

Hemodynamic effects of knee-joint tamponade

^{99m}Tc-diphosphonate scintimetry in growing dogs

Ebbe Stender Hansen^{1,2}, Tine Brink Henriksen², Ivan Noer³ and Cody Büniger¹

We studied the influence of joint effusion on juxtaarticular vascularity and bone metabolism of the immature knee in puppies by dynamic and static ^{99m}Tc-diphosphonate scintimetry. Unilateral joint tamponade of 10 KPa (75 mmHg), introduced by intraarticular dextran-70 infusion, resulted in quantitatively similar scintimetric changes in an angiographic Phase I (0-20 sec), a blood pool Phase II (20-256 sec), and a bone-uptake Phase III (2 h). The uptake was reduced by 20 percent in the distal femoral epiphysis, by 15 percent in the distal femoral growth plate in Phases II-III, and by 8 percent in the proximal tibial growth plate in Phase III. The main part of scintimetric changes during joint tamponade could be ascribed to altered epiphyseal and metaphyseal intraosseous hemodynamics.

Studies on growth disturbances in experimental chronic arthritis¹³ and hemarthrosis¹⁴ using sequential ^{99m}Tc-diphosphonate scintimetry have demonstrated a marked decrease in tracer uptake in juxtaarticular growth plates consistent with the hypoplastic metaphyseal growth and the disturbed longitudinal growth of femur observed both clinically^{1,10,12} and experimentally.^{6,14,17} This depression of growth-plate metabolism may be caused by hemodynamic changes secondary to joint effusion.^{2,19} Previous observations on the effect of knee-joint tamponade on juxtaarticular hemodynamics using radioactive microspheres have been inconclusive with respect to affection of metaphyses and growth plates.^{2,3,4,5} We report the impact of joint effusion on the uptake of ^{99m}Tc-diphosphonate in the juvenile dog knee.

Materials and methods

Animals

Seven 13-week-old mongrel dogs weighing 6-9 kg were used.

Design of the study

Initially, control dynamic and static ^{99m}Tc-diphosphonate scintigraphy of both knees was performed. At a second scintigraphic examination 1 week later, the intraarticular pressure of the right knee was raised to 10.0 KPa (75 mmHg) by elevation of a bottle of isotonic dextran-70 (Macrodex® 60 mg/mL with sodium chloride) connected to an intraarticular cannula (Micro-lance, gauge 21) placed with the tip in the patellofemoral compartment. After 30 minutes' equilibration, dynamic scintigraphy was performed. The increased knee-joint pressure was maintained until static scintigraphy was executed after 2 hours.

The knee joints contained 9 (7-10) mL fluid at the selected pressure level. After aspiration, the uptake ratio increased by 0.04 in the femoral growth plate (NS), by 0.03 in the femoral epiphysis ($P < 0.05$), and by 0.02 in the tibial growth plate (NS). No detectable amounts of radioactivity were found by gamma-camera counting of the syringes containing fluid aspirated from joints.

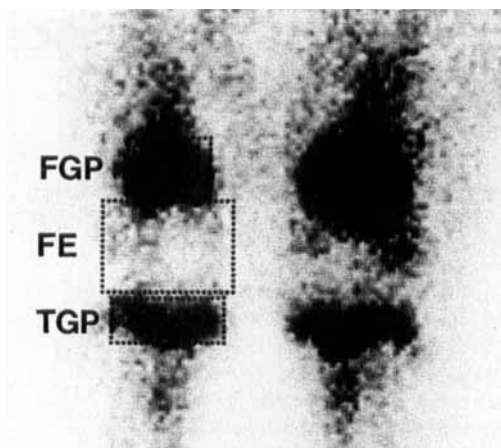
The mean (SEM) brachial systolic blood pressure before dynamic scintigraphy was 128 (7) mmHg, and this increased insignificantly to 144 (14) mmHg at the time of delayed static scintigraphy. No relationship between systolic blood pressure and change in count ratio was observed.

Scintigraphy

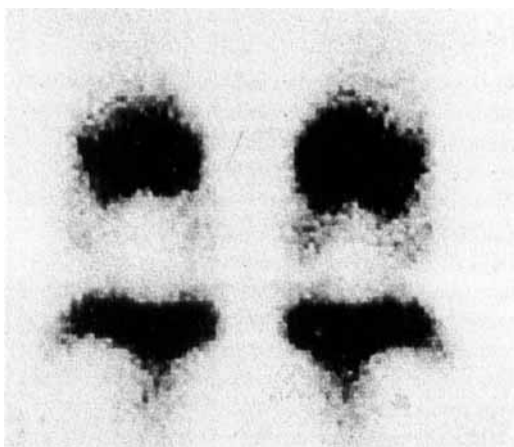
The scanning equipment used consisted of a gamma camera (General Electric Maxi 61), equipped with an

Århus Orthopedic Hospital¹, University of Århus Institute of Experimental Clinical Research², and Department of Clinical Physiology³, County Hospital, Randers, Denmark

Correspondence: Dr. Ebbe Stender Hansen, Århus Orthopedic Hospital, Randersvej 1, DK-8200 Århus N, Denmark



Dynamic blood-pool image. The scintimetric procedure is illustrated: Bilaterally identical box regions of interest were created around activity representing the distal femoral growth plate (FGP), the distal femoral epiphysis (FE), and the proximal tibial growth plate (TGP).



