Decreased blood perfusion in canine tibial diaphysis after filling with acrylic bone cement compared with inert bone wax

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Sixteen dogs had one tibia filled with acrylic PMMA bone cement and the opposite, control tibia filled with inert bone wax. After 1, 4, and 12 weeks, the blood perfusion in diaphyses was measured with Sc-46 labeled microspheres. The blood flow rates increased from 1 to 4 weeks and dropped to about the 1-week level after 12 weeks on both sides, with the acrylic side lower than the control side. On both sides, Disulphine Blue staining of the bones showed severe endosteal avascularity after 1 and 4 weeks and massive periosteal apposition after 4 and 12 weeks. The initial increase in blood flow is considered due to periosteal apposition, and the differences in blood flow rates are attributed to avascularity caused by the polymerization heat and toxicity of the acrylic cement.

Bone damage after cementation of a prosthesis into tubular bone with acrylic (PMMA) bone cement might be caused by reaming of the medullary cavity (Danckwardt-Lilliestrom 1969, Rhinelander et al. 1979), filling of the canal (Sund and Rosenquist 1983, 1984), heat production during polymerization (Mjöberg 1986), and toxic effect of excessive monomer leakage (Feith 1975).

The aim of this study was to investigate the combined adverse effects of polymerization heat and monomer toxicity in an experimental model where the control side was surgically prepared in an identical manner, but the medullary canal filled with an inert bone wax (Howard and Kelley 1969, Rodrigues and Carvalho 1983). Because no prosthesis was inserted, forces were not transmitted to the interface between the cement and bone.

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Material and methods

Sixteen mongrel dogs with closed epiphyseal lines, weight 20–30 kg, were premedicated with propionylpromazine (Combelen® Vet) 0.1 mg/kg and atropin 0.02 mg/kg and anesthetized with thiomebumal sodium (Leopental®). Endotracheal intubation was performed and the anesthesia was maintained with Immobilon® Vet (etorphine 0.125 mg/mL, acepromazine 0.4 mg/mL) 0.04 mL/kg initially and supplemented with smaller doses later as needed.

Operative procedure

Access to the proximal tibia was obtained through the patella tendon, which was divided longitudinally. Corpus Hoffa was left intact in order to stay extraarticular. The tibial medullary cavity was opened anterior to the corpus Hoffa, and was reamed with hand-driven reamers to a diameter of 8–9 mm. The medullary cavity was curetted, brushed, and flushed with saline several times and sucked. Radiopaque PMMA bone cement (Palacos®) was injected on one side with a cement gun through a specially designed injection tube (Ø 6.5 mm) small enough to pass all the way down into the medullary canal. The cement

was introduced from the bottom up as the tube was retracted. The cement was pressurized with a custom-made pressurizer until it had cured. The contralateral tibia was filled in a similar fashion with bone wax (Ethicon®) containing 15 percent w/w zirconium dioxide, which is the same radiopaque as contained in commercial acrylic cement.

Postoperative radiographs confirmed adequate filling of the tibial diaphyses. A prophylactic antibiotic, 1 g ampicillin i.m., was given for 3 days. No infections were encountered. All the animals recovered rapidly, and stood with full weight bearing on the operated on legs a few hours after the operation.

Bone perfusion investigations

The dogs were killed after 1 week (2 dogs), 4 weeks (6 dogs), and 12 weeks (8 dogs). Immediately before the following investigation, premedication with propionylpromazine 0.1 mg/kg and anesthesia with thiomebumal sodium 12.5 mg/kg was administered. The dogs were intubated and ventilated with 20 percent O_2 / 80 percent N_2O using a Servo respirator. The anesthesia was maintained with fentanyl (Haldid®) 0.2–0.4 mg i.v. Muscle relaxation was obtained with intermittent doses of pancuronium bromide (Pavulon®), 2 mg per dose. The anesthesia was monitored with ECG, aortic blood pressure, and analysis of blood gases.

The dogs were placed supine on the operating table and the carotid arteries were exposed. The right carotid artery was catherized (Cava Fix® 14 G) into the left ventricle. The abdominal aorta was cannulated through the left carotid artery in a similar fashion. The position of the catheters was checked with an image intensifier and pressure recording.

After 30-min steady circulatory state, microspheres (Nen-Track®; 10^7, 15 microns, spheres labeled with 500 micro Ci Sc-46 suspended in 5 mL 10 percent Dextran with 0.01 percent Tween 80) were injected into the left ventricle during 30 s (Tøndevold 1982), followed by flushing with 10 mL saline. Preceding the injection by 30 s, a suction pump (Braun, West Germany) was started, and reference blood samples were obtained from the aorta at a constant rate of 2.5 mL/min for 4 min.

