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RELATIONSHIPS BETWEEN OXYGEN AND CARBON DIOXIDE TENSIONS AND ACID-BASE BALANCE IN ARTERIAL BLOOD AND IN MEDULLARY BLOOD FROM LONG BONES IN DOGS

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By means of an invasive technique the relations between arterial and medullary gas tensions (PO_2 and PCO_2), and arterial and medullary acid-base balance (pH and standard bicarbonate) were determined in long bones in seven anaesthetized dogs.

A semilogarithmic correlation was found between the arterial oxygen tension and the oxygen tension in the medullary blood. Between the arterial carbon dioxide tension and the medullary blood carbon dioxide tension a linear correlation was demonstrated. A linear correlation was also found between arterial pH and standard bicarbonate values and the corresponding values obtained from medullary blood.

With regard to the parameters investigated no difference was demonstrated between epiphyseal, metaphyseal or diaphyseal medullary blood.

Key words: aetiology; blood supply; bone; femur head; osteoarthritis; physiology; regional blood flow

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Measurements of long bone medullary oxygen tension (PO_2), carbon dioxide tension (PCO_2) and acid-base balance most often are made on medullary blood taken from bones suffering from some pathological condition (Woodhouse 1962, Brookes & Helal 1968, Brookes 1971, Pujol et al. 1973). Only in the study of Pujol et al. (1973) is information given about the corresponding arterial values.

The purpose of the present investigation was to determine the normal correlations between arterial and long bone medullary gas tensions and acid-base balance in the anaesthetized dog.

MATERIAL AND METHODS

Seven mongrel dogs weighing 29–42 kg were used for the experiment. All dogs were more than 2 years old. The dogs were all premedicated with propionylpromazin (Combilen®), and anaesthesia was induced with thiopenthal given intravenously. After oro-tracheal intubation anaesthesia was maintained with halothane-N_2O-O_2. Muscle relaxation was provided by intermittent doses of pancuronium bromide. Ventilation was performed with a Servo®-900 ventilator.

Arterial blood pressure was continuously measured from the right brachial artery on an Ellab monitor using a Statham P 23Db transducer.

Arterial oxygen tension (PaO_2), arterial carbon dioxide tension ($PaCO_2$) and pH were monitored continuously using an artificial arterial-venous shunt. This was prepared by cannulating the right carotid artery and left external jugular vein and, after heparinization (300 i.u./kg body weight), pumping the output of the carotid artery through a special blood gas cuvette (Henningsen 1968) back into the external jugular vein.

Electrocardiogram and rectal temperature were continuously monitored.

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Metal cannulas with a diameter of 2 mm were introduced into the bone marrow of the left femoral epiphysis, the right femoral metaphysis and the right humeral diaphysis. A 1.8 mm drill was used to penetrate the cortex. Correct positioning of the cannula tips in the middle of the bone marrow was ensured by X-ray examination.

PO_2, PCO_2, pH and standard bicarbonate were determined on a Radiometer ABL 1 blood gas analyser. One ml samples drawn anaerobically by slight aspiration of arterial blood from the brachial artery and of medullary blood from the femoral epiphysis, metaphysis and the humeral diaphysis were investigated.

The fraction of inspired oxygen (FiO_2) and the ventilation were at first adjusted to give a PaO_2 of about 100 mmHg and $PaCO_2$ of about 40 mmHg, read on the continuous blood gas analyser. After an equilibration period of 10 minutes in which arterial PO_2, PCO_2 and pH remained constant, samples were at the same time drawn from the arterial catheter and the bone marrow cannulas. Hereafter, with a constant $PaCO_2$ (40 mmHg), FiO_2 was varied and samples were drawn at various values of PaO_2.

After termination of this part of the study PaO_2 was kept constant at about 100 mmHg, and $PaCO_2$ was varied.

Hypercapnia was obtained by the addition of CO_2 to the inspired gas mixture. Hypocapnia was obtained by hyperventilation. Samples were drawn at various values of $PaCO_2$.

Equilibration periods of at least 10 minutes were used prior to every sampling.

