

Sudden death attributable to exercise-induced pulmonary hemorrhage in racehorses: Nine cases (1981–1983)

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Summary: Pathologic changes are described in 11 horses that died during racing or training; 9 died of acute pulmonary hemorrhage (exercise-induced pulmonary hemorrhage), 1 died of exsanguination, and 1 died of CNS trauma. Cardiac lesions were not found in any horse. Severe engorgement of pulmonary vessels, with hemorrhage into alveoli, airways, interstitium, and subpleural tissues, was observed in all 9 horses that died of exercise-induced pulmonary hemorrhage. Infiltration of eosinophils and/or lymphocytes around vessels and airways was seen in 6 horses. Focally extensive fibrosis was observed in the pleura and interstitium of 6 horses, and collections of siderophages were seen in the fibrous tissue and in the airways. Focal occlusion of bronchioles with inspissated mucus, such as that associated with small airway disease, was found in 4 horses. Underlying respiratory tract lesions, particularly those associated with small airway disease or bronchiolitis, may have a role in fatal pulmonary hemorrhage.

Sudden death in seemingly healthy horses most often is attributed to diseases of the cardiovascular system, such as myocarditis,¹⁻³ rupture of the heart, aorta, or large arteries,^{4,5} ruptured chordae tendineae,⁶ and atrial dysrhythmia.⁷ Nevertheless, in a recent study of 25 horses, 21 of which died during racing or training, only 7 of the 21 (33%) had lesions sufficient to explain the sudden death.⁸ The objective of the study reported here was to determine the incidence and cause of sudden death in exercising horses.

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Criteria for selection of cases

Between January 1981 and July 1983, all horses that died suddenly during racing or training at 2 Pennsylvania racetracks were transported to the necropsy facility of the George D. Widener Hospital at the University of Pennsylvania School of Veterinary Medicine. During the study period, approximately 12,000 races were run, with approximately 9 horses/race. Year-round racing was conducted at both racetracks, and approximately 1,500 Thoroughbreds were housed at each facility. Horses that were euthanatized because of breakdown or other injuries were excluded before referral to the university. Also excluded were horses that died suddenly, but not while racing or training (eg, a horse found dead in its stall one morning was not included). Complete necropsy was performed within 4 to 6 hours of death and included examination of all thoracic and abdominal organs. Tissue specimens were obtained for histologic examination from lungs, liver, kidneys, and organs that appeared abnormal. Multiple lung tissue specimens (>10) were obtained from all horses, including specimens from the cranial, lateral caudal, central dorsal caudal, and hilar regions of both lungs and from the accessory lung lobe. All tissue specimens were fixed in neutral-buffered 10% formalin, and lung specimens were submerged under absorbant towels. After fixation, tissue specimens were embedded in paraffin, and 5- μ m sections were cut and were stained with hematoxylin and eosin. Selected sections were treated with Giemsa, toluidine blue, and Masson trichrome stains.

Results

During the period of the study, 11 horses died suddenly without apparent cause of death. Age ranged from 2 to 9 years, and the group included females, geldings, and stallions, representing a reasonable sample of the total population racing at the 2 tracks. Death did not have apparent seasonal incidence.

Two horses died during training; the others died while racing. All the latter horses had completed three fourths of the race. All were in apparent good health immediately before their fatal exercise.

