and died immediately or as they were transported to the next race checkpoint (**Table 2**). Lesions commonly detected in dogs with race-related deaths included rhabdomyolysis (ie, skeletal muscle degeneration and necrosis; n = 15), enteritis (10), gastritis (10), gastric ulceration (10), aspiration pneumonia (8), centrilobular hepatocellular necrosis (6) or centrilobular hepatic fibrosis (3), gastric dilatation (3), and cardiac myodegeneration and necrosis (3). Among the 23 dogs, most deaths were attributed to aspiration of gastric contents (n = 6; 26.1%), aspiration pneumonia (3; 13.0%), acute blood loss (3; 13.0%), or sled dog myopathy (2; 8.7%). Other causes of death were reported for 2 (8.7%) dogs. The cause of death was undetermined for 7 (30.4%) dogs; the lesions identified in each of these dogs were considered of insufficient severity or clinical importance to cause death. Lesions indicative of abuse or neglect were not identified in any dog. All dogs examined were in adequate to good body condition.

Rhabdomyolysis—Focal rhabdomyolysis (skeletal muscle necrosis) was evident in 15 dogs. Pathologic changes were similar in each affected dog. The size of rhabdomyolytic foci ranged from minute areas that were recognizable only microscopically to large areas that affected an entire muscle. A wide variety of muscles were affected, and lesions did not develop in any 1 specific muscle predominantly. All muscles from which samples were routinely collected as part of the standard postmortem evaluation as well as the serratus ventralis, interosseous, adductor, pectoral, temporalis, diaphragm, infraspinatus, intercostal, and masseter muscles were affected. Muscles with grossly apparent foci were streaked with pallor and were sometimes surrounded by fascial edema. Microscopically, rhabdomyolysis was inconsistently evident (**Figure 1**). Lesions were multiphasic, and myocytes within and between affected muscles were in different stages of degeneration and repair. Degenerate myocytes were swollen and had sarcoplasmic vacuolar change and loss of cross-striations. Necrotic myocytes were hypereosinophilic with sarcoplasmic hyalinization and nuclear pyknosis. De-

Table 1—Lesions and presumptive cause of death identified in 23 dogs that died during competition in the Iditarod Trail sled dog races in 1994 through 2006.

Presumptive cause of death	Dog No. (year of death)	Age (y), sex	Approximate race distance completed (km [miles])	Lesions
Aspiration of regurgitated gastric contents	2 (2006)	4, M	1,125 (700)	Peracute BP, GU, rhabdomyolysis, centrilobular hepatic fibrosis, moderate lymphocytic thyroiditis, and mild plasmacytic enteritis
	9 (2004)	5, M	645 (400)	Peracute BP, gastric dilatation, rhabdomyolysis, mild renal tubular epithelial necrosis, and moderate lymphocytic and erosive gastritis
	13 (1999)	3, M*	1,000 (620)	Peracute BP, GU, CHDN, and rhabdomyolysis
	15 (1997)	3, M*	1,400 (870)	Peracute BP, GU, gastric dilatation, CHDN, and mild lymphoplasmacytic gastritis
Aspiration pneumonia	4 (2006)	4, M	400 (250)	Acute BP, moderate lymphoplasmacytic gastritis, moderate lymphoplasmacytic and eosinophilic enteritis, and rhabdomyolysis
	5 (2005)	2, F	1,590 (990)	Acute BP, multifocal gastric erosion, small intestinal intussusception, mild lymphoplasmacytic enteritis, and rhabdomyolysis
	12 (2000)	3, M*	1,495 (930)	Acute BP, GU, CHDN, rhabdomyolysis, mild lymphocytic gastritis, and mild eosinophilic enteritis
	19 (1997)	5, M	465 (290)	Acute BP, GU, mild lymphoplasmacytic and neutrophilic enterocolitis, centrilobular hepatic fibrosis, membranous glomerulopathy, cardiac myodegeneration, and rhabdomyolysis
Acute blood loss	7 (2005)	3, F	1,000 (620)	GU, mild cardiac myodegeneration, mild lymphoplasmacytic and eosinophilic enteritis, and rhabdomyolysis
	8 (2004)	6, M	1,430 (890)	GU, mild lymphocytic gastritis, mild plasmacytic enteritis, and testicular interstitial cell tumor
	14 (1998)	5, M	1,400 (870)	GU, mild lymphoplasmacytic gastritis, CHDN, and rhabdomyolysis
Pulmonary edema	11 (2001	3, M	595 (370)	Severe pulmonary edema, gastric dilatation, multifocal proliferative and granulomatous alveolitis, rhabdomyolysis, and mild cardiac myodegeneration
Sled dog myopathy	16 (1997)	4, M	645 (400)	Severe rhabdomyolysis, mild renal tubular epithelial necrosis, centrilobular hepatic fibrosis, and cerebral and coronary angiopathy
	23 (1994)	5, F	645 (400)	Severe rhabdomyolysis; mild lymphoplasmacytic gastritis; fatty infiltration of approaches to the atrioventricular node, the atrioventricular node, bundle of His with disruption of the bundle of His; pulmonary edema and congestion; and acute centrilobular hepatic congestion
Brain edema	21 (1995)	NK, F	Unrecorded	Brain edema with neuronal degeneration and astrocytic swelling, multifocal pulmonary hemorrhages, and rhabdomyolysis
Accidental strangulation or drowning (per history)	20 (1996)	3, F	190 (120)	Pulmonary emphysema
Undetermined	1 (2006)	5, M	1,660 (1,030)	Mild lymphoplasmacytic gastritis, focal dermal necrosis of prepuce, and tonsillar foreign-body granuloma
	3 (2006)	3, M	885 (550)	Mild lymphocytic gastritis
	6 (2005)	4, F	1,785 (1,080)	CHDN and mild lymphoplasmacytic enteritis
	10 (2003)	5, M	1,785 (1,110)	CHDN, rhabdomyolysis, and thymic hemorrhage
	17 (1997)	8, F*	660 (410)	Luminal large intestinal hemorrhage and mild eosinophilic and plasmacytic enteritis
	18 (1997)	1, F	260 (160)	Rhabdomyolysis, mild cardiac myodegeneration, mild lymphoplasmacytic and neutrophilic pneumonia, mild lymphoplasmacytic and neutrophilic enterocolitis, and lymphocytic thyroiditis with follicular atrophy
	22 (1995)	NK, F	870 (540)	Multifocal pulmonary hemorrhages and mild lymphoplasmacytic gastritis

*Denotes neutered dog.
M = Male. F = Female. BP = Bronchopneumonia. GU = Gastric ulceration. CHDN = Centrilobular hepatocellular degeneration and necrosis. NK = Not known.