The dogs then received 30 mL Disulphine Blue 7.5 percent i.v., and were killed 30 min later by an overdose of mebumal sodium i.v.

The stripped tibiae were divided longitudinally with a saw. Alternately, the medial and lateral half of the bone was divided into 1-cm-long pieces and placed in test tubes. These samples were weighed on a Metler precision balance scale, subtracting the weight of the test tubes, and gamma radiation scintillation counts in a well-type scintillation counter (Packard® Auto-Gamma Scintillation Spectrometer) were performed.

The other halves of the tibiae were freeze cut on a hard-tissue cryostat, and the specimens were photographed for grading of the disulphine staining. The grading of the periosteal apposition and unstained areas was based on visual impression (Table 1), and not on actual measurements that had failed to produce valid results.

Table 1. Canine tibial diaphysis filled with bone wax or bone cement, evaluated with Disulphine Blue staining, concerning unstained areas and periosteal apposition, and cortical blood flow (mL/100 g/min)

Identification	Part[a]	Disulphine Blue staining		Perfusion	
		Unstained Wax/cement	Apposition Wax/cement	Wax	Cement
1 week					
01	L	+++/+++	+/–	6.3	2.9
06	M	+++/+++	+/+	5.5	3.7
4 weeks					
01	M	+/++	++/+	29.7	25.7
07	L	+/+++	++/+	24.6	12.2
25	M	+/++	++/+	18.1	14.3
26	L	+/+	++/++	27.7	24.3
27	M	++/+	++/+	14.8	11.0
28	L	+/++	+++/+	16.7	14.4
12 weeks					
04	M	–/–	+++/++	10.0	8.0
05	L	+/+	++/++	3.2	2.1
22	L	–/–	++/+	19.4	12.3
23	M	–/–	+++/+	7.9	5.3
24	L	–/+	++/+	6.1	5.2
32	M	–/–	+/+	3.5	5.3
33	L	–/–	++/+	7.4	5.8
34	M	–/–	+++/++	11.1	10.2

[a] M medial, L lateral part of tibia used for perfusion measurements.
– No unstained areas or periosteal apposition, + just visible unstained areas or apposition, ++, +++ increasing unstained areas extending further through the cortex or increasing periosteal apposition.

Calculation

Blood flow rates were calculated after correcting for the physical decay.

Blood flow rate (mL/100 g/min) = (Activity/100 g tissue x 2.5 mL/min)/Activity of reference sample.

Diaphyseal blood flow rates were calculated as the mean values of the five central specimens (5–10 g tissue) of the tibial diaphysis.

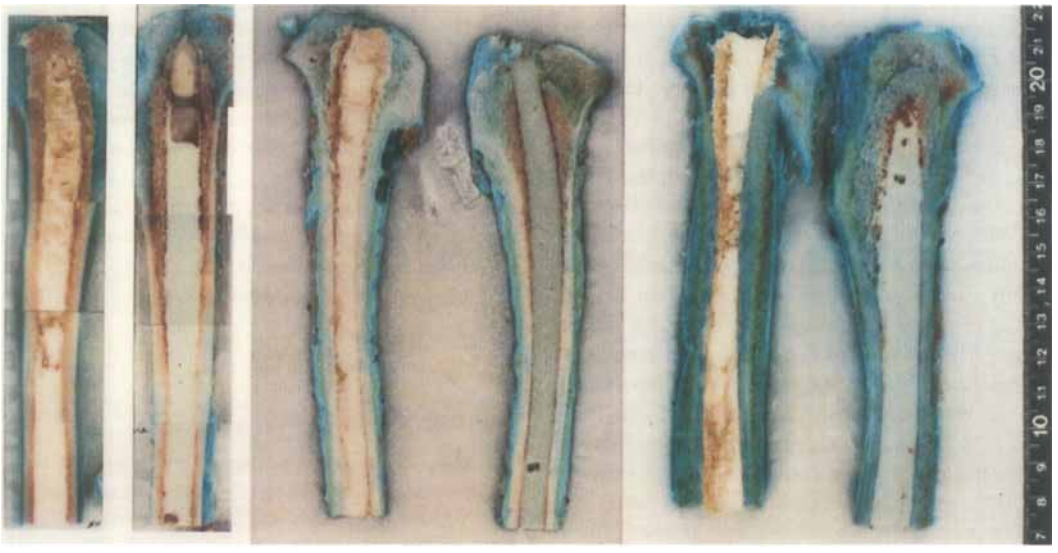

Figure 1. Longitudinal intravital Disulphine Blue stained sections of canine tibiae, 1 (left pair, 06), 4 (middle pair, 25), and 12 (right pair, 23) weeks after filling of the medullary cavity with bone wax (left bone of a pair) or bone cement (right bone of a pair).

