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Tissue vitality in septic gonitis

^{99m}Tc-DPD scintimetry in puppies

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After a single intraarticular injection of 10^9 *Staphylococcus aureus* in 12 puppies, septic arthritis developed in all the experimental knees after 48 hours. A considerable variability in scintigraphic appearance was observed. The juxtaarticular growth plates showed either unchanged or slightly decreased uptake except in 1 dog exhibiting a definite increase in tracer uptake. The epiphyseal uptake showed no consistent pattern. The intraarticular pressure of the arthritic joints increased significantly, but was not related to the tracer uptake pattern.

We conclude that delayed joint scintigraphy as a single investigation in early septic arthritis does not provide diagnostic information and may be misleading.

In septic arthritis, scintigraphy has been reported to display increased juxtaarticular uptake (Gilday et al. 1975), normal or slightly "cold" joint images (Lisbona & Rosenthall 1977, Murray 1982, Minikel et al. 1983) or localized photon deficient regions in otherwise "hot" joints (Murray 1982, Minikel et al. 1983). However, the scintigraphic appearance may also depend on the duration of disease, the specific joint involved, and the scintigraphic technique used (Gilday et al. 1975, Murray 1980, Gandsman et al. 1983).

A quantitative measure of the uptake of bone-seeking isotopes can be obtained by scintimetry (Bauer et al. 1980, Deutsch et al. 1981, Wingstrand et al. 1985 a + b, Nutton et al. 1985). This technique has been shown to improve the assessment of subchondral bone and growthplate metabolism in juvenile chronic arthritis (Hansen et al. 1985, 1986).

The aim of this study was to assess scintimetric changes in early septic arthritis of the juvenile knee in relation to the intraarticular joint pressure and to locate the uptake by contact autoradiography.

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Materials and methods

The study included 12 mongrel puppies, 10 (8–14) weeks old, weighing 9.7 (5.5–15.6) kg. In Brietal® anesthesia (methohexital, 7 mg/kg) after premedication with Combelen® (10-(3-dimethyl-aminopropyl)- propionyl phenothiazine, 0.1% 0.5 ml s.c.), septic arthritis of the right knee was induced by a single intraarticular injection of 10^9 *Staphylococcus aureus* isolated from a human joint.

Scintigraphy. Joint scintigraphy was performed initially and after 48 hours by means of a gamma camera (General Electric Maxi 61) equipped with a low-energy, ultra high-resolution converging collimator. The examinations were carried out under anesthesia (Immobilon® vet., etorfin-acepromazin) 2 hours after intravenous injection of 15–20 mCi ^{99m}Tc-DPD (99m-labeled technetium 2,3-dicarboxypropane- 1,1diphosphonate). Both anteroposterior and sagittal projections in the supine position were used. To obtain optimal resolution and minimal side-to-side variation, contact between knees and collimator was secured.

Regional scintimetric analysis. Three anatomic regions of interest representing the distal femoral growth plate (FGP), the distal femoral epiphysis (FE), and the proximal tibial growth plate (TGP) were analyzed by sagittal scans using a data-processing system (General Electric Star) interfaced with the camera. The count ratio between arthritic and control limb was calculated for the three regions (CR_{FGP}, CR_{FE}, and CR_{TGP}). The counts were corrected for radioactive decay in the time interval between data acquisition of the arthritic and the control limb. Previous control studies of the scintimetric technique applied have revealed an interindividual and intraindividual coefficient of variation of 8 per cent and 5 per cent, respectively (Hansen et al. 1986).

Intraarticular pressure. The intraarticular pressure (IAP) was measured bilaterally after 48 hours by a fluid-filled, electromanometric pressure-recording system. The knees were kept in neutral position with the needle in the intercondylar compartment (Bünger et al. 1983). The atmospheric pressure at knee level served as a reference.

Histology. Tissue specimens were fixed in formalin, stained with hematoxylin-eosin, and examined in a light microscope.

Contact autoradiography. In 1 dog, the uptake of tracer was located by contact autoradiography. Two hours after injection of 25 mCi ^{99m}Tc-diphosphonate, the knees were dissected free, embedded in an aqueous solution of carboxymethyl cellulose, and frozen by immersion in hexane cooled by solid CO_2 at -75°C. The frozen knees were sectioned progressively in the coronal plane using a heavy cryomicrotome until the cut surface was approximately at midarticular level. An X-ray film was then attached to the surface and left in the dark for 18 hours (Christensen & Krogsgård 1981).