Table 2—Historical findings that preceded death in 23 dogs that died during competition in the Iditarod Trail sled dog races in 1994 through 2006.

Dog No.	History
1	Collapsed suddenly while resting at a checkpoint approximately 20 minutes following a physical examination during which no abnormalities were detected; died immediately.
2	Developed unsteady gait, then collapsed shortly thereafter; died immediately.
3	Musher stopped team to untangle lead dogs. Dog collapsed within moments of stopping; died immediately.
4	Substandard performance, but no abnormalities were detected via physical examination. After a distance of approximately 40 miles later, dog collapsed suddenly during racing. Dog was hospitalized for pneumonia and died within 48 hours.
5	Dog was carried in to the checkpoint with coughing and respiratory distress. Musher reported that the dog had aspirated. Dog was hospitalized for pneumonia and died within 48 hours.
6, 7, 9, 11, 14, 17, 18, and 19	Collapsed suddenly during racing; died immediately.
8	Substandard performance, but no abnormalities were detected via physical examination. After a distance of approximately 120 miles later, dog collapsed suddenly during racing; died immediately.
10	Collapsed suddenly during racing. Seemed to recover, was returned to team, then refused to run shortly thereafter. Died on carriage to next checkpoint.
12 and 15	Stopped pulling, then collapsed shortly thereafter; died immediately.
13	Collapsed suddenly during racing, vomited, then died.
16	Developed abnormally stiff gait. After a distance of approximately 40 miles, collapsed suddenly during racing; died immediately.
20	Hesitated when traversing standing water and became tangled in neckline; died shortly thereafter.
21	History not available.
22	Developed unsteady gait, then collapsed shortly thereafter. Developed respiratory distress during carriage to the next checkpoint; died.
23	Collapsed suddenly during racing; died immediately. Musher reported that the dog had squatted frequently prior to death.

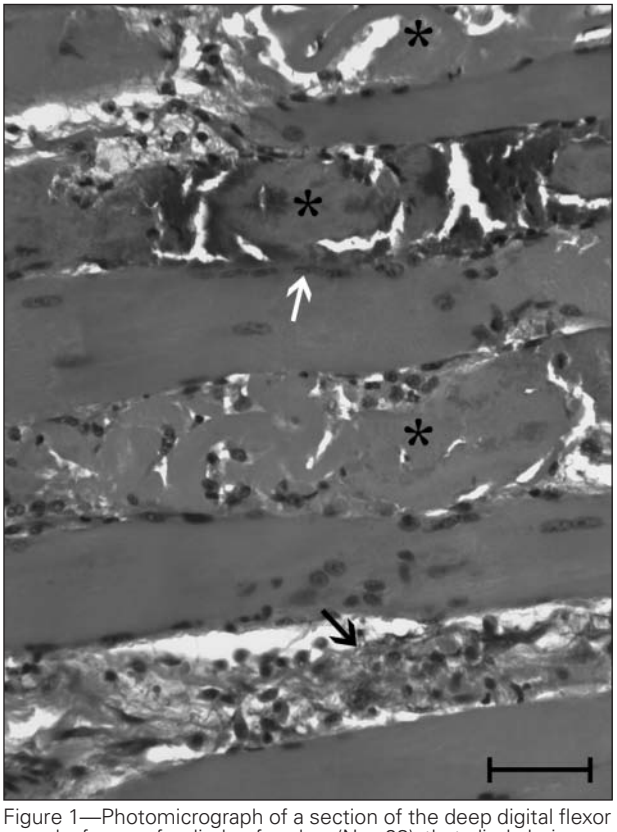

Figure 1—Photomicrograph of a section of the deep digital flexor muscle from a forelimb of a dog (No. 23) that died during an Iditarod Trail sled dog race. The presumptive cause of death was sled dog myopathy. Severe rhabdomyolysis is evident in this tissue. Notice the signs of necrosis including vacuolation, swelling, and fragmentation of sarcoplasm (asterisks); features of regeneration including centralization of nuclei, proliferation of satellite cells (white arrow), and infiltration of myofiber by macrophages (black arrow) are also present. H&E stain; bar = 50 µm.

generate and necrotic myocytes were often mineralized. Features of regeneration included centralization of nuclei with multiple nuclei aligned in rows, sarcoplasmic basophilia, and myosatellite cell proliferation. Areas of myocyte loss were inconsistently infiltrated with neutrophils, lymphocytes, plasma cells, and macrophages. Four dogs with rhabdomyolysis (dogs 7, 11, 18, and 19) had concurrent mild myocardiocyte degeneration and necrosis.

Four dogs with rhabdomyolysis (dogs 9, 16, 18, and 23) were apparently affected with sled dog myopathy; sled dog myopathy was considered the cause of death for 2 of these dogs (dogs 16 and 23). This condition has historically been associated with race-related deaths and is characterized by widespread and large foci of rhabdomyolysis.[4] In the present study, sled dog myopathy was characterized by large, grossly evident foci of rhabdomyolysis that affected several muscles; in some instances, an entire muscle or muscles not used for locomotion (masseter, temporalis, and intercostal muscles) were affected. In 1 dog (dog 16), there was microscopic evidence of pigmentary renal tubular epithelial necrosis: sloughed necrotic epithelial cells and globular eosinophilic material that was consistent with myoglobin were detected within renal tubules.

