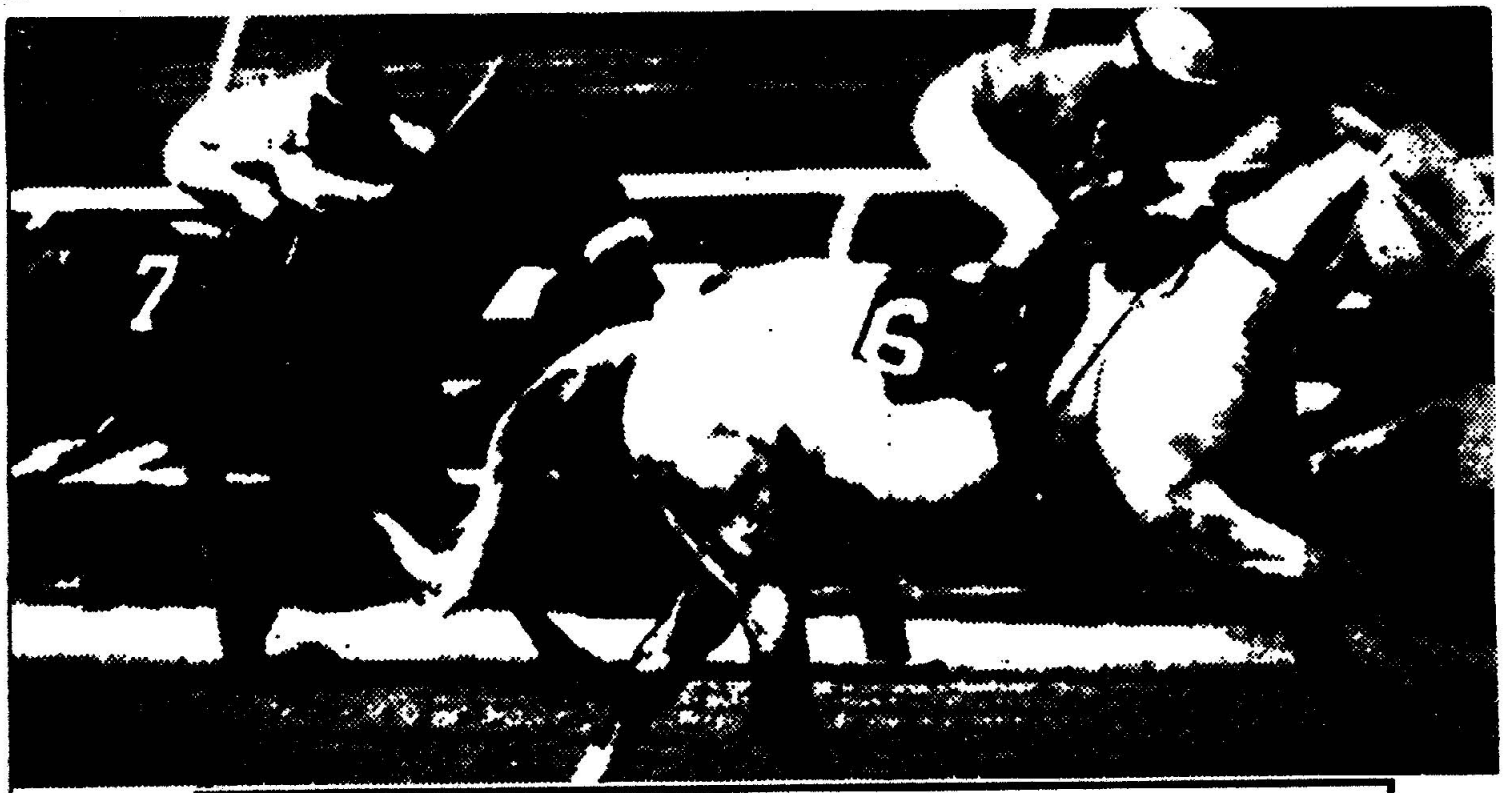

A WORKSHOP

Exercise-Induced Pulmonary Hemorrhage Findings, Part 2

Moderator

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A workshop on Exercise-Induced Pulmonary Hemorrhage was held by the Association of Racing Commissioners International Drug Testing and Quality Assurance Program, on January 3, 1991, in Cincinnati. Equine Practice *is pleased to present the proceedings of the workshop. Part 1 was presented in* Equine Practice, *January 1992, Vol. 14, No. 1, page 19, and Part 3 will appear in a future issue.*

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Etiology and Pathogenesis

The etiology and pathogenesis of exercise-induced pulmonary hemorrhage (EIPH) outlined were:

- The events that trigger episodes of EIPH are unknown and the relationship between initial episodes of EIPH and the well-characterized end-stage lung disease associated with this condition is poorly understood. Factors that may be involved in the etiology of EIPH include small airway disease,[12-14] upper airway disease,[15] increased blood viscosity, and cardiac output along with the high pressures in the pulmonary and bronchial circulations of exercising horses.[16,17] Echinocytosis is also a possible etiology.[18,19]
- No evidence is available to show that defects in blood clotting are in any way associated with episodes of EIPH. However, the 50% increase in hematocrit and the twofold or greater increase in blood viscosity associated with intense exercise may contribute to the occurrence of EIPH.[20]
- Opinion is divided on the role of the very substantial (four- to fivefold) increases in pulmonary vascular pressure associated with strenuous exercise in the pathogenesis of EIPH. Some authorities hold that these increases are not carried over to the pulmonary capillaries, and are not, by themselves, sufficient to cause blood vessel rupture and produce EIPH. This relationship is also thought to hold when negative airway pressures are greatly increased, as occurs in natural or induced laryngeal hemiplegia.