Statistics. The Student's *t*-test for paired observations was used for evaluation of scintimetric data. Pearson's linear correlation analysis was applied to analyze the relationship between IAP and the count ratio in FGP, FE, and TGP. *P* values less than 0.05 were considered significant.

Results

All the experimental knees were warm and swollen after 6 hours. Leukocyte counts increased from 6.9 (4.6–9.7)$\times 19^9$ per litre to 19.3 (12.6–31.6)$\times 10^9$ per litre after 48 hours. Body temperature raised 1° C. In 5 dogs, sepsis was suspected, and Methicillin®, 100 mg/kg, was therefore administered thrice daily.

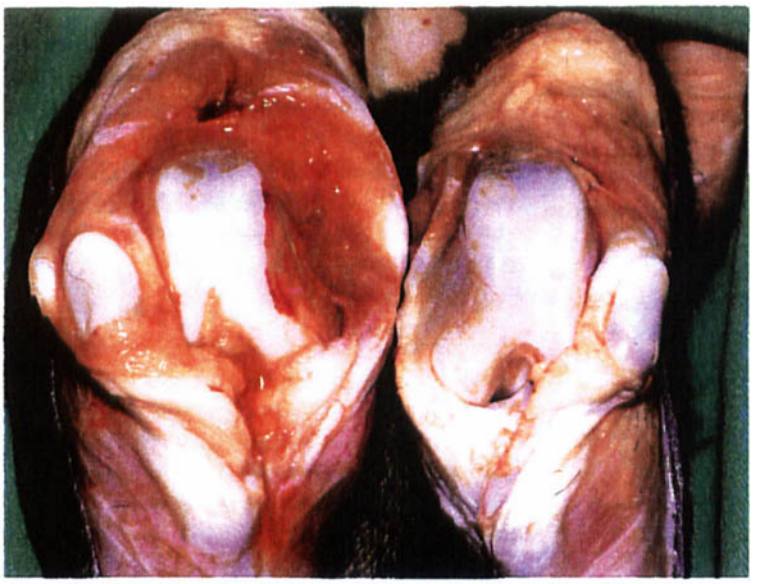
Pathoanatomy. Staphylococcus aureus was isolated from the experimental knee in all the dogs after 48 hours. At dissection the experimental knees had purulent effusion, synovial hyperemia, and periarticular edema (Figure 1a). Radiography showed increased soft-tissue shadows, but no bone changes.

The histologic preparations showed acute synovial inflammation with polymorphonuclear cell infiltration and perivascular edema. Focal disruption of the synovial lining was present in all the experimental knees. Areas of superficial cartilage destruction with invasion of polymorphonuclear cells were observed (Figure 1b). The contralateral knees exhibited normal histologic features.

Joint scintigraphy (Figure 2). The scintigrams showed a moderate reduction in tracer uptake in five knees (Figure 2b). In one knee, tracer uptake in the distal femoral epiphysis was entirely absent (Figure 2c). Another dog had a markedly increased uptake in both juxtaarticular growth plates (Figure 2d). In the remaining dogs, the scintigraphic joint images were essentially unchanged.

Scintimetry (Figure 2a, Table 1) In the growth plates, one dog (no. 2) had a nearly twofold uptake of ^{99m}Tc-DPD, with a CR_{FGP} of 1.68 and a CR_{TGP} of 1.92. This knee clearly deviated from the rest, in which a slight to moderate reduction in the growth plate uptake was found. If dog no. 2 is excluded from statistical analysis, this reduction was significant ($P < 0.01$). In 4 dogs, however, the reduction was less than 8 per cent, and hence, within the coefficient of variation of the scintimetric method.

The epiphyseal uptake showed no consistent pattern. Five dogs had increased and 7 reduced uptake. CR_{FE} varied between 0.30 and 1.50.



