

STUDIES ON THE PHYSIOPATHOLOGY OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN THE HORSE. VII. PERCENTAGE VENOUS ADMIXTURE

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ABSTRACT

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The percentage venous admixture was calculated in 21 clinically normal horses and ponies and in 13 horses and ponies with chronic obstructive pulmonary disease (COPD). The oxygen contents of pulmonary end-capillary blood, arterial and mixed venous blood were calculated from blood and respiratory gas values and substituted in the shunt equation.

The mean percentage venous admixture of the COPD subjects was significantly greater than that of the normal subjects. It was concluded that a larger proportion of alveoli in the lungs of COPD subjects were hypoventilated than that of alveoli of the normal lungs.

INTRODUCTION

The concentration of O₂ in expired gas is determined by the relationship between alveolar ventilation and pulmonary capillary blood flow (Comroe, Forster, Dubois, Briscoe & Carlsen, 1962; Nunn, 1969). According to Comroe *et al.* (1962), uneven alveolar ventilation relative to alveolar blood flow is the commonest cause of hypoxaemia in human clinical medicine. The difference between the partial pressures of oxygen in alveolar gas and arterial blood ($\Delta A-aPO_2$) while breathing air is a composite measure of direct anatomical shunts as well as the shunts due to the perfusion of under- and non-ventilated alveoli (Bartels, Severinghaus, Forster, Briscoe & Bates, 1954). A significant increase in the $\Delta A-aPO_2$ value may therefore be assumed to indicate increased direct shunt and/or hypoventilation of a greater proportion of alveoli. If physiological right-to-left shunts remain unchanged, it may be indicative of hypoventilation alone.

As discussed at length by Nunn (1969), much depends on what is meant by "alveolar PO₂", and how it is measured or calculated. In the original studies by Haldane & Priestley (1905), alveolar gas was defined as gas sampled at the end of a forced expiration. At that time it was not appreciated that alveoli were unequally perfused with pulmonary blood and that consequently the end-expiratory gas sample consisted of a mixture of gases from both perfused alveoli and from non- or partially-perfused alveoli. However, in 1946, Riley, Lilienthal, Proemmel & Franke re-stated the concepts of gas exchange by considering the lung as 3 separate compartments from a gas exchange point of view. The 3 compartments were: (a) alveoli which are not perfused at all, (b) perfused and ventilated alveoli, i.e. "ideal alveoli", and (c) perfused but non-ventilated alveoli, i.e. the shunt component of the pulmonary circulation. Riley *et al.* (1946) thus drew a clear distinction between end-expiratory gas, which was a mixture of alveolar dead space gas and functional alveolar gas, and "ideal" alveolar gas, which originated only from alveoli taking part in gas exchange.

The significance of the Riley approach was that it enabled physiologists and clinicians to calculate the amount of venous admixture with pulmonary end-capillary blood which provided a convenient index of the relative amount of right-to-left shunt. Nunn (1969), however, noted that it was neither strictly accurate nor did it identify the anatomical pathway of the shunt. The method has been utilized to estimate the extent of lung dysfunction in man. Nunn (1969) stated that current opinion postulated a random distribution of ventilation throughout the lung in many forms of chronic lung disease.

Gillespie & Tyler (1969) determined the magnitude of the pulmonary vascular shunt in horses by means of the modified equation of Finley, Hill & Bonica (1963). They showed that, in subjects with emphysema, the pulmonary vascular shunt (i.e. the shunt due to non-ideal alveoli) was significantly higher than in clinically normal control subjects. Sasse (1971) drew attention to the following factors which may be of significance in cases of chronic obstructive pulmonary disease (COPD) and which might be expected to cause inequalities of perfusion throughout the lung:

(a) thrombotic emboli in the lung such as those described by Mitchell, Silvers, Dart, Petty, Vincent, Ryan & Filley (1968);

(b) compression of pulmonary veins as a result of elevated intrathoracic pressure; and

(c) destruction of the pulmonary vascular bed as in emphysema.

These studies were carried out to compare the percentage venous admixture in the blood of horses with COPD with that of clinically normal horses.

