Pulmonary Hemorrhage in Exercising Horses: A Review

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Epidemiologic surveys have contributed significantly to our understanding of pulmonary hemorrhage in exercising horses but much remains to be learned about the mechanisms which predispose to its occurrence. Recent review articles (*Clarke,* 1985; *Pascoe* and *Raphel,* 1982) have summarized much of this information and highlight the need for research efforts to focus on the pathophysiology of this condition in horses (*Pascoe,* 1985).

Historical Background

Epistaxis has been reported as a problem in some racing Thoroughbreds for at least 300 years (*Markham,* 1681). Subsequent reports suggested that epistaxis occurred in 0.5–2.5 percent of racing Thoroughbreds (*Cook,* 1974). With the development of flexible fiberoptic endoscopy it became apparent that although some horses manifested epistaxis after exercise a much larger percentage (45–75%) had endoscopic evidence of pulmonary hemorrhage without showing epistaxis (*Pascoe* and *Raphel,* 1982). These observations focussed attention on the lung rather than the nose as the probable source of hemorrhage and subsequent studies have endeavored to define the problem and assess the efficacy of medications used for treatment of EIPH.

Definition and Diagnosis

Exercise-induced pulmonary hemorrhage (EIPH) is defined as bleeding from the lungs as a consequence of exercise. Definitive diagnosis is established by endoscopic observation of blood in the tracheobronchial airways. Although endoscopy can be performed at the completion of exercise previous clinical experience has suggested that examination within 30–90 minutes of the completion of exercise will provide the best opportunity for recognition of blood in the airways. If blood is absent at the initial examination but EIPH is strongly suspected a second examination 30 minutes later is recommended. Recognition of epistaxis should not preclude endoscopic examination of the tracheobronchial airways as other sites, e. g, the nasal turbinates, ethmoturbinates or gutteral pouches need to be eliminated as potential sources of hemorrhage.

If endoscopic examination is not possible, cytologic examination of a tracheobronchial aspirate may be considered. Observation of macrophages containing intracytoplasmic droplets of hemosiderin is strongly suggestive of recent pulmonary hemorrhage (*Beech,* 1975). These hemosiderophages may be recovered in a transtracheal aspirate for several weeks after an episode of EIPH (*Whitwell* and *Greet,* 1984).

Epidemiology

Endoscopic studies have shown that pulmonary hemorrhage has been associated with most common types of equine exercise, a notable exception being endurance events (*Pascoe* and *Raphel,* 1982). The incidence has varied from 0–75% depending on the type and intensity of exercise studied (*Clarke,* 1985). More recent cytologic (*Whitwell* and *Greet,* 1984) and histologic studies (*Mason, Collins* and *Watkins,* 1983) have strengthened the concept that most if not all Thoroughbred horses in training experience pulmonary hemorrhage. EIPH has been observed in Thoroughbreds, Standardbreds, Quarter Horses, Appaloosas and Polo ponies and occurs with a similar frequency irrespective of geographical location (*Clarke,* 1985).

Pulmonary hemorrhage is usually first noted in two year olds when they commence training and although some studies have suggested that the frequency may be higher in older horses, exercise intensity appears to be a more consistent feature than the horses age or sex. *Burrell* (1985) recently reported observing EIPH after cantering in Thoroughbred racehorses, although generally galloping at speeds greater than 14 m/s is required to induce EIPH. Although the likelihood of detecting EIPH increases with the intensity and duration of exercise the minimum intensity and duration necessary to produce EIPH remains to be established.

There appears to be no clear relationship between performance, and EIPH as judged by race finishing position although studies to determine the effect of EIPH on an individual horses performance need to be conducted. *Soma* et *al.* (1985) have suggested that continued episodes of EIPH may be associated with declining performance. *Mason* et *al.* (1984) found no correlation between EIPH and track surface, trainers, location of stables or type of bedding.

