Pulmonary vascular pressures of exercising Thoroughbred horses with and without endoscopic evidence of EIPH

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Manohar, Murli, and Thomas E. Goetz. Pulmonary vascular pressures of exercising Thoroughbred horses with and without endoscopic evidence of EIPH. J. Appl. Physiol. 81(4): 1589–1593, 1996.—Exercise-induced pulmonary hemorrhage (EIPH) is a common occurrence in racehorses. The objective of this study was to compare pulmonary vascular pressures of healthy Thoroughbred horses with and without postexertion endoscopically detectable fresh blood in the trachea. The nasopharynx, larynx, and trachea (down to the carina) of horses were examined weekly with an endoscope 55–60 min postexertion, and the diagnosis of EIPH was confirmed by the presence of fresh blood in the trachea. Measurements of heart rate and right atrial, pulmonary arterial, and pulmonary arterial wedge pressures were made during quiet rest and during treadmill exercise performed at 14.5 m/s on a 5% uphill grade. This workload elicited maximal heart rate of the horses. Mean pulmonary capillary pressure was estimated to be halfway between the mean pulmonary arterial pressure and the mean pulmonary arterial wedge pressure. These data from 7 healthy sound exercise-trained horses that were positive on 12 consecutive occasions (at 1-wk intervals) for the postexercise presence of fresh blood in the trachea were compared with those in 8 healthy horses that were consistently negative for the evidence of fresh blood in the trachea on postexercise endoscopic examination over 12–16 wk. The heart rate and the right heart and/or pulmonary vascular pressures in the two groups of horses were similar at rest. Exercise was attended by a large significant (P < 0.05) increase in these pressures and heart rate in both groups. However, statistically significant differences between endoscopically EIPH-positive and endoscopically EIPH-negative horses for heart rate and right atrial and pulmonary vascular pressures were not found during exercise. Thus these data revealed that the magnitude of exercise-induced right atrial as well as pulmonary arterial, capillary, and venous hypertension in endoscopically EIPH-positive horses that are otherwise healthy is quite similar to that in endoscopically EIPH-negative horses during comparable exertion.

EXERCISE-INDUCED PULMONARY HEMORRHAGE (EIPH) is frequently observed in racehorses. On the basis of postexercise endoscopic detection of fresh blood in the trachea, it has been reported that the incidence of EIPH in racing Thoroughbred (9) and Standardbred (2) horses probably exceeds 75%. It is commonly held in “racing circles” that EIPH contributes to exercise intolerance, i.e., loss of stamina and/or performance, even though definite proof is lacking (2, 9). Although it has been demonstrated that hemosiderin-laden macrophages could be recovered in the tracheobronchial washings from all Thoroughbreds in training (11), the fact remains that unless overt epistaxis occurs, the diagnosis of EIPH in racehorses is made on endoscopic examination of the airway performed ~60 min postexercise (9). Furthermore, the decision in competitive racing as to whether a racehorse is prescribed furosemide administration for prevention and/or management of EIPH is also based on the endoscopic observation of fresh blood in the trachea after a race (Dr. R. Jensen, Illinois Racing Board, personal communication).

Recent work has demonstrated that exercising horses develop marked pulmonary arterial, capillary, and venous hypertension (3–6), and it is believed that the high transmural (intravascular minus perivascular alveolar) pulmonary capillary pressure exerted on the blood-gas barrier, which has to be quite thin (0.3–0.6 µm) to provide for diffusion of respiratory gases, probably contributes to stress failure of pulmonary capillaries (10), resulting in EIPH. Despite this recognition, to our knowledge there have been no reports comparing pulmonary vascular pressures of horses that exhibit EIPH with those that do not. Thus the primary objective of this study was to compare the rest and exercise values of pulmonary vascular pressures of Thoroughbred horses in which fresh blood is detected on postexercise endoscopic examination of the trachea with those in which fresh blood is not detected on the postexercise endoscopic examination of the airway. In our experiments, horses performed high-intensity short-term exercise at maximal heart rate.

MATERIALS AND METHODS

Horses. Experiments were carried out on 15 Thoroughbred horses (7 fillies and 8 geldings) aged 2.5–5 yr and weighing between 375 and 523 kg. The horses were divided into two groups (EIPH-positive and EIPH-negative groups), designated as endoscopically EIPH-positive (n = 7) and endoscopically EIPH-negative (n = 8) horses. The horses were housed in an air-conditioned building and were accustomed to being handled by people. They were fed a diet of alfalfa hay and oats, and free access to water was provided. The horses were healthy, sound, and received routine treatments meeting veterinary medical standards for the equine species. Our protocols and procedures were approved by the Institutional Laboratory Animal Care and Use Committees.

