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Heliox-induced Changes in the Breathing Mechanics of Ponies during Exercise

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ABSTRACT. The changes occurring in breathing mechanics of exercising ponies when heliox is substituted for air are reported. Respiratory airflow, tidal volume (V_T) and transpulmonary pressure (Ptp) were simultaneously measured in 5 healthy ponies (255 ± 15 kg) at rest (breathing air) and while they exercised for 6 min on a treadmill. During exercise they first breathed air (2 min), than heliox (2 min) and then air again (2 min). Tidal volume (V_T), respiratory rate (f_R), minute volume ($\dot{V}_E$), maximum Ptp changes, total pulmonary resistance (R_L), mechanical work of breathing per liter (Wrm l^{-1}), mechanical work per min ($\dot{W}$rm), dynamic compliance and pulmonary inertance were calculated. Heliox breathing significantly increased f_R and $\dot{V}_E$ while V_T remained unchanged. R_L was reduced by 50% of its "air value", Wrm l^{-1} decreased, while $\dot{W}$rm remained unchanged. Pulmonary inertance dropped to 30% of its "air value". These observations suggest that in ponies, turbulent resistance and pulmonary inertance could be mainly responsible for the increases of R_L and Wrm l^{-1} during exercise.

Key words. Respiration; exercise; resistance unloading; heliox breathing; ponies; horses.

INTRODUCTION

In previous studies in horses, it has been suggested that a potential mechanical limitation to ventilation during strenuous exercise could result from increases in total pulmonary resistance,[2,5] mechanical work of breathing,[3] and inertial pressure losses.[4] With the high flow rates recorded during strenuous exercise, physical factors such as turbulence and friction increase dramatically, which in turn induce an increase in flow resistance and the work of breathing. Because these physical factors are related to gas density, it can be predicted that they will be reduced by breathing a gas of low density. Therefore, it may be anticipated that the ratio of the work of breathing per cycle (Wrm) to tidal volume (V_T), would be improved with helium-oxygen (heliox) breathing.

The present study attempts (1) to assess any changes that occur in ventilation and mechanics of breathing when heliox is substituted for air and (2) to analyse whether these modifications can be adequately explained by changes in friction, turbulence and inertance.

MATERIALS AND METHODS

Five healthy ponies aged 2.5 to 4 years and weighing 255 ± 15 kg (mean ± SEM) were used. They were healthy on clinical examination, endoscopic examination of the upper airways, and arterial blood gas analysis performed at rest.

All experiments were carried out on a treadmill located outdoors and were performed twice for each subject over a 1–2 day interval. The 10 results were averaged for each parameter. Respiratory airflow ($\dot{V}$) was measured with a No. 5 Fleisch pneumotachograph mounted on a tightly fitting mask and coupled to a differential pressure trans-

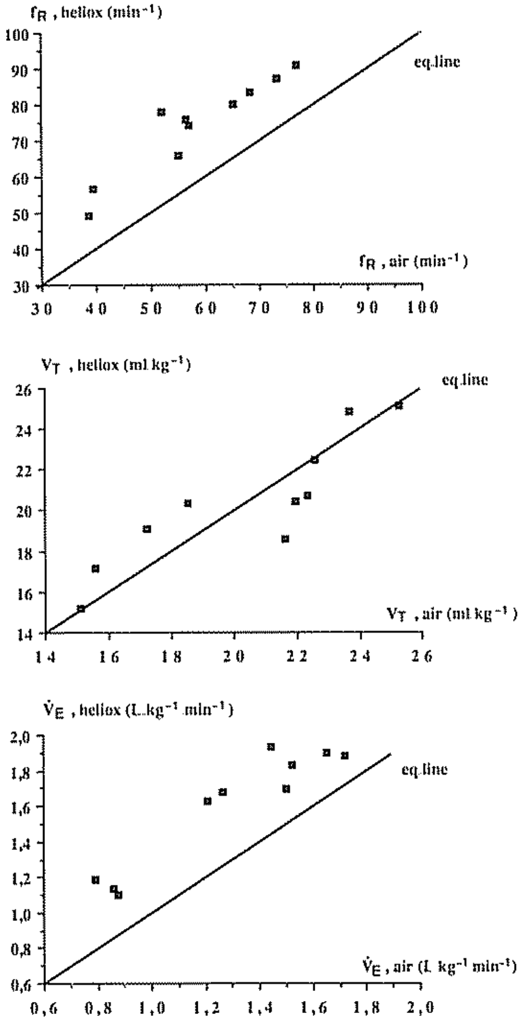

Fig 1 Respiratory frequency (f_R), tidal volume (V_T) and minute volume ($\dot{V}_E$) in ponies running on a treadmill while breathing either air or heliox ($n = 10$). "eq. line" represents the identity line.

