EQUINE VETERINARY JOURNAL
Equine vet. J. (1995) **27** (4) 240-241

Editorials

Racing horses, nitroglycerin and exercise induced pulmonary haemorrhage (EIPH)

Exercise induced pulmonary haemorrhage (EIPH) is endemic in racing horses, although not confined to Thoroughbreds or even to the horse. The disorder has been reported in racing greyhounds, (King and Raskin 1991) and a recent study by Akbar *et al.* (1994) confirmed the condition in racing camels in the Gulf region. Although the latter authors were careful not to draw any hard conclusions about the incidence of EIPH in camels based on the limited number of animals examined, the study suggests that the frequency of EIPH in camels may be similar to its frequency in Standardbreds.

The condition of EIPH has been recognised for at least 300 years and, for 280 of those years, it was known only as post race 'bleeding' from the nostrils; although on rare occasions, racing horses died in the immediate post race period from massive pulmonary haemorrhage. In 1974, Cook suggested that the blood originated in the lungs and, in 1980, Pascoe introduced the term EIPH after endoscopic surveys of Thoroughbred racehorses at several North American racetracks confirmed the lung as the site of haemorrhage and also discovered that a high percentage of racing horses were affected (Pascoe *et al.* 1981). More recently, Whitwell and Greet (1984) have shown that 100% of horses in training that were sampled yield pulmonary haemosiderophages, suggesting that EIPH is a widespread problem of horses in training.

Throughout the 300 year history of EIPH, horse owners and trainers have attempted to prevent this condition. Historical approaches included administration of conjugated oestrogens, oxalates, bioflavinoids and other substances and water deprivation. The latter was apparently effective and probably led to the use of frusemide (Tobin 1981). Today, frusemide is the most commonly used medication for prevention of EIPH and has been the medication of choice for over 20 years. Frusemide attained this position by virtue of its apparent efficacy. Veterinarians administered frusemide prophylactically and horsemen believed it reduced the incidence of EIPH; and administration to racehorses was soon established in North America.

How does frusemide produce its effects? For 20 years on American racetracks, the conventional wisdom was that EIPH was due to hypertension associated with the stress of physical exertion. Not surprisingly, backstretch wisdom of a generation ago has been corroborated by recent research confirming that frusemide may reduce blood pressure in the pulmonary system (Manohar *et al.* 1994).

Recently, West *et al.* (1993) have shown clearly that EIPH is caused by the exceptionally high pulmonary capillary blood pressures generated in racing horses. The capillary blood pressures in the pulmonary circulation are the highest ever measured in mammals, and the fact that they lead to 'stress failure' (rupture) of pulmonary capillaries is not surprising. Rather, physiologists are surprised (because the alveolar-capillary membrane must be very thin for efficient gas transfer) that the pulmonary capillaries of horses can withstand these high pressures for significant periods without rupture.

The sequelae of repeated episodes of EIPH are significant. Following disruption of the alveolar-capillary membrane, all the components of blood enter the pulmonary interstitium and alveoli. Microthrombi and impaired microcirculation result. As healing occurs, scar tissue forms, which interferes with expansion and contraction of the lungs and also impedes gas exchange. Repeated extravasation of blood eventually causes the end-stage lesions reported by O'Callaghan *et al.* (1987).

Hypoxaemia is a common sequel in human patients that have experienced maladaptive repair of lung tissue following injury. The horse is unique among athletic animals in its tendency to become hypoxaemic during intense exercise. All other equids evaluated (e.g. ponies) maintain normoxia during maximal exercise.

The pulmonary circulation developed as a low pressure system through which blood could replenish its oxygen content while eliminating carbon dioxide. Because minimal thickness of the blood-gas membrane facilitates diffusion of these gases, a low pressure system is necessary to allow maximal gas exchange. However, high gas exchange, expressed as $\dot{V}O_{2max}$, is a quality associated with elite human distance runners and is probably also a trait in elite equine athletes. Because high cardiac output is required for high $\dot{V}O_{2max}$ and high pulmonary artery pressure is a consequence of high cardiac output, superior horses probably have high cardiac outputs (and, in consequence, high pulmonary artery pressures) and may be more prone to EIPH than horses with lower performance capacity.

The irony of the equine alveolar-capillary membrane is that it is too thick to allow sufficient gas exchange (resulting in arterial hypoxaemia during intense exercise) and too thin to protect against the high pulmonary capillary pressures generated during intense exercise, resulting in EIPH. It appears that the cardiopulmonary vascular system of the racehorse approaches or has reached the physiological limitations of mammalian systems.

There are a number of lessons from these findings. The

first is that EIPH is an integral part of horseracing as we know it today. The champion horse runs at the very edge of what flesh, bone and pulmonary capillaries can withstand. When horses repeatedly bleed into their lungs during periods of intense exercise, lung damage is cumulative and may eventually limit the racing career of the individual.

Therefore, EIPH is a serious condition in racing horses, and prevention or reduction of the incidence is an important concern. West *et al.* (1993) have proposed 2 approaches to this problem: strengthening of the alveolar-capillary membrane or, perhaps from a more practical viewpoint, reducing the pressure in the pulmonary circulatory system during exercise.