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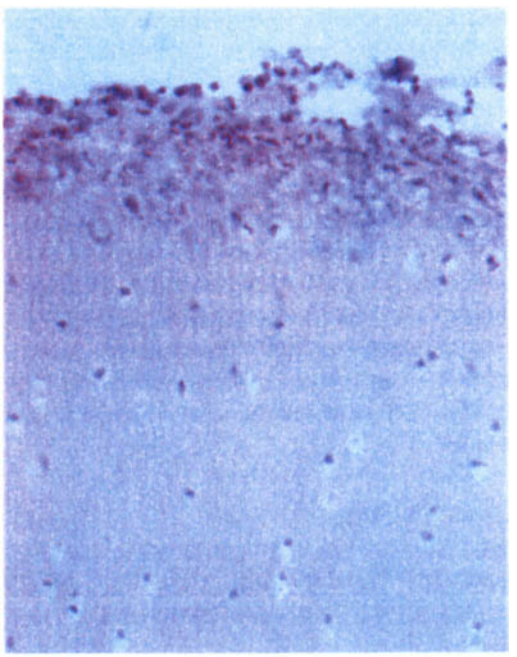

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Figure 1. Forty-eight hours after injection of *Staphylococcus aureus* in juvenile dog knee.
A. Purulent synovial fluid, synovial hyperemia, and periarticular swelling in the right arthritic joint. The left knee is normal.
B. Histology. Septic knee with superficial destruction of the tibial articular cartilage with polymorphonuclear cell infiltration. Hematoxylin-eosin × 25.

Table 1. Scintimetry and intraarticular pressure (IAP). Count ratio between arthritic and control knee in distal femoral growth plate (CR_{FGP}), distal femoral epiphysis (CR_{FE}), and proximal tibial growth plate (CR_{TGP}) before the induction (0 hours) and after 48 hours of septic arthritis

Dog no.	CR_{FGP} 0h	CR_{FGP} 48h	CR_{FE} 0h	CR_{FE} 48h	CR_{TGP} 0h	CR_{TGP} 48h	IAP 48h (KPa)
1	1.04	0.92	1.08	0.30	1.14	1.13	2.0
2[a]	1.07	1.68	1.05	0.89	0.96	1.92	2.7
3	1.11	1.05	1.10	0.99	1.10	1.10	[b]
4	1.09	1.03	1.21	1.34	1.02	0.96	[b]
5	1.04	0.75	0.99	0.85	0.92	0.84	3.3
6	0.97	0.65	1.01	0.75	0.99	0.85	2.7
7	1.09	1.06	1.00	0.87	1.18	0.92	2.0
8	1.15	1.13	0.94	0.82	1.03	0.85	2.9
9	1.04	0.68	0.95	1.50	1.04	0.74	3.1
10	1.00	0.76	1.02	1.22	1.00	1.01	2.7
11	0.97	0.80	1.00	1.24	0.97	0.79	4.0
12	1.00	0.87	0.95	1.31	1.07	0.83	1.7

[a] Excluded from statistical analysis.
[b] Pressure measurements failed for technical reasons.