MATERIALS AND METHODS

Subjects

Twenty-one clinically normal horses and ponies and 13 COPD subjects of the series described previously (Littlejohn, 1980) were used. All subjects were given a full clinical examination, including determination of rectal temperatures.

Blood gas determinations

The partial pressures of O₂ and CO₂ in arterial and venous blood samples were determined by the methods described by Littlejohn & Bowles (1981). Oxygen contents of blood samples were calculated using the Blood Gas Calculator (Severinghaus, 1966) and assuming an O₂ capacity of 1.34 ml per g of haemoglobin.

The partial pressures of O₂ and CO₂ in mixed expired gas samples were determined by means of Radiometer PO₂ and PCO₂ electrodes types E5046 and E5036 respectively.

Calculations

The calculation of percentage venous admixture was carried out according to the following equation (Nunn, 1969).

$$\text{Percentage venous admixture} = 100 \times \frac{C\acute{c}O_2 - CaO_2}{C\acute{c}O_2 - C\bar{v}O_2} \quad (1)$$

where $C\acute{c}O_2$ = content of oxygen in pulmonary end-capillary blood

CaO_2 = content of oxygen in arterial blood

$C\bar{v}O_2$ = content of oxygen in venous blood

Since the oxygen content of pulmonary end-capillary blood cannot be measured directly, it was derived by calculating the alveolar PO₂ (i.e. the "ideal" alveolar PO₂ as defined by Riley *et al.*, 1946). The ideal alveolar PO₂ was then assumed to be equal to the pulmonary end-capillary blood PO₂, from which the O₂ content was calculated.

The ideal alveolar partial pressure of oxygen (PAO₂) was calculated by inserting the appropriate values obtained for each subject in the following equation derived by Filley, Macintosh & Wright (1954):

$$PAO_2 = PIO_2 - PaCO_2 \frac{PIO_2 - \bar{P}EO_2}{\bar{P}ECO_2} \quad (2)$$

where PaCO₂ = partial pressure of carbon dioxide in arterial blood,

PIO₂ = partial pressure of oxygen in inspired air and $\bar{P}EO_2$, $\bar{P}ECO_2$ = partial pressures of oxygen and carbon dioxide respectively in mixed expired gas

Mixed expired gas was collected in a meteorological balloon, using a mask similar to that used by Sasse (1971).

The determination of percentage venous admixture was then made by substituting the appropriate values in the equation (1) above.

RESULTS

The mean values for PAO₂, ΔA-aPO₂ and percentage venous admixture are shown in Table 1. Percentage saturations and O₂ contents of arterial, mixed venous and pulmonary end-capillary blood are also tabulated.

The mean percentage O₂ saturation of arterial blood of the COPD subjects was highly significantly lower than that of the normal subjects. Conversely, the mean percentage venous admixture of the COPD subjects was highly significantly greater than that of the normal subjects. The PaO₂ of normal subjects was highly significantly higher than that of the COPD horses and consequently also the A-aPO₂ difference. There was no significant difference between the mean values for PAO₂ of normal and COPD horses. The frequency distributions of the percentage venous admixture are shown in Fig. 1.

DISCUSSION

Since a comparison of the arterial PO₂ of the 2 groups of subjects disclosed a highly significant mean difference, it was not surprising to find that parameters which were calculated from equations involving the PaO₂ values also showed highly significant differences between normal and COPD subjects. Thus the percentage O₂ saturation of arterial blood, the A-aPO₂ difference and the percentage venous admixture all had highly significant differences. The mean percentage venous admixture of the COPD subjects was more than 3 times that of the normal group.

Gillespie & Tyler (1969) recorded a highly significant difference in A-aPO₂ difference between normal and emphysematous horses. They also calculated the percentage pulmonary vascular shunt of normal and emphysematous horses by administering 100% oxygen and obtained mean percentages of 5,24 and 8,90 respectively, a result which was not statistically significant but which nevertheless recorded a trend which the findings of the present studies strongly support.