Statistical analyses were performed with a Wilcoxon test for paired data and the Mann-Whitney test for unpaired data.

Results

Blood flow rates were higher in the tibia filled with wax than in the tibia filled with acrylic PMMA bone cement (Table 1). Median diaphyseal blood flow rates after 1 week were 3.3 mL/100 g tissue/min on the cemented side compared with 5.9 mL/100 g/min, on the control side. The blood flow rates increased to 14.4 mL/100 g/min and 21.4 mL/ 100g/min, respectively, after 4 weeks and declined to 5.5 mL/100 g /min (P = 0.004) and 7.7 mL/100 g/min (P = 0.007), respectively, at 12 weeks. The differences between the two legs were significant after 4 weeks (P = 0.03). The relative differences were most pronounced after 4 weeks, but leveled out after 12 weeks to absolute values resembling the 1-week results. No differences in blood flow rates between medial and lateral parts of tibiae were encountered.

The disulphine staining showed after 1 week a complete lack of bluish coloring in diaphyseal cortex, possibly indicating necrosis, and only very slight periosteal apposition. There were no visible differences between bones filled with wax and with PMMA. After 4 weeks, unstained areas were still present at the inner part of the cortex, whereas the outer parts had become stained. The unstained areas were generally larger in the bones filled with PMMA compared with the bones filled with wax. A heavily stained periosteal apposition on all the bones was encountered, but was most pronounced in the bones filled with wax. After 12 weeks, all the areas of cortex were stained in a speckled fashion, and no larger avascular areas could be found in bones filled with wax or in bones filled with PMMA. The apposition of bone was even larger than after 4 weeks, and was largest in the bones filled with wax (Figure 1, Table 1).

Discussion

Former studies on the effect on bone of intramedullary application of PMMA cement have all been dealing with a control operation consisting of removal of bone marrow (Feith 1975, Rhinelander et al. 1979, Sund and Rosenquist 1983) without filling of the medullary cavity with an inert material. The blood supply to cortical bone is mainly derived from the medullary cavity (Brookes 1971, Rhinelander 1972), and thus the cortex becomes avascular when the bone marrow is removed (Trueta and Cavadias

1955, Danckwardt-Lilliestrom 1969), apart from a narrow rim just beneath the periosteum. If the medullary cavity is left empty after reaming, the endosteal blood flow can regenerate rapidly, and the revascularization can take place from both the periosteum and endosteum (Dankwardt-Lilliestrom 1969). This process differs from what happens when the marrow cavity is filled with cement and revascularization can only take place from periosteum. Consequently, we found that a model for testing the biological response to cement must include a control operation with filling of the medullary cavity. Other authors have inserted a precured bone cement rod into the medullary cavity as a control (Feith 1975, Linder 1977). Such procedures cannot effectively fill the medullary cavity, because in a pilot series of 5 animals we found that if the medullary cavity was not completely filled with bone wax, a heavy, blue-stained line occurred between the wax and the bone within a few weeks, indicating that the endosteal blood circulation had been reestablished.

Bone wax is a material with well-documented harmless effects on bone (Howard and Kelley 1969, Rodrigues and Carvalho 1983), and was chosen as inert filler. Bone wax is softer than bone cement. However, because no force transmission occurred, and because there were no signs of endosteal revascularization due to displacement of the wax, this was not considered a disadvantage.

When measuring blood flow in slices of bone, the flow rates are an expression of the combined flow in the original cortex and in the subperiosteal apposition. The deep-blue staining of the subperiosteal apposition compared with the light-blue staining or in avascular areas complete lack of staining of the original cortex indicate that most of the rise in blood flow rate must be attributed to the subperiosteal apposition.

Many explanations for the subperiosteal apposition after intramedullary interventions have been suggested. Trueta and Cavadias (1955, 1964) suggested that the ischemia caused by interruption of the medullary circulation provokes proliferation of periosteal vessels with accompanying new-bone formation. Zucman et al. (1968) found bone marrow subperiosteally after reaming rabbit tibiae, and they believed that these marrow cells gave rise to callus formation. We believe that the formation of new bone subperiosteally can be attributed to the operative procedure of reaming and filling, although the actual mechanism remains obscure. The difference in blood flow rates between the two legs must then be attributed to the difference in the filling materials. Thus, the heat generation during polyme
and the release of toxic substances from the cement might be the factors responsible for the more pronounced avascularity and less subperiosteal apposition leading to lower flow rates on the cemented side. This accords with de Waal Malefijt (1988), who found more pronounced periosteal bone formation on goat femur in which an uncemented hip prosthesis had been inserted than in the femurs that had received a cemented prosthesis.

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