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HEMODYNAMICS OF THE JUVENILE KNEE IN RELATION TO INCREASING INTRA-ARTICULAR PRESSURE

An Experimental Study in Dogs

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The relationships between intraosseous pressure and regional blood flow in the juxta-articular epiphyses were determined in the knees of immature dogs. Intraosseous pressures were continously registered in one knee. Regional blood flow rates were simultaneously determined by the microsphere technique before and after venous tamponade of both knee joint capsules.

During complete venous tamponade the intraosseous pressure of the distal femoral epiphyses rose 268%, while flow increased 122%. A concurrent 20-fold flow increase of the knee capsule and 3–4-fold flow increase of the proximal femoral bone was observed. Evacuation of the knee joints resulted in an immediate drop of the intraosseous pressure of the distal femoral epiphyses, whereas hyperaemia prevailed for at least half an hour and was most pronounced in the distal femoral epiphyses and knee joint capsule. Intraosseous pressure registration did not significantly influence regional blood flow.

It is suggested that the changes of intraosseous pressures during knee joint tamponade reflect changes in the venous outlet resistance. The results demonstrate the significance of intra-articular pressure increase on the hemodynamics of the juxta-articular tissues of the knee and proximal femoral bone. These findings may be of importance in the pathogenesis of growth disturbances observed in juvenile degenerative arthritis.

Key words: bone blood flow; dogs; intra-articular pressure; intraosseous pressure; juvenile arthritis; knee joint; microspheres

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Experimental studies of the knee joint have documented an interdependency between intra-articular pressure and intraosseous pressure of the juxta-articular bones (Arnoldi et al. 1979, Bünger et al. 1981). The relationship is most pronounced in knee joints with preserved epiphyseal plates (Lucht et al. 1981). Juvenile degenerative arthritis of the knee is usually accompanied by overgrowth of the distal femoral epiphysis and juxta-articular osteoporosis (Duthie et al. 1972, Goel et al. 1974, Benz 1980). These bone changes are generally regarded to be due to inflammatory hyperaemia and disuse (Brattström 1963, Stein & Duthie 1981). A causative influence of knee joint tamponade must be considered too.

The relationship between intra-articular pressure and intraosseous pressure in the knee joint has been documented by means of direct bone cannulation with fluid filled electromanometer systems (Arnoldi et al. 1979, Lucht et al. 1981, Bünger et al. 1981). Uncertainty exists as to what

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degree this traumatic pressure measurement influences the regional hemodynamics of bone (Wilkes & Visscher 1975). Likewise the intraosseous pressure changes regarding bone blood flow in the knee are not sufficiently clarified (Bünger et al. 1982).

The aim of this study was to analyse the influence of intraosseous pressure measurements on blood perfusion of the juvenile knee and to investigate the relationship between juxta-articular intraosseous pressure and regional blood flow rates during various degrees of knee joint tamponade.

METHODS

General

Six mongrel puppies (13.2–14.5 kg) 5 months old were premedicated with 0.5 ml 0.1% Combelin ® (10-(3-dimethylaminopropyl)propionyl phenothiazine). Anaesthesia was induced by intravenous Brietal ® (methohexital) 7 mg per kg and after orotracheal intubation maintained by halothane 0.5–1.5 per cent through a constant volume respirator. Muscle relaxation was obtained by intermittent doses of Pavulon ® (pancuronium bromide). Polyethylene catheters were inserted into the brachial arteries for blood pressure recording and arterial blood gas analyses. A central vein catheter served as central venous pressure recording and as a route for administration of small volumes of sodium bicarbonate (7.5 per cent) in case adjustment of blood gasses and pH was needed. Cardiac output and core temperature was measured on a Cardiac Output Computer – 9520 ® (Edwards Laboratories) with a Swan-Ganz ® flow-directed thermodilution catheter (model 93-132-5F) placed in a pulmonary artery via an external jugular vein. The correct position of the catheter tip was secured by pressure wave recording and fluoroscopy.

The dogs were placed in supine position with the hips in 90° flexion, 45° abduction and neutral rotation, whereas the knee was kept in 90° flexion in order to avoid changes of bone hemodynamic secondary to altered joint position (Bünger et al. 1981).