ducer (Validyne M145) with catheters (4 mm ID, 6 mm OD, 220 mm long). Tidal volume (V_T) was obtained by numerical integration of the $\dot{V}$ signal and was electronically corrected for BTPS.

Esophageal pressure (Pes) was measured with an esophageal balloon catheter (4 mm ID, 6 mm OD, 220 mm long) coupled to a pressure transducer (Bentley, Trantec M800). The pressure in the mask (Pm) was also recorded using a catheter (4 mm ID, 6 mm OD, 220 mm long) and a pressure transducer. Transpulmonary pressure (Ptp) was calculated as the difference between Pes and Pm.[1]

A giant non-rebreathing Hans Rudolph valve (Model 7280) was fitted to the Fleisch pneumotachograph. The inspiratory side of the valve was connected by a hose (100 mm ID, 150 cm long) to a 1 000 l bag containing ≈ 79 % He and ≈ 21 % O_2, and 65 % saturated with H_2O vapor at ambient temperature. A manual 3-way stopcock valve (60 mm ID) placed between the hose and the bag allowed switching between air and heliox breathing.

Calibration of the pneumotachograph was performed with both air and He. The pressure transducers were carefully calibrated under both static and dynamic conditions, before and after each experiment. Static calibration was carried out with a water manometer. Dynamic calibration was performed by checking the frequency response and amplitude of signals with a sinusoidal pump generating alternating pressures in a closed flask. Frequencies up to 10 Hz and pressure changes up to 5 kPa were used. The frequency response characteristics of the system consisting of the pneumotachograph, the pressure transducer, the connector catheters, and the pressure recording system were matched up to 10 Hz for phase compatibility. In all cases, the amplitude responses were flat.

Throughout each experiment, the heart rate (HR) was recorded on a telemetric electrocardiographic system (Danica Electronica, DK 2880).

Measurements of Pes, Pm, V_T, $\dot{V}$ and HR were first made during quiet air breathing following a 5 min rest period on the treadmill. The ponies then trotted for a 6 min period on the treadmill at a speed of 3.0 m s^{-1} and an incline of 5°. First they breathed air, then heliox, and then air again, each for a period of 2 min. The tracings were recorded during the last 30 seconds of the rest period, air breathing, heliox breathing and

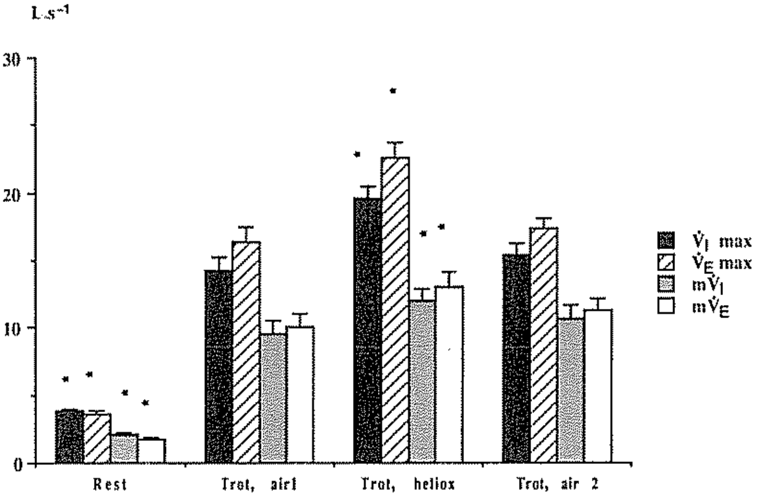

Fig. 2. Inspiratory peak and mean airflows ($\dot{V}_I$max and m$\dot{V}_I$ respectively) and expiratory peak and mean airflows ($\dot{V}_E$max and m$\dot{V}_E$) in ponies at rest, during exercise with air breathing (air$_1$), with heliox breathing and with air breathing again (air$_2$) ($n = 10$). *Significantly different from "trot air$_1$" values with $p < 0.001$

air breathing. Ten regular and artefacts free cycles were used for calculation.