The repeatability of observations of EIPH has been of interest because of its importance in designing studies to evaluate the efficacy of medication used for treating EIPH. Because confirmation requires endoscopic observation a number of factors can influence the recording of a positive result. These include the site of hemorrhage within the lung, the volume of extravasated blood, the time of bleeding relative to the time of examination and the efficiency of mucociliary clearance and the site of observation within the lungs. Recognizing these variables, attempts have been made to establish the repeatability of EIPH observations (*Pascoe* and *Raphel,* 1982). Based on a recent study it appears that observations after at least four consecutive exercise periods are necessary to establish the repeatability of EIPH for on individual horse (*Pascoe, McCabe, Franti* and *Arthur,* 1985).

No correlation has been reported between upper airway abnormalities (e. g., laryngeal hemiplegia, pharyngeal lymphoid hyperplasia) and EIPH (*Pascoe* and *Raphel,* 1982; *Raphel,* 1982).

Clinical Features

Physical and clinical examination without benefit of endoscopy or tracheobronchial cytology is not a reliable means of diagnosing EIPH. Most horses show no apparent discomfort during bleeding episodes and coughing is not a reliable sign because it can be initiated by a variety of stimuli such as inhaled dirt or grass, increased respiratory secretions as a result of exercise or exacerbation of preexisting bronchiolitis. Swallowing is a more consistent sign and is often the first indication of EIPH noted by astute trainers. Abnormal respiratory patterns are also uncommon and their detection warrants additional investigation for more serious pulmonary disease. At rest, horses known to experience EIPH cannot be differentiated from non-bleeders on the basis of physical examination, electrocardiogram, hematology, biochemical or hemostatic tests. Perturbations in any of these examinations suggests concurrent systemic disease which requires additional careful examination.

Thoracic radiographs provide useful information but are not necessarily diagnostic. Although previous studies ascribed a regional pattern in the thoracophrenic angle as indicative of EIPH (*O'Callaghan* and *Goulden,* 1982; *Pascoe, O'Brien, Wheat* and *Meagher,* 1983), recent studies (*Pascoe* and *O'Callaghan,* unpublished observation) suggest that this finding is relatively uncommon and probably indicative of more serious pulmonary disease. Correlation of radiographic signs with pathologic features is needed to establish patterns suggestive of EIPH.

Pathophysiology

Recent studies have focused on the lung as the source of hemorrhage in EIPH. However, several fundamental questions concerning the source of the blood and the mechanisms which produce pulmonary hemorrhage during or after exercise in horses remain to be answered. Pathologic descriptions of the lungs of bleeders have been few and usually incomplete. *Robertson* (1913) believed that the blood seen in the lungs was inspired during exercise and caused death by asphyxiation. Endoscopic studies do not support this observation. *Mahaffey* (1962) reported that hemorrhage occurred from rupture of alveolar capillaries, but could find no histologic evidence to indicate why this happened.

In subsequent reports, other investigators (*Cook,* 1974; *Johnson, Garner, Hutcheson* and *Merriam,* 1973; *Rooney,* 1970) have noted several common features. These included observing areas of hemorrhage in the dorsal region of the caudal lung lobes which were characterized by blood filled alveoli and bronchioles, variable degrees of interstitial fibrosis, microabscesses and macrophages with intracytoplasmic hemosiderin. In the most extensive, published survey *Mason* et *al.* (1983) examined 117 Thoroughbred horses and found consistent gross evidence for a specific regional location for hemorrhage in the dorsal caudal lung lobe. In the collapsed lung these areas were bilaterally symmetrical, purple in color and were surrounded by apparently normal lung. This discoloration was interpreted as evidence of previous hemorrhage. The most striking histological change was widespread bronchiolitis with little or no associated mucus production. Hemosiderophages were seen in some alveoli and there was some evidence of alveolar scarring.

Recently *O'Callaghan, Pascoe* and *Tyler* (1985, unpublished observations) have corroborated these gross pathology findings in a group of 24 Thoroughbred horses with a confirmed history of EIPH. A similar distribution of gross discoloration was noted on the collapsed lung. After inflation it was noted that the discoloration was caused by light brown or bronze pigment staining of the dorsal and dorso-lateral surface of the caudal lung lobe. The fine surface pattern of pigment distribution suggests that it was located in the interstitium. At the time of writing, microscopic examination had not been completed but preliminary evidence suggest that the pigment staining resulted from hemosiderin deposition within the interstitium. Gross observation of fixed slices of lung show that these areas of pigment staining are associated with increased bronchial arterial supply and extend from the dorsal surface into the parenchyma and are associated with evidence of airway disease. Histologic examination will hopefully allow more accurate description of the relationship of these observations.

