Anti-inflammatory agent, dexamethasone, does not affect exercise-induced arterial hypoxemia in Thoroughbreds

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Manohar, Murli, Thomas E. Goetz, Aslam S. Hassan, Tracy DePuy, and Sarah Humphrey. Anti-inflammatory agent, dexamethasone, does not affect exercise-induced arterial hypoxemia in Thoroughbreds. J Appl Physiol 93: 99–106, 2002. First published March 15, 2002; 10.1152/japplphysiol.01186.2001.—In view of the suggestion that pulmonary injury-induced release of histamine and/or other chemical mediators from airway inflammatory and mast cells contribute to the exercise-induced arterial hypoxemia (EIAH) in human athletes, we examined the effects of pretreatment with a potent anti-inflammatory agent, dexamethasone, on EIAH and desaturation of hemoglobin in horses. Seven healthy sound, exercise-trained Thoroughbreds were studied in the control (no medications) experiments, followed in 7 days by intravenous dexamethasone (0.11 mg·kg⁻¹·day⁻¹ for 3 consecutive days) studies. Blood-gas measurements were made at rest and during incremental exercise leading to maximal exertion at 14 m/s on a 3.5% uphill grade. Galloping at this workload induced pulmonary hemorrhage in all horses in both treatments, thereby indicating that stress failure of pulmonary capillaries had occurred. In both treatments, significant EIAH, desaturation of hemoglobin, hypercapnia, acidosis, and hyperthermia developed during maximal exercise, but significant differences between the control and dexamethasone treatments were not discerned. The failure of pretreatment with dexamethasone to significantly affect EIAH suggests that pulmonary injury-evoked airway inflammatory response may not play a major role in EIAH in racehorses. However, our observations in both treatments that EIAH developed quickly (being evident at 30 s of exertion) and that its severity remained unaffected by increasing exercise duration (to 120 s) suggest that EIAH has a functional basis, probably related to significant shortening of the transit time for blood in the pulmonary capillaries as cardiac output increases dramatically.

HUMAN SUBJECTS OFTEN EXHIBIT exercise-induced arterial hypoxemia, which is known to limit exercise performance (8, 27). Recently, it was suggested that capillary stress failure (i.e., pulmonary injury)-induced histamine (and possibly other chemical mediators) release from airway inflammatory and mast cells contributes to the exercise-induced arterial hypoxemia in human athletes (1, 25–27). In support of this argument are the observations that plasma histamine concentration increases in exercising human subjects (1, 25–27) and that inhaled nedocromil sodium, a well-known stabilizer of inflammatory and mast cells used in the management of asthma (6), as well as diphenhydramine HCl, an H₁-receptor antagonist, significantly attenuated or alleviated the exercise-induced arterial hypoxemia in human subjects (7, 9, 26).

Similar to human athletes, horses are known to exhibit significant exercise-induced arterial hypoxemia (2, 3, 10, 13, 15, 21–23, 34, 36, 37). Also, because of the high transmural [intracapillary minus perivascular (alveolar)] force exerted onto the blood-gas barrier (17–20, 24) relative to its strength, the incidence of capillary stress failure (4, 38) induced exercise-induced pulmonary hemorrhage (EIPH) in racehorses is rather high (>75%; Refs. 14, 33). Furthermore, histological evidence has been presented that autologous blood introduced into the alveoli of horses with EIPH evokes an inflammatory response (35). Also, there have been reports that racehorses experiencing repeated episodes of EIPH have obstructive small-airway disease (16), wherein release of leukotrienes, histamine, and other inflammatory mediators plays a role (28). In view of these reports (16, 28, 35) and the suggestion that pulmonary injury-induced release of histamine (and/or other chemical mediators) from airway inflammatory and mast cells contributes to the exercise-induced arterial hypoxemia in healthy human subjects (1, 25–27), we became interested in evaluating the role of airway inflammation in bringing about arterial hypoxemia in exercising Thoroughbreds. Although the precise chain of events leading to exercise-induced arterial hypoxemia via the latter mechanism (1, 25–27) remains to be elucidated, it was suggested that inflammatory chemical mediators, particularly histamine, being potent capillary permeability promontants, contribute to the reported interstitial pulmonary edema (29) and, in turn, to ventilation-perfusion mismatching within the lungs, resulting in arterial hypoxemia (26, 27).

