Pulmonary Gas Exchange, Anaerobic Metabolism, and EIPH Unchanged by Nasal Strip Application in Exercising Thoroughbreds

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Two sets of experiments, using 7 healthy exercise-trained Thoroughbred horses were carried out in random order, 7 days apart. No differences were observed between the nasal strip group and controls as far as pulmonary gas exchange, anaerobic metabolism monitors, or the incidence of EIPH. Author’s address: University of Illinois, College of Veterinary Medicine, Urbana, IL 61802. © 2001 AAEP.

1. Introduction
Exercise-induced pulmonary hemorrhage (EIPH) has been the subject of much investigation and documentation in the past 30 years since the observation that post-racing bleeding (previously thought to be of nasal origin, i.e., epistaxis) was, in fact, of pulmonary origin.1,2 Numerous studies have suggested that the primary etiopathogenesis is linked to stress failure of pulmonary capillaries due to the extremely high transmural pulmonary capillary pressures that occur during strenuous exercise in horses.3–6 It has also been suggested that bleeding may be a result from asphyxia or associated with upper respiratory tract obstruction.7,8 Work from Kansas recently suggested that the use of an equine nasal dilator strip9 may introduce a new concept for the prevention of EIPH by enhancing nostril dilation.9–12 The present study was undertaken to further explore the potential benefits of nasal strips.

2. Materials and Methods
The experiments were carried out using 7 healthy, sound Thoroughbred horses (2 fillies and 5 geldings), 2.5- to 5-years-old and weighing between 431–509 kg. Exercise, training, dewormings, immunizations, housing and diet, and our experimental protocols were approved by the Institutional Laboratory Animal Care and Use Committees.

Exercise training was carried out over a period of 7 weeks using a walk, trot increasing to cantering and galloping to a maximum treadmill belt speed of 14 m/s for 120 seconds. EIPH was demonstrated in all horses at 14 m/s on a 3.5% uphill gradient, and this work rate was selected for the trials.

On the day of the study, the abdominal aorta was catheterized percutaneously.13 Cardiac catheters (8F) 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 the left jugu-
lar vein. Catheter placement was confirmed by oscillographic recordings of the characteristic phasic blood pressure wave forms. Thus, simultaneous sampling of aortic and mixed venous blood as well as continuous monitoring of core temperatures could be made during the experiments. After catheter placement, the horses stood on the treadmill for 50 min before pretesting blood-gas tensions, blood pH, and lactate/ammonia studies were taken.8

Experimental Design and Protocol
All horses were studied in two sets of experiments: control and nasal strip. The sequence of the experiments was randomized for every horse, and they were carried out at 7-day intervals.

Control Study
In these experiments, measurements were first made in duplicate (5 minutes apart) on quietly standing horses (rest #1 and #2) when heart rate and pulmonary vascular pressures had been stable for 10 to 15 min. Then exercise was performed in the following manner on the high speed treadmill set at a 3.5% uphill grade. Beginning with a walk at 2 m/s for 60 sec, belt speed was raised in increments of 1 m/s every 60 sec until the speed was 6 m/s. After the horses had trotted for 60 sec at 6 m/s, belt speed was raised to 8 m/s (canter) for 60 sec, and then to 14 m/s. Horses galloped at 14 m/s on a 3.5% uphill grade for 120 sec. Thereafter, the belt speed was first decreased to 5 m/s (trot) for 60 sec and then to 2 m/s (walk) for 5 min before stopping the treadmill.

Epistaxis was not seen in any of the horses during the training period. Endoscopic examination eliminated the presence of pharyngeal, or laryngeal disease (e.g., lymphoid hyperplasia or laryngeal hemiplegia).

In the above incremental exercise protocol, along with core temperature measurement, simultaneous aortic and pulmonary arterial blood samples were obtained for determining blood–gas tensions, pH, hemoglobin concentration, hemoglobin-O2 saturation and O2 content at 55 sec of trotting at 6 m/s, at 55 sec of cantering at 8 m/s, at 30, 60, 90, and 120 sec of galloping at 14 m/s on a 3.5% uphill grade, at 60 sec of trotting at 5 m/s as well as at 2 min of walk at 2 m/s. Hereafter, the measurements at 5 m/s and 2 m/s are also referred to as recovery data. Pulmonary arterial blood samples were also obtained pre-exercise (at rest) and at 2 min of walk at 2 m/s (during recovery) for lactate analysis as described above. For plasma ammonia assays, mixed-venous blood samples were obtained pre-exercise (at rest), upon immediately completing exercise at 8 and 14 m/s on a 3.5% uphill grade, as well as at 2 min of walk at 2 m/s during recovery.