Respiratory frequency (f_R), inspiratory and expiratory time (t_I and t_E), the ratio of t_I to the total time of the breathing cycle (t_I/t_T), peak inspiratory and expiratory $\dot{V}$ ($\dot{V}_I$max and $\dot{V}_E$max), V_T, mean inspiratory and expiratory $\dot{V}$ (m$\dot{V}_I$ and m$\dot{V}_E$), minute volume ($\dot{V}_E$), minimal and maximal Ptp (Ptpmin and Ptpmax), as well as the maximal Ptp change (maxΔPtp) were calculated. The recorded traces also allowed computation of total pulmonary resistance (R_L) and mechanical work of breathing per liter (Wrm l^{-1}) and per min ($\dot{W}$rm).

The inspiratory and expiratory volume accelerations were calculated as the slope of the flow changes at the beginning of inspiration and of expiration. These values were obtained for exercising ponies while breathing air and heliox.

The following parameters were also calculated: pulmonary inertance (IL), i.e. the ratio of the inertial pressure changes to the total change in volume acceleration;[4] the dynamic compliance (Cdyn), i.e. the amplitude of V_T

Table 1. *Inspiratory and expiratory times (t_I and t_E), t_I to total breathing time ratio (t_I/t_T), minimal and maximal transpulmonary pressures (Ptpmin and Ptpmax) and maximal transpulmonary pressure changes (maxΔPtp) at rest, during exercise with air breathing (air$_1$), with heliox breathing and with air breathing again (air$_2$) in ponies ($n = 10$, mean ± SEM)*

Values	Units	Rest	air$_1$	heliox	air$_2$
t_I	s	1.64±0.13	0.55±0.04	0.43±0.03***	0.52±0.07
t_E	s	2.13±0.23	0.53±0.05	0.41±0.03***	0.51±0.06
t_I/t_T	%	44±1	51±1	52±1	51±1
Ptpmin	kPa	−0.98±0.04	−1.81±0.13	−1.56±0.09*	−1.99±0.11
Ptpmax	kPa	−0.23±0.14	0.78±0.23	0.39±0.18**	0.61±0.24
maxΔPtp	kPa	0.75±0.13	2.59±0.29	1.95±0.20***	2.60±0.26

*Significantly different from air$_1$ values with $p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

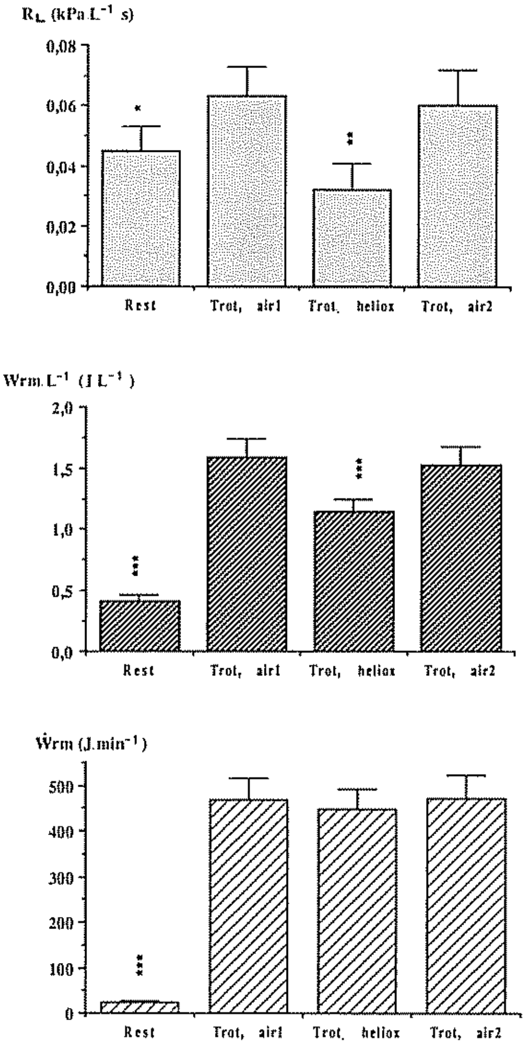

Fig 3 Total pulmonary resistance (R_L), mechanical work of breathing per liter (Wrm l^{-1}) and mechanical work per min ($\dot{W}rm$) in ponies at rest, during exercise with air breathing (air_1), with heliox breathing and with air breathing again (air_2) ($n=10$). **Significantly different from "trot air_1" values with $p<0.01$; ***$p<0.001$