Delayed static ^{99m}Tc -diphosphonate bone scan.

Figure 1. The influence of joint effusion on ^{99m}Tc -diphosphonate uptake in the juvenile dog knee. The intraarticular pressure was artificially elevated to 10 kPa in the right knee, while the left knee served as the control.

ultra-high resolution, converging collimator, and interfaced with a data-processing system (General Electric Star).

The dogs were premedicated with 0.5–1.0 mL Combelen[®] vet. (propionyl promazine 10 mg/mL), anesthetized with Immobilon[®] vet. (etorfin 0.125 mg + acepromazine 0.4 mg/mL), and were positioned supine on the scanning table with the hips extended and neutrally rotated, the knees nearly extended. The limb position was secured with adhesive tape and sandbags. The collimator was placed parallel to the floor and in

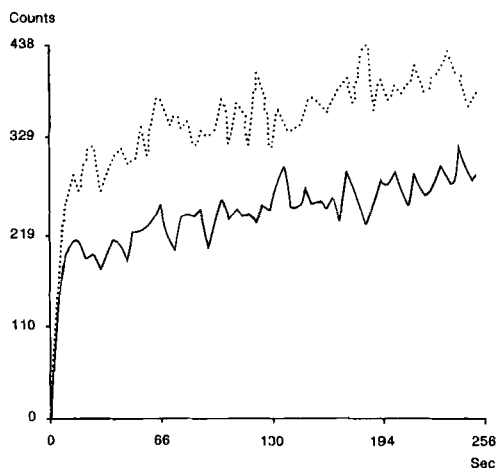


Figure 2. Dynamic activity versus time curves from the right experimental knee (—) and left control knee (.....) in the distal femoral epiphysis.

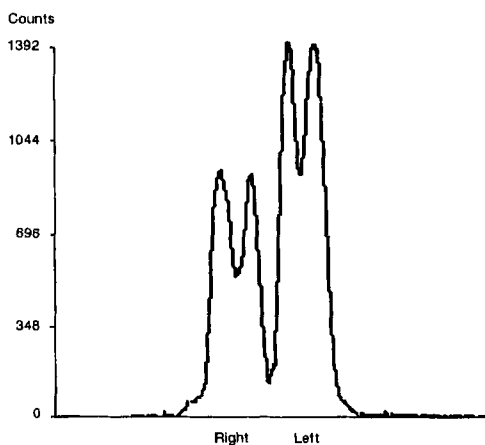


Figure 3. Static uptake profile across the distal femoral epiphysis. Uptake was reduced in the right knee, while the left knee served as the control. The two smaller peaks within each large peak, representing the lateral and medial femoral condyles, respectively, contribute equally to the overall decrease in epiphyseal uptake of ^{99m}Tc -DPD.

contact with both patellae. Each examination consisted of a dynamic and a delayed static anteroposterior study between which the dogs were kept anesthetized with an unchanged knee position. Dynamic scintigraphy comprising 64 frames at 4-second intervals, total 256 seconds, was acquired immediately after i.v. bolus injection of 400–450 mBq ^{99m}Tc -DPD (99m -technetium labeled 1,2 dicarboxypropane 3,3 diphosphate)^{9,15}. Delayed static scintigraphy was performed after 2 hours.

Table 1. ^{99m}Tc -DPD three-phase scintimetry of immature dog knees during unilateral joint tamponade (10kPa). Uptake ratio (N 7) between experimental and control joint in the distal femoral growth plate, distal femoral epiphysis, and proximal tibial growth plate. Control scintimetry (C), experimental scintimetry (E), and difference between the two (E-C). Mean SEM

		Angiography Phase I (0-20 s)	Blood pool Phase II (20-256 s)	Bone uptake Phase III (2 h)
Femoral growth plate	C	1.07 0.03	1.00 0.01	0.99 0.02
	E	0.91 0.08	0.86 0.02	0.85 0.02
	E-C	-0.15 0.08	-0.14 0.01***	-0.14 0.02**
Femoral epiphysis	C	1.06 0.03	1.00 0.01	1.00 0.02
	E	0.86 0.06	0.78 0.02	0.80 0.02
	E-C	-0.20 0.08*	-0.22 0.02***	-0.20 0.02**
Tibial growth plate	C	1.07 0.02 ^a	1.03 0.01 ^a	1.04 0.02
	E	0.99 0.08	0.95 0.03	0.95 0.02
	E-C	-0.08 0.09	-0.07 0.03	-0.09 0.02**

^aDifferent from 1.00, $P < 0.05$.