Pressure recording system

With image intensifier control metal cannulae (Radner® biopsy cannulae) with an inner diameter of 1.5 mm were inserted transcutaneously and extra-articularly from the medial side of the knee joint into the distal femoral metaphysis (FM), distal femoral epiphysis (FE) and proximal tibial epiphysis (TE). After flushing with heparin-saline solution (10 000 U/l), the Radner cannulae, the artery and central vein catheters were connected to a five-channel pressure recording system (Siemens strain gauge transducers 746, Siemens pressure amplifier 863, Siemens Mingograph 805) via polyethylene manometer tubes (Portex®, inner diameter 1.5 mm, length 200 cm). To prevent clotting, a constant perfusion system was established with heparin-saline solution (10 000 U/l) at a rate of 5 ml/h using a Unita I heavy duty pump (Braun Melsungen AG). The intra-articular pressure of the knees (P_J) was raised by elevating a bottle of Rheomacrodex® connected to a needle (Terumo®, 1.20 × 38 mm) inserted into the femoro-patellar compartment of the knees.

Blood flow measurements

The microsphere method with reference blood sampling (Domenech et al. 1969) was used to measure the regional blood flow. NEN–TRAC microspheres (New England Nuclear), 15 μm in diameter, were labelled with ^{141}Ce, ^{113}Sn, ^{46}Sc and ^{51}Cr and used in four different flow measurements in each dog. The spheres were suspended in 10% Dextran with 0.01% Tween 80 added. A volume of 4 ml microsphere solution containing 5.0×10^6 spheres was used at each flow determination. To secure adequate dispersal of the spheres the batch was agitated for 5 min on a Whirlimixer® before injection. A catheter (6.0 F, pig tail) was inserted into the left ventricle of the heart via the left carotid artery for sphere injection. Another catheter (6.0 F, no end curve) was advanced into the aorta descendens via the right carotid artery to the level of the second lumbar vertebrae for reference blood sampling and connected to a reversed Unita I heavy duty pump, which was started about 30 s before sphere injection at a calibrated rate of 1.96 ml/min. The spheres were injected over a period of 30 s followed by flushing with 5 ml heated (37°C) heparin-saline. The reference blood sampling was continued 3 min after sphere injection.

After the last flow measurement the dogs were sacrificed with a saturated dose of potassium chloride. The hind limbs were dissected and knee joint synovial and capsule biopsies were taken at the level of the inferior patellar pole. Cancellous bone biopsies with a diameter of 0.8 cm were taken with a bone biopsy drill (Bordier®) from the distal femoral metaphyses, trochlea patella, medial and lateral condyle of the distal femoral epiphyses and from the proximal tibial epiphyses. Cortical bone from femoral diaphyses was isolated. Patellae and proximal femoral epiphyses were freed from soft tissue and sampled with articular cartilage. All tissue samples were divided into approximately 2-g pieces and placed in preweighed plastic vials to a maximum height of 2 cm for gamma radiation counting.

The reference blood samples and tissue samples were counted in a 4-channel scintillation system with the channels set for the 4 principal energies for the four isotopes. The counts in each channel were corrected for background and cross talk from the other isotopes. The total counts for the single reference blood sample and the single tissue biopsy were calculated. The regional blood flow rate was calculated using the equation (Hales 1974):

Regional blood flow rate ml/100 g × min^{-1} =

$$\frac{\text{Counts/100 g tissue} \times V}{\text{Counts of reference sampling}}$$

where V is the reference sample rate (ml/min).

Experimental procedures

Intraosseous pressures were continuously monitored in one knee. Control blood flow was measured ½ h after insertion of the bone cannulae, but before cannulation of the knee joint cavities. The second flow measurement was done ½ h after raising P_J to 30 cm of H_2O in both knees. The third flow determination followed ½ h after raising P_J to 100 cm H_2O. The last flow determination (control II) was performed ½ h after normalization of intra-articular pressure (P_J = O H_2O) in both joints. Steady state was controlled before and after flow determination by means of cardiac output, mean arterial pressure, central venous pressure, core temperature and blood gases including pH. The perfusion in the pressure-recording system was stopped 3 min prior to blood flow determinations.