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Glucocorticoids possess potent anti-inflammatory and immunosuppressive actions, and, because of these well-known properties, their therapeutic use in a variety of inflammatory, allergic, and autoimmune diseases in animals and humans is prevalent (31). It is well known that systemically administered synthetic analogs of adrenoglucocorticoids, viz., dexamethasone and triamcinolone, are particularly effective in the treatment of obstructive small-airway disease (heaves) in horses, wherein release of leukotrienes, histamine, and cytokines from airway inflammatory cells has been demonstrated (28). The multiple mechanisms cited for the anti-inflammatory effects of glucocorticoids include the inhibition of phospholipase A₂, causing suppression of the production of arachidonic acid and its metabolites; inhibition of histamine release from the basophils and mast cells; as well as suppression of the production and release of cytokines and acute-phase reactants in macrophages, endothelial cells, lymphocytes, and monocytes (31). Thus, in view of the suggestion that pulmonary injury-induced release of chemical mediators from airway inflammatory and mast cells contributes to exercise-induced arterial hypoxemia (1, 7, 9, 25–27) and that introduction of autologous blood into the airways of horses evokes an inflammatory response (35), we hypothesized that the potent anti-inflammatory and immunosuppressive properties of dexamethasone (curtailing the number of inflammatory cells invading the airways as well as diminishing or inhibiting their release of various chemical mediators; Refs. 28, 31) would attenuate or suppress the development of interstitial pulmonary edema, which, through diminished impediment to O₂ diffusion and/or an improvement in ventilation-perfusion mismatching, may mitigate arterial hypoxemia in galloping Thoroughbreds. Thus our objective in the present study was to examine the effects of pretreatment with intravenous (IV) dexamethasone, at a dose known to alleviate obstructive small-airway disease (28), on the arterial hypoxemia and desaturation of hemoglobin in horses performing high-intensity exercise capable of eliciting maximal heart rate and inducing EIPH. Dexamethasone is a synthetic analog of the adrenoglucocorticoids, with ~25-fold anti-inflammatory potency of cortisol (31).

**MATERIALS AND METHODS**

**Horses**

Experiments were carried out on seven healthy, sound Thoroughbred horses (3 fillies, 4 geldings), 3–6 yr old and weighing 454.1 ± 13.6 kg. They were exercise trained for a period of 7 wk before the blood-gas and hemodynamic studies were undertaken. 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 dewormed periodically and were inoculated with tetanus toxoid and strangles vaccine. Our protocols and procedures were approved by the Institutional Laboratory Animal Care and Use Committees.

**Exercise Training**

After familiarization with walking, trotting, cantering, and galloping on the high-speed treadmill for 1 wk, all horses were exercise trained for a period of 7 wk before the blood-gas and hemodynamic studies were undertaken. Our exercise-training regimen has been described in detail previously (10, 19–23).

**Work Intensity Eliciting EIPH**

Because occurrence of EIPH demonstrates that capillary stress failure-related pulmonary injury has indeed occurred (4, 12, 38), for the present study we intended to use a workload capable of eliciting EIPH consistently. Trials to ascertain work intensity needed to elicit maximal heart rate and EIPH were undertaken on completion of the above-described exercise training. In agreement with our laboratory’s previous work (10, 18, 20–23), it was observed that galloping at 14 m/s on a 3.5% uphill grade not only elicited maximal heart rate but also induced EIPH in all horses as demonstrated by the presence of fresh blood in the trachea on postexercise arterial endoscopic examination (14, 17, 33). It was also observed that these horses could not sustain galloping at 14 m/s on a 3.5% uphill grade for >120 s despite vigorous humane encouragement. Thus this workload, i.e., 14 m/s on a 3.5% uphill grade, was selected for further experimentation because it represented a strenuous effort eliciting maximal heart rate and EIPH in the experimental horses.

**Experimental Design and Protocol**

All horses were studied in the control as well as the dexamethasone treatments. Because glucocorticoid administration can have prolonged effects on various physiological functions (31), all horses were first studied in the control experiments, followed in 7 days by the IV dexamethasone studies. All experimentation was carried out in an air-conditioned laboratory, where the ambient temperature was maintained at 20–21°C.

