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Bone reaction to the implant of intramedullary pins of three different metals in rat femur

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A bone–implant interface is influenced by several factors, such as chemical composition of the implanted material, stress transfer at the interface and the biology of the living model. Histological and vascular tree injection methods were used to assess the response to intramedullary pins, cast in different metallic alloys and implanted in the medullary canal of rat femora. A remarkable endosteal reaction, with an absence of major damage of the medullary vascular supply, was observed. Remodelling of this woven bone led to the formation of a lamellar bony shell around the pins, while in sham operations (pin inserted and soon removed) the former was completely resorbed in about 20 days. Mechanical trauma seems to be sufficient to evoke the response of the endosteum, which does not differ from that observed in the normal repair process of diaphyseal fractures. Bone grew very close to the metal surface, but a thin connective membrane or a layer of amorphous material was present at the interface with stainless steel, Co–Cr and titanium pins. Histology of the interface suggests that the implants were not mechanically neutral; these observations may be correlated to the thin layer of bone observed around hip cementless prosthetic stems in patients.

1. Introduction

Extensive investigations have been carried out to study bone changes following the suppression of intramedullary circulation [1–7]; an even more complex pattern of phenomena is observed when the medullary canal is reamed and filled with a metallic implant or bone cement, including necrosis of the inner envelope of diaphyseal bone, periosteal and endosteal apposition, revascularization of the diaphysis through new, circumferential medullary cavities if the original canal is obstructed by the implanted material, and remodelling of the necrotic bone [8–14]. Undoubtedly suppression of the vascular supply is the cause of bone necrosis; however, other factors, such as bone marrow pressure forced into the cortical Volkmann and Havers canals, also play a role in the observed phenomena [15, 16]. When a prosthetic stem is inserted, the occurrence of the former phenomena characterize the biological reaction to the implant and are the main factors which determine the primary stability of the prosthesis.

In this study thin intramedullary pins were implanted in order to minimize the medullary damage and evaluate the pattern of the endosteal response at different intervals and to different types of metallic alloys.

2. Materials and methods

In total, 30 male, Sprague-Dawley rats, with a weight of about 250 g, were used. Under phenobarbital anaesthesia both knee joints were exposed through an external parapatellar incision. A hole was drilled with a dental burr below the intercondylar notch of the femoral epiphysis and a metallic wire 0.8 mm in diameter was inserted into the medullary canal of each femur until it fitted the spongious bone of the proximal metaphysis (Fig. 1). The distal end of the wire was cut below the level of the articular cartilage.

Of the rats, 9 were implanted on both sides with a stainless steel wire (316L, ISO 5832/1), 9 with Co–Cr (ASTM F75) and 9 with pure titanium (ASTM F67). Sham operations were performed in 9 animals: in these the pin was removed before closure of the wound. The animals were housed three per cage and they were able to walk soon after recovery from anaesthesia.

From each group 3 rats were sacrificed 10, 20 and 30 days after insertion of the pins; 3 days before

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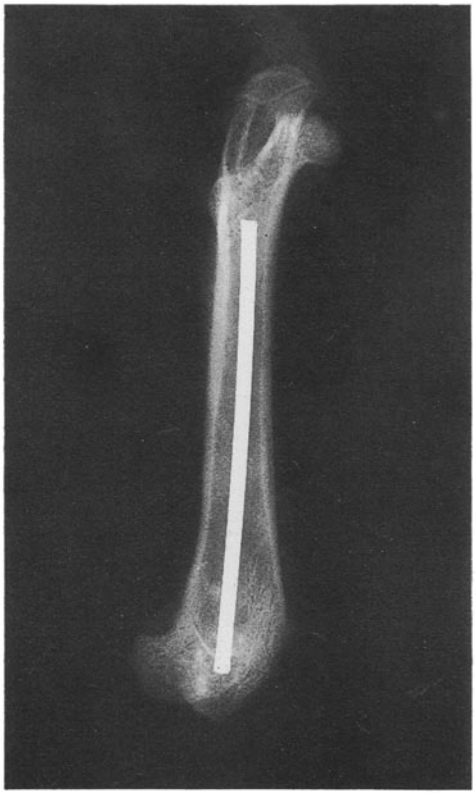

Figure 1 X-ray of the femur with intramedullary pin.