Statistics and calculations. Least squares regression lines were calculated. Correlation coefficients (r) were calculated and Student's *t*-test was applied to the correlation coefficients. The level of significance (Student's *t*-test) for the regressions and for differences between epiphyseal, metaphyseal and diaphyseal values at the various arterial values was taken as $P < 0.05$. Calculations of hyperbolas indicating 95 per cent confidence limits around the regression lines were done by means of the formula $s_y =$

$$1.984 \times s_{(x \cdot y)} \times \sqrt{1 + \frac{1}{n} + \frac{(x - \bar{x})^2}{\Sigma(x - \bar{x})^2}}$$

(Snedecor 1956). $s_{(x \cdot y)}$ = sample standard deviation of the regression coefficient, n = number of correlative samples, $\bar{x}$ = mean values of abscissa values.

RESULTS

The correlations between corresponding values of PO_2, PCO_2, pH and standard bicarbonate in medullary and arterial blood are shown in Table 1 and Figures 1–4. Each of the regression lines was drawn on the basis of at least 89 measurements. Only results obtained when mean arterial blood pressure was above 70 mmHg have been used for the calculations.

No differences could be demonstrated between blood samples obtained from epiphyseal, metaphyseal or diaphyseal blood. The shaded areas on the figures indicate the widest 95 per cent confidence limits.

Oxygen tensions (Figure 1). When arterial oxygen tensions were below 80 mmHg, changes in PaO_2 caused almost identical changes in medullary oxygen tensions. Above this level, however, only small increases were seen in medullary oxygen tensions as arterial oxygen tensions increased. In this study PaO_2 varied between 26 and 492 mmHg and medullary PO_2 between 22 and 135 mmHg. The best fit of correlation seemed to be

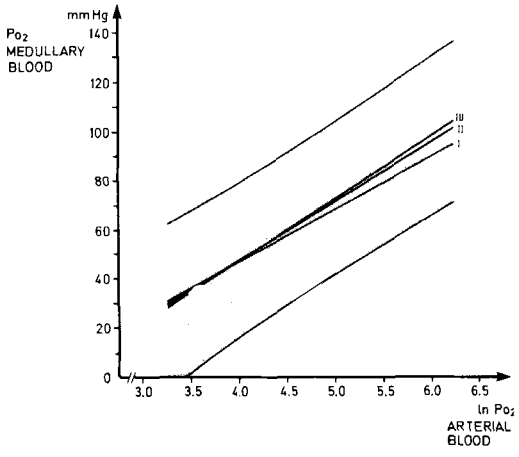

Figure 1. Least square regressions of medullary epiphyseal (I), metaphyseal (II) and diaphyseal (III) PO_2 in relation to natural logarithm of arterial PO_2 (PaO_2). Shaded area indicates the broadest 95 per cent confidence limits.
I: $P_{epiphysis}O_2 = 21.53\ lnPaO_2 - 39.65$, $r = 0.76$, $P < 0.001$
II: $P_{metaphysis}O_2 = 24.35\ lnPaO_2 - 49.80$, $r = 0.74$, $P < 0.001$
III: $P_{diaphysis}O_2 = 26.00\ lnPaO_2 - 57.94$, $r = 0.69$, $P < 0.001$

Table 1. Correlations between arterial and medullary (epiphyseal, metaphyseal and diaphyseal) blood gas tensions (PO_2 and PCO_2) and acid-base balance (pH and standard bicarbonate) in seven anaesthetized dogs. Regression equations, equations for hyperbolas indicating 95% confidence limits (s), number of correlative samples (n), correlation coefficients (r) and significance (P) of correlation coefficients are shown