Exercise training. Initially, the horses exercised on the high-speed treadmill set at 0% grade (on the flat). Starting with a walk at 2 m/s for 60 s, belt speed was raised in increments of 1 m/s every 60 s until the horses had trotted at 6 m/s for 60 s. Belt speed was then raised to 8 m/s for 60 s, to 10 m/s for 60 s, and finally to 14.2–14.5 m/s for 120 s. Thereafter, belt speed was reduced to 5 m/s for 60 s and then to 2 m/s for 5–7 min before the treadmill was stopped. Exercise was performed in this manner 3 days/wk for a period of 4–5 wk. For the next 3 wk, this incremental exercise...
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regimen was performed with the treadmill set at 3.5% uphill grade. Henceforth, the horses were exercised twice per week to maintain conditioning.

EIPH-positive and EIPH-negative groups. The horses were categorized as EIPH positive or EIPH negative based on the results of endoscopic examinations of the airway performed 55–60 min after exertion at 14.2–14.5 m/s on a 3.5% uphill grade over a period of 12–16 wk. Each horse was examined endoscopically a minimum of 12 consecutive times at weekly intervals; endoscopic examination of the nasopharynx, larynx, and trachea (down to the carina) was performed by using a flexible fiber-optic endoscope (Pentax Fiberscopes, Orangeburg, NY), and the presence of fresh blood in the airway was regarded as indicative of the occurrence of EIPH (2, 9).

None of the 15 horses in this study exhibited epistaxis (blood at the nostrils) on any occasion. However, there were seven horses that exhibited fresh blood in the trachea on 12 consecutive weekly endoscopic examinations performed 55–60 min postexertion; these horses were designated as EIPH-positive horses. In the other eight horses, blood was not found on any occasion in the trachea on weekly postexercise endoscopic examinations of the airway; they were designated as EIPH-negative horses.

Our characterization of EIPH-positive and EIPH-negative horses based on the presence of fresh blood in the trachea during postexercise endoscopic examination of the airway in the above-described manner is consistent 1) with the routine veterinary medical practice of detecting EIPH in horses performing competitively at racetracks and 2) with the criterion for racehorses to become eligible for prerace furosemide administration for prevention and/or management of EIPH (Dr. R. Jensen, Illinois Racing Board, personal communication).

Work intensity for maximal heart rate. Trials were carried out to ascertain the work intensity at which maximal heart rate was achieved. It was observed that the heart rate of horses during exertion at 14.2 m/s on a 3.5% uphill grade (215 ± 4 beats/min) was not different from that during exercise at 14.5 m/s on a 5% uphill grade (214 ± 3 beats/min). Thus, for the present study, the latter workload was selected because it represented a more strenuous effort performed at maximal heart rate.

Experimental procedure. Our hemodynamic procedures have been described in detail previously (3–6); therefore, only a brief description is given here. On the day of the study, cardiac catheters (7F) equipped with tip manometers and fluid-filled lumens (Millar Instruments, Houston, TX) were advanced via the left jugular vein so as to simultaneously record phasic right atrial, right ventricular, pulmonary arterial, and pulmonary arterial wedge pressures. The in vivo catheter-manometer signals were matched with corresponding fluid-filled pressure signals obtained by using conventional transducers (Statham/Gould, Oxnard, CA) zeroed at the level of the point of the shoulder. The data were displayed on an oscillographic recorder (E for M, Lanexa, KS), and mean pressures were obtained by electronic integration of the phasic pressure signals.

Experimental protocol. The same experimental protocol was used for the two groups of horses. Hemodynamic measurements were first made in standing horses when heart rate and right heart and/or pulmonary vascular pressures had been stable for ~10–15 min. Thereafter, exercise was performed on a high-speed treadmill set at 5% uphill grade. Exercise began with a walk at 2 m/s for 60 s. Belt speed was increased in increments of 1 m/s every 60 s until the speed was 6 m/s. After the horses trotted for 60 s at 6 m/s, belt speed was raised to 8 m/s for 60 s and then to 14.5 m/s. Horses performed exercise at 14.5 m/s at 5% uphill grade for 90 s. Thereafter, belt speed was decreased to 5 m/s for 60 s and then to 2 m/s for 5 min before the treadmill was stopped.

At 55–60 min after exercise, careful endoscopic examination of the nasopharynx, larynx, and trachea (down to the carina) was undertaken by using a flexible fiber-optic endoscope (2, 9).