Enteritis—Enteritis was detected in 10 dogs, of which 2 had concurrent colitis (dogs 18 and 19) and 2 had concurrent gastritis (dogs 8 and 12). Gross changes suggestive of enteritis or colitis (ie, nonformed feces consistent with diarrhea) were lacking in all cases. Enteritis ranged from mild (n = 9) to moderate (1); histologically, the inflammation was classified as eosinophilic, plasmacytic, plasmacytic and eosinophilic, or lymphoplasmacytic and neutrophilic. Colitis was histologically characterized by hemorrhage or lymphoplasmacytic and neutrophilic inflammation. Colitis was mild in both of the affected dogs. The specific etiology of enteritis or colitis was not determined for any of the dogs.

Gastritis and gastric ulceration—Among the 23 dogs, 10 had gastritis. Gastritis was characterized as mild (n = 7), moderate (2), and severe (1) and consisted of

lymphocytic, lymphoplasmacytic, or lymphofollicular inflammation with or without erosive inflammation.

Eight dogs were affected with gastric ulceration. In each of these dogs, gastric ulceration appeared to play a role in their deaths. Of the ulcer-associated deaths, 5 were attributed to aspiration of gastric content and 3 were attributed to anemia or hypovolemic shock associated with blood loss. Ulcers were characterized as acute (dogs 3 and 19), subacute (dogs 11, 12, and 15), chronic (dog 13), and combined acute and chronic (dogs 7 and 14). Ulcers were multifocal in 8 dogs, ranging in number from 2 to > 20 ulcers. Ulcers affected the fundic mucosa in all dogs and pyloric mucosa in only 1 dog (dog 13). In 7 dogs, ulcers were associated with gastric foreign bodies including booties (dogs 2 and 19), straw (dogs 8, 12, 13, and 14), and rocks (dog 13). One dog (dog 10) without gastric ulceration was reported to have gastric foreign material consisting of straw. Gastric ulceration was associated with diffuse gastritis in 3 dogs (dogs 12, 14, and 15).

In 5 dogs with gastric mucosal lesions (dogs 1, 3, 4, 8, and 14), spiral-shaped bacteria were identified microscopically. These organisms were tightly spiraled (8 to 12 µm in length), had colonized superficial mucous and gastric pits, and were occasionally present within the cytoplasm of parietal cells. Dog 8 also had round yeasts (3 to 4 µm in diameter) within gastric pits.

Bronchopneumonia—Bronchopneumonia was diagnosed in 8 dogs and was ascribed to aspiration of gastric content in each case. Lesion characterization ranged from peracute to acute. Gross findings were similar for all dogs: lungs were diffusely congested and edematous. Brown-tinged fluid or ingesta was usually present within airways. Acute bronchopneumonia was further distinguished by cranioventral areas of the lungs that failed to collapse; were firm; and, in some instances, had dark-brown areas of discoloration. Histologically, bronchopneumonia was centered on airways that contained foreign material, including pleomorphic amphophilic substance, plant material, and portions of skeletal muscle. Peracute bronchopneumonia was associated with alveoli filled with fluid, fibrin, multifocal hemorrhage, and mild infiltrates of neutrophils and macrophages. Acute bronchopneumonia additionally featured suppurative inflammation and alveolar septal necrosis and also inconsistent findings of bronchiolar epithelial necrosis, venous thrombosis, fibrinoid vascular necrosis, and intralesional colonies of bacteria (**Figure 2**). Gastric lesions were present in all dogs with bronchopneumonia.

Hepatocellular disease—Centrilobular hepatocellular degeneration and necrosis were evident in 6 dogs and was classified as mild to moderate. Three additional dogs had mild centrilobular hepatic fibrosis. Features of chronic passive hepatic congestion (ie, hemosiderin accumulation and congestion of sinusoids) were generally lacking in these cases. Gross hepatic lesions consisted of inconspicuous tan to yellow parenchymal discoloration and accentuated lobular patterns. Myocardiocyte degeneration was identified in one of the dogs with hepatic lesions (dog 19). Most dogs with hepatocellular necrosis also had rhabdomyolysis (dogs 10, 12, 13, and 14). Of the dogs with hepatic necrosis, vitamin E concentration in hepatic tissue was assessed in dogs 14 and 15; the value in dog 15 was minimally decreased (**Table 3**). Dog 23 had pulmonary congestion and edema, together with hepatic centrilobular congestion, which were suggestive of acute heart failure; this dog also had cardiac conduction system defects, as described in another report.[3]

Cardiac findings—Subjectively, the heart of every dog in the study was proportionately large in relation to the lungs and thoracic cavity, compared with heart size in pet dogs. Heart weight (left and right ventricles with interventricular septum) as a percentage of body weight was determined for dog 2 (0.78%), dog 3 (0.79%), dog 4 (0.90%), dog 8 (0.91%), dog 10 (1.20%), and dog 21 (1.02%). Microscopic foci of myocardiocyte degeneration and necrosis were identified in 4 dogs; each of these dogs also had foci of rhabdomyolysis, and 2 (dogs 18 and 19) had low hepatic vitamin E concentrations.