Statistics

Mean values and standard error of the mean (SEM) were calculated from all recorded parameters. The effect of bone cannulation and the hemodynamic response to changes in intra-articular pressure were examined by a two-way analysis of variance. Comparison of the means was performed by use of the corresponding modified t-test (Armitage 1974). A linear analysis of correlation was applied to examine the relationship between intraosseous pressure and regional blood flow. *P*-values less than 0.05 were considered significant.

RESULTS

Intraosseous pressures (Table 1)

The control pressures showed a P_{FM} of 5.0 ± 1.4 mmHg, a P_{FE} of 4.8 ± 0.9 mmHg and a P_{TE} of 9.0 ± 1.6 mmHg (Table 1). A rise of P_J to 30 cm of H_2O resulted in a significant rise of P_{FE}, while only a minimal increase of P_{FM} and P_{TE} was observed. At a P_J of 100 cm = 73.5 mmHg just below the mean arterial pressure, the P_{FE} further increased to 268% of the control pressure, while the P_{FM} and P_{TE} increased 30% and 53% respectively. A decrease of P_J to zero cm H_2O was followed by an immediate fall of P_{FE} to approximately the control I value, while no changes were observed regarding P_{FM} and P_{TE}.

Control regional blood flow rates (RBF) (Table 2)

The overall RBF of the cannulated right distal femoral epiphyses was 12.2 ± 1.4 ml/100 g × min^{-1} in comparison with a RBF on the left side of 13.0 ± 2.2 ml/100 g × min^{-1}. They were not significantly different. At the sites of pressure registration in the proximal tibial epiphyses and distal femoral epiphyses of the right knees the RBF were nonsignificantly elevated. However, a significant decrease in RBF of the right trochlea patella was encountered.

Regional blood flow in relation knee joint pressure (Table 3)

Despite great interindividual differences in control flow between the dogs, a uniform increase in

Table 1. Intraosseous pressures (P) (mmHg) (mean ± SEM) in the right knee of six dogs in relation to knee joint pressure

	Intra-articular pressure				
	Control I	30 cm H_2O	60 cm H_2O	100 cm H_2O	Control II
P_{FM}	5.0±1.4	6.3±0.9	6.9±1.3	7.5±1.2	7.5±1.2
P_{FE}	4.8±0.9	10.7±2.2	14.5±3.0	17.7±4.1	7.7±1.1
P_{TE}	9.0±1.6	11.4±1.6	14.0±2.5	13.8±1.9	13.6±2.5

Table 2. Control regional blood flow rates in the right knee subjected to intraosseous pressure registration in relation to flow rates in the left knee of six dogs

	Right knee	Left knee
	ml × 100 g^{-1} × min^{-1} mean ± SEM	
Distal femoral metaphysis	6.0±1.9	7.5±3.2
Trochlea patella	12.5±3.5	17.4±4.0*
Medial condyle	14.1±2.8	11.6±1.9
Lateral condyle	9.5±1.4	10.2±1.8
Patella	9.5±1.7	11.5±2.0
Knee joint capsule	1.1±0.5	0.8±0.5
Proximal tibial epiphysis	15.8±4.5	13.9±4.8

* Statistically significant difference ($P < 0.05$).

RBF of all tissue samples was observed during elevation of P_J. This suggests increased blood flow of the whole femoral bone during elevation of knee joint pressure. At a P_J of 100 cm H_2O the flow increase proximal to the knee joint was 3–4-fold, whereas the flow increase in the juxta-articular bones of the knee was about 2-fold. The location with the most marked flow increase was the knee joint capsule. Reduction of the knee joint pressure to 0 cm H_2O was followed by a decrease of RBF rates proximal to the knee joint, but compared to the control values a state of hyperaemia was still present. In the patella and distal femoral epiphysis a more marked hyperaemia prevailed with flow rates exceeding the values measured during knee joint tamponade. This was contrary to RBF of the proximal tibial epiphyses, which decreased. A profound hyperaemia was present in the knee joint capsule half an hour after evacuation of the knee joint capsule.

