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# OBSERVATIONS ON LONG BONE MEDULLARY PRESSURES IN RELATION TO ARTERIAL $PO_2$, $PCO_2$ AND pH IN THE ANAESTHETIZED DOG

ERIK TØNDEVOLD, JØRGEN ERIKSEN & ERIK JANSEN

Department of Orthopaedic Surgery T-2, Department of Anaesthesiology, Gentofte Hospital, Hellerup, and Department of Anaesthesiology, Herlev Hospital, Herlev, Denmark

To investigate the influence of variations in arterial oxygen tensions ($PaO_2$), arterial carbon dioxide tensions ($PaCO_2$), and arterial pH on long bone medullary pressures, seven anaesthetized dogs were investigated.

Comparing the control medullary pressures, i.e. the mean medullary pressures obtained at the normal range of $PaO_2$ (75–110 mmHg) with the mean medullary pressures corresponding to the range of $PaO_2$ of $<75$ mmHg, statistically significant ($P < 0.05$) decreases were seen in both epiphyseal, metaphyseal and diaphyseal medullary pressures, from $27.6 \pm 5.0$ to $15.5 \pm 3.6$ mmHg, from $23.5 \pm 2.9$ to $13.9 \pm 2.3$ mmHg and from $27.7 \pm 3.9$ to $18.3 \pm 2.5$ mmHg (all mean values $\pm$ s.e. mean), respectively.

Hyperoxia, hypocapnia, hypercapnia or metabolic acidosis had no effect on medullary pressures in any of the regions studied.

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

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According to Shim (1968) the factors controlling medullary blood flow may be divided into neural, hormonal and metabolic. Results obtained by Shim & Patterson (1967) suggest that the metabolic control mechanism is the most potent one, and that this control mechanism is related to the oxygen and carbon dioxide tensions ($PaO_2$ and $PaCO_2$), the pH and the acid metabolites of the arterial blood.

Although no direct correlation might be expected between medullary blood flow rates and medullary pressures, several investigators have found obvious relationships between these two parameters: a low medullary pressure means a low blood flow, and a high medullary pressure means either a high blood flow or a medullary congestion of blood due to obstruction of the venous outflow (Shaw 1963, Axuma 1964, Weinman et al. 1963, Keck & Kelly 1965).

The purpose of this study was to investigate if variations in the arterial $PaO_2$, $PaCO_2$ and pH caused any changes in the long bone medullary pressures (epiphyseal, metaphyseal or diaphyseal) in the anaesthetized dog.

## MATERIAL AND METHODS

The investigation was performed on seven mongrel dogs (weight 29–42 kg). Anaesthesia and some of the monitoring procedures have pre-

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viously been described (Eriksen et al. 1979). The medullary pressure was measured through metal cannulas (diameter 2 mm) placed with their tips in the bone marrow of the left femoral epiphysis, the right femoral metaphysis and the right humeral diaphysis. To penetrate the cortex of the bone a 1.8 mm drill was used. No leakage of medullary blood was seen when the metal cannulas were placed in the bones. S & W AE 840 transducers and S & W BAP amplifiers were used for the measurements of medullary pressures. Arterial blood pressures were measured by means of a catheter placed in the left branchial artery. Central venous pressures (CVP) were measured in the superior caval vein via a catheter introduced into the left branchial vein. Recording was made on Statham P 23Db transducers using Ellab M5-BCM amplifiers.

X-ray examinations confirmed the correct positioning of the metal cannulas centrally in the bone marrow and of the CVP catheter.

The fraction of inspired oxygen ($FiO_2$) was at first adjusted to give an arterial oxygen tension ($PaO_2$) of about 100 mmHg and an arterial carbon dioxide tension ($PaCO_2$) of about 40 mmHg. After an equilibration period of 10 minutes in which $PaO_2$, $PaCO_2$ and pH were kept constant using a continuous blood gas analyser (Henningsen 1968), the following parameters were registered simultaneously: $PaO_2$, $PaCO_2$ and arterial pH (all determined in 1 ml samples on a Radiometer ABL 1 blood gas analyser), medullary pressures (epiphyseal, metaphyseal and diaphyseal), mean arterial pressure (MAP), CVP and temperature.

Variations in $PaO_2$ were obtained by changing the $FiO_2$ while $PaCO_2$ and arterial pH were kept constant. Registration of the above-mentioned parameters was made 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 addition of $CO_2$ to the inspired gas mixture, hypocapnia by hyperventilation. Registration of parameters took place at various values of $PaCO_2$.