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

Scintimetry

Initially, a horizontal uptake profile extending across both limbs was moved proximally and distally to explore the location of changes in uptake. Box regions of interest were then created on summed images of all dynamic frames and similarly on static images around activity representing the distal femoral growth plate, the distal femoral epiphysis, and the proximal tibial growth plate (Figure 1). Identical regions were used in experimental and control knees. Dynamic-count versus time curves were generated in each region (Figure 2). The first 20 seconds were referred to as the angiographic Phase I, during which uptake reflected blood flow through the region. The remainder of the dynamic study was considered as the blood pool Phase II. Curve integrals corresponding to these two dynamic phases were calculated in each region of interest. The delayed static study represented the bone uptake Phase III. Count ratios between experimental (right) knee and the corresponding control (left) knee were calculated in the three anatomic regions and uptake phases.

Statistics

The mean and the standard error of the mean (SEM) were calculated for all the parameters. The Student's two-tailed t -test for paired observations was used for evaluation of changes in count ratios and blood pressure.

Results

In control scintimetries the count ratio between right and left knee had coefficients of variation ranging from 0.02 to 0.08, and varied around unity except in the tibial growth plate, where dynamic uptake was slightly increased in the right knee (Table 1).

During elevated intraarticular pressure, decreased uptake was observed in the juxtaarticular epiphyses and metaphyses, while no changes were found more proximally in the femur or more distally in the tibia. Scintimetric changes were quantitatively similar in the three uptake phases. Femoral epiphyseal uptake decreased by 20 percent in all the phases; the medial and lateral femoral condyles were equally affected (Figure 3). Uptake in the distal femoral growth plate was reduced by 15 percent in Phases II and III. The tibial growth-plate uptake was reduced by 8 percent in Phase III.

Discussion

This study has demonstrated decreased uptake of ^{99m}Tc -DPD in both epiphyses and growth plates in response to elevated intraarticular pressure of the growing dog knee, the femoral epiphysis being the most sensitive. The good numerical agreement between dynamic and static scintimetry suggests that decreased blood flow is the primary mechanism involved. This was in contrast to the findings in chronic arthritis,

where delayed growth-plate uptake of ^{99m}Tc -DPD was reduced to a greater extent than dynamic uptake,^{15,16} presumably due to decreased growth-plate mineralization⁸ in addition to reduced blood flow in arthritis.

The most likely explanation of the decreased epiphyseal blood flow during joint tamponade is increased venous resistance at the outlet from bone due to extraosseous compression of epiphyseal veins. Accordingly, previous investigations found the intraosseous pressure of the distal femoral epiphysis to be increased by knee-joint tamponade,^{2,4,11,18} as well as by selective ligation of the medial genicular vein.⁵ Epiphyseal blood flow measured with radioactive microspheres was unchanged with a joint pressure at 50 percent of mean arterial pressure,¹¹ which was taken as evidence of compensatory precapillary vasodilation. Another study⁴ showed progressive hyperemia of the entire limb with increasing degrees of knee tamponade and increasing intraosseous pressure levels, which was explained by activation of autoregulatory mechanisms of both local and systemic nature. However, halothane was used for anesthesia, and it is quite possible that progressive halothane-induced vasodilation accounted for the diffuse increment in limb blood flow in that study. Because we did not observe changed uptake in bone remote from the joint, the present experiment speaks against systemic autoregulation. Later studies relating epiphyseal hemodynamics to intraarticular pressure^{2,3} resulted in decreased epiphyseal flow at 13

KPa, as we found in the current experiment at 10 KPa. A slow gradual increase was tolerated better than a sudden introduction of joint tamponade,² which also suggests autoregulation of epiphyseal hemodynamics. The precise nature of these autoregulatory mechanisms still remains to be settled.^{11,18} We found no evidence of increased vulnerability of the medial over the lateral femoral condyle, as reported previously².

The present finding of decreased growth-plate uptake is somewhat surprising considering that knee-joint tamponade does not consistently elicit an intraosseous-pressure response in the distal femoral metaphysis.^{4,7,18} The metaphyseal bone cannulae in the previous studies may, however, have been placed centrally, where the intraosseous pressure reflects marrow pressure, rather than in peripheral metaphyseal bone mainly drained by epiphysio-metaphyseal veins susceptible to compression during joint tamponade. Another possible mechanism could be reflex arteriolar constriction activated by the epiphyseal engorgement. The venoarterial reflex has, however, never been demonstrated in bone.