divided by the elastic pressure change which is the difference in total pressure between the beginning and the end of inspiration.

Significant differences between (1) air and heliox breathing and (2) "air" before and "air" after heliox breathing were assessed by a Student's *t*-test for paired data, with $p<0.05$ accepted as significant. Mean results ± SEM are presented.

RESULTS

Fig. 1 illustrates the changes induced by heliox breathing in f_R, V_T and $\dot{V}_E$ in the form of identity relationships. Each point on these graphs compares the data on air to the data on the heliox mixture obtained from 10 experiments. In response to respiratory unloading, i.e. change from air to heliox, $\dot{V}_E$ increased significantly ($p<0.001$) by a mean of 27%. This ventilatory increase was exclusively due to an increase in f_R ($p<0.001$), with no consistent changes in V_T. Mean and peak inspiratory and expiratory $\dot{V}$ increased (Fig. 2) and t_I and t_E decreased, significantly in both cases, while t_I/t_T remained unchanged (Table 1). Heliox breathing also induced a substantial decrease in maxΔ Ptp ($p<0.001$) (Table 1).

R_L, which increased significantly ($p<0.05$) from rest to trot, was reduced to a value smaller than its rest value during trotting with heliox (Fig. 3). Wrm l^{-1} was also reduced ($p<0.001$), but $\dot{W}rm$ remained unchanged (Fig. 3). The inspiratory and expiratory volume accelerations increased ($p<0.05$) when the ponies were switched from air to heliox breathing (Table 2), and pulmonary inertance was reduced from 19.78 ± 0.07 to 6.5 ± 0.42 10^{-4} kPa l^{-1} s^2.

For each experiment, the individual values of Cdyn calculated at rest, during exercise with air breathing and during exercise with heliox breathing are shown in Fig. 4. The mean rest value of Cdyn was 8.62 ± 0.69 l kPa^{-1}. In 8 out of the 10 experiments, Cdyn became negative during exercise with air breathing. The values of Cdyn were positive again during heliox breathing and were significantly greater than the rest values.

HR was 42±4 bpm at rest and 163±3 bpm while trotting with air breathing. The latter value remained unchanged throughout the 6 min trot period.

For all parameters, there were no differ-

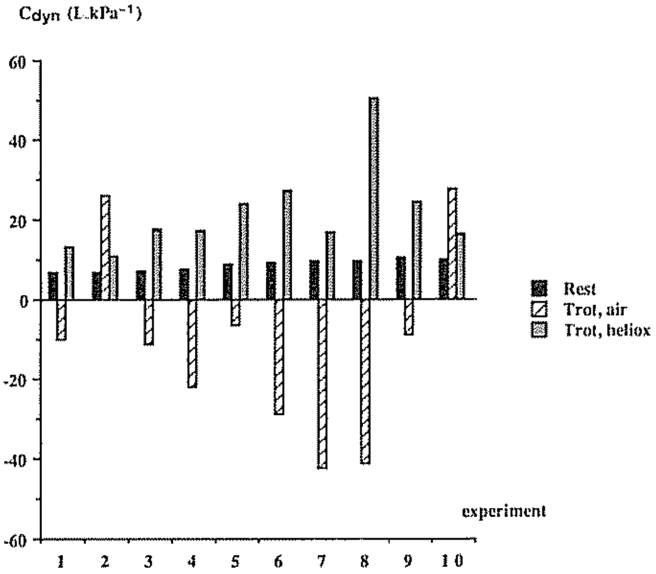

Fig 4. Individual dynamic compliance (Cdyn) in ponies at rest, during exercise with air breathing, and during exercise with heliox breathing ($n = 10$).

ences between the "air" values before and after heliox.