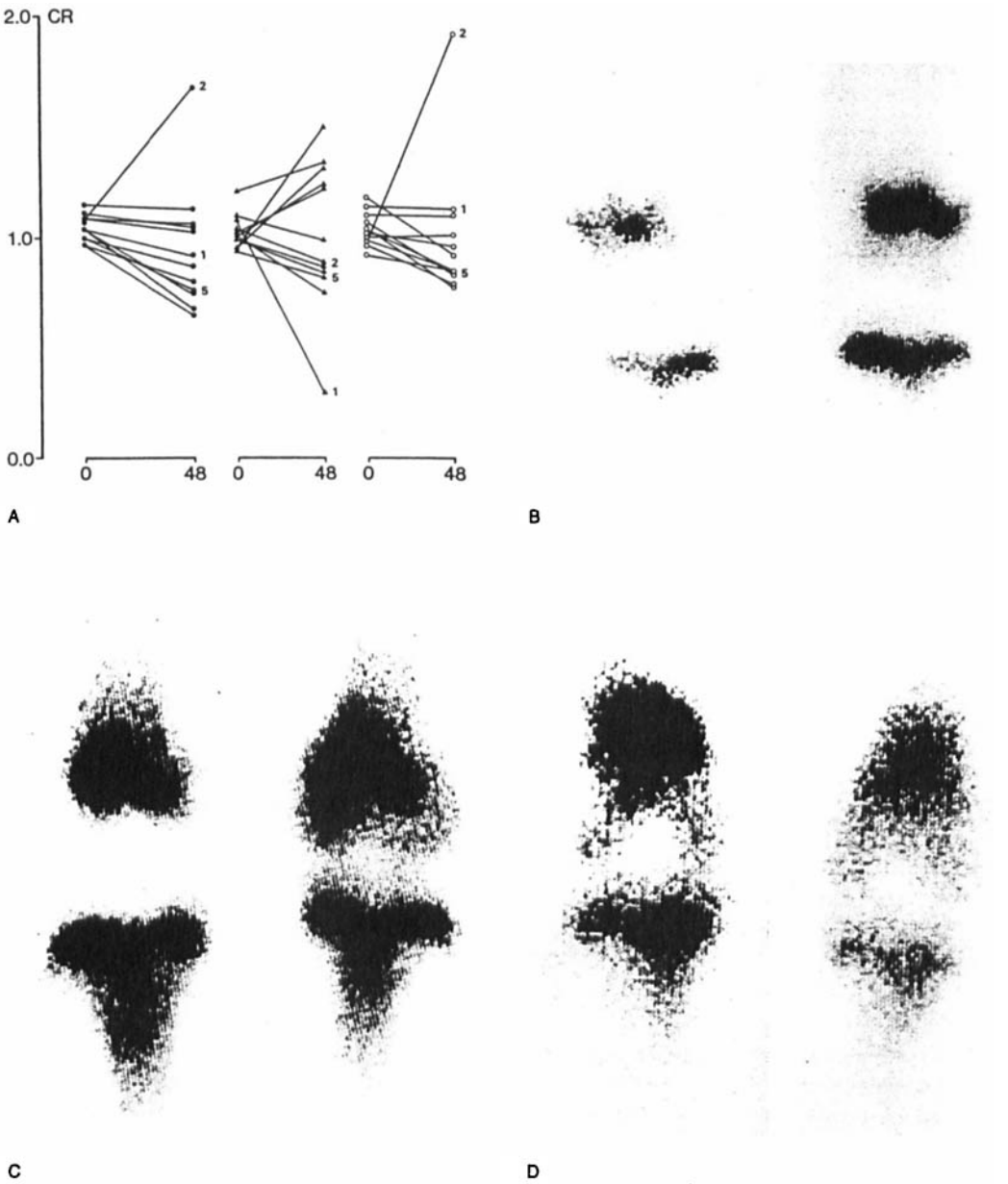

Figure 2. ^{99}mTc-DPD scintigraphy and scintimetry in early septic arthritis of juvenile dog knees.
A. Count ratio (CR) between arthritic and control knee in distal femoral growth plate •, distal femoral epiphysis ▲, and proximal tibial growth plate ○ initially and after 48 hours. The numbers 5, 1, and 2 refer to the cases shown in this figure: b, c, and d, respectively.
B. Case 5. A moderate reduction in tracer uptake in the arthritic knee. Arthritic knee to the left, control to the right in figures b, c, and d.
C. Case 1. The arthritic knee showed no uptake of ^{99m}Tc-DPD in the distal femoral epiphysis compared with the control.
D. Case 2. Arthritic knee with an increased uptake in the growth plates compared with the control.

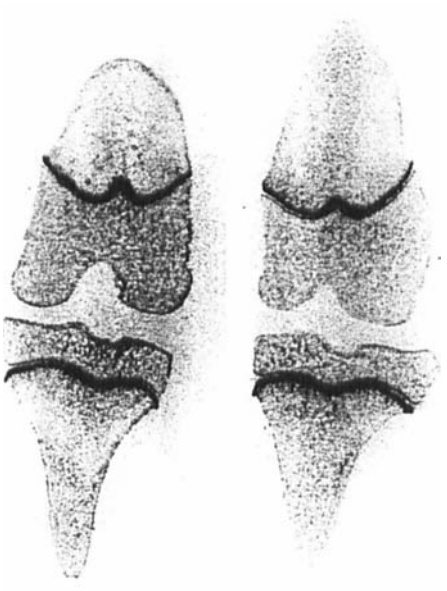

Figure 3. ^{99m}Tc-diphosphonate contact autoradiography of arthritic (to the left) and control knees 48 hours after induction of septic arthritis. The uptake of radionuclide was located in the calcification layer of the growth plates and the subchondral epiphyseal bone, where the activity was increased in the arthritic joint.

Contact autoradiography (Figure 3). The uptake of ^{99m}Tc-diphosphonate was located by contact autoradiography in a knee with reduced growth plate uptake and increased epiphyseal uptake according to scintimetry. In both experimental and control joints, growth plate uptake was localized to a narrow zone at the metaphyseal junction. The epiphyseal uptake was confined mainly to a thin bone layer at the periphery of both juxtaarticular epiphyses. This subchondral uptake was increased in the arthritic joint, whereas no change in the central epiphyseal bone had occurred.