**Control study.** In these experiments, horses received no medication(s). On completion of the blood-gas, pH, and hemodynamic measurements (in duplicate) on quietly standing horses when heart rate and aortic and pulmonary vascular pressures had been stable for at least 10–15 min, exercise was performed on the high-speed treadmill set at a 3.5% uphill grade in the following manner. Beginning with a walk at 2 m/s for 120 s, the belt speed was raised in increments of 1 m/s every 60 s until the speed was 6 m/s. After the horses had trotted at 6 m/s for 60 s, belt speed was raised to 8 m/s for 60 s and then to 14 m/s. On completion of 120 s of galloping at 14 m/s on a 3.5% uphill grade, the belt speed was decreased to 5 m/s. After the horses had trotted at 5 m/s for 60 s, the belt speed was decreased to 2 m/s and the horses were walked for 5 min before the treadmill was stopped. In this exercise protocol, along with continuous core temperature measurement, simultaneous aortic and pulmonary arterial (mixed venous) blood samples were obtained for determining blood-gas tensions, pH, hemoglobin concentration, hemoglobin O₂ saturation, and O₂ content at 55 s of trotting at 6 m/s; at 55 s of exercise at 8 m/s; at 30, 60, 90, and 120 s of galloping at 14 m/s on a 3.5% uphill grade; and at 120 s of walk at 2 m/s. Pulmonary arterial blood samples were also obtained preexercise (at rest), at 60 s of exercise at 8 m/s, and at 120 s of walk at 2 m/s for determining lactate concentration in duplicate by using a chemical assay (Sigma Diagnostics, Sigma Chemical, St. Louis, MO).
Dexamethasone study. For these experiments, our dexamethasone dosage was based on the widely used therapeutic dose (0.10 mg·kg⁻¹·day⁻¹) for horses afflicted with obstructive small-airway disease (heaves), wherein release of various inflammatory mediators, viz., leukotrienes, histamine, and cytokines, is known to play a role (28). Thus, in these experiments, horses received IV dexamethasone (0.11 mg·kg⁻¹·day⁻¹) for 3 consecutive days. Ninety minutes after the last injection of dexamethasone, resting data were obtained (in duplicate) on quietly standing horses when heart rate and aortic and pulmonary vascular pressures had been stable for 10–15 min. Thereafter, exercise was performed on the high-speed treadmill set at a 3.5% uphill grade in exactly the same manner as described above for the control study. Along with continuous measurement of core temperature, simultaneous arterial and mixed venous blood samples were obtained for determining blood-gas tensions, pH, hemoglobin concentration, hemoglobin O₂ saturation, O₂ content, and lactate concentration at the same intervals as in the control study (see above).

Experimental Procedures

On the day of the study, after local anesthesia in the 17th intercostal space, the abdominal aorta was percutaneously catheterized as described previously (10, 20–23). Thereafter, after local infiltration of 2% lidocaine HCl, cardiac catheters (8F) equipped with a tip manometer (Millar Instruments, Houston, TX), fluid-filled lumen, and a thermistor (Edward Laboratories, Santa Clara, CA) were advanced into the pulmonary artery via introducers inserted into the left jugular vein. The locations of various catheters were confirmed by monitoring the characteristic phasic blood pressure waveforms on an oscillographic recorder (E for M, Lanexa, KS). Besides blood pressure monitoring, these catheters permitted simultaneous sampling of the aortic and pulmonary arterial (mixed venous) blood as well as continuous monitoring of the pulmonary arterial blood (core) temperature during the experiments. After catheter placement, horses stood quietly on the treadmill for ~45–50 min before blood-gas and pH studies were undertaken.

Blood-gas tensions, pH, hemoglobin concentration, hemoglobin-O₂ saturation and O₂ content were determined by using a carefully calibrated blood-gas analyzer/CO-oximeter (ABL520 system, Radiometer, Copenhagen, Denmark), and all blood-gas tension and pH data were corrected to the simultaneously measured pulmonary artery blood temperature. The calibration of our blood-gas/pH analyzer/CO-oximeter was checked frequently and was verified by using tonometered solutions of known blood-gas tensions, pH, hemoglobin concentration, and O₂ saturation. In the present study, O₂ extraction (%) was calculated as (arterial-to-mixed venous blood O₂ content gradient/arterial blood O₂ content) × 100.

For lactate determinations (10, 21), the mixed venous blood samples obtained at various steps of the protocol were immediately deproteinized with chilled perchloric acid (8% wt/vol). After centrifugation, the supernatant fluid was harvested for lactate assays (Sigma Diagnostics, Sigma Chemical), which were carried out in duplicate.