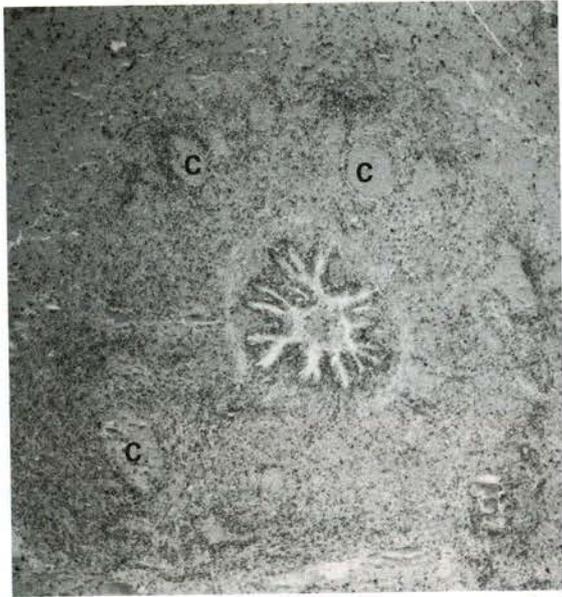


Figure 1—Photomicrograph of a bronchus of horse 3, in which severe hemorrhage separates the various layers—lining epithelium, submucosa, muscularis, and peribronchiolar tissue. Notice bronchial cartilage (c) in outer layers and minimal hemorrhage in lumen. H&E stain; $\times 26$.

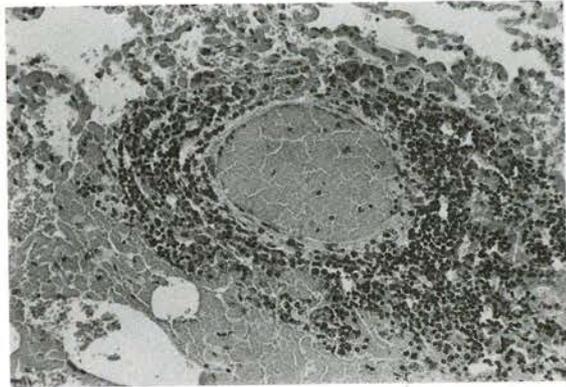


Figure 2—Photomicrograph of a small vein in the lung of horse 5, in which the various layers of the wall contain numerous eosinophils. H&E stain; $\times 105$.

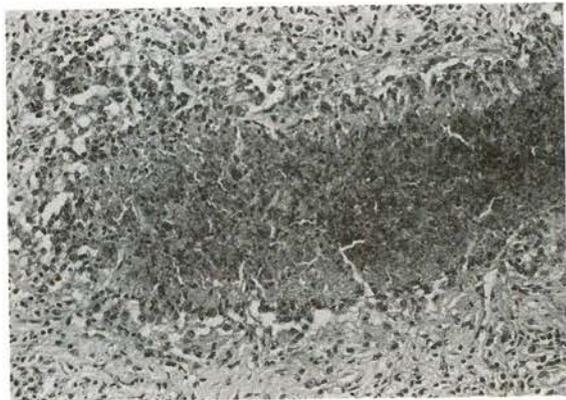


Figure 3—Photomicrograph of a focus of necrotic eosinophils surrounded by fibrous tissue, lymphocytes, macrophages, and giant cells in an area of severely congested and hemorrhagic lung. H&E stain; $\times 110$.

Of the 11 horses, 9 died apparently from exercise-induced pulmonary hemorrhage (EIPH). The nasal cavity, trachea, and bronchi of all 9 horses, except No. 3, were filled with bloodstained froth. The lungs were deep red to black, with a few normal-appearing pink areas in the cranial portion. The lungs were heavy, and felt moderately firm, consistent with being blood-filled. In horses 3 and 5, multiple deep red nodules (1 to 3 cm in diameter) were scattered throughout the lung parenchyma. Focal fibrosis of the pleura, evident as thick white areas over the lung surface, was seen in horses 1 through 5 and horse 9. Some of these areas felt firm and extended into the lung parenchyma. Pathologic changes that could have accounted for the sudden death were not observed in any other system, and macroscopic cardiac lesions were not observed in any horse.

Microscopic examination of the lungs of all 9 horses revealed engorgement of the pulmonary arteries, veins, and capillaries, with hemorrhage into alveoli, bronchioles, bronchi, interstitium, and subpleural tissue. The severity of the engorgement and hemorrhage varied from almost nonexistent to massive in various areas of the lung, but the caudal portion of the lung lobes was the site of the most severe hemorrhage. Pleural and interstitial fibrosis or marked eosinophilic bronchitis and bronchiolitis were accompanied by severe hemorrhage. Some airways with severe eosinophilic and lymphocytic infiltration had extensive hemorrhage, and the lining epithelium, submucosa, muscular layer, cartilage, and peribronchial tissue were separated widely by areas of hemorrhage (Fig 1). Infiltration of eosinophils around and within walls of airways and blood