TABLE 1 The A-aPO₂ difference, the oxygen saturation and content of pulmonary end-capillary, arterial and mixed venous blood and the percentage venous admixture of normal and COPD subjects

		Normal n = 21	COPD n = 13	Difference of means	Significance
Mean PaO ₂	kPa Mean SE ±	10,33 0,97	8,07 1,33	2,26	t = 5,91 P < 0,001
Mean PAO ₂	kPa Mean SD ±	13,28 0,44	13,04 0,80	0,24	t = 0,81 NS
Mean A-aPO ₂ difference	kPa Mean SD ±	2,94 0,99	4,95 0,21	2,01	t = 5,54 P < 0,001
% S _c	Mean SD ±	97,4 0,2	97,2 0,3	0,2	t = 2 NS
% S _a	Mean SD ±	94,2 1,6	86,4 10,6	7,8	t = 3,33 P < 0,001
% S _v	Mean SD ±	61,2 8,6	60,6 8,7	0,58	t = 0,19 NS
ℓℓ O ₂ content pulmonary end capillary	Mean SD ±	0,177 0,019	0,182 0,014	0,005	t = 0,9 NS
ℓℓ O ₂ content arterial blood	Mean SD ±	0,171 0,017	0,163 0,025	0,008	t = 1,05 NS
ℓℓ O ₂ content mixed venous blood	Mean SD ±	0,110 0,020	0,114 0,022	0,004	T = 0,53 NS
percentage venous admixture	Mean SD ±	8,8 3,9	26,5 16,6	17,7	t = 4,72 P < 0,001

S = oxygen saturation
 c = pulmonary end-capillary blood
 a = arterial blood
 v = mixed venous blood
 ΔA-aPO₂ = difference between ideal alveolar and arterial PO₂
 ℓℓ content = litres oxygen per litre of blood

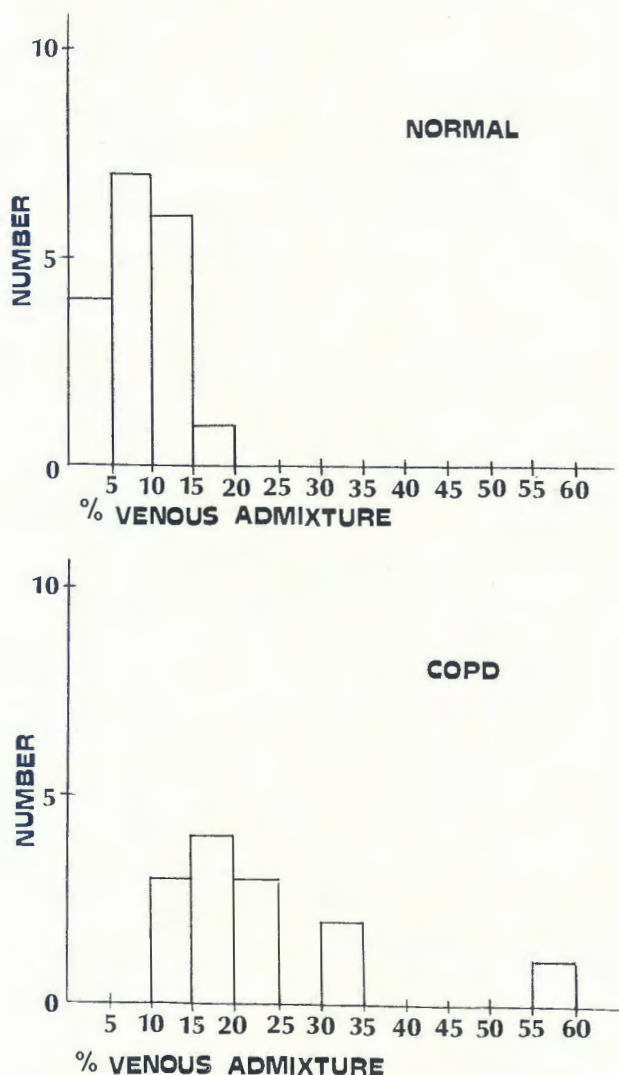


FIG. 1 Frequency distributions of percentage venous admixture in normal and COPD horses

The finding that the mean oxygen content of the arterial blood of COPD subjects was not significantly lower than that of the normal subjects, while the mean PaO_2 of the former was significantly lower, is clearly due to the fact that, at the upper (arterial) portion of the O_2 -HB dissociation curve, large decreases in PaO_2 cause only small decreases in arterial blood oxygen saturation and content.