Postexercise Airway Endoscopic Examination

In both treatments, with use of a flexible fiber-optic endoscope (Pentax Fiberscopes, Orangeburg, NY), careful endoscopic examination of the nasopharynx, larynx, and trachea (up to the carina) was undertaken 45–50 min postexercise (14, 17, 33). The presence of fresh blood in the airway(s) was regarded as indicative of the occurrence of EIPH (14, 17, 33).

Statistical Analysis of the Data

All data were subjected to repeated-measures, split-plot design analysis of variance procedure (32) by using the SAS statistical software package (SAS version 8.1, SAS Institute, Cary, NC), and the treatment comparisons were made by using the least squares significant difference method (32). Data for the control as well as the dexamethasone treatments were also individually subjected to Newman-Keuls multiple-range test (Ref. 32; SAS version 8.1, SAS Institute) to determine the significant effects of work intensity and duration within each treatment. For all statistical analyses, the level of significance was set at \( P < 0.05 \). The statistical power of comparisons for various variables in the present study exceeded 80%. The data are presented as means ± SE.

RESULTS

Changes in Core Temperature

Dexamethasone administration did not significantly affect the core temperature of standing or exercising horses. The incremental treadmill exercise protocol used in the present study caused a significant, progressive rise in core temperature as work intensity and exercise duration increased. At 120 s of galloping at 14 m/s on a 3.5% uphill grade, mean core temperature had increased 3.0°C above the preexercise values in both treatments, and statistically significant differences between the control and dexamethasone experiments could not be discerned.

Changes in Arterial O₂ Tension and Hemoglobin O₂ Saturation

Arterial values of O₂ tension and hemoglobin O₂ saturation in quietly standing horses were unaffected by dexamethasone administration (Fig. 1). Whereas these variables were well maintained during submaximal exercise performed at 6 and 8 m/s in both treatments, a statistically significant \( (P < 0.0001) \) reduction in arterial O₂ tension and hemoglobin O₂ saturation was observed during galloping at 14 m/s on a 3.5% uphill grade. Statistically significant differences between the control and dexamethasone experiments could not be demonstrated, however. At 120 s of galloping at 14 m/s on a 3.5% uphill grade in the control and dexamethasone experiments, the arterial O₂ tension was 69.8 ± 3.6 and 70.5 ± 3.2 Torr, respectively. Whereas in going from 30 s to 120 s of galloping at 14 m/s on a 3.5% uphill grade, arterial O₂ tension did not register a statistically significant change in either treatment, arterial hemoglobin O₂ saturation decreased progressively with increasing exercise duration as exercise-induced hyperthermia, hypercapnia (Fig. 2), and metabolic acidosis (Fig. 3) intensified, causing a rightward shift of the hemoglobin-O₂ dissociation curve. At 120 s of galloping at 14 m/s on a 3.5% uphill grade in the control and dexamethasone experiments, the arterial hemoglobin O₂ saturation was 82 ± 4 and 83 ± 4%, respectively, and statistically significant differences between treatments were not discerned.
Changes in Mixed Venous $O_2$ Tension and Hemoglobin $O_2$ Saturation

Preexercise values of these variables were similar in the control and dexamethasone experiments (Fig. 1). During exercise, work intensity-related significant reductions in these variables were observed in both treatments, but statistically significant differences between treatments were not found.

Changes in Arterial and Mixed Venous Blood CO₂ Tension

Dexamethasone administration did not cause statistically significant changes in arterial CO₂ tension of standing horses (Fig. 2). In both treatments, whereas submaximal exercise was attended by a significant reduction in arterial CO₂ tension, significant hypercapnia developed during galloping at 14 m/s on a 3.5% uphill grade. However, statistically significant differences between the control and dexamethasone treatments could not be demonstrated.

As expected, in both treatments mixed venous blood CO₂ tension increased progressively with incremental exercise protocol used in the present study. At 60 and 120 s of galloping at 14 m/s on 3.5% uphill grade in the control study, the mixed venous blood CO₂ tension approached $110 \pm 7$ and $136 \pm 9$ Torr, respectively. Corresponding values in the dexamethasone experiments were $106 \pm 7$ and $130 \pm 10$ Torr, respectively, and statistically significant differences ($P < 0.0001$) between the control and dexamethasone treatments were not discerned. In both treatments, the mixed venous-to-arterial CO₂ tension gradient also increased progressively with increasing work intensity. At 60
and 120 s of galloping at 14 m/s on a 3.5% uphill grade in the control study, the mixed venous-to-arterial blood CO₂ tension gradient was 57/11006 and 79/11006 Torr, respectively. Corresponding values in the dexamethasone experiments were 55/11006 and 77/11006 Torr, respectively, and statistically significant differences (P < 0.8191) between the control and dexamethasone treatments were not found.