Regression equation	Equation for hyperbola indicating 95 % confidence limits (s_y)	Number of correlative samples (n)	Correlation coefficient (r)	Significance of correlation coefficient
$P_{epiphysis}O_2 = 21.53 \ln PaO_2 - 39.65$	$\pm 21.60 \sqrt{1.01 + \frac{(x-4.85)^2}{31.27}}$	92	0.76	$P < 0.001$
$P_{metaphysis}O_2 = 24.35 \ln PaO_2 - 49.80$	$\pm 25.73 \sqrt{1.01 + \frac{(x-4.85)^2}{31.27}}$	92	0.74	$P < 0.001$
$P_{diaphysis}O_2 = 26.00 \ln PaO_2 - 57.94$	$\pm 31.65 \sqrt{1.01 + \frac{(x-4.85)^2}{31.27}}$	92	0.69	$P < 0.001$
$P_{epiphysis}CO_2 = 0.87\, PaCO_2 + 7.39$	$\pm 9.34 \sqrt{1.01 + \frac{(x-37.38)^2}{304711936}}$	90	0.94	$P < 0.001$
$P_{metaphysis}CO_2 = 0.97\, PaCO_2 + 4.21$	$\pm 7.59 \sqrt{1.01 + \frac{(x-37.17)^2}{212226624}}$	89	0.96	$P < 0.001$
$P_{diaphysis}CO_2 = 0.92\, PaCO_2 + 6.12$	$\pm 9.17 \sqrt{1.01 + \frac{(x-37.27)^2}{172633321}}$	90	0.95	$P < 0.001$
$pH_{epiphysis} = 0.764\, pH_a + 1.673$	$\pm 0.361 \sqrt{1.01 + \frac{(x-7.27)^2}{0.931225}}$	91	0.88	$P < 0.001$
$pH_{metaphysis} = 0.812\, pH_a + 1.329$	$\pm 0.310 \sqrt{1.01 + \frac{(x-7.27)^2}{0.931225}}$	91	0.78	$P < 0.001$
$pH_{diaphysis} = 0.887\, pH_a + 0.771$	$\pm 0.186 \sqrt{1.01 + \frac{(x-7.27)^2}{0.931225}}$	91	0.95	$P < 0.001$
$st.bic._{epi.} = 0.56\, st.bic._a + 6.34$	$\pm 4.15 \sqrt{1.01 + \frac{(x-16.54)^2}{202476}}$	90	0.56	$P < 0.001$
$st.bic. = 0.43\, st.bic._a + 9.01$	$\pm 4.73 \sqrt{1.01 + \frac{(x-16.53)^2}{198878}}$	90	0.40	$P < 0.001$
$st.bic._{dia.} = 0.52\, st.bic_a + 7.12$	$\pm 4.33 \sqrt{1.01 + \frac{(x-16.51)^2}{208332}}$	90	0.53	$P < 0.001$

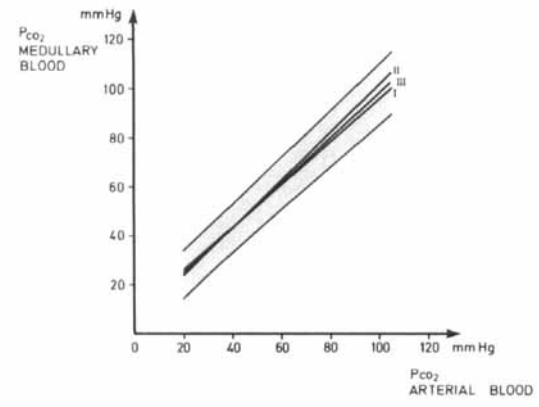

Figure 2. Least squares regressions of medullary epiphyseal (I), metaphyseal (II) and diaphyseal (III) PCO_2 in relation to arterial PCO_2 ($PaCO_2$). Shaded area indicates the broadest 95 per cent confidence limits.
I: $P_{epiphysis}CO_2 = 0.87 \quad PaCO_2 + 7.39, \quad r = 0.94, \quad P < 0.001$
II: $P_{metaphysis}CO_2 = 0.97 \quad PaCO_2 + 4.21, \quad r = 0.96, \quad P < 0.001$
III: $P_{diaphysis}CO_2 = 0.92 \quad PaCO_2 + 6.12, \quad r = 0.95, \quad P < 0.001$