Relationship between intraosseous pressure and RBF

The correlation between RBF of the distal femoral metaphyses and pressure was not significant (R = 0.2181). However, in the juxta-articular epiphyses the relationship was significant during control state and during increasing P_J (Fig. 1) (R = 0.5809, $P < 0.01$). After evacuation of the knee joint the persisting high RBF of the juxta-articular bones was not reflected by increased intraosseous pressure (Fig. 2).

Central hemodynamics

During the experiments no changes were observed in CVP and blood gases. The initial MAP was 80 ± 5 mmHg and cardiac output 1.73 ± 0.13 l/min; at the end of the experiment (control II) the MAP had risen to 90 ± 17, while cardiac output was unchanged (1.75 ± 0.18 l/min). This reflects increased peripheral resistance in some dogs at the end of the experiments.

DISCUSSION

The development of radioactive microspheres has provided a direct and reliable method for study of

Table 3. Blood flow in ml/(100 g × min) ±SEM in the lower hindlimbs of six dogs in relation to elevation of knee joint pressure

Anatomical site	Intra-articular pressure			
	Control I	30 cm H_2O	100 H_2O	Control II
Caput femoris epiphysis	8.4±1.4	18.7±4.2	29.5±5.8	22.3±4.0
Femoral diaphysis	5.4±0.7	12.8±2.3	20.6±3.7	18.8±3.8
Distal femoral metaphysis	6.7±1.8	10.4±2.9	18.4±4.2	13.2±3.0
Trochlea patella	14.9±3.5	17.9±3.3	30.9±5.6	31.2±6.5
Patella	10.5±1.3	15.2±1.6	22.8±3.9	35.9±5.6
Knee joint capsule	0.9±0.3	4.7±0.9	18.7±5.1	83.0±16.7
Medial femoral condyle	12.8±1.7	18.0±2.7	26.7±5.1	32.2±5.3
Lateral femoral condyle	9.9±1.1	14.1±2.2	25.9±3.9	28.5±4.3
Proximal tibial epiphysis	13.3±3.3	15.7±1.9	37.6±8.6	26.9±5.6

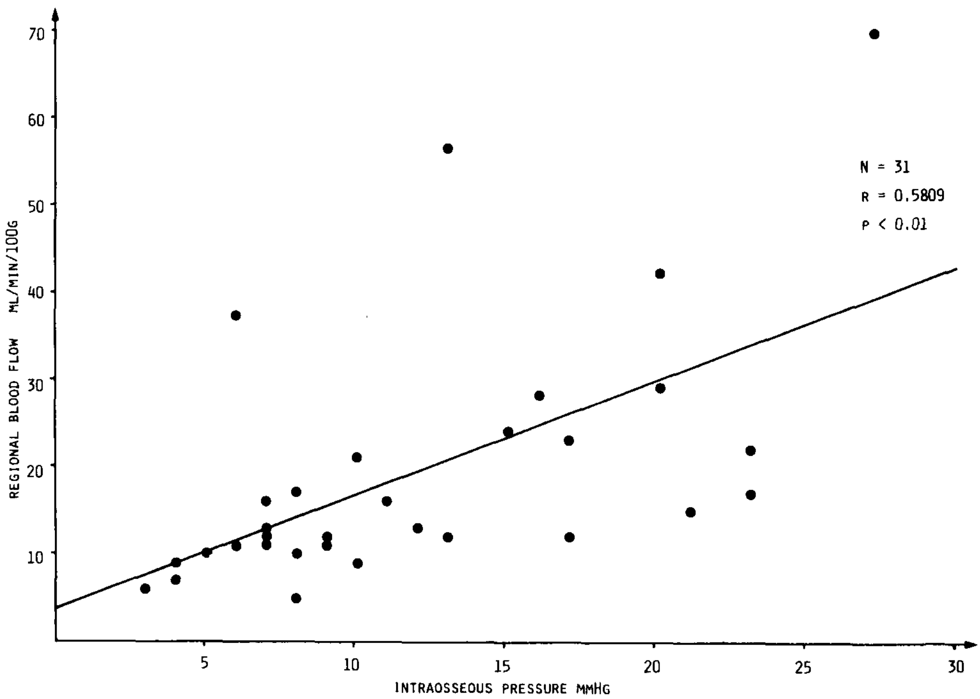

Figure 1. The correlation between regional blood flow rates and intraosseous pressure of the juxta-articular epiphyses of the right knee in six immature dogs during control conditions and increasing intra-articular pressure.