vessels was observed in horses 3, 5, 7, and 9 (Fig 2), and lymphocytes were seen in similar locations in horses 1, 3 through 5, 7, and 9. The severity of the infiltration varied from location to location within the lung—almost nonexistent in some and severe in others. The most severe changes were in the dorsal caudal and hilar areas, but in some horses, multiple, severely affected areas seemed to be randomly distributed. Multiple oblong, oval, or circular foci of degenerating eosinophils resembling parasite migration tracks were observed in the pulmonary parenchyma of horses 3 and 5 (Fig 3). Alternatively, these might have been bronchioles, with attenuated or sloughed bronchial epithelial lining, plugged by bronchial casts of necrotic eosinophils. These eosinophil-containing foci were most numerous within the aforementioned dark red nodules that were visible in the lungs of these 2 horses.

Focally extensive fibrosis of the pleura and interstitium, often including the area around large vessels and airways, were observed in 6 of the horses. Groups of macrophages laden with hemosiderin also were seen within this fibrous tissue, particularly at the junction of the pulmonary parenchyma and the deep layers of the pleura. In horses 1 through 4, 7, and 9, groups of siderophages also were seen in

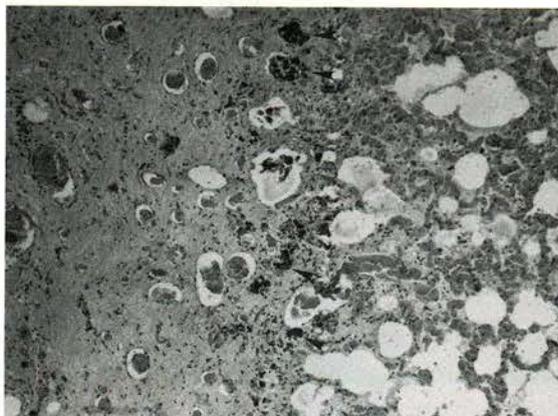


Figure 4—Photomicrograph of a focus of pleural fibrosis, in which are seen congested capillaries and groups of siderophages (arrows). H&E stain; $\times 40$.

airways (Fig 4), peribronchial connective tissue, alveolar walls, and alveolar lumens. Siderophages infrequently were observed in the alveoli of all horses. Severe focal mucoid bronchiolitis was seen in horses 1 and 3 through 5. In affected areas, the bronchioles and several bronchi were occluded completely with plugs of inspissated mucus and cellular debris (Fig 5). Degenerating inflammatory cells were scattered throughout the lining epithelium, and lymphocytes, eosinophils, and neutrophils infiltrated the bronchiolar walls and peribronchial connective tissue.

In these 9 horses, sudden death was attributed to pulmonary failure secondary to fulminant EIPH. Of the 9, 4 had had epistaxis at the time of death and 5 had previous history of EIPH; the EIPH history of the other 2 horses was unknown.

Horses 10 and 11 were included in the study because they had died during exercise without apparent traumatic cause of death. However, at necropsy, horse 10 had hemoperitoneum attributable to severance of the right internal iliac artery secondary to fracture of the right pubic bone. Other tissue specimens did not have pathologic changes.

Horse 11 had multiple fractures of the left forelimb and third and fourth cervical vertebrae, with macroscopic evidence of spinal cord compression. Other tissues did not have pathologic changes, with the exception of mild pulmonary hemorrhage and eosinophilic peribronchitis in multiple lung specimens.

Sudden death in these 11 exercising horses was attributed to EIPH in 9 horses, exsanguination in 1 horse, and CNS trauma in 1 horse.