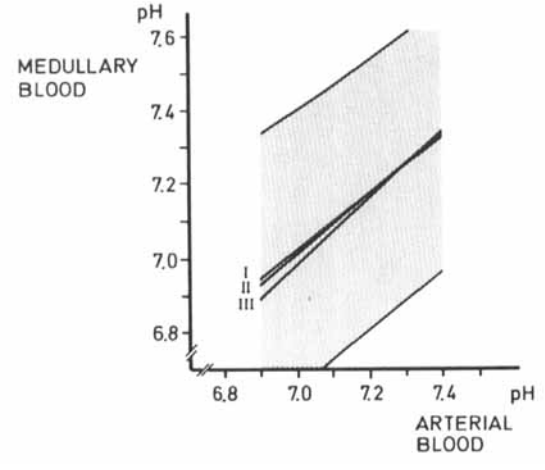

Figure 3. Least square regressions of medullary epiphyseal (I), metaphyseal (II) and diaphyseal (III) pH in relation to arterial pH (pH_a). Shaded area indicates the broadest 95 per cent confidence limits.
I: $pH_{epiphysis} = 0.764 \quad pH_a + 1.673, \quad r = 0.88, \quad P < 0.001$
II: $pH_{metaphysis} = 0.812 \quad pH_a + 1.329, \quad r = 0.78, \quad P < 0.001$
III: $pH_{diaphysis} = 0.887 \quad pH_a + 0.771, \quad r = 0.95, \quad P < 0.001$

semilogarithmic, mean correlation coefficient (r) was 0.73 ($P < 0.001$).

Carbon dioxide tensions (Figure 2). Linear correlations were found between medullary PCO_2 and $PaCO_2$, mean correlation coefficient (r) = 0.95 ($P < 0.001$). $PaCO_2$ varied between 20 and 103 mmHg. Medullary PCO_2 varied between 20 and 102 mmHg.

pH (Figure 3). Linear correlations with a mean correlation coefficient (r) of 0.91 ($P < 0.001$) were found between pH values in arterial and medullary blood. The range for arterial pH was 6.92–7.41. The range for medullary pH values was 6.88–7.43.

Standard bicarbonate (Figure 4). The best fit of correlation seemed to be a straight line with a mean correlation coefficient (r) of 0.50 ($P < 0.001$). The arterial standard bicarbonate varied in the study between 10 and 20 mmol/l.

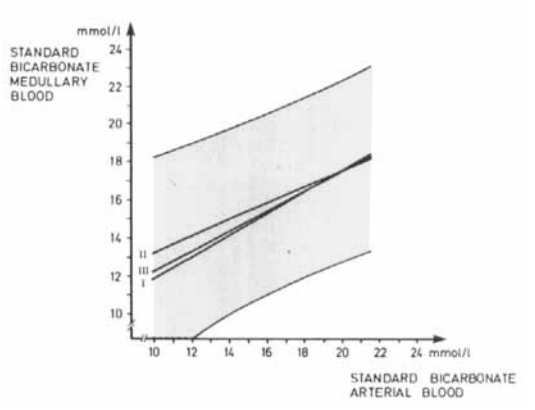

Figure 4. Least square regressions of medullary epiphyseal (I), metaphyseal (II) and diaphyseal (III) standard bicarbonate in relation to arterial standard bicarbonate ($st.bic._a$). Shaded area indicates the broadest 95 per cent confidence limits.
I: $st.bic._{epiphysis} = 0.56 \quad st.bic._a + 6.34, \quad r = 0.56, \quad P < 0.001$
II: $st.bic._{metaphysis} = 0.43 \quad st.bic._a + 9.01, \quad r = 0.40, \quad P < 0.001$
III: $st.bic._{diaphysis} = 0.52 \quad st.bic._a + 7.12, \quad r = 0.53, \quad P < 0.001$

DISCUSSION

In this study we have determined the relationships between PO_2, PCO_2, pH and standard bicarbonate in arterial blood and in medullary blood taken from three different places in long bones: the epiphysis, the metaphysis and the diaphysis. With regard to the parameters tested no differences in composition were found between the three types of medullary blood.

The vascular arrangement in long bones has been studied in detail by Trueta & Harrison (1953), Brånemark (1959), Trueta & Morgan (1960) and Brookes (1971). The blood reaches the bone marrow through an afferent artery. In the bone marrow long wide sinusoids make up a functional lattice in which osteoblastic cells are distributed, and in which ionic and gas exchange between blood and surrounding tissues takes place. From the sinusiods the blood flows through collecting venules back into hte systemic circulation.

We do believe that the samples of medullary blood we have investigated in this study represent sinusoidal blood, but we are also aware that this could be a matter of dispute. The perforating technique used to obtain the samples is rather traumatic to the tissues and consequently, around the cannula tip, some of the normal vascular and bony structures may have been destroyed. Furthermore, the tip of the cannula might have been placed near either a predominantly arterial or venous end of the sinusoid. However, because of the large number of samples investigated most of these sources of error have been overcome, and we believe that the measured PO_2, PCO_2, pH and standard bicarbonate values are representative of the milieu in which osteoblastic cells are situated.