Recognizing that the lung has two circulations, the pulmonary and bronchial arterial circulations and that there appears to be a relatively specific regional location for the hemorrhage tempts speculation on possible mechanisms which might predispose to EIPH. A number of hypotheses have been tendered (*Clarke,* 1985; *Cook,* 1974; *Robinson* and *Derksen,* 1980) and while each has its merits, additional information from pathology and physiology studies is necessary to corroborate these ideas.

Based on the limited information available, the most tenable hypothesis seems to suggest that small airway disease may predispose to EIPH. Because horse lungs have poor collateral ventilation (*Robinson* and *Sorenson,* 1978), partial or complete airway obstruction from small airway disease might predispose to uneven expanding forces on segments of lung subtended by such abnormal airways. Vessels adjacent to these diseased areas of lung would be subjected to tremendous increases in local perivascular pressures because of the interdependence of lung tissue and such distending pressures may be sufficient during exercise to produce vessel rupture or tissue tearing and subsequent hemorrhage. Subsequent damage to the tissue with continued tearing could eventually be expected to produce grossly visible lesions within the lung. If in fact histological evidence supports the dorsal and dorsolateral areas as being the only regions involved, then based on evidence in dogs regional pleural pressure changes may be greater in this location predisposing to additional stresses on the lung tissue during exertion.

Unfortunately these ideas do not explain why the small airway disease occurred initially or if in fact it is the initial predisposing factor. An equally tenable hypothesis could suggest that mechanical stresses applied to the dorsocaudal lung during maximal exertion may cause lung tissue tearing and hemorrhage which predisposes to small airway disease and subsequent airway obstruction and its possible se-

quelae. The apparent bronchial arterialization of these abnormal areas of lung is probably a normal repair response to lung injury (*Cudcowicz,* 1968) but once established may also contribute to the bleeding observed in EIPH.

Therapy

The variety of current treatment modalities highlights our limited understanding of the pathophysiology of EIPH. Treatment is largely empirical and usually directed at prophylaxis. Reports of the efficacy of available preparations are largely ancedotal and unsupported by clinical trials. Supportive treatment is not usually required as hemorrhage ceases soon after racing in most horses; blood being cleared from the airways within six hours. A small number of horses continue to bleed for several days after racing. These horses usually show signs of systemic disease and should be evaluated for concurrent pulmonary disease and treated accordingly.

Massive fatal episodes of hemorrhage occur rarely but because of their catastrophic significance in equine spectator sports they have contributed greatly to the controversy surrounding regulation of EIPH and epistaxis in competitive equine events.

The more common therapeutic agents used for treating EIPH positive horses include furosemide, conjugated estrogens, hesperidin-citrus bioflavinoids, vitamin C, coagulants, clenbuterol, disodium cromoglycate and a variety of nonspecific feed supplements. Hesperidin-citrus bioflavinoids used as a feed supplement have been shown not to be effective in controlling EIPH (*Sweeney* and *Soma,* 1984).

Furosemide is permitted as a prerace medication for registered bleeders in most racing states in North America. Its continued use is surrounded by controversy because of difficulty in establishing its efficacy in treating EIPH and because of the potential problems that the associated diuresis causes with urinary detection of prohibited medications. Most studies have shown that furosemide (200–400 mg IV, 1–3 hours preexercise) does not stop pulmonary hemorrhage (*Pascoe, Ferraro, Cannon, Arthur* and *Wheat,* 1981; *Sweeney* and *Soma,* 1984) but may be effective in reducing pulmonary hemorrhage in most horses (*Pascoe* et *al.,* 1985). The rationale for using furosemide was based on the concept that EIPH may have been caused by pulmonary edema, however the association of pulmonary edema with EIPH remains to be proven.

Ipratroprium was shown to be effective in 2 horses in multiple trials but needs additional evaluation before a sound recommendation can be made (*Sweeney, Soma, Bucan* and *Ray,* 1984). Without an improved understanding of the pathophysiological mechanisms involved in EIPH it is difficult to provide a rational basis for therapy.

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