Intraarticular pressure. For technical reasons, the IAP could not be assessed in two dogs. IAP in the arthritic joints was elevated to 2.7 (1.7–4.0) KPa ($P < 0.001$). In the control joints, IAP was slightly negative (−1.1– −0.3) KPa. No relationship between IAP and uptake of ^{99m}Tc-diphosphonate could be demonstrated for the femoral growth plate ($r = -0.22$, NS), femoral epiphysis ($r = 0.32$, NS), or tibial growth plate ($r = -0.17$, NS).

Discussion

Our dogs had pronounced septic arthritis with rapid development of joint swelling, periarticular edema, local tenderness, fever, and an elevated leukocyte count. Yet, the scintigraphic changes were subtle and inconsistent. In some dogs the uptake of ^{99m}Tc-DPD was essentially unchanged. Others had "cold" joint images, mostly due to a decreased growth-plate uptake. In one dog, there was complete absence of tracer in the distal femoral epiphysis. Only 1 dog had increased tracer uptake in bone adjacent to the infected joint. The most likely reason for the slight changes in uptake of ^{99m}Tc-DPD was that substantial metabolic disturbance in bone had not yet occurred at the early stage of arthritis investigated.

The sequence of events during septic arthritis has been studied in several experimental models. After intraarticular injection of *Staphylococcus aureus* in rabbit knees, over 90 per cent of the bacteria are cleared from the joint cavity within 30 minutes (Johnson et al. 1970). Residual organisms surviving this first line of defense, then, initiate the arthritis, which is progressive once established (Nagel et al. 1966, Schurman et al. 1975). Goldenberg et al. (1983) found that synovitis develops within the first day, depletion of glycosaminoglycans from the articular cartilage occurs after 2 days, and irreversible cartilage changes prevail after 5 days of joint infection. To our knowledge, early subchondral bone involvement in septic arthritis has not been reported. Our observations suggest that metabolic bone changes occur late in septic arthritis, i.e., at a time when the articular cartilage already may have suffered damage.

The most consistent scintimetric finding was that showing reduced growth plate uptake. A similar observation was reported in chronic Carrageheenan-induced arthritis (Hansen et al. 1986) and in chronic hemarthrosis (Hansen et al. 1985) of immature dog knees. Hence, it appears that decreased ^{99m}Tc-DPD uptake may be seen in synovitis of any origin. In one knee, we found a markedly increased growth plate uptake. This pattern is similar to the general scintigraphic appearance in juvenile osteomyelitis of the metaphyses of long bones (Gilday et al. 1975, Majd & Frankel 1976, Maurer et al. 1981). A possible explanation of this exceptional scintigraphy is infectious spread to the metaphyses. As the

growth plates separate the epiphyseal and metaphyseal circulation, septic spread has most likely occurred directly from the joint cavity to the metaphyseal bone. This would suggest a joint anatomy resembling that of the juvenile hip with capsular insertions beyond the growth plates. Clinically, such a case has been reported by Murray (1982).

Regarding the observed tracer uptake in the epiphyseal region, a number of factors may contribute to the variability. In normal puppies, a moderate elevation of intraarticular pressure induces increased subchondral blood flow in the juvenile knee (Bünger 1987) consistent with the increased subchondral tracer uptake demonstrated autoradiographically in 1 dog with increased epiphyseal uptake. The presence of synovitis, however, renders the distal femoral epiphysis susceptible to ischemia at lower pressure levels, apparently because of increased vascular resistance caused by inflammation (Bünger et al. 1983). The poor correlation between intraarticular pressure and epiphyseal tracer uptake may be due to interindividual variations in the inflammatory vascular resistance, as well as to variations in the anatomic relationship between joint capsule and epiphyseal vascularity. The absence of tracer uptake in the distal femoral epiphysis in 1 dog may be due to tamponade secondary to elevated joint pressure. Septic thrombosis with infarction of the entire epiphysis is another possible explanation (Murray 1982).

In conclusion, we found evidence of a decreased growth plate metabolism and, in most cases, an altered epiphyseal metabolism after 48 hours of septic arthritis, although the changes in uptake of ^{99m}Tc-DPD were slight. Regional differences in uptake, which can only be appreciated by scintimetry, may counterbalance each other and give the impression of a negative scintigraphy. Hence, delayed ^{99m}Tc-diphosphonate scintigraphy must be considered unreliable in the early diagnosis of septic arthritis.

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