Measurements and data analysis. Hemodynamic data were obtained for rest and for exercise at 8 m/s on a 5% uphill grade and at 14.5 m/s on a 5% uphill grade. Measurements were made over all consecutive cardiac cycles recorded during 20–45 s of exercise at 8 m/s on a 5% uphill grade and over all consecutive cardiac cycles recorded during 15–60 s of exercise at 14.5 m/s on a 5% uphill grade. Mean pulmonary capillary pressure was estimated (3–6, 10) as 1⁄2(mean pulmonary arterial pressure + mean pulmonary arterial wedge pressure). Heart rate was determined from the phasic right ventricular pressure recordings.

The data from both groups of horses were subjected to split-plot design analysis of variance (8) by using the SAS statistical software package (SAS Institute, Cary, NC). Individual data sets for endoscopically EIPH-positive and endoscopically EIPH-negative groups were also subjected to analysis of variance followed by Newman-Keuls multiple-range test (8) to determine the effects of work intensity. A probability level of P < 0.05 was regarded as being statistically significant, and the data are presented as means ± SE.

RESULTS

Significant differences in heart rate, mean right atrial pressure, or pulmonary vascular pressures were not found between the groups of horses either at rest or during exercise (Figs. 1–6). In both groups, exercise resulted in significant tachycardia and in right atrial as well as pulmonary arterial, capillary, and venous hypertension. During exercise at 14.5 m/s on a 5% uphill incline, mean right atrial, mean pulmonary arterial, mean pulmonary arterial wedge, and mean pulmonary capillary blood pressures of endoscopically EIPH-positive horses approached 61 ± 4, 96.5 ± 4.0, 225

**Fig. 1.** Heart rate of exercise-induced pulmonary hemorrhage (EIPH-positive horses was similar to that of EIPH-negative horses both at rest and during exertion. *Significantly different from 8 m/s as well as 14.5 m/s for same group of horses, P < 0.05. **Significantly different from 14.5 m/s for same group of horses, P < 0.05.**
70.1 ± 3.3, and 83.3 ± 3.6 mmHg, respectively. Exercise also caused a significant increment in the pulmonary arterial pulse pressure (Fig. 3), and the pulmonary perfusion pressure gradient increased significantly from 5 ± 1 mmHg at rest to 27 ± 1 mmHg.

Postexercise endoscopic examination of the airway revealed fresh blood in the trachea of each of the seven horses belonging to the EIPH-positive group. However, blood was not detected in the airways on the postexercise endoscopic examination in any of the horses belonging to the EIPH-negative group.

**DISCUSSION**

Our data have demonstrated that right atrial, pulmonary arterial, pulmonary capillary, and pulmonary venous pressures of Thoroughbred horses that exhibit fresh blood in the trachea during postexercise endoscopic examination are not different from those that do not exhibit fresh blood in the trachea postexercise; this was true at rest as well as during strenuous exertion. These data also confirmed earlier observations (3–6) that galloping horses develop significant pulmonary arterial, capillary, and venous hypertension.

It has been suggested that the incidence of EIPH may increase with age, but conclusive evidence is lacking.
In the present study, an age-related trend for the occurrence of EIPH was not observed. Interestingly, the youngest horse (2.5 yr old) in this study belonged to the EIPH-positive group. It should be noted that all of our horses had previously raced competitively in Illinois and/or other US racing jurisdictions.

Recently, mean pulmonary arterial pressure of a 3-yr-old Thoroughbred filly that experienced EIPH (based on postexercise endoscopic examination of the airway) was reported to be 138 mmHg during exertion at 13.5 m/s, when the heart rate approached 210 beats/min (10). This exercise value of mean pulmonary arterial pressure from the EIPH-positive filly (10) exceeded values (89–105 mmHg) reported from EIPH-negative horses exercised at similar or higher workloads in previous studies (3–6). In horse racing circles, this has been interpreted as meaning that the pulmonary vascular pressures of Thoroughbreds that exhibit fresh blood in the trachea postexercise endoscopy of the airway may be higher than those in horses that do not exhibit fresh blood in the trachea postexercise. Support for this is often provided by citing data from a preliminary report (1) where three Thoroughbred horses (undescribed EIPH status) exercised at 10 m/s [a much lower workload than in the present and previous (3–6) studies] had mean pulmonary arterial and mean left atrial pressures of 115 and 70 mmHg, respectively. It is worth noting that neither of these reports (1, 10) compared the pulmonary vascular pressures of EIPH-positive and EIPH-negative horses. Because our experiments sought to clarify this issue, we studied horses that were consistently negative (n = 8) or positive (n = 7) for EIPH during postexercise airway endoscopic examinations (a minimum of 12 consecutive times at weekly intervals) over 12–16 wk of performing high-intensity treadmill exercise (cf. EIPH-positive and EIPH-negative groups in MATERIALS AND METHODS). Also, the same hemodynamic procedures were employed to obtain data from both groups of horses. Our data (Figs. 3–6), thus obtained, do not support the view that pulmonary vascular pressures of endoscopically EIPH-positive horses that are otherwise healthy exceed those in the endoscopically EIPH-negative horses either at rest or during high-intensity exercise performed at the same workloads. We remain cognizant, however, that none of our horses exhibited epistaxis, and, therefore, our data may not relate to the latter situation.