During the investigation a spontaneous acidotic drift in the arterial blood was observed in all dogs. Usually this metabolic acidosis was treated by infusion of bicarbonate, but before such treatment and at normal values of $PaO_2$ (about 100 mmHg) and $PaCO_2$ (about 40 mmHg) registration of parameters was made at various values of arterial pH.

Equilibration periods of at least 10 minutes, during which stable values were maintained by the continuous blood gas analyser, preceded each registration of parameters.

In an earlier paper we have shown that long bone medullary pressure remained constant and did not change with increasing arterial blood pressure, when the mean arterial blood pressure (MAP) was above 80 mmHg (Tøndevold et al. 1979). Consequently, the present study will only deal with results obtained when MAP was above 80 mmHg.

All medullary pressures in this study are given as "real" medullary pressures, i.e. the measured medullary pressures minus the corresponding central venous pressures. This has been done because of the obvious influence venous obstruction has on the medullary pressures (Azuma 1964, Keck & Kelly 1965).

### *Calculations*

*Medullary pressures/$PaO_2$.* The measurements used for this part of the study were taken at stable values of $PaCO_2$ and arterial pH, i.e. a $PaCO_2$ of between 35–45 mmHg and an arterial pH of 7.36–7.46. Different ranges of $PaO_2$ were selected (<75, 75–110, 111–200, 201–300, and >300 mmHg) and within these ranges the mean values ± s.e. mean of $PaO_2$ and the mean values ± s.e. mean of the corresponding epiphyseal, metaphyseal and diaphyseal medullary pressures were calculated. The normal range of $PaO_2$ was taken as 75–110 mmHg and the corresponding medullary pressures within this range were the control values.

*Medullary pressures/$PaCO_2$.* The measurements used for this part of the study were taken at stable values of $PaO_2$, that is a $PaO_2$ of 75–110 mmHg. Variations in arterial pH were allowed as long as these variations were due to changes in $PaCO_2$. Within different ranges of $PaCO_2$ (<35, 35–45, and >45 mmHg) the mean values ± s.e. mean of $PaCO_2$ and the mean values ± s.e. mean of the corresponding medullary pressures were calculated. The normal range of $PaCO_2$ was taken as 35–45 mmHg and the corresponding medullary pressures within this range were used as control values.

*Medullary pressures/arterial pH.* Medullary pressures used for this part of the study were taken at stable values of $PaO_2$ (75–110 mmHg) and $PaCO_2$ (35–45 mmHg). The ranges of arterial pH used for the calculations were <7.26, 7.26–7.35, and 7.36–7.46. The mean values ± mean of arterial pH and the mean values ± s.e. mean of the corresponding medullary pressures within these ranges were calculated. The normal range for arterial pH was taken as 7.36–7.46 and the corresponding medullary pressures were the control values.

The Mann-Whitney rank sum test was used for statistical analysis of the results obtained. The level of significance for differences was chosen as $P < 0.05$.

## RESULTS

In Table 1 and Figure 1 the corresponding values of $PaO_2$ and epiphyseal, metaphyseal, and diaphyseal pressures are shown. Comparing the mean medullary pressures within the range of $PaO_2$ of 75–110 mmHg (the control medullary pressures) and <75 mmHg, the decreases in the epiphyseal, metaphyseal and diaphyseal regions were from 27.6 mmHg to 15.5 mmHg, from 23.5 mmHg to 13.9 mmHg, and from 27.7 mmHg to 18.3 mmHg, respectively. The mean medullary pressures in all three regions corresponding to the range of $PaO_2$ of <75 mmHg were significantly ($P < 0.05$) lower than the values obtained at all higher levels of $PaO_2$.

Increases in $PaO_2$ above 75 mmHg had no influence on medullary pressures.

No significant differences could be demonstrated between the mean epiphyseal, metaphyseal or diaphyseal medullary pressures within the different ranges of $PaO_2$.

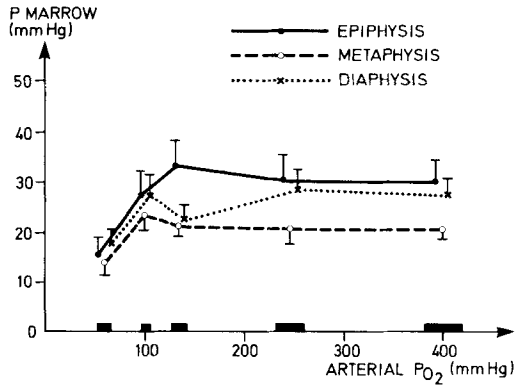


*Figure 1. Long bone epiphyseal, metaphyseal and diaphyseal medullary pressures ($P_{marrow}$) in relation to the arterial oxygen tension ($PaO_2$). Mean values ± 1 s.e. mean of the medullary pressures obtained within different ranges of arterial $PaO_2$ (< 75, 75–110, 111–200, 201–300 and > 300 mmHg) are shown in relation to the mean arterial $PaO_2$ within these ranges. The horizontal bars on the abscissa indicate the mean values ± 1 s.e. mean of arterial $PaO_2$ within the above-mentioned ranges of arterial $PaO_2$.*