Vitamin E and selenium concentrations in hepatic tissue—Hepatic vitamin E and selenium concen-

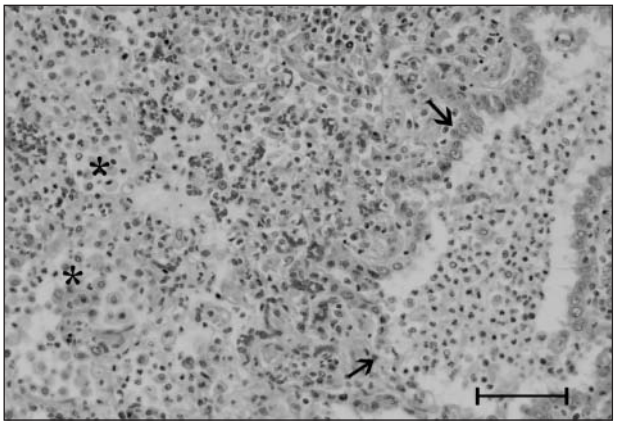

Figure 2—Photomicrograph of a section of lung tissue obtained from a dog (No. 4) that died during an Iditarod Trail sled dog race. The presumptive cause of death was aspiration pneumonia. The dog had acute bronchopneumonia. Notice the extent to which alveoli (asterisks) and a bronchiole (arrows) are filled with neutrophils, mononuclear leukocytes, fibrin, and edema. H&E stain; bar = 50 µm.

Table 3—Vitamin E and selenium concentrations in hepatic tissue obtained from 7 dogs that died during competition in the Iditarod Trail sled dog races in 1994 through 2006.

Dog No.	Vitamin E (µg/g [reference range])	Selenium (µg/g [reference range])
11*	1,520 (median = 175)	3.07 (0.7–2.5)
14†	570‡	0.61 (0.5–1.5)
15	129 (139–249)	0.63 (0.5–1.5)
16	65 (139–249)	0.68 (0.5–1.5)
17	112 (139–249)	0.84 (0.5–1.5)
18	77 (139–249)	0.61 (0.5–1.5)
19	77 (139–249)	1.00 (0.5–1.5)
20	570‡	0.54 (0.5–1.5)

Liver samples were analyzed for vitamin E and selenium concentrations at the following laboratories: *Kansas State Veterinary Diagnostic Laboratory, Kansas State University and †Analytic Sciences Laboratory, University of Idaho. Samples from the remaining 6 dogs were analyzed at the Veterinary Diagnostic Laboratory, Oregon State University. ‡No reference range established.

trations were evaluated in 8 dogs (Table 3). Vitamin E concentration in hepatic tissue was confirmed to be low in 5 of the 7 dogs (dogs 15, 16, 17, 18, and 19). Three of those dogs were affected with rhabdomyolysis, including dog 16, which died as a result of sled dog myopathy and dogs 18 and 19, which were affected with myocardiocyte degeneration and necrosis. Hepatic selenium concentration was within reference limits in all dogs evaluated.

Race distance—For the entire study population, the mean ± SD approximate distance completed in the race prior to death was 995 ± 500 km (range, 190 to 1,785 km). Mean approximate distances completed by dogs with different disease conditions were as follows: dogs with rhabdomyolysis (n = 8), 932 ± 485 km (range, 260 to 1,785 km); dogs with potential sled dog myopathy (4), 548.8 ± 192.5 km (range, 260 to 645 km); dogs with enteritis (11), 1,017 ± 542 km (range, 260 to 1,740 km); dogs with gastritis (10), 1,048 ± 454 km (range, 400 to 1,660 km); dogs with gastric ulceration (8), 1,164 ± 346 km (range, 465 to 1,495 km); dogs with bronchopneumonia (8), 1,015 ± 469 km (range, 400 to 1,590 km); and dogs with centrilobular hepatocellular necrosis (6), 1,470 ± 284 km (range, 1,000 to 1,785 km). Median race distances completed for dogs with and without a particular condition were compared, and significant differences were identified only between dogs with and without sled dog myopathy (≤ 645.0 vs 1,062.5 km, respectively; $P \leq 0.10$) and between dogs with and without centrilobular hepatic necrosis (1,447.5 vs 652.5 km, respectively; $P \leq 0.05$).

Discussion

Little is known about lesions associated with prolonged physical exertion in animals; in particular, there is sparse information regarding the pathologic conditions that are common among long-distance racing dogs during races. Results of the present study indicated that aspiration of gastric contents, aspiration pneumonia, and acute blood loss secondary to gastric ulceration were the most common causes of death among endurance-racing sled dogs. As with humans and horses, the cause of death was undetermined for a considerable fraction of race-related dog deaths. Lesions commonly identified in the study population included rhabdomyolysis, enteritis, gastritis, gastric ulceration, centrilobular hepatocellular necrosis or hepatic fibrosis, gastric dilation, and cardiac myodegeneration and necrosis.

In the present study, aspiration of regurgitated or vomited gastric content was associated with death in 6 of 23 (26.1%) dogs. Peracute bronchopneumonia was microscopically evident in each of these dogs but was of insufficient severity to explain death. Aspiration of refluxed gastric content without subsequent severe pneumonia may result in sudden death through several mechanisms: asphyxia secondary to airway obstruction, vagally mediated apnea or bradycardia, or anaphylactic or septicemic shock.[5] In 3 (13.0%) other dogs, death did not occur immediately following aspiration of gastric content but occurred at some time later as a result of acute bronchopneumonia. For those dogs, the mechanism of death presumably involved respiratory insufficiency or septicemic shock.

Gastric disease seemed to be an important predisposing factor for aspiration pneumonia because all dogs with aspiration pneumonia in the present study had concurrent gastritis, gastric ulceration, or erosion. However, gastric mucosal lesions are common among competing sled dogs that do not die during a race.[6] Furthermore, one can speculate that gastric ulceration may have developed as a result of stress, secondary to acute aspiration pneumonia. Therefore, further investigation is needed to determine the risk for pneumonia associated with these lesions in long-distance racing dogs.