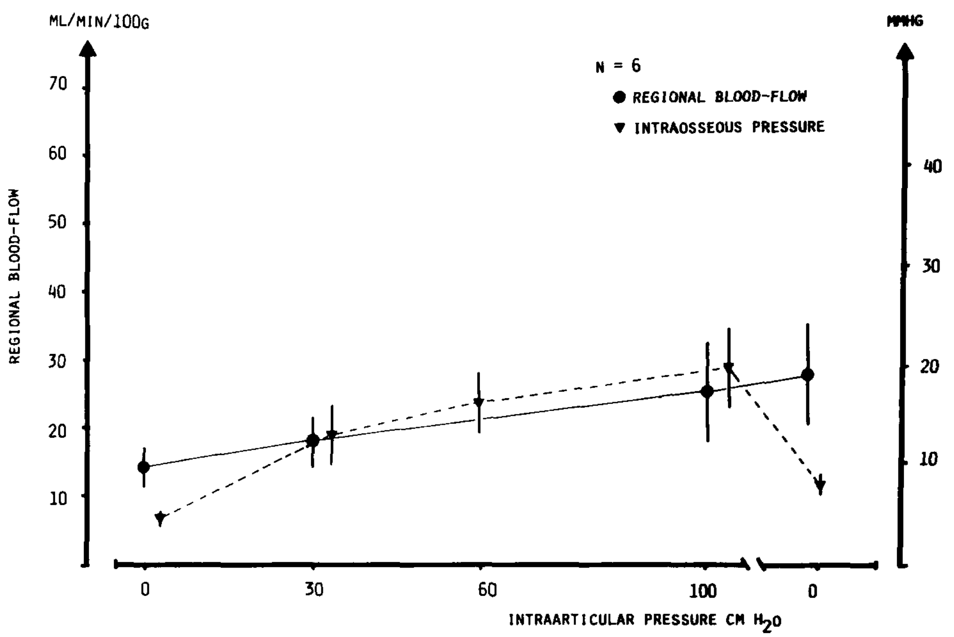

Figure 2. Regional blood flow rates and intraosseous pressure of the distal femoral epiphyses during changes of intra-articular pressure in six immature dogs.

blood perfusion so long as some essential conditions are fulfilled (Hales 1974, Rudolf & Heymann 1967). The microspheres must mix uniformly with blood at the site of injection. We have injected the spheres into the left ventricle, which is sufficient when measuring peripheral blood perfusion (Buckberg et al. 1971). The injection of spheres and reference sampling must not alter the central hemodynamics nor must the embolization of spheres influence the microcirculation. A moderate, gradual increase in peripheral resistance was observed during the present experiments, while no changes in cardiac output, blood pressure, and blood gasses were observed in relation to spheres injection. The most probable explanation of the peripheral resistance increase is an initial vasodilatation caused by premedication. From the last flow measurements we were able to detect both vasodilatation and vasoconstriction. This suggests that previous injected spheres did not impair the responsiveness of the microcirculation of bone and joint capsule. The microspheres must be trapped during the first passage through the tissue of interest. Spheres with a size of 15µm as used in this study have been found to lodge in the Haversian arteries of cortical bone and in the trabecular vessels of cancellous bone (Okubo et al. 1979). Additionally more than 99% of 15µm spheres are trapped during the first circulation (Tøndevold & Eliasen 1982), while the use of 7–10µm spheres causes underestimation of bone blood flow, probably due to arterio-venous shunting (Gross et al. 1979). Finally, enough microspheres must be injected to ensure accurate blood flow measurement. According to Buckberg et al. (1971) the statistical variation in flow determinations is approximately 10% when at least 400 spheres are found in the tissue biopsy as well as in the reference blood sample. The bilateral simultaneous flow determinations in the femoral heads in this study showed a mean variation of 13% (range 3–33%). However, the assumption that there is the same blood flow in the femoral heads in one individual has been questioned (Launders et al. 1981). The number of spheres used in the present study was theoretically sufficient to measure tissue blood flow in 1-g biopsies with an accuracy of 10% when the RBF was not below 10 ml/100 g × min.