Table 2 and Figure 2 show the corresponding values of $PaCO_2$ and epiphyseal, metaphyseal and diaphyseal medullary pressures. At the normal range of $PaCO_2$ (35–45 mmHg) the control epiphyseal, metaphyseal and diaphyseal mean medullary

*Table 1. Long bone medullary pressures ($P_{epiphysis}$, $P_{metaphysis}$, and $P_{diaphysis}$) in seven anaesthetized dogs in relation to different ranges of the arterial oxygen tension ($PaO_2$). Mean values ± s.e. mean of $PaO_2$ and mean values ± s.e. mean of the corresponding medullary pressures within the ranges have been calculated. The control medullary pressures are the mean medullary pressures within the normal range of $PaO_2$ (75–110 mmHg)*

| Number of observations | Arterial oxygen tension ($PaO_2$) (mmHg) Range | Mean ± s.e. mean within the range | Medullary pressures (P) (mmHg) $P_{epiphysis}$ Mean ± s.e. mean | $P_{metaphysis}$ Mean ± s.e. mean | $P_{diaphysis}$ Mean ± s.e. mean |
|---|---|---|---|---|---|
| 8 | <75 | 59.9 ± 5.9[x] | 15.5 ± 3.6[x] | 13.9 ± 2.3[x] | 18.3 ± 2.5[x] |
| 10 | 75–110 (normal range) | 101.6 ± 1.5 | 27.6 ± 5.0 (control medullary pressures) | 23.5 ± 2.9 | 27.7 ± 3.9 |
| 10 | 111–200 | 134.1 ± 7.1 | 33.3 ± 5.2 | 21.3 ± 2.5 | 22.4 ± 2.7 |
| 8 | 201–300 | 246.5 ± 12.2 | 30.6 ± 4.9 | 20.6 ± 3.0 | 28.5 ± 4.1 |
| 9 | >300 | 401.7 ± 16.7 | 30.2 ± 4.3 | 20.4 ± 1.6 | 27.3 ± 3.1 |

Within the respective medullary region [x]: $P < 0.05$ indicates significance of difference from the control medullary pressure.

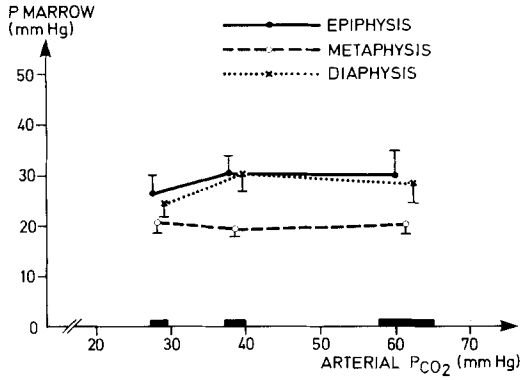


*Figure 2. Long bone epiphyseal, metaphyseal and diaphyseal medullary pressures ($P_{marrow}$) in relation to the arterial carbon dioxide tension ($PaCO_2$). Mean values ± 1 s.e. mean of the medullary pressure obtained within different ranges of arterial $PaCO_2$ (35, 35–45, and > 45 mmHg) are shown in relation to the mean arterial $PaCO_2$ within these ranges. The horizontal bars on the abscissa indicate the mean values ± 1 s.e. mean of arterial $PaCO_2$ within the above-mentioned ranges of arterial $PaCO_2$.*

pressures were 30.5 mmHg, 19.5 mmHg and 30.1 mmHg, respectively. Variations in $PaCO_2$ caused no significant changes in any of the medullary pressures. At the normal range of $PaCO_2$ the mean medullary metaphyseal pressure was significantly lower than both the mean epiphyseal medullary pressure and the mean diaphyseal medullary pressure. At the ranges of $PaCO_2$ of <35 mmHg and >45 mmHg no differences between the medullary pressures were demonstrated.