Nasal Strip Study
In these experiments, measurements were first made on quietly standing horses (without the nasal strip) when heart rate and pulmonary vascular pressures had been stable for 10 to 15 min (hereafter, these pre-nasal strip measurements are referred to as rest #1). Then, carefully following the manufacturer’s instructions supplied with the product, an equine nasal dilator strip9 was applied. Five minutes later, resting measurements (rest #2) were completed and, thereafter, exercise was initiated. Exercise was performed on the treadmill set at a 3.5%/uphill grade, exactly in the same manner as described for the control study (see above). Sampling intervals and procedures for handling the arterial and mixed-venous blood for various measurements during exercise and recovery were identical to those in the control study.14

Post-Exercise Airway Endoscopic Examination
In the control as well as the nasal strip experiments, using a flexible fiberoptic endoscope,9 careful endoscopic examination of the nasopharynx, larynx, and trachea (up to the carina) was undertaken 45 to 50 min post-exercise. The presence of fresh blood in the airway was regarded as indicative of the occurrence of EIPH. A “grading” standard for degree of EIPH was not adopted as our previous observations have shown unreliability in such techniques.4,9 In the present study, immediate pre-exercise endoscopic examination of the airways was not performed; however, our extensive clinical and experimental experience indicates that fresh blood is not normally present in the airways of healthy horses.

Measurements and Data Analysis
In the present study, the O2 extraction (%) was calculated as (arterial to mixed venous O2 content gradient/arterial O2 content) × 100. All data were subjected to repeated measures, split-plot design analysis of variance (ANOVA15) using the SAS statistical software package6 and treatment comparisons were made using the least squares significant difference method.15 Data for the control and the nasal strip experiments were also individually subjected to analysis of variance followed by Newman Keuls multiple range test15 to determine the significant effects of work intensity within each treatment. For all statistical analyses, the level of significance was set at p < 0.05, and the data are presented as mean ± 1 SEM.

3. Results
The ANOVA revealed that between horses and the controls versus nasal strip interaction, effects were not statistically significant for any of the variables in this study. The statistical power for various variables in this study exceeded 80%.

The peak in core temperatures in both experiments (mean Δ = 3.4°C) occurred at 120 sec of galloping at 14 m/s on a 3.5% uphill grade.

In both groups (control and nasal strip), arterial O2 tensions recorded at 120 sec of galloping on a 3.5% uphill grade demonstrated hypoxemia, 72.9 ±
1.6 and 73.4 ± 2.1 mm Hg, respectively. Statistically significant differences between the control and nasal strip experiments were not found. Arterial and mixed venous blood hemoglobin-O2 saturations were 85.0 ± 1.7 and 86.5 ± 2.2%, respectively (not statistically significant). Arterial blood CO2 tensions were 44.6 ± 0.7 and 45.1 ± 1 mm Hg at rest and reached 50.8 ± 1.8 and 50.2 ± 1.7 mm Hg in control and nasal strip horses at maximal exercise.

Arterial blood pH values were 7.15 ± 0.031 and 7.146 ± 0.041, respectively. At 120 sec of galloping at 14 m/s on a 3.5% uphill grade, control and nasal strip horses recorded mixed venous blood O2 content reductions to 2.2 ± 0.2 and 2.2 ± 0.3 ml/dl, respectively (not significant).

In control and nasal strip experiments, the corresponding values for O2 extraction were 91.4 ± 0.8% and 91.4 ± 1.0%, respectively. In both control and nasal strip studies, large significant increments in mixed-venous blood lactate and plasma ammonia concentrations were observed in response to maximal exercise. Blood lactate concentration means in mM/l at rest were 0.48 ± 0.02 for controls and 0.53 ± 0.02 for nasal strip. After high intensity exercise, they rose to 17.41 ± 2.42 and 16.75 ± 3.02, respectively. Plasma ammonia concentrations in μM/l were 4.6 ± 3.0 for controls and 3.5 ± 1.2 for nasal strip. These rose to 172.3 ± 56.8 and 169.11 ± 68.12, respectively. There were no statistically significant differences between the two treatments at any step of the experimental protocol.

Post-exercise airway endoscopic examination revealed that all horses demonstrated EIPH in the control and in the nasal strip experiments.