The intraosseous pressure registration in the juxta-articular bones of the knees in immature dogs in previous studies (Bünger et al. 1981, 1982) and in the present study has shown a surprising uniformity with values from 8 to 14% of mean arterial pressure. The P_{FE} level is consistently below the P_{TE} and P_{FM} level. This accords with previous observations in immature dogs (Bouteiller et al. 1979, Azuma 1964) and demonstrates a separation of the three vascular beds. The interdependency between P_J and P_{FE} in this study was in accordance with our previous observations. (Bünger et al. 1981, 1982).

The interpretation of intraosseous pressure and its reflection on bone blood perfusion has been a matter of debate. The current opinion is that the pressure measured with transcortical bone cannulation is a mean pressure of a pool of mixed arterial and venous blood extravasated within the bone marrow or cancellous bone compartment (Azuma 1964, Shim et al. 1972, Wilkes & Visscher 1975). The small variations in intraosseous pressure levels in our series indicate that using continuous or intermittent perfusion of the pressure recording system secures a constant pressure-measuring field. The blood perfusion was not significantly affected by pressure registration although a moderate hyperaemia was present in the medial femoral condyle and tibial epiphyses after bone cannulation. This correlates with recent observations by Bouteiller et al. (1979) who found a moderate hyperaemia following bone cannulation of the trochanteric and diaphyseal bone. The significantly decreased flow in trochlea patella might represent a "steal phenomenon".

In the juvenile knee the almost complete intra-articular location of distal femoral epiphysis would seem to indicate an influence of increasing intra-articular pressure on the epiphyseal hemodynamics. The discrepancy between the proximal and distal bone blood flow increase indicates that the venous drainage of the knee capsule, patella and distal femoral epiphysis is impaired during increasing P_J. The abrupt fall of P_{FE} after evacuation of the knee joint together with increasing blood perfusion strongly supports this view. Surprisingly the increased P_J not only released local hyperaemia of the knee joint, but also a regional increased RBF proximal to the knee. The triggering mechanism may be the increased intraosseous pressure acting on vascular pressure receptors, activation of stretch receptors in the knee joint capsule or a metabolic stimulus. The most convenient explanation is activation of both local and regional regulatory mechanisms. Pharmacological stimulation of beta-receptors in the knee joint capsule has been shown to produce a marked increase in clearance rate of intra-articular ^{133}Xe in dogs and humans, indicating increased capsular blood flow rate (Dick et al. 1971). A stimulation of beta-receptors in the knee joint capsule due to increased intra-articular pressure may have been one of the local regulatory mechanisms responsible for the changes observed in the present study. The flow response pattern to increased intra-articular pressure was similar in the patella, distal femoral epiphysis and knee capsule. This supports the hypothesis of a common regulatory mechanism of the articular blood flow in which arterio-venous shunts at the synovial-epiphyseal junction are suggested to play an important role (Liew & Dick 1981). The hyperaemia in femoral bone proximal to the knee during tamponade was observed both in cancellous and compact bone. Recent studies using microsphere technique have provided quantitative evidence that bone and marrow are under reflex control (Gross et al. 1979). Previous studies have indicated that bone and marrow vessels are influenced by neurogenic factors. Electrical stimulation of sympathetic nerves produces vasoconstriction in bone measured by venous outflow collection (Drinker & Drinker 1916), while lumbar sympathectomy increases bone blood flow (Trotman & Kelly 1963). Thus, bone and marrow vessels are innervated and appear to have a resting sympathetic tone. The sympathetic nervous system probably plays a major role in the regional regulatory mechanisms activated during increased intra-articular pressure in the present study.

The results of the present study emphasize the significance of acute intra-articular pressure increase in relation to the local hemodynamics of the knee and the regional blood perfusion of the proximal femoral bone. It can be suggested that an elevation of intra-articular pressure following chronic juvenile arthritis may affect the hemodynamics of both the knee and the bones of the limb.

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