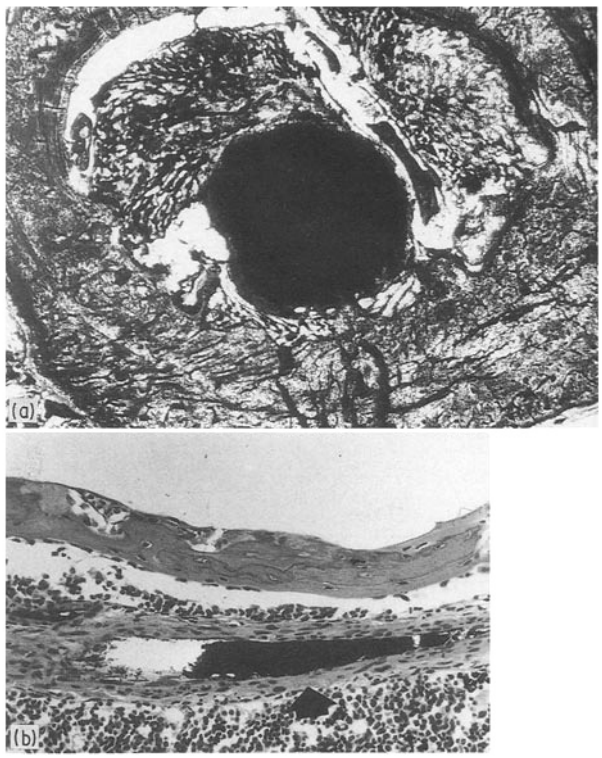

Figure 2 (a) The medullary vessels injected by indian ink are not disturbed by the intramedullary pin. (Resin, 300 μm, unstained section, × 15.5.) (b) Detail of a medullary vessel injected by indian ink near the lamellar bony shell (arrow). (Paraffin, 7 μm, haematoxilin–eosin, × 62.)

termination, tetracycline (30 mg kg^{-1}) was injected intraperitoneally. They were sacrified by inhalation of an overdose of ether and soon thereafter the aorta was incannulated and the cava was cut to allow reflux of blood. About 100 ml indian ink were injected under pressure into the distal aorta. Both femora were cleaned from soft tissues and fixed in neutral formalin for 2 weeks. The right femur was decalcified in EDTA and before embedding in paraffin the implants were gently removed from the distal end of the bone; sections were stained with haematoxylin–eosin. The left femur was embedded undecalcified in Technovit resin. Sections 300 μm thick were cut with a diamond low-speed saw and mounted unstained. Other sections were ground to 15 μm thickness with an Exact apparatus, stained with haematoxylin–eosin and mounted as routinely.

Sections of the distal metaphysis and of different levels of the diaphysis were studied at intervals of about 3 mm.

3. Results

In the midshaft of the femur the pin filled approximately one-quarter of the medullary area; this proportion was even lower in the more distal and proximal sections of the diaphysis. Medullary arteries (branches of nutrient artery) were injected in all the bones examined and thin sinusoids spread radially from them to the endosteal surface (Fig. 2).

In the control group, at 10 days the pin trail was filled by haematoma; at later intervals it had undergone fibrous substitution in some animals while in others it remained unchanged. Woven bone was present and could fill the entire medullary area or just a part of it. At 20 days most of this bone had undergone resorption and at 30 days no trace of it remained. Neither necrosis of the cortical bone nor enhanced periosteal apposition were evident.

The implanted animals showed the same endosteal reaction as controls, but with two main differences:

1. at 20 days a large quantity of woven bone was still present;
2. remodelling of woven bone led to the formation of a bony shell around the pin.

The latter showed a progressive organization from primary to lamellar bone, with collagen fibres and osteocytic lacunae oriented in a plane parallel to the surface of the implant (Fig. 3). The connection of this shell of bone to the cortex was produced either by contact of the pin with the endosteum or by a bony isthmus (Fig. 4).

Bone remodelling of the cortex was not enhanced in either