While stress failure of pulmonary capillaries (10) may occur at high transmural (intravascular minus perivascular/alveolar) pulmonary capillary pressures, the question arises as to why some horses consistently exhibit fresh blood in the trachea postexercise, whereas others may not, despite similarity of intravascular pulmonary capillary pressures during strenuous exertion (Fig. 6). Several possibilities may be considered. First, it needs to be emphasized that in the context of stress failure of pulmonary capillaries, the key variable (6, 10) is the transmural (intravascular minus perivascular) pulmonary capillary pressure. Given the similarity of pulmonary capillary blood pressure values during exertion in the endoscopically EIPH-positive and EIPH-negative horses (Fig. 6), it may be suggested that there may be differences in the perivascular alveolar pressure of EIPH-positive and EIPH-negative horses during exertion. To our knowledge, measurements of alveolar pressure in galloping EIPH-positive and EIPH-negative Thoroughbreds have not been made to date. Second, it is possible that there may be differences between EIPH-positive and EIPH-negative horses in terms of the strength of the blood-gas barrier. The strength of the blood-gas barrier is primarily in its connective and elastic tissue components (10). Studies comparing this aspect of the blood-gas barrier in EIPH-negative vs. EIPH-positive horses may also have used our knowledge. Third, the endoscopic diagnosis of EIPH in this study was based on the postexercise macroscopic detection of fresh blood in the trachea. Although it has been demonstrated that all Thoroughbreds in training had hemosiderin-laden macrophages in the tracheobronchial washings several days postexercise (11), the fact remains that, at present, postexercise endoscopic examination of the airway is accepted as the most practical method of detecting EIPH in competitive horse racing (2, 9) and that only those racehorses that exhibit fresh blood in the trachea become eligible for prerace furosemide administration for prevention/management of EIPH. Chronologically, because racehorses are exercised frequently, tracheobronchial washings cannot determine with certainty whether a particular episode of high-intensity exercise caused EIPH. Finally, it remains to be definitively determined whether EIPH originates from the pulmonary circulation; the bronchial circulation may be the culprit instead (7, 9).

It is difficult to explain why our values of various pulmonary vascular pressures from both groups of horses (Figs. 2–6), which exercised at a much higher workload (14.5 m/s on a 5% uphill grade), were less than the values reported from a filly exercised at 13.5 m/s in the study by West et al. (10) and in the three

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**Fig. 6. Changes in estimated mean pulmonary capillary pressure with exercise are shown for EIPH-positive and EIPH-negative horses.**

During exercise at 14.5 m/s on a 5% uphill grade, mean pulmonary capillary pressure increased to ~3-fold of its value at rest, and there were no statistically significant differences between 2 groups. *Significantly different from 8 m/s as well as 14.5 m/s for same group of horses, P < 0.05. **Significantly different from 14.5 m/s for same group of horses, P < 0.05.

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horses exercised at 10 m/s in a preliminary report (1). One likely possibility is that the differences in these studies may be related to the different reference sites for pressure signals. In the present and previous (3–6) studies, pressure signals were referenced at the level of the point of the shoulder. Whereas Jones et al. (1) did not note the referencing of their pressure signals, West et al. (10) referenced the mean pulmonary arterial pressure at the level of the right atrium (it was, however, not described how the latter was established). In large animals, the hydrostatic pressure effect (due to gravitational force acting on a column of fluid) can be substantial and may account for these disparities.

In conclusion, our data have demonstrated that right heart and/or pulmonary vascular pressures of horses that exhibit fresh blood in the trachea on postexercise endoscopic examination are similar to those of endoscopically EIPH-negative horses both at rest and during high-intensity short-term exercise.

The authors gratefully acknowledge the excellent technical assistance of Beth Saupe, Donald Lantz, Eileen Sullivan, Richard Griffin, and Jay E. Koble in carrying out these experiments.

This work was supported in part by a grant-in-aid from the Illinois Department of Agriculture Equine Research Funds. The high-speed treadmill at the University of Illinois College of Veterinary Medicine was procured with financial support from the Illinois Thoroughbred and Standardbred Breeders Fund.

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Received 21 February 1996; accepted in final form 23 May 1996.

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