The amount of oxygen available for medullary metabolism depends on medullary blood flow rate and arterial oxygen content. The rate of medullary flow was not investigated in this study and some of the inhomogeneity characterizing our results might be explained by an unstable flow rate. A decreased flow with an unchanged oxygen consumption will lead to an increased oxygen extraction from the blood flowing through the area and vice versa, a relation which earlier had been proposed as a way of estimating the medullary flow (Ingebrigsten et al. 1963).

We did not find any significant difference between simultaneously measured oxygen tensions in epiphyseal, metaphyseal or diaphyseal medullary blood. Brookes (1965, 1967) has found decreased blood flow in epiphyseal zones, using an isotope technique for flow estimation. Our technique cannot reject this hypothesis.

With the exception of the work of Pujol et al. (1973), most information about human medullary oxygen tensions are given without details concerning simultaneously measured arterial oxygen tensions (Woodhouse 1962, Brookes & Helal 1968). Furthermore, all samples in these studies have been drawn from bones suffering from some pathological condition. Assuming a normal arterial oxygen tension of about 100 mmHg and assuming that our results of animal experiments could be transferred directly to humans, most measurements of oxygen tension in human medullary blood given in the literature would lie within our 95 per cent confidence limits.

Linear correlations with narrow 95 per cent confidence limits were also found between arterial and medullary carbon dioxide tensions. A raised PCO_2 in bone marrow stimulates osteoblastic differentiation and promotes calcification, both essential aspects of bone production (Richards & Brookes 1969). From other studies too, it is known that active osteogenesis is dependent on an increased PCO_2 (Wilmer 1965). The highest medullary PCO_2 values have been found in impacted fractures of the femoral neck in which a PCO_2 of 77 mmHg has been measured (Brookes & Helal 1968).

Anaesthesia induced hypoventilation with a grave acidosis could not induce changes in medullary PCO_2 to that extent.

The medullary pH values are difficult to

interpret. Changes in medullary pH could be due to changes in medullary PCO_2 and/or to variations in local metabolism. An increased anaerobic glycolysis because of either reduced medullary flow or reduced oxygen content in medullary blood, or both, will contribute to changes in pH. However, as good correlations were seen to arterial pH, medullary pH values will also depend on arterial PCO_2 and systemic metabolism.

Alkaline drift and especially an elevated pH are found when cancellous bone is formed, whereas a reduced pH is supposed to be the local stimulus for cells possessing osteogenic potency, hereby provoking an increased calcification (Brookes 1971).

Standard bicarbonate is the bicarbonate concentration of fully oxygenated blood at 38° Celsius, when the PCO_2 has been adjusted to 40 mmHg (Astrup et al. 1960). By adjusting the PCO_2 to 40 mmHg, alterations in bicarbonate in blood secondary to changes in PCO_2 disappear and the standard bicarbonate therefore exclusively describes metabolic acid-base changes. The correlations found between arterial and medullary standard bicarbonate values were not as good as for the other parameters tested even if a mean correlation coefficient (r) of 0.50 and $P < 0.001$ was seen. Some of the scatter round the regression line could be explained by variations in local pH giving large variations in the standard bicarbonate concentration. Arterial values in this study indicate a metabolic acidosis. During the investigation the dogs were treated with saline intravenoulsy which dilutes plasma bicarbonate and results in a dilutional acidosis. Low haemoglobin values too will change standard bicarbonate (Siggaard-Andersen 1963).

In presenting our results no attention has been paid to variations in blood pressure as long as this parameter lay within the normal range. Variations in local blood flow were not measured. Our results are obtained during circumstances simulating the clinical conditions during which medullary blood samples could be taken. Therefore, the correlations given in this study represent a tool for further investigations, primarily of a clinical nature.

In this study close correlations were found between simultaneously measured gas tensions and acid-base balance in arterial and medullary blood from long bones in the dog. No significant differences in these parameters could be demonstrated in samples taken at the same time from three different places in long bones: the epiphysis, the metaphysis and the diaphysis.

Information about gas tensions and acid-base balance in medullary blood should never be given without information about corresponding arterial values.

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