Pulmonary aspiration of gastric material results initially from reflux of stomach contents into the esophagus. Oral expulsion of gastric content during competition is not an infrequent occurrence among endurance-racing sled dogs.[b] Such an expulsion event provides an opportunity for aspiration of gastric material. Iditarod Trail veterinarians have conjectured that during periods of high-intensity exercise, sled dogs may develop gastroesophageal reflux, a disorder that is known to affect human athletes and that is thought to be influenced by exertion-associated reduction in the barrier pressure of the lower esophageal sphincter.[7] In addition, dogs with gastric mucosal lesions may also have the propensity to vomit or regurgitate. Nevertheless, inhalation of refluxed material would seem to additionally require impairment of the swallowing, gag, or cough reflex. Anatomic abnormalities or lesions suggestive of neurologic or muscular conditions that might impair upper airway function (such as atrophy of the cricoarytenoideus dorsalis muscle) were not identified in any dog in our study. It might be speculated that labored breathing or other factors associated with exercise could impair protective mechanisms that prevent aspiration. Anecdotal impressions propose that cough may be inhibited in humans during exercise.[8] Further research is needed to identify conditions of racing sled dogs that may disturb upper airway function and elucidate whether upper airway reflexes are compromised during periods of exertion.

Although acute respiratory distress syndrome may develop in dogs following aspiration of gastric content, microscopic lesions suggestive of acute respiratory distress syndrome (including type II pneumocyte hyperplasia and hyaline membrane formation[9]) were not prominent in any dog in the present study. Morphologic features of pneumonia consistent with H3N8 influenza–viral pneumonia, such as extensive pulmonary and pleural hemorrhage, were not identified in any of the study dogs.[10]

Aside from aspiration pneumonia, the dogs in our study population generally lacked histologically apparent airway lesions. This was surprising because endurance-racing sled dogs typically have airway inflammation and respiratory reactivity that is increased, compared with nonracing control dogs, similar to so-called ski asthma in human cold-weather atheletes.[11]

Gastric disease may predispose athletic dogs to regurgitate or vomit, thereby providing an opportunity for aspiration-associated death. Furthermore, gastric ulceration may result in death because of associated acute or chronic blood loss or by provision of a portal for bacterial transposition and subsequent development of septicemia. Acute blood loss attributable to gastric

ulceration accounted for deaths of 3 of the 23 (13.0%) dogs in the present study. Sled dogs are known to have a predisposition for development of gastric ulceration and erosion after sustained strenuous exercise.[6,12,13] Gastrointestinal mucosal lesions are also common among exercising humans and horses.[14-17]

Gastric ulcers may form via direct mucosal injury, hypersecretion of gastric acid, gastric mucosal ischemia, or interference with gastroprotective prostaglandins, often as a result of nonsteroidal anti-inflammatory drug or glucocorticoid treatments.[18] The pathogenesis of exercise-associated gastric ulceration in dogs is unknown but may involve altered gastric blood supply during periods of exertion, increased stomach acidity associated with high-fat diets, and stress-associated prostaglandin suppression. The administration of nonsteroidal anti-inflammatory drugs or systemic glucocorticoids to dogs participating in the Iditarod Trail races is prohibited. In the present study, the stomachs of most dogs that died with gastric ulceration contained foreign material including straw, booties, and rocks. This material is believed to be an incidental finding and not involved in ulcerogenesis; the ingestion of these items may have been a result of pica secondary to gastric discomfort and could have promoted regurgitation or vomiting.

The spiral-shaped bacteria localized to gastric mucosal lesions in 5 dogs in the present study are believed to represent large *Helicobacter* spp because of their morphologic features and location.[19] Similar bacteria have been observed in gastric biopsy specimens of racing sled dogs.[6] The role of these organisms in gastritis or gastric ulceration in dogs is uncertain; however, they are believed to be more commensal than pathogenic organisms.[18]

Gastritis and enteritis were common among dogs with race-related death. Of the 23 dogs in the study population affected with gastritis or enteritis, histologic changes were nonspecific and usually mild, and in no instance was a primary etiologic agent identified. The prevalence of gastrointestinal inflammation in conditioned sled dogs is unknown; however, diarrhea is recognized as a common condition.[20] It is unclear whether these lesions are exercise related or are more strongly influenced by the unique husbandry of sled dogs. Inflammation of the gastrointestinal mucosa does not seem to be prevalent among human or equine athletes.

Further study is needed to determine the causes of gastritis and enteritis among sled dogs. The presence of several enteric pathogens has been identified in sled dogs with diarrhea, including *Salmonella* spp, *Campylobacter* spp, *Clostridium perfringens*, rotavirus, coronavirus, parvovirus, *Giardia* spp, *Cryptosporidium* spp, and coccidia; however, a causative role for any of those organisms has not been determined. *Salmonella enterica* is commonly isolated from feces of dogs competing in the Iditarod Trail races, but there is no correlation of that infection with the presence of diarrhea.[21] Sled dogs are fed a variety of feedstuffs that are not commonly fed to pet dogs, including high-fat commercial dog foods, beef, horse meat, meat from various trapped animals, fish, entire chickens, and lamb fat; most of these are provided raw and often frozen. There is increasing evidence that feeding raw meat contaminated with *S enterica* to adult Greyhounds can result in infection and clinical salmonellosis.[22]

Foci of rhabdomyolysis (skeletal muscle necrosis) were identified in 14 of the 23 (60.1%) dogs in the present study. The presence of small foci of skeletal muscle injury is not surprising because a substantial proportion of dogs that are removed from the Iditarod Trail race have focal muscle injuries including muscle strains and tears. However, in dogs that died because of rhabdomyolysis, lesions were severe; almost always multifocal; and, in some cases, present in nonlocomotor muscles. Therefore, direct muscle injury does not universally account for rhabdomyolysis in sled dogs. The concurrent cardiac myonecrosis provides additional evidence for systemic disease, such as that which develops from nutritional derangements, toxicoses, and metabolic abnormalities, rather than representing damage associated with exertion of isolated muscle groups. All rhabdomyolytic lesions were multiphasic, suggesting ongoing or multiple episodes of injury.

Four dogs in the present study were considered to have some degree of sled dog myopathy, a disorder that has been historically recognized as a cause of race-associated deaths.[4] Sled dog myopathy is characterized by large foci of rhabdomyolysis that affects several muscles, sometimes in association with secondary myoglobinuria and renal tubular epithelial necrosis. Myoglobinuria is thought to damage renal tubular epithelial cells via obstruction of renal tubules with myoglobin casts, direct toxic effects, or induction of reduced renal blood flow.[23] Severe rhabdomyolysis may result in death as a consequence of acute renal failure, lactic acidosis, and severe hyperkalemia. In dog 23 in our study, severe rhabdomyolysis coincided with defects of the cardiac conduction system, including fatty infiltration of the conduction system leading into and out of the atrioventricular node, the atrioventricular node itself, and the bundles of His.[3] In that dog, it was speculated but not confirmed that excessive potassium was released from the degenerating and necrotic muscle, which then caused sudden conduction system failure in a heart that already had a weakened conduction system. Dogs affected with sled dog myopathy generally died earlier in the race (lower median distance completed) relative to the entire study population.

The cause of sled dog myopathy is unknown; the pathogenesis may involve oxidative stress, electrolyte derangement, lipid disorders, mitochondrial injury, or metabolic alterations. Exertional rhabdomyolysis in horses has been postulated to be predisposed by abnormal skeletal muscle calcium homeostasis, polysaccharide storage myopathy, electrolyte abnormalities, and selenium deficiency.[23] Sarcoplasmic inclusions, such as those associated with equine polysaccharide storage disease,[24] were not observed in any dogs of the present study.

Three dogs with varying degrees of rhabdomyolysis had low hepatic vitamin E concentration. Deficiency of this antioxidant is thought to result in rhabdomyolysis as a result of free radical–mediated cell membrane damage.[25] Exercise has been associated with lower plasma concentrations of vitamin E in endurance sled dogs; however, there is no association between prerace plasma vitamin E concentration and risk for development of exertion-associated rhabdomyolysis, and administration of an antioxidant supplement fails to at-

tenuate exercise-induced increases in plasma creatine kinase activity in sled dogs.[26,27] These findings imply that rhabdomyolysis in sled dogs is not entirely attributable to oxidant stress. Mushers and trail veterinarians have speculated that the incidence of fatal sled dog myopathy declined after dogs were given supplemental vitamin E. However, because information about sled dog myopathy is now widely disseminated among the mushers, the diligence of mushers in removing dogs that have collapsed, are reluctant to run, or have generalized stiffness or erratic gait from the race may be principally accountable.

Centrilobular hepatocellular degeneration and necrosis, or fibrosis, was observed in 9 dogs of the present study. Dogs affected with this lesion generally died later in the race (higher median distance completed) relative to the entire study population. Interestingly, serum alkaline phosphate, alanine transaminase, aspartate aminotransferase, and lactate dehydrogenase activities are greater than the reference range in sled dogs following racing.[28] Centrilobular hepatopathies are typically associated with ischemia or toxin-mediated injury because hepatocytes in this area are furthest from arterial blood supply and are therefore most prone to hypoxia.[29] Furthermore, activity of the mixed-function oxidase system, which may bioactivate toxic metabolites, is high in centrilobular hepatocytes. The importance of this lesion in race-associated dog deaths is unclear. Centrilobular congestion, degeneration, and necrosis can also represent nonspecific processes associated with poor oxygenation in a dying animal with reduced cardiac output. The centrolobular lesions were mild in all dogs in our study; thus, the potential for hepatic insufficiency that could result in death seems low. Additionally, lesions suggestive of hepatic insufficiency, such as icterus, were absent in all dogs. The pathogenesis of the centrolobular lesion is also unknown but could include exercise-associated cardiac insufficiency, ischemia resulting from gastric ulcer-associated blood loss or dehydration, oxidative stress associated with vitamin E deficiency or hyperthermia, or exposure to various hepatotoxins. Increased intestinal permeability has been identified in endurance-racing sled dogs[13]; disruption of the intestinal mucosal barrier may allow hepatotoxic substances to shower the liver through the portal circulation.[29] If storage conditions are inappropriate, there is potential for the distinctive foods fed to sled dogs to harbor hepatotoxins (eg, aflatoxin synthesized by certain fungi), although this would not be expected to cause the type of lesions observed in these dogs. Although certain fish may contain organochlorines that are also capable of causing hepatocellular necrosis, exposure to levels sufficient to cause liver lesions seems unlikely. The cause of hepatocellular necrosis in racing dogs requires further investigation.

Subjective biventricular hypertrophy was common among dogs that died during race competition. When measured, heart weight as a percentage of body weight exceeded the reference range established for pet dogs.[30] This finding is not surprising because echocardiographic and ECG studies have revealed that sled dogs that have completed endurance training often have cardiac hypertrophy.[31-34] These changes are thought to represent physiologic adaptation of the heart in athletic individuals to sustained exercise, rather than manifestation of cardiovascular disease.

Pulmonary hemorrhages, an exercise-induced lesion associated with sudden death in horses,[35] were detected in only 2 dogs. These lesions were of unknown clinical relevance.

Of the 23 dogs in the present study, 7 (30.4%) lacked lesions or were considered to have lesions of insufficient severity or clinical importance to explain death. The cause of death for dogs that lacked major lesions is puzzling, and fatal cardiac arrhythmias are often considered in such cases. In an ECG study of 319 trained sled dogs, cardiac arrhythmias, including atrial and ventricular premature contractions, second-degree atrioventricular block, and paroxysmal ventricular tachycardia, were identified in 13 (4.1%).[32] Cardiac conduction system lesions have been identified in some dogs that died during race competition[3] and also in 1 dog in the present study (dog 23). A thorough examination of the conduction system is quite difficult; therefore, it is possible that cardiac conduction system lesions were underreported. Because of resource limitations, the cardiac conduction systems from dogs 1 to 20 in the present study were not examined in a thorough, systematic manner, which can involve examination of 800 to 1,200 histologic sections of each heart. Although cardiac hypertrophy seems typical of the athletic canine heart, given that this lesion has the potential to sustain aberrantly propagated cardiac impulses (ie, re-entry phenomenon),[36] its role in cases of unexpected death that lack other clinically relevant lesions is uncertain. Small foci of myocardiocyte degeneration and necrosis may be capable of causing fatal conduction disturbances. Although such lesions were detected in dogs of the present study, their potential for involvement in death is also difficult to determine.

In mammals, ischemia to vital organs (ie, heart and brain) can result in cellular necrosis and death; however, such lesions are not microscopically apparent unless survival is prolonged for several hours following the insult.[37] In addition, certain fatal physiochemical alterations fail to result in gross or microscopic lesions (eg, derangement in body temperature, electrolyte or acid-base imbalance, and toxic substances or metabolic diseases that interfere with certain essential cellular biochemical pathways). Airway obstruction attributable to exercise-induced bronchoconstriction or laryngospasm results in acute dyspnea in human atheletes.[38,39] These physiologic derangements could explain sled dog deaths for which explicatory lesions are lacking, but have not been identified in sled dogs to our knowledge.

In humans, cardiac abnormalities including malformations, coronary artery disease or anomalies, hypertrophic cardiomyopathy, and myocarditis are the most common cause of exercise-related sudden death.[40,41] Lesions are lacking to explain death in a substantial proportion of the remaining cases of exercise-related sudden death, and cardiac arrhythmias are often implicated. Conditioned horses that die suddenly during racing usually lack lesions sufficient to account for death[42]; recognized causes include vascular rupture and exercise-induced pulmonary hemorrhage,

although fatal cardiac arrhythmias have similarly been incriminated in horses with insufficient lesions.[43] Similarly, a substantial proportion of conditioned sled dogs that die during competition lack lesions to account for death. However, in contrast to equine and human athletes, unexpected death of endurance-racing dogs may result from aspiration pneumonia, gastric mucosal lesions, and sled dog myopathy.

In the present study, most dogs that died during racing unexpectedly collapsed and died without previous clinical signs, regardless of the cause. Some dogs that died were reported by the musher to have substandard performance, and although no abnormalities could be detected via physical examination, the dogs died later in the race. Therefore, Iditarod Trail veterinarians recommend that a musher retire a dog from the race under such circumstances. In premier sled dog races such as the Iditarod Trail, Copper Basin, and the Yukon Quest, dogs that display clinical signs suggestive of aspiration pneumonia, gastric ulceration, or sled dog myopathy are required to be released from competition. Mushers remove affected dogs from harness and carry them to the next checkpoint where a veterinarian can evaluate their condition.

The risk for death that lesions detected in our study population pose to conditioned dogs competing in endurance races is unknown. Estimation of cause-specific mortality rates would be superior to crude death rate and proportional mortality rates for assessing risk for sudden death. However, data describing the total time that dogs were at risk during the study period were not available. Epidemiologic investigation to identify risk factors for death among endurance-racing dogs is warranted but is probably limited by the infrequency of race-related death and its multifactorial nature.

a. Minitab 14.0, Minitab Inc, State College, Pa.
b. Nelson S, Chief Veterinarian, Iditarod Trail Sled Dog Race: Personal communication, 2006.

References

1. Hinchcliff KW, Reinhart GA, Burr JR, et al. Metabolizable energy intake and sustained energy expenditure of Alaskan sled dogs during heavy exertion in the cold. *Am J Vet Res* 1997;58:1457–1462.
2. Cantor GH. 1995 ISDVMA guide to sled dog necropsies. In: *1995 Iditarod Trail sled dog race musher's/veterinarian's handbook*. Wasilla, AK: Iditarod Trail Committee, 1995;47–53.
3. Bharati S, Cantor GH, Leach JB, et al. The conduction system in sudden death in Alaskan sled dogs during the Iditarod Race and/or during training. *PACE* 1997;20:654–663.
4. Blake J. Sled dog myopathy. In: Schmidt KE, ed. *The musher and veterinary handbook*. 2nd ed. Wakefield, Mass: International Sled Dog Veterinary Medical Association, 2001;13–14.
5. Byard RW. Sudden infant death syndrome. In: Byard RW, ed. *Sudden death in infancy, childhood and adolescence*. 2nd ed Cambridge: Cambridge University Press, 2004;491–574.
6. Davis MS, Willard MD, Nelson SL, et al. Prevalence of gastric lesions in racing Alaskan sled dogs. *J Vet Intern Med* 2003;17:311–314.
7. Maddison KJ, Shepherd KL, Hillman DR, et al. Function of the lower esophageal sphincter during and after high-intensity exercise. *Med Sci Sports Exerc* 2005;37:1728–1733.
8. Widdicombe J, Singh V. Physiological and pathophysiological downregulation of cough. *Respir Physiol Neurobiol* 2006;150:105–117.
9. Parent C, King LG, Walker LM, et al. Clinical and clinicopathologic findings in dogs with acute respiratory distress syndrome: 19 cases (1985–1993). *J Am Vet Med Assoc* 1996;208:1419–1427.
10. Crawford PC, Dubovi EJ, Castleman WL, et al. Transmission of equine influenza virus to dogs. *Science* 2005;310:482–485.
11. Davis MS, McKiernan BS, McCullough S, et al. Racing Alaskan sled dogs as a model of "ski asthma". *Am J Respir Crit Care Med* 2002;166:878–882.
12. Davis MS, Willard MD, Nelson SL, et al. Efficacy of omeprazole for the prevention of exercise-induced gastritis in racing Alaskan sled dogs. *J Vet Intern Med* 2003;17:163–166.
13. Davis MS, Willard MD, Williamson KK, et al. Sustained strenuous exercise increases intestinal permeability in racing Alaskan sled dogs. *J Vet Intern Med* 2005;9:34–39.
14. Murray MJ, Schusser GF, Pipers FS, et al. Factors associated with gastric lesions in Thoroughbred racehorses. *Equine Vet J* 1996;28:368–374.
15. Begg LM, O'Sullivan CB. The prevalence and distribution of gastric ulceration in 345 racehorses. *Aust Vet J* 2003;81:199–201.
16. Choi SC, Choi SJ, Kim JA, et al. The role of gastrointestinal endoscopy in long-distance runners with gastrointestinal symptoms. *Eur J Gastroenterol Hepatol* 2001;13:1089–1094.
17. Moses FM. Gastrointestinal bleeding and the athlete. *Am J Gastroenterol* 1993;88:1157–1159.
18. Simpson KN. Diseases of the stomach. In: Ettinger SJ, Feldman EC, eds. *Textbook of veterinary internal medicine*. 6th ed. St Louis: Elsevier Saunders, 2005;1310–1331.
19. Simpson KN, Neiger R, DeNovo R, et al. ACVIM consensus statement: the relationship of *Helicobacter* spp infection to gastric disease in dogs and cats. *J Vet Intern Med* 2000;14:223–227.
20. Long RD. Treatment of common injuries in endurance racing sled dogs. *Compend Contin Educ Pract Vet* 1993;15:434–437.
21. Cantor GH, Nelson S, Vanek JA, et al. *Salmonella* shedding in racing sled dogs. *J Vet Diagn Invest* 1997;9:447–448.
22. Morley PS, Strohmeyer RA, Tankson JD, et al. Evaluation of the association between feeding raw meat and *Salmonella enterica* infections at a Greyhound breeding facility. *J Am Vet Med Assoc* 2006;228:1524–1532.
23. Bartsch RC, McConnell EE, Imes GD, et al. A review of exertional rhabdomyolysis in wild and domestic animals and man. *Vet Pathol* 1977;14:314–324.
24. Valentine BA, McDonough SP, Chang YF, et al. Polysaccharide storage myopathy in Morgan, Arabian, and Standardbred related horses and Welsh-cross ponies. *Vet Pathol* 2000;37:193–196.
25. Cellular adaptations, cell injury, and cell death: mechanisms of cell injury. In: Kumar V, Abbas AK, Fausto N, eds. *Robbins and Cotran pathologic basis of disease*. 7th ed. Philadelphia: Elsevier Saunders, 2005;14–19.
26. Piercy RJ, Hinchcliff KW, DiSilvestro RA, et al. Effect of dietary supplements containing antioxidants on attenuation of muscle damage in exercising sled dogs. *Am J Vet Res* 2000;61:1438–1445.
27. Piercy RJ, Hinchcliff KW, Morley PS, et al. Vitamin E and exertional rhabdomyolysis during endurance sled dog racing. *Neuromuscul Disord* 2001;11:278–286.
28. Burr JR, Reinhart GA, Swenson RA, et al. Serum biochemical values in sled dogs before and after competing in long-distance races. *J Am Vet Med Assoc* 1997;211:175–179.
29. Cullen JM, MacLachlan NJ. Liver, biliary system, and exocrine pancreas. In: McGavin MD, Carlton WW, Zachary JF, eds. *Thomson's special veterinary pathology*. 3rd ed. St Louis: Mosby Inc, 2001;81–124.
30. Turk JR, Root CR. Necropsy of the canine heart: a simple technique for quantifying ventricular hypertrophy and valvular alterations. *Compend Contin Educ Pract Vet* 1983;5:905–910.
31. Stepien RL, Hinchcliff KW, Constable PD, et al. Effect of endurance training on cardiac morphology in Alaskan sled dogs. *J Appl Physiol* 1998;85:1368–1375.
32. Hinchcliff KW, Constable PD, Farris JW, et al. Electrocardiographic characteristics of endurance-trained Alaskan sled dogs. *J Am Vet Med Assoc* 1997;211:1138–1141.
33. Constable PD, Hinchcliff KW, Olson JL, et al. Athletic heart syndrome in dogs competing in a long-distance sled race. *J Appl Physiol* 1994;76:433–438.
34. Constable PD, Hinchcliff KW, Olson JL, et al. Effects of endurance training on standard and signal-averaged electrocardiograms of sled dogs. *Am J Vet Res* 2000;61:582–588.
35. Gunson DE, Sweeney CR, Soma LR. Sudden death attributable to exercise-induced pulmonary hemorrhage in racehorses: nine cases (1981–1983). *J Am Vet Med Assoc* 1988;193:102–106.
36. Cardiac arrhythmias and their electrocardiographic interpreta-

tion. In: Guyton AC, Hall JE, eds. *Textbook of medical physiology*. 9th ed. Philadelphia: WB Saunders Co, 1996;149–158.
37. Cellular adaptations, cell injury, and cell death: morphology of cell injury and necrosis. In: Kumar V, Abbas AK, Fausto N, eds. *Robbins and Cotran pathologic basis of disease*. 7th ed. Philadelphia: Elsevier Saunders, 2005;19–23.
38. Parsons JP, Mastronarde JG. Exercise-induced bronchoconstriction in athletes. *Chest* 2005;128:3966–3974.
39. McFadden ER, Awadski DK. Vocal cord dysfunction masquerading as exercise-induced asthma. A physiologic cause for "choking" during athletic activities. *Am J Respir Crit Care Med* 1996;153:942–947.
40. Eckart RE, Scoville SL, Campbell CL, et al. Sudden death in young adults: a 25-year review of autopsies in military recruits. *Ann Intern Med* 2004;141:829–834.
41. Maron BJ, Epstein SE, Roberts WC. Causes of sudden death in competitive athletes. *J Am Coll Cardiol* 1986;7:204–214.
42. Gelberg HB, Zachary JF, Everitt JI, et al. Sudden death in training and racing Thoroughbred horses. *J Am Vet Med Assoc* 1985;187:1354–1356.
43. Kiryu K, Machida N, Kashida Y, et al. Pathologic and electrocardiographic findings in sudden cardiac death in racehorses. *J Vet Med Sci* 1999;61:921–928.