The mean difference between ideal alveolar PO_2 and PaO_2 ($\Delta\text{A-APO}_2$) in COPD subjects was more than twice that of the normal subjects—a highly significant result. Factors influencing the magnitude of the A-aPO_2 difference were discussed exhaustively by Nunn (1969) and may be summarized as follows: (a) The magnitude of the total venous admixture; (b) the alveolar PO_2 , for example, a loss of 1 vol per cent of oxygen from blood with a PO_2 of 700 mm Hg causes a fall in the blood PO_2 of 325 mm Hg. However, if the initial PO_2 were 100 mm Hg, the loss of 1 vol per cent would cause a fall of only 35 mm Hg, and most of the loss of O_2 would be from haemoglobin and not from physical solution as in the case of high PO_2 ; (c) the shape and position of the oxygen dissociation curve of the subject's blood; (d) the temperature, pH and acid-base status of the blood; (e) the haemoglobin concentration; (f) alveolar ventilation and (g) the cardiac output.

In the 2 groups of subjects discussed in this series of investigations, there were no significant differences between the mean PAO_2 values, mean acid-base values,

mean rectal temperatures and mean haemoglobin concentrations (Littlejohn, 1978). Factors associated with an abnormally large A-aPO_2 difference and venous admixture may thus have been alveolar ventilation and/or cardiac output. Since the cardiac output of horses with emphysema was not significantly different from that of normal horses (Gillespie & Tyler, 1969), alveolar hypoventilation remains the major consideration in a discussion of venous admixture in horses with COPD.

It should be emphasized that the concept of venous admixture is simply a useful means of quantitating the combined effect of anatomical and pathological shunts and it must be carefully distinguished from the physiological situation. The venous admixture is not a measure of the anatomical shunt; it is simply a measure of the amount of venous admixture which would be required to produce the observed A-aPO_2 difference if all alveoli were functioning ideally (Nunn, 1969). As was pointed out by Nunn (1969), the calculated venous admixture is at best an index rather than a precise measurement of the amount of venous blood which is being mixed with blood from ideally functioning alveoli.

The venous admixture as defined above does not distinguish anatomical shunt from shunt effects due to unequal distribution of pulmonary ventilation to pulmonary perfusion. However, administration of oxygen enables one to determine anatomical shunt, because the inhalation of 100% oxygen eliminates the shunt effect caused by inadequate ventilation (Nunn, 1969). An attempt was made to quantitate these 2 factors in 2 subjects with COPD by administering 100% oxygen for 40 min, after which period of equilibration stable blood oxygen levels were achieved. The percentage venous admixture was then determined by the same methods as described for subjects breathing air. The results are given in Table 2.

TABLE 2 The percentage venous admixture, anatomical shunt and pulmonary vascular shunt in 2 COPD subjects E1 and E7

Subject	% venous admix. (breathing air)	% anatomical shunt (breathing 100% oxygen)	% pulmonary vascular shunt
E1	18	8	10
E7	24	7	17

In the above 2 subjects, it appeared that shunt effects produced by unequal distribution of pulmonary ventilation to perfusion provided the major proportion of the total venous admixture. It is of interest that the anatomical shunts calculated for subjects E1 and E7 were close to the mean venous admixture obtained from normal subjects (Table 1).

These findings with regard to venous admixture thus indicated that maldistribution of pulmonary ventilation was the major factor in the genesis of hypoxaemia in this series of horses with COPD. They also provided support for the conclusion of Gillespie & Tyler (1969) that the larger total shunt in their horses with emphysema was very likely due to the above factor superimposed on the anatomic shunt.

Further support for this conclusion is provided by the fact that the increased alveolar dead space in many COPD horses is associated with an increase in PaCO_2 and not a decrease in end-tidal PCO_2 (Littlejohn & Bowles, 1982), because hypoventilation, whether caused by bronchiolar spasm, bronchiolitis or emphysema, has the effect of diminishing the PO_2 and increasing the PCO_2 of blood flowing from affected alveoli. This inadequately oxygenated blood mixes with the highly oxygenated blood flowing from normally functioning alveoli to produce arterial blood of reduced PO_2 and increased PCO_2 .

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