4. Discussion
Our primary objective in the present study was to determine whether the application of an external nasal dilator strip might improve exercise-induced arterial hypoxemia and hypercapnia, diminish blood lactate and ammonia concentrations at constant workload, or diminish the incidence of EIPH in strenuously exercising Thoroughbred horses. The results of the present study clearly demonstrated that the application of an external nasal dilator strip did not achieve these benefits. Our findings are similar to recent observations in human subjects performing maximal exercise, wherein it was demonstrated that the application of the nasal dilator strip did not affect VO2\text{max}, maximal ventilation, and indices of perceived exertion/dyspnea and it was concluded that the external nasal dilator strip did not enhance exercise performance. However, it should also be noted that a reduction in VO2 during sub-maximal exercise with a nasal dilator strip as well as a delay in the onset of oral breathing in human athletes have been reported. This discrepancy in the human data may be related to observations being made in so-called “responders” vs. “nonresponders.” A substantial between-subject variation in the compliance of the lateral nasal vestibule wall has been reported in the human population, which may account for the reported differences between “responders” and “nonresponders.” Whether a similar situation exists in the Thoroughbred horse population is not known as yet; however, as discussed below, it should be noted that the morphology/physiology of the equine nostril is quite different from that of the human nose. Although only 7 horses were used in the present study, it should be noted that the data were highly consistent among horses as indicated by the fact that, in the analysis of variance, the between horse as well as the horse × treatment interaction effects were not significant for any of the variables examined in the present study.

In the present study, the highest workload used was 14 m/s on a 3.5% uphill grade. That this workload indeed represented a strenuous effort for our horses was indicated by the facts that a) this workload elicited maximal heart rate of horses; b) this workload could not be sustained for > 120 sec despite vigorous humane encouragement; and c) it induced EIPH in all horses in both treatments. Similar to previous reports, at submaximal workloads, our horses exhibited hyperventilation and the arterial blood O2 tension as well as hemoglobin-O2 saturation were well maintained in the control as well as the nasal strip studies. We also observed a significant reduction in arterial PO2 and de-saturation of hemoglobin during galloping at 14 m/s on a 3.5% uphill grade in both studies, but statistically significant differences between the control and the nasal strip experiments were not found. Although “relative” hypoventilation (as evidenced by the increased P\text{ACO2} during galloping at 14 m/s on a 3.5% uphill grade) and ventilation:perfusion inequality also contribute, the exercise-induced arterial hypoxemia in horses is believed to be due primarily to the diffusion limitation caused by a dramatically shortened transit time for blood in the pulmonary capillaries as cardiac output increases approximately 7- to 8-fold. Since we did not observe significant benefit to gas exchange in the lungs of exercising horses upon the application of the nasal strip, the question remains whether application of an external nasal dilator strip indeed decreases nasal resistance to airflow in horses. At present, our knowledge regarding changes in total as well as regional pulmonary resistance in exercising horses is limited and somewhat controversial. For example, whereas Art et al 18,19 observed a significant increase in total pulmonary resistance of galloping horses, Slocombe et al 20 reported that significant changes in total pulmonary resistance did not occur during exercise even though it was reported that upper airway resistance had decreased significantly during galloping. By contrast, it is noteworthy that Art and Lekeux 18,19 have presented data indicating a significant increment in the overall equine upper airway resistance as well as in its components, that is, the nasopharyngeal and laryngeal-tracheal resistances, during heavy exercise. Despite some dis-
agreement, it is generally believed that during quiet breathing in resting horses, 50% of the total pulmonary resistance results from the nasal passages, 30% from the remaining upper airways, and 20% from the intra-thoracic airways. In strenuously exercising horses, despite physiologic adjustments, for example, a dramatic dilatation of the external nares, full abduction of the larynx, and bronchodilation, which increase the cross-sectional area of the respiratory tree. Art and colleagues have shown that the relative contribution of the various airway segments to the total pulmonary resistance does not change. At present, however, data are not available to assess the individual contribution of the segments of the nasal passage (i.e., nostril vs. the nasal meatus) to resistance to airflow through them in exercising horses. Since the application of an adhesive nasal strip did not significantly affect the various parameters examined in our study, it may be argued that the application of the nasal strip may not have made a significant contribution to lowering the total pulmonary resistance of galloping horses. However, further work is warranted to document whether this is indeed the case.