Frusemide apparently reduces peak pulmonary circulatory pressure. However, it also reduces systemic circulatory pressure, produces unwanted effects on drug detection and is not particularly effective as a preventative of pulmonary haemorrahge (Sweeney *et al.* 1990). Furthermore, there is evidence that frusemide may delay the onset of muscle fatigue during maximal exercise (Harkins *et al.* 1993). The ideal prophylactic agent for EIPH is a medication that would reduce blood pressure in the pulmonary circulation while exerting minimal effects on other body systems.

Given these circumstances and in order to protect the health and welfare of racing horses, it is important to identify agents that can reduce the incidence of EIPH. Since frusemide is not especially effective in preventing EIPH and has undesirable side effects, it appears reasonable to investigate the potential therapeutic value of other agents to reduce the incidence of EIPH.

In this issue (p275) Manohar extends his classic studies on EIPH to nitroglycerin. This author shows that infusion of nitroglycerin rapidly and effectively reduces pulmonary capillary blood pressure in the standing horse and suggests that pulmonary capillaries have a certain basal sympathetic tone that is diminished by nitroglycerin infusion. The next and more critical experiments are those to determine if nitroglycerin infusion can exert a similar effect on pulmonary capillaries in exercising horses without substantially altering cardiac output, thereby becoming a candidate agent for reducing the incidence of exercise induced hypertension and pulmonary haemorrhage in racing horses.

The work described by Manohar (1995) represents a step in this direction. How successfully nitroglycerin reduces pulmonary capillary pressure in exercising horses remains to be seen. What is important, however, is that an attempt is being made to identify agents that will reduce the incidence of EIPH in racing horses, thereby protecting the health and welfare of those animals.

The traditional view is that therapeutic agents should not be administered immediately prior to a race; and that horses should compete on the basis of receiving only natural feed. But can this traditional view be sustained? It is not supported by consensus opinion in North America, where the racing industry has taken substantial steps to ensure that, with appropriate veterinary supervision, nearly all racehorses may receive frusemide. Taking into account the widespread incidence and cumulative effects of EIPH, specific prophylactic medication to prevent or ameliorate the condition might seem to be both logical and acceptable.

J. D. HARKINS
T. TOBIN
Maxwell H. Gluck Equine Research Center
University of Kentucky
Lexington
Kentucky 40546, USA.

References

Akbar, S.J., Derksen, F.J., Billah, A.M. and Wemery, U. (1994) Exercise induced pulmonary hemorrhage in racing camels. *Vet. Rec.* **135**, 624-625 (Abstr.)

Cook, W.R. (1974) Epistaxis in the racehorse. *Equine vet. J.* **6**, 45-58.

Harkins, J.D., Hackett, R.P. and Ducharme, N.G. (1993) Effect of furosemide on physiologic variables in exercising horses. *Am. J. vet. Res.* **54**, 2104-2109.

King, R.R. and Raskin, R.E. (1991) Intrabronchial hemorrhage in greyhound dogs after racing. In: *Proceedings 7th International Racing Greyhound Symposium.* 18-21.

Manohar, M. (1995) Effects of glyceryl trinitrate (nitroglycerin) on pulmonary vascular pressures in standing Thoroughbred horses. *Equine vet. J.* **27**, 275-279

Manohar, M., Hutchens, E. and Coney, E. (1994) Frusdemide attenuates the exercise-induced rise in pulmonary capillary blood pressure in horses. *Equine vet. J.* **26**, 51-54.

O'Callaghan, M.W., Pascoe, J.R., Tyler, W.S. and Mason, D.K. (1987) Exercise-induced pulmonary hemorrhage in the horse: results of a detailed clinical, post mortem and imaging study II. Gross lung pathology. *Equine vet. J.* **19**, 389-393.

Pascoe, J.R., Ferraro, G.L., Cannon, J.H., Arthur, R.M. and Wheat, J.D. (1981) Exercise-induced pulmonary hemorrhage in racing Thoroughbreds: a preliminary study. *Am. J. vet. Res.* **42**, 703-707.

Sweeney, C.R., Soma, L.R., Maxson, A.D., Thompson, J.E., Holcombe, S.J. and Spencer, P.A. (1990) Effects of furosemide on the racing times of Thoroughbreds. *Am. J. vet. Res.* **51**, 772-778.

Tobin, T. (1981) *Drugs and the Performance Horse.* Charles C. Thomas, Springfield, Illinois.

West, J.B., Mathieu-Costello, O., Jones, J.J., Birks, E.K., Logemann, R.B., Pascoe, J.R. and Tyler, W.S. (1993) Stress failure of pulmonary capillaries in racehorses with exercise-induced pulmonary hemorrhage. *J. appl. Physiol.* **75**, 1097-1109.

Whitwell, K.E. and Greet, T.R.C. (1984) Collection and evaluation of tracheobronchial washes in the horse. *Equine vet. J.* **16**, 499-508.