Discussion

All horses of this study had lesions sufficient to explain their sudden death during exercise. This differed appreciably from the report of Gelberg et al,⁸ who found a 32% probability of such lesions. The majority (82%) of the horses of our study had pulmonary lesions sufficient to explain the sudden death. In the study of Gelberg et al,⁸ the authors

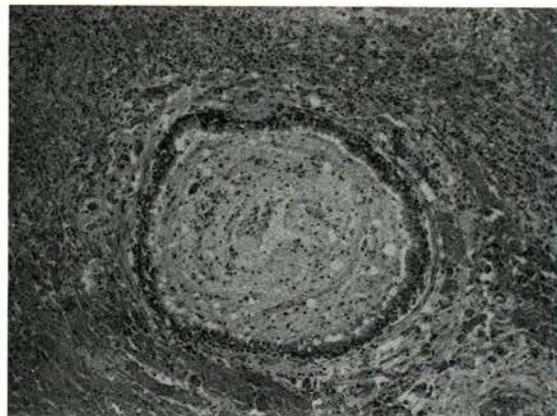


Figure 5—Photomicrograph of mucoid bronchiolitis. The lumen is plugged with mucus and degenerating inflammatory cells. Peribronchiolar connective tissue is infiltrated with lymphocytes and eosinophils, and capillaries are engorged. H&E stain; $\times 46$.

speculated that sudden death most likely was associated with exercise-induced acute cardiovascular failure; this conclusion was reached despite the fact that only 2 horses had histologic evidence of myocardial disease. Of course, a microscopic lesion causing conduction disturbance, with subsequent heart failure, may have been overlooked.

Epistaxis during or after exercise long has been recognized as a serious problem in racehorses.⁹ Its origin in the lungs was suggested,¹⁰ but was not confirmed until fiberoptic endoscopy was used widely.^{11,12} Because of its association with exercise, the condition has become known as EIPH. Morbidity of EIPH, its relation to age, and its association with various situations, has been described,¹¹⁻¹³ as has the effect of treatment with various drugs.^{12,14-17} Occurrence of EIPH is not random, and it is observed consistently in individual horses.^{12,17}

Despite its occurrence in 45 to 86% of racing horses, data are not available on the death rate of horses with EIPH. Our study indicated that EIPH was the cause of death in 82% of the Thoroughbred racehorses that died suddenly (while exercising) of causes unrelated to musculoskeletal trauma. Thus, EIPH should be considered as the most common cause of sudden death in exercising Thoroughbred racehorses.

During the period of the study reported here, approximately 12,000 races were run; therefore, we found the death rate of horses with EIPH to be 1 death/1,500 races.

There is only limited understanding of the pathophysiologic mechanism of EIPH. It is associated with atrial fibrillation,¹⁸ but in human beings, atrial fibrillation is associated with increased left atrial and pulmonary wedge pressures.¹⁹ Paroxysmal atrial fibrillation has been reported in racehorses,²⁰⁻²³ with most horses reverting to normal sinus rhythm within 24 hours. If transient arrhythmia develops in a horse during a race, it might not be detected. Thus, many apparently healthy horses may be exercising with

such arrhythmias, and may be at risk for development of EIPH. Exercise-induced pulmonary hemorrhage may be triggered by the asphyxia that develops during breath-holding after horses leave the starting gate.²⁴ Another hypothesis is that upper airway obstruction, as seen in horses with laryngeal hemiplegia, may initiate pulmonary bleeding during maximal exercise.²⁵

Alternative explanations for EIPH have included subclinical respiratory disease resulting in bronchospasm precipitated by exercise.^{10,26,27} In our horses, subclinical chronic bronchitis may have been involved, especially in old horses.²⁶ Bronchiole obstruction and/or scarring might contribute to local increases in perivascular pressure,^{26,27} and perhaps might result in pulmonary hemorrhage. Of the horses of this study, 6 had fibrous pulmonary scars, and 4 had eosinophilic bronchiolitis.

In a recent study,²⁸ extensive small airway disease was observed in close association with the vascular changes in lungs of horses with EIPH. Bronchiolitis was suspected as the early lesion, and increased number and size of bronchial arteries may have resulted.²⁸ We also suspect that the eosinophils in eosinophilic bronchiolitis associated with allergic lung disease²⁹ may have a role in alveolar hemorrhage. In the guinea pig, eosinophils contain a metalloprotein that degrades type-I and type-III collagen, which constitute the bulk of lung and blood vessel collagen.³⁰ Thus, eosinophils could damage the integrity of lung blood vessels and alveolar walls so that increased pulmonary perfusion and intermittent higher airway pressure associated with exercise might precipitate pulmonary hemorrhage. Cytologic findings in tracheobronchial aspirates from many Thoroughbred racehorses were suggestive of small airway disease,³¹ and evidence of past pulmonary hemorrhage was detected in many of the horses.