The morphology of the equine nose is quite different from that of the human nose. The skeleton of the lateral wall of the horse’s nose is incomplete rostral to the nasoincisive notch and this so-called “soft” portion of the equine nose contains a unique structure known as the false nostril. The latter is a diverticulum of the nasal passage which opens into the dorsal lateral aspect of the true nostril. In an exercising horse, the effacement of the false nostril is brought about by the action of several muscles, namely, the dorsal and ventral levator nasi, the dilator naris lateralis, the dilator naris apicalis, and the levator nasabialis. As the lateral nasal wall is pulled taut upon contraction of these muscles in an exercising horse, the anterior nasal cavity becomes almost circular (from being comma-shaped at rest). The equine nasal strip covers a portion of the false nostril and its beneficial effect on nasal resistance to airflow during strenuous exertion may result from its ability to minimize/prevent dynamic collapse of the lateral wall of the nostrils. Although it is difficult to discern the exact reasons for the lack of a beneficial effect of the nasal strip on the aerobic (gas exchange) and anaerobic (lactate and ammonia production) variables in strenuously exercising horses in the present study, the following possibilities may be considered: a) Because active contraction of above mentioned muscles tightly stretches the lateral nasal wall in healthy horses performing strenuous exercise, a significant dynamic collapse of the lateral nasal wall may not occur. In fact, as yet there have been no direct reports documenting dynamic collapse of the lateral nasal wall in strenuously exercising horses. b) In a maximally exercising horse, the lateral nasal wall may be maximally stretched upon contraction of the above mentioned muscles such that the application of a passive device (adhesive nasal strip) is unable to cause a further stretching of the nasal wall. c) Finally, it is also plausible that although application of the nasal strip may help lower the nasal resistance to airflow in exercising horses, the change may be of an insufficient magnitude to significantly affect the physiologic parameters examined in the present study.

In exercising horses, the significant rise in blood temperature, hypercarbia, and marked acidosis shift the hemoglobin-O2 dissociation curve to the right, thereby facilitating increased O2 unloading from hemoglobin at the working muscles. The extent of hyperthermia, hypercarbia, and acidosis observed in the nasal strip study were not different from that in the control study. In the control as well as the nasal strip studies, there was a progressive significant exercise-induced reduction of a similar magnitude in the mixed-venous blood O2 tension and hemoglobin-O2 saturation. The reduction in mixed-venous blood O2 tension associated with the increased O2 delivery to the working muscles helps to expand the partial pressure gradient for O2 diffusion across the blood-gas barrier, thereby facilitating pulmonary O2 transfer.

In exercising horses, arterial blood O2 content is known to increase dramatically due to the significant increase in hemoglobin concentration caused upon release of the splenic erythrocyte reservoir. The extent of the increment in arterial O2 content of horses in the present study was also similar between the control and the nasal strip experiments and was accompanied by a large reduction in the mixed-venous O2 content in both sets of experiments as O2 extraction approached 91.4%. At constant workload, the close similarity of the arterial to mixed venous O2 content gradient and O2 extraction between the control and the nasal strip experiments suggests that the aerobic metabolic O2 requirements were probably similar for the two sets of experiments.

In the present study, we also determined mixed-venous blood lactate and plasma ammonia concentrations as indices of anaerobic metabolism. This was done in the context that the reduced work of breathing (caused by lowered nasal resistance to airflow) in the nasal strip experiments would diminish the metabolic O2 requirements of the respiratory muscles, thus allowing increased O2 availability to the working muscles which, at constant workload, should decrease reliance on anaerobic metabolism. However, this appears to have not been the case in the nasal strip experiments in the present study.

In the present study, although large significant increments in blood lactate and plasma ammonia concentrations were observed in the control and the nasal strip studies, statistically significant differences were not observed between the two treatments at any step of the protocol. Finally, in the present study, airway endoscopy revealed that the occur-
rence of EIPH was also unaffected by the application of an external nasal dilator strip. All horses had experienced EIPH in both treatments as demonstrated by the presence of fresh blood in the trachea, larynx or pharynx. The fact that statistically significant differences in any of the above parameters were not observed in strenuously exercising horses following application of the external nasal dilator strip raises doubts regarding meaningful benefits to its use in racehorses.

In conclusion, our data demonstrated that application of an external nasal dilator strip neither improved the exercise-induced arterial hypoxemia and hypercapnia, nor did it diminish the lactate and ammonia production or the incidence of EIPH in Thoroughbreds performing strenuous exercise.

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References and Footnotes


*Pentax Fiberscopes, Orangeburg, NY.
*SAS version 6.12, SAS Institute, Cary, NC.