The findings of this investigation indicate that the presence of knee-joint effusion influences the local bone circulation adversely in epiphyses as well as in growth plates. Increased joint pressure probably contributes to the development of the growth disturbances associated with juvenile chronic arthritis and related inflammatory joint conditions of childhood.

References

1. Ansell B M, Bywaters E G L. Growth in Still's disease. *Ann Rheum Dis* 1956;15:295-319.
2. Büniger C. Hemodynamics of the juvenile knee. Joint effusion and synovial inflammation studied in dogs. *Acta Orthop Scand* 1987;58(Suppl 222):1-104.
3. Büniger C. Regional blood flow and intraosseous pressure changes of the juvenile knee in experimental arthritis. In: *Bone Circulation* (Eds. Arlet J, Ficat R P, Hungerford D.S). Williams & Wilkins, Baltimore 1984:216-21.
4. Büniger C, Hjerminnd J, Bülow J. Hemodynamics of the juvenile knee in relation to increasing intra-articular pressure. An experimental study in dogs. *Acta Orthop Scand* 1983;54(1):80-7.
5. Büniger C, Bülow J, Hjerminnd J, Harving S. Hemodynamics of the juvenile dog knee in relation to increased venous outlet resistance. *Pflugers Arch* 1983;399(2):129-33.
6. Büniger C, Büniger E H, Harving S, Djurhuus J C, Jensen O M. Growth disturbances in experimental juvenile arthritis of the dog knee. *Clin Rheumatol* 1984;3(2):181-8.
7. Büniger C, Harving S, Hjerminnd J, Büniger E H. Relationship between intraosseous pressures and intra articular pressure in arthritis of the knee. An experimental study in immature dogs. *Acta Orthop Scand* 1983;54(2):188-93.
8. Christensen S B, Krogsgaard O W. Localization of Tc 99m MDP in epiphyseal growth plates of rats. *J Nucl Med* 1981;22(3):237-45.
9. Deutsch S D, Gandsman E J, Spraragen S C. Quantitative regional blood flow analysis and its clinical application during routine bone scanning. *J Bone Joint Surg (Am)* 1981;63(2):295-305.
10. Duthie R B, Matthews J M, Rizza J M, Steel W M, Woods C G. The management of musculo-skeletal problems in haemophilias. Blackwell Scientific Publications, Oxford 1972.
11. Ewald H, Holm I E, Bülow J, Büniger C. Effect of indomethacin on regulation of juxta-articular bone blood flow during joint tamponade. An experimental study in puppies. *Scand J Clin Lab Invest* 1989;49(3):273-7.

12. Goel K M, Rawson S P, Shanks R A. Radiological assessment of fifty patients with juvenile rheumatoid arthritis: correlation with clinical and laboratory abnormalities. *Pediatr Radiol* 1974;2(1):51-9.
13. Hansen E S, Holm I E, Bünger C, Noer I, Christensen S B, Knudsen V. ^{99m}Tc DPD uptake in juvenile arthritis. Scintimetry and autoradiography of the knee in dogs. *Acta Orthop Scand* 1986;57(4):299-304.
14. Hansen E S, Hjortdal V E, Noer I, Christensen S B, Holm I E, Bünger C. ^{99m}Tc DPD uptake in juvenile hemarthrosis. Scintimetry and autoradiography of the knee in dogs. *Orthopedics* 1989;12(3):441-7.
15. Hansen E S, Hjortdal V E, Noer I, Holm I E, Ewald H, Bünger C. Three phase (^{99m}Tc) diphosphonate scintimetry in septic and nonseptic arthritis of the immature knee: an experimental investigation in dogs. *J Orthop Res* 1989;7(4):543-9.
16. Hansen E S, Noer I, Henriksen T B, Hjortdal V E, Søballe K, Bünger C. The influence of synovial effusion on juxtaarticular ^{99m}Tc DPD uptake in arthritis of the immature dog knee. *J Orthop Rheumatol* 1989. In press.
17. Hoaglund F T. Experimental hemarthrosis. The response of canine knees to injections of autologous blood. *J Bone Joint Surg (Am)* 1967;49(2):285-98.
18. Holm I E, Ewald H, Bülow J, Bünger C. Vasoactive substances in subchondral bone of the dog knee. *J Orthop Res* 1989. In press.
19. Wingstrand H. Transient synovitis of the hip in the child. *Acta Orthop Scand* 1986;57(Suppl 219):1-61.

Acknowledgements

Financial support from the Danish Rheumatism Association and the Medical Faculty, University of Århus, is gratefully acknowledged.