DISCUSSION

The ventilatory effect of unloading during exercise was shown here to cause an increase in $\dot{V}_E$ which was exclusively due to an increase in f_R, with no consistant changes in V_T. In addition, the increased airflows with gas of low density were associated with smaller pleural pressure changes. These changes are in keeping with those observed in similar studies performed on humans[14,17] and on ponies.[15] The intrinsic (force velocity) properties of skeletal muscles, neural reflexes diminishing central drive[8] and/or chemoreflexes are mechanisms thought to contribute to load compensation. They could explain the increase of flow achieved with less pressure. The sharp and immediate increase in f_R when heliox was breathed was not compensated by a simultaneous decrease in V_T, thus, $\dot{V}E$ increased. Although arterial gas tensions were not measured here, similar experiments performed on humans and ponies have shown that the increased $\dot{V}_E$ results in an alveolar hyperventilation and arterial hypocapnia.

In humans,[12] horses,[16] cattle[10] and ponies[2] the relative contribution of the upper airways resistance (Ruaw) to R_L has been shown to be about 80%. This important relative contribution of Ruaw is partly due to

Table 2. *Inspiratory and expiratory volume accelerations ($\ddot{V}_I$ and $\ddot{V}_E$, respectively) during air and heliox breathing (mean ± SEM)*

$\ddot{V}_I$ air $l\ s^{-2}$	$\ddot{V}_E$ air $l\ s^{-2}$	$\ddot{V}_I$ heliox $l\ s^{-2}$	$\ddot{V}_E$ heliox $l\ s^{-2}$
467.6±46.4	490.2±55.2	545.4±36.9*	585.8±35.4*

*Significantly different from air values with $p < 0.05$.

the occurrence of turbulence in that part of the respiratory tract.[19] In exercising horses, more than in other species, turbulence may become of major importance for two reasons. First, during strenuous exercise, peak flows as high as 80 l s^{-1} are reached,[5] and consequently, the Reynolds number is much greater than its critical value. Secondly, horses are unable to bypass the considerable resistance of the nasal cavities[2] by switching from nasal to oronasal breathing. The fact that changing from air to heliox breathing decreased R_L by 51% confirms the importance of turbulence in the upper airways of ponies. Indeed, the frictional pressure losses (P) produced by $\dot{V}$ in tubes are a function of the flow rate, tube geometry and fluid physical properties. The relationship between these parameters is defined by the flow pattern, which in turn is largely determined by the Reynolds number (Re):

$$Re = d\nu\rho/\mu$$

where d is tube diameter, ν gas velocity, ρ gas density and μ the gas viscosity. At low Re, the flow is laminar with a parabolic velocity profile and the pressure drop is entirely due to viscous forces. This is the case in the peripheral airways, as described by the Poiseuille equation:

$$P = C_1\mu\dot{V}.$$

At high Re, when turbulent flow is fully developed (e.g. at the outlet of a localized constriction or orifice as in the larynx or in the nasal cavities), the pressure losses are entirely inertial and

$$P = C_2\rho\dot{V}^2.$$

This means that the resistance in the central and upper airways is more dependent on gas density and flow and less dependent on viscosity, while the opposite is true in the peripheral airways.[19] Substitution of a heliox mixture for air decreases the density of the respired gas (×0.345) and only slightly alters the viscosity. Therefore, the substantial changes in R_L observed during the present experiments are mainly attributable to the changes occurring in the fluid dynamics, and especially to the reduction of the turbulent resistance in the upper airways.

The method used to measure IL and its validity are discussed elsewhere.[4] The inertance, as measured in this study, is mainly due to the air. Because the density of the heliox mixture is about 0.345 that of air, heliox breathing induced a decrease of about 60% in IL. Therefore, the decrease in Wrm l^{-1}, although explained largely by the decrease in R_L, could be also due partly to the decrease in pressure necessary for volume acceleration.