Changes in Arterial pH and Mixed Venous Blood Lactate Concentration

Preexercise values of these variables were similar in the control and dexamethasone experiments (Fig. 3). In both treatments, although arterial pH was well maintained during submaximal exercise, a significant, progressive acidosis developed during galloping at 14 m/s on a 3.5% uphill grade as exercise duration progressed to 120 s. Statistically significant differences between control and dexamethasone treatments regarding arterial pH (P < 0.3198) and blood lactate concentration (P < 0.2613) could not be discerned, however.

Changes in Arterial-to-Mixed Venous Blood O₂ Content Gradient and O₂ Extraction

In standing horses, hemoglobin concentration, arterial and mixed venous blood O₂ contents, arteriovenous O₂ content gradient, and O₂ extraction were unaffected by dexamethasone administration (Fig. 4). Because of splenic release of erythrocyte reservoir, hemoglobin concentration of exercising horses was observed to increase significantly (P < 0.0001) in both treatments; at 120 s of galloping at 14 m/s on a 3.5% uphill grade, arterial hemoglobin concentration had approached 22.0 ± 0.4 and 21.6 ± 0.4 g/dl in the control and the dexamethasone treatments respectively, and statistically significant differences were not discerned. Concomitantly, a significant (P < 0.0001) increment of a similar magnitude in arterial blood O₂ content was also observed during exercise, whereas work intensity-related similar changes occurred in the mixed venous blood O₂ content in both treatments. Consequently, arterial-to-mixed venous blood O₂ content gradient of exercising horses increased significantly (P < 0.0001) in both treatments. At 120 s of galloping at 14 m/s on a 3.5% uphill grade in the control and the dexamethasone experiments, arterial-to-mixed venous blood O₂...
content gradient was 22.4 ± 1.2 and 21.7 ± 0.9 ml O₂/dl blood, respectively, as O₂ extraction approached 90.7 ± 0.8 and 91.0 ± 0.9%, respectively. Statistically significant differences between the control and dexamethasone treatments were not found.

**DISCUSSION**

Our primary objective in the present study was to examine whether pretreatment with an anti-inflammatory agent (dexamethasone) would affect the development and/or severity of arterial hypoxemia in horses performing strenuous exercise capable of inducing stress failure of pulmonary capillaries. In this context, our data revealed that IV dexamethasone [administered at a dose known to alleviate obstructive small-airway disease (heaves) in horses; Ref. 28] did not significantly affect the development of arterial hypoxemia and desaturation of hemoglobin or their severity (Fig. 1) during short-term high-intensity exercise that caused pulmonary injury as evidenced by the occurrence of EIPH. These findings suggest that pulmonary injury-evoked airway inflammatory response is unlikely to play a major role in bringing about arterial hypoxemia in galloping Thoroughbreds. Although the reasons for divergent findings of the present study vis-à-vis reports in human subjects after nedocromil and diphenhydramine inhalation (7, 9, 26) are difficult to discern, species differences cannot be ruled out.

In view of the negative findings of the present study vis-à-vis human experiments with nedocromil and diphenhydramine (7, 9, 26), it is important to note that a discrete causal relationship between pulmonary injury and airway inflammation-induced release of histamine (and/or other chemical mediators) and exercise-induced arterial hypoxemia has not been established. In fact, Wetter et al. (39) reported that, although plasma histamine increased in exercising women, it was inversely correlated with severity of arterial hypoxemia at end exercise. Furthermore, it was recently demonstrated that preexercise IV administration of an anti-histaminic agent, tripelennamine HCl (a known H₁-receptor antagonist), failed to affect the arterial hypoxemia and desaturation of hemoglobin in Thoroughbreds performing high-intensity exercise that induced EIPH (23). Thus it was concluded that pulmonary injury and airway inflammation-induced histamine release may not play a major role in bringing about arterial hypoxemia in exercising horses (23).