The medullary pressures obtained at different values of arterial pH are shown in Table 3 and Figure 3. At the normal range of arterial pH (7.36–7.46) the mean medullary pressures found were: epiphyseal = 27.5 mmHg, metaphyseal = 20.8 mmHg, and diaphyseal = 27.2 mmHg. Metabolic acidosis, not even severe (pH 7.26), caused no changes in mean epiphyseal, metaphyseal or diaphyseal medullary pressures. At the range of pH of 7.26–7.35 the mean metaphyseal medullary pressure (20.8 mmHg) was lower than the mean medullary pressures in the epiphyseal region (27.6 mmHg) and in the diaphyseal region (27.2 mmHg). No differences were observed between the mean medullary pressures at the ranges of pH below 7.26 and 7.36–7.46.

The control medullary pressures used in the three sections of the study were identical.

## DISCUSSION

In this study we have shown a lowering of epiphyseal, metaphyseal and diaphyseal

*Table 2. Long bone medullary pressures ($P_{epiphysis}$, $P_{metaphysis}$, and $P_{diaphysis}$) in seven anaesthetized dogs in relation to different ranges of the arterial carbon dioxide tension ($PaCO_2$). Mean values ± s.e. mean of $PaCO_2$ and mean values ± s.e. mean of the corresponding medullary pressures within the ranges have been calculated. The control medullary pressures are the mean medullary pressures within the normal range of $PaCO_2$ (35–45 mmHg)*

| Number of observations | Arterial carbon dioxide tension ($PaCO_2$) (mmHg) Range | Mean ± s.e. mean within the range | Medullary pressures (P) (mmHg) $P_{epiphysis}$ Mean ± s.e. mean | $P_{metaphysis}$ Mean ± s.e. mean | $P_{diaphysis}$ Mean ± s.e. mean |
|---|---|---|---|---|---|
| 22 | <35 | 28.5 ± 0.8 | 26.6 ± 3.3 | 20.5 ± 1.9 | 24.2 ± 2.4 |
| 15 | 35–45 (normal range) | 38.7 ± 1.0 | 30.5 ± 3.4 (control medullary pressures) | 19.5 ± 1.5[x] | 30.1 ± 3.2 |
| 11 | >45 | 61.5 ± 3.6 | 30.1 ± 4.8 | 20.6 ± 2.3 | 28.4 ± 3.7 |

Within the normal range of $PaCO_2$ [x]: $P < 0.05$ indicates that the mean metaphyseal medullary pressure is significantly different from the mean epiphyseal medullary pressure and the mean diaphyseal medullary pressure.

medullary pressures, when $PaO_2$ decreased below 75 mmHg, whereas neither hyperoxia, hypocapnia, hypercapnia nor metabolic acidosis seemed to have any influence on medullary pressures in the long bones in the anaesthetized dog.

The problems connected with the measurement of long bone medullary pressures by means of intramedullary metal cannulas have been discussed in several studies (Stein et al. 1957, Herzig & Root 1959, Azuma 1964). The medullary pressures measured in this way correlate qualitatively well with the haemodynamic changes in the bone marrow. A fall in medullary pressure indicates a decrease in bone marrow blood flow and a rise is due to either an increased blood flow or an intraosseous congestion of blood (Azuma 1964, Shim 1968).

Hypoxia is the most powerful stimulus of sympathetic activity, and with increased sympathetic activity circulatory priorities are established by vasoconstriction in tissues of no immediate importance, permitting increased circulation in vital organs (Folkow et al. 1961). The bone marrow does not seem to be among the vital organs: intravenous injections of adrenaline or noradrenaline or a direct stimulation of the cut peripheral end of the abdominal sympathetic trunk resulted in decreases in medullary pressures (Herzig & Root 1959). Furthermore, Drinker & Drinker (1916) have shown that the arterioles of the bone marrow are supplied with sympathetic nerve fibres with a vasoconstrictor function. The results obtained in this study where a decrease in $PaO_2$ (<75 mmHg) was followed by a decrease in long bone medullary pressures correlate well with the above-mentioned studies.

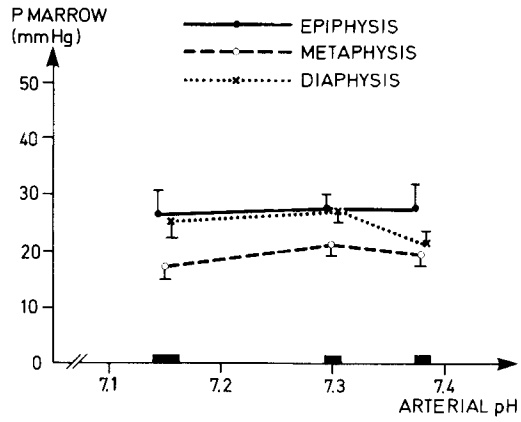


*Figure 3. Long bone epiphyseal, metaphyseal and diaphyseal medullary pressures ($P_{marrow}$) in relation to the arterial pH. Mean values ±1 s.e. mean of the medullary pressures obtained within different ranges of arterial pH (<7.26, 7.26–7.35, 7.36–7.46) are shown in relation to the mean arterial pH within these ranges. The horizontal bars on the abscissa indicate the mean values ±1 s.e. mean of arterial pH within the above mentioned ranges of arterial pH.*