The overestimation of Cdyn in large animal breathing with high f_R and V_T has been reported.[2,11] The error in the computation of Cdyn results from the fact that in diseased or exercising large animals the inertance, and consequently the inertial pressures, are no longer negligible. Classically, Cdyn is measured at points of zero $\dot{V}$ and may be defined by the equation:[9]

$$\text{measured Cdyn} = \frac{V_T}{\Delta Pel - [\omega^2 V_T\, IL]}$$

where ΔPel is the change in elastic pressure and $\omega = 2\Pi f$, f being the respiratory frequency in Hz. $[\omega^2 V_T IL]$ is generally considered to be negligible, but in large animals with large IL, f_R and V_T, $[\omega^2 V_T IL]$ becomes very important, and during exercise its absolute value can be greater than ΔPel. This explains why, in these specific conditions, Cdyn is overestimated and may even be negative.[13]

In conclusion, heliox breathing in exercising ponies induced (1) the same modified breathing pattern previously reported for man, (2) a sharp decrease in R_L and Wrm l^{-1} suggesting that the increase in R_L during exercise is mainly due to increased turbulence in the extrathoracic airways and (3) a sharp decrease in IL suggesting that the increase of Wrm l^{-1} is partly associated with the high inertial pressures.

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Alleviation of Exercise-induced Hypoxemia Utilizing Inspired 79% Helium 20.95% Oxygen

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ABSTRACT We investigated the effect of reducing gas density on arterial and mixed venous PO_2 and PCO_2, pulmonary artery (PAP) and esophageal pressures (ESP), and ventilatory and cardiac frequencies (fR, HR) during treadmill exercise in the horse. Four horses were exercised for 4 min on separate occasions at 10 m s^{-1} and 11–13 m s^{-1} while breathing ambient air (time 0–2 min) and then when gas density was reduced by substituting helium (He–O_2) for nitrogen in the inspirate (time 2–4 min). At 10 m s^{-1} and 11–13 m s^{-1} He–O_2 produced increases in PaO_2 from 63.1 (8.41) to 86.5 (11.53) mm Hg (kPa) and from 62.2 (8.29) to 75.7 (10.09) mmHg (kPa). At both work rates, He–O_2 induced a 6 mmHg (0.79 kPa) decrease in $PaCO_2$ and a 11–14 mmHg (1.46–1.86 kPa) decrease in peak inspiratory to expiratory ESP difference. Mean PAP, HR, and mixed venous PO_2 and PCO_2 did not change with He–O_2. The data show that the hyperventilation produced by He–O_2 could not explain the increased PaO_2.

Key words. Horses; blood gases; ventilation; esophageal; pulmonary artery.

INTRODUCTION

Strenuously exercised horses routinely develop hypoxemia and hypercapnia concurrent with severe acidosis.[2–5,8,10,11] Accordingly, hypotheses have been advanced suggesting that ventilation is mechanically restricted, because of the 1 : 1 phase locking of breath to stride frequency.[5,8] At a locked breath frequency (single breath time of approximately 200–250 ms), tidal volume and, therefore, alveolar ventilation are inadequate to maintain arterial blood gas homeostasis.[5] Consequently, hypoventilation produces hypercapnia and hypoxemia, despite the increased ventilatory stimulation of acidosis. However, extending exercise time reduced the $PaCO_2$ to hypocapnic values yet PaO_2 remained unchanged.[5] This means that despite increased alveolar ventilation ($\dot{V}A$) either ventilation-perfusion ($\dot{V}/\dot{Q}$) worsened or diffusion impairment increased. Recent studies demonstrated during heavy exercise that $\dot{V}/\dot{Q}$ mismatch and hypoventilation accounted for approximately 25% of the hypoxemia; shunt, 1%; and diffusion limitation, nearly 70%.[11] The question of relative contributions to hypoxemia by either hypoventilation or $\dot{V}/\dot{Q}$ mismatch remains unresolved.

To gain insight into the contribution of the hypoventilation to hypoxemia, we have alleviated the hypoventilation by reducing airway resistance using low density He instead of N_2 in the inspired gas.

METHODS

Three Quarterhorses and one Thoroughbred (495 ± 32 kg SEM, age 4–8 years) free of any known disease were studied. These animals were experienced in running on a high speed treadmill and in appropriate physical condition to complete the exercise protocol.

Exercise protocols and gas administration

Each horse exercised on the treadmill (3° incline) at 2 m s^{-1} for 2 min followed by 4 min at 10 m s^{-1} and on a separate occasion