The commonly mentioned possible causes of exercise-induced arterial hypoxemia in horses include the so-called “relative” alveolar hypoventilation (Fig. 2), ventilation-perfusion inhomogeneity, and the diffusion limitation related to the significantly shortened transit time for blood in the pulmonary capillaries as cardiac output increases dramatically (2, 3, 10, 13, 15, 21–23, 36, 37). Whereas the similarity of arterial CO₂ tension between the control and dexamethasone studies (Fig. 2) indicated similarity of alveolar ventilation in exercising horses, for unexplained reasons Prefaut et al. (26) reported a significant rise in arterial CO₂ tension of athletes performing maximal exertion after nedocromil inhalation. Alveolar-to-arterial O₂ tension gradient was not determined in the present study; however, the following observations suggest that the respiratory exchange ratio may not have been affected by dexamethasone administration. 1) Throughout the experimental protocol, arterial-to-mixed venous blood O₂ content gradient (Fig. 4) and O₂ extraction in the dexamethasone treatment were not different from the control study, indicating similarity of the aerobic metabolism in the two treatments. 2) Also, because acidosis (Fig. 3A), mixed venous blood CO₂ tension as well as mixed venous-to-arterial blood CO₂ tension gradient (cf. RESULTS), and lactate production (Fig. 3B) were not significantly different between the control and dexamethasone treatments, it is suggested that anaerobic metabolism of exercising horses was unaffected as well. Thus it is unlikely that O₂ uptake, CO₂ production, and respiratory exchange ratio were significantly affected by dexamethasone administration. This coupled with the finding that dexamethasone administration did not significantly affect arterial CO₂ and O₂ tensions (Figs. 1 and 2) suggests that the alveolar-to-arterial O₂ tension gradient may not have changed significantly between the control and dexamethasone treatments. However, because ventilation-perfusion inhomogeneity probably does not play a major role in bringing about the exercise-induced arterial hypoxemia in racehorses, the possibility remains that dexamethasone administration may have affected ventilation-perfusion inequality without significantly affecting the efficiency of pulmonary gas exchange.

In our experiments, arterial hypoxemia was already well developed by 30 s of galloping at 14 m/s on a 3.5% uphill grade, and further significant changes in the arterial O₂ tension did not occur as exercise duration progressed to 120 s (Fig. 1). According to the hypothesis that capillary stress failure (4, 12, 38)-related pulmonary injury-evoked airway inflammatory and mast cell histamine release (1, 25–27) leads to interstitial pulmonary edema (29), an accentuation of the arterial hypoxemia would be expected with increasing exercise duration as interstitial pulmonary edema intensifies over time. The fact that this was not the case in our control and/or dexamethasone experiments (Fig. 1), or in previous studies (10, 21–23), argues against a significant role for structural changes in the blood-gas barrier (4, 12, 29, 38) in bringing about the exercise-induced arterial hypoxemia. Further support for this argument is provided by the observation that, during a repeat bout of strenuous exercise performed 6 min after the first exercise bout that caused stress failure of pulmonary capillaries, an accentuation of the arterial hypoxemia could not be demonstrated (21). Similar observations were also reported in human subjects (5,
11, 30), and it was concluded that capillary stress failure-related structural changes in the blood-gas barrier are probably not responsible for the exercise-induced arterial hypoxemia (5, 11, 21, 30). The findings that arterial hypoxemia developed rather quickly, being evident at 30 s of galloping at 14 m/s on a 3.5% uphill grade, and that its severity was not significantly affected by increasing exercise duration in either treatment (Fig. 1) are consistent with the thesis that exercise-induced arterial hypoxemia in racehorses more likely has a functional basis, probably related to significant shortening of the transit time for blood in the pulmonary capillaries as cardiac output increases dramatically (21–23).

A pertinent issue to the present study is whether the occurrence of EIPH evokes airway inflammatory response in horses. Although bronchoalveolar lavage was not performed in our experiments, it should be noted that Tyler et al. (35) demonstrated that introduction of autologous blood into the alveoli of horses (e.g., with EIPH) evoked airway inflammatory response. In the present study, all horses were first studied in the control experiments wherein they experienced EIPH. Thus, based on the findings of Tyler et al., it is presumed that airway inflammatory response may have developed before dexamethasone administration was begun.

In conclusion, the results of the present study demonstrated that pretreatment with IV dexamethasone failed to significantly affect the development and severity of arterial hypoxemia and desaturation of hemoglobin in Thoroughbreds performing strenuous exercise that caused pulmonary injury as evidenced by the occurrence of EIPH. The failure of pretreatment with a potent anti-inflammatory agent to significantly modify exercise-induced arterial hypoxemia suggests that pulmonary injury-evoked airway inflammatory response is unlikely to play a major role in bringing about arterial hypoxemia in galloping Thoroughbred horses.

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REFERENCES