These facts are interpreted as evidence that pulmonary blood vessels do not easily rupture and that pathological change must be present to allow pulmonary vessels to rupture and cause EIPH.

Other authorities, however, point to the fact that pulmonary capillaries in the rabbit have been shown to rupture at pressures as low as 40 Torr[21] and suggest that this pressure is well within the range that may be attained in equine pulmonary capillaries during intense exercise. These authorities suggest that rupture of healthy pulmonary capillaries is theoretically possible, based simply on the possible substantial pressure increases in the pulmonary circulation during intense exercise. Another factor that may contribute to rupture of pulmonary capillaries is the presence of bronchial artery-pulmonary artery anastomoses, which may also contribute to EIPH.[1]

- The nature of any local pathological changes that may be associated with the initial rupture of pulmonary vessels is unknown. It is thought that local inflammatory lesions causing small airway disease are a likely predisposing cause of EIPH and may precede the hemorrhagic lesions. On the other hand, EIPH may occur in the normal horse and lead to inflammatory lesions and small airway disease.
- The role of intra-alveolar hemorrhage in the early development of EIPH is unclear. It may be that hemorrhage alone is sufficient to initiate development of the proliferative changes seen in the chronic EIPH lesion and this possibility is being investigated.
- The source of the hemorrhage (i.e., does the blood come from the bronchial or pulmonary circulation?) in EIPH is unknown. While the pulmonary circulation cannot be ruled out as the source of the hemorrhage, a more appealing speculation is that the hemorrhage comes from the bronchial circulation, although it may enter the pulmonary circulation through bronchopulmonary anastomoses, with the hemorrhage ultimately occurring from a ruptured pulmonary blood vessel.[1]
- The dominant characteristic of the mature EIPH lesion is bronchial artery proliferation and an increased number of bronchopulmonary anastomoses. This requires substantial neovascularization in the lesion and such newly developing blood vessels may be particularly prone to rupture, increasing the number and severity of EIPH incidents.[22]
- Although there is no direct supporting evidence, it is likely that once lesions are established the pathological changes are progressive and irreversible. The lesions appear to continue to develop and can eventually become substantial with unique location, geometry, and micropathological characteristics.[22]
- The mature or end-stage lesion first becomes apparent in the dorsal or highest portion of the caudal lobe of both lungs and extends cranially. The lesions are generally bilaterally symmetrical and some authors suggest that the lower margin of the lesion is horizontal. Grossly, the lesions are raised, blue in color, and readily distinguishable from normal lung tissue. Additionally, areas of apparently normal lung tissue may be interspersed between the lesions.[1]
- While the location, apparent limits on the extent of the lesion, and the pathology of the lesion are unique, there are no clearly understood reasons for the specific location, symmetry, and limits on extent of the lesions.
- While the end-stage lesions in lungs described previously are readily recognized during postmortem examination, no reports of less developed

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lesions or areas of such proliferative changes have been obtained from necropsy laboratories. Such lesions need to be specifically searched for in necropsy examinations of racing horses in order to explore the early stages of development of chronic EIPH lesions.

- A simple, noninvasive screening technique to locate and identify lesions associated with EIPH in racing horses would greatly help investigation of this condition.
- Because EIPH occurs in virtually all horses, the distinction between an EIPH and a non-EIPH horse is arbitrary and difficult to define. One consequence of this is that it would be extremely difficult at this time to investigate the possibility of a genetic component in the development of EIPH.

Micropathology

Micropathology findings relating to EIPH included:

- The characteristic lesions of end-stage EIPH lungs consist of destruction of alveolar tissue, extensive proliferation of the bronchial blood vessels, and greatly increased numbers of bronchial pulmonary anastomoses. The development of new blood vessels (angiogenesis) and the increased number of anastomoses provide a potential source for systemic arterial blood to enter pulmonary capillaries and then the airways.[1]

Effects on Performance

Effects on performance resulting from EIPH are listed as follows.

- In attempting to assess the effects of EIPH on performance one must bear in mind that all horses exercising strenuously suffer some degree of EIPH. The effects of EIPH on the performance of a racing horse are likely, therefore, to be directly related to the severity of the hemorrhage in any given episode of EIPH.
- Mild episodes of EIPH apparently have little or no effect on the racing performance of horses. The possibility that mild episodes of EIPH may occur concomitantly with pulmonary edema and have an effect on performance needs to be investigated.
- Horses that bleed from the nose (epistaxis) and those that pull up in a race clearly suffer a reduction in performance due to EIPH. The number of episodes of EIPH that prevent a horse from finishing its race is apparently small, since many horses that bleed from the nose suffer no apparent reduction in performance.

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- Reports of EIPH causing horses to slow down during races to swallow blood or to swerve or other behavioral changes are anecdotal and have not been systematically studied. This is despite the fact that the rules of racing in certain jurisdictions are based on these reports.
- A small but significant number of horses die acutely during races from causes unrelated to musculoskeletal trauma. Opinions differ as to the role of EIPH in the deaths of such horses.

Some researchers hold that the lesions in horses dying of acute pulmonary hemorrhage during a race are generally not those of classical EIPH. On the other hand, other workers consider fulminating EIPH to be the most common cause of nontraumatic death in racing horses and estimate that about 80% of horses dying in this way succumb to fulminating EIPH. This analysis estimates an overall death rate from fulminating EIPH is about one death per 1500 races,[28] with the remainder dying from causes unrelated to EIPH or musculoskeletal trauma.

- The effects of EIPH on performance are likely to be progressive and cumulative and ultimately there may be substantial wastage of racing horses due to EIPH. ■

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Editor's Note: Part 3 of the EIPH Workshop will appear in a future issue of *Equine Practice*.