*Table 3. Long bone medullary pressures ($P_{epiphysis}$, $P_{metaphysis}$, and $P_{diaphysis}$) in seven anaesthetized dogs in relation to different ranges of arterial pH. Mean values ± s.e. mean of arterial pH and mean values ± s.e. mean of the corresponding medullary pressures within the ranges have been calculated. The control medullary pressures are the mean medullary pressures within the normal range of arterial pH (7.36–7.46)*

| Number of observations | Arterial pH Range | Arterial pH Mean ± s.e. mean within the range | Medullary pressures (P) (mmHg) $P_{epiphysis}$ Mean ± s.e. mean | $P_{metaphysis}$ Mean ± s.e. mean | $P_{diaphysis}$ Mean ± s.e. mean |
|---|---|---|---|---|---|
| 14 | <7.26 | 7.15 ± 0.020 | 26.4 ± 4.2 | 16.8 ± 1.8 | 25.4 ± 3.2 |
| 21 | 7.26–7.35 | 7.30 ± 0.005 | 27.6 ± 2.4 | 20.8 ± 1.5[x] | 27.2 ± 2.0 |
| 17 | 7.36–7.46 (normal range) | 7.38 ± 0.006 | 27.5 ± 4.1 (control medullary pressures) | 19.5 ± 2.0 | 21.5 ± 2.0 |

Within the range of arterial pH of 7.26–7.35 [x]: $P < 0.05$ indicates that the mean metaphyseal medullary pressure is significantly different from the mean epiphyseal medullary pressure and the mean diaphyseal medullary pressure.

High arterial oxygen tensions cause a small increase in peripheral resistance and a slight decrease in cardiac output (Cotes et al. 1963) both apparently not sufficient to produce any changes in medullary pressures.

The systemic responses to hypercapnia contain elements of local depression and general autonomic stimulation. The circulatory stimulation of central origin consists of increased sympathetic activity and of increased sympathetic activity and of increased plasma levels of adrenaline and mentioned above a decreased medullary blood flow therefore would be expected to be followed by a decrease in medullary pressures. Other investigators (Cumming 1962 and Shim & Patterson 1967) have found an increased medullary blood flow during hypercapnia. This might perhaps be due to a specific effect of carbon dioxide, which is known to produce peripheral vasodilatation (Cullen et al. 1969). That no medullary pressure variations were demonstrated in this study might be due to different $PaCO_2$ increments or different species.

An influence of hypocapnia on medullary pressures has not been described and no such influence was seen in this study.

Post & Shoemaker (1962) found an increase in blood outflow from the upper and lower venous efflux systems of the femur in the unanaesthetized dog after infusion of small doses of hydrochloric acid. A metabolic acidosis did not produce any medullary pressure changes in this study, even if a decreased pressure had been expected because of the severe effects acidosis has on the haemodynamics. The "spontaneous" acidosis seen in our dogs might be explained as a dilutional acidosis, caused by the intravenous treatment with saline, which will dilute the plasma bicarbonate.

The conditions during metabolic alkalosis were not investigated.

In spite of an adequate arterial blood pressure (MAP > 80 mmHg) (Tøndevold et al. 1979) severe circulatory disorders seem to occur in the bone marrow during a decreased $PaO_2$ (<75 mmHg) with significant decreases in medullary pressures in epiphyseal, metaphyseal and diaphyseal regions.

The orthopaedic patient is often prone to arterial hypoxia brought about by his positioning (horizontal, Trendelenburg), his age (often elderly patients), the presence of pneumonia, sequelae of anaesthetics, fat embolism etc.

The results of our study may perhaps suggest a solution to some unsolved aetiological problems in the orthopaedic field. At the same time, however, they emphasize the importance of maintaining sufficient arterial oxygen tensions in orthopaedic patients by oxygen therapy, early mobilization, chest physiotherapy, treatment of infections etc.

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Correspondence to: Erik Tøndevold, M.D., Department of Orthopaedic Surgery T-2, Gentofte Hospital, DK-2900 Hellerup, Denmark.