In conclusion, only 4 of the 9 horses that died from pulmonary hemorrhage had epistaxis at the time of death, although all but 1 had blood-stained froth in the airways at necropsy. Thus, pulmonary hemorrhage cannot be ruled out as the cause of death solely because of lack of blood in the nares. Necropsy should include thorough examination of the lungs for the signs of EIPH—deep red to black, heavy, firm lungs, and bloodstained froth in the airways. Detailed examination of the heart and larynx for predisposing lesions also should be performed.

Although the study was designed to include only horses with nontraumatic causes of death, 2 horses that died from trauma were included because of the lack of external signs of such trauma. Because our study indicated that EIPH was the apparent cause of death in the majority (82%) of exercising Thor-

oughbred racehorses, complete necropsy was necessary to rule out a traumatic cause of death.

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Book Review: Decision Making in Small Animal Soft Tissue Surgery

This textbook consists of 10 sections based on body systems. Each section comprises chapters that contain algorithms and specific comments on how decisions regarding surgical patients should be made. In the preface, the authors state that the intention of the book is to "complement, not to replace existing textbooks." Practicing veterinarians and students of veterinary medicine will find this text helpful in organizing their thoughts and developing a disciplined approach to patient care.

As with most textbooks that contain contributions from several authors, the content varies from section to section. The editors are to be complimented for minimizing variations in quality. Of particularly good quality are the discussions of acute and chronic diarrhea and neoplastic disorders. This may be attributable in part to the fact that these topics lend themselves well to the format used in the text. Topics that require judgment on the part of the veterinarian before using the algorithms are not well suited to this. This problem is exemplified by the discussion of management of traumatic wounds. The decision-making process is clearly described, but unless the veterinarian has accurately assessed the wound before following the algorithm, it is difficult to

arrive at the intended conclusion. A similar comment could be made regarding the discussion of biliary tract trauma.

Because nearly all topics were handled in the space of 2 pages, including the algorithms, decisions had to be made regarding what material was to be included. In the discussion of megaesophagus, as well as the discussion of vascular ring anomalies, a Heller's myotomy of the lower esophageal sphincter is recommended for treatment of spasm or stricture of the lower esophageal sphincter. The need for this procedure in veterinary medicine is quite limited, and it is used infrequently. The overall poor prognosis associated with surgical treatment of persistent right aortic arch is not emphasized in this section. In the discussion of airway obstruction, it is unclear as to why castellated laryngofissure was the only technique illustrated for treatment for laryngeal paralysis.

Another problem with the algorithm format is illustrated by the section on heartworm disease: In the algorithm accompanying this discussion, the recommendation is made that the presence of liver and kidney disease in conjunction with evidence of right-sided heart disease should be considered an indication that adult worms be removed

via pulmonary arteriotomy. It is doubtful that this statement can be universally applied to all animals in this category. The statement also is made that uncomplicated bile peritonitis is aseptic and does not require abdominal drainage. Although it is probably true that uncomplicated bile peritonitis does not require drainage of the abdominal cavity, it is misleading to imply that this is an aseptic condition. In the algorithm accompanying the discussion of linear intestinal foreign bodies, the reader is informed that surgery is invariably required. Recent reports suggest that, in certain instances, these may be managed expectantly.

Potential purchasers of this text should be aware of the intention of the editors and the limitations of the text. Within this context, the text succeeds in its mission and should be a valuable asset to veterinary practitioners and veterinary students seeking to improve their management of small animals requiring surgery.—[*Decision Making in Small Animal Soft Tissue Surgery*. By Allen G. Binnington and Joanne R. Cockshutt. 232 pages; illustrated. B. C. Decker Inc, Burlington, Canada. 1988. Available in USA from CV Mosby Co, 11830 Westline Industrial Dr, St Louis, MO 63146. Price \$40.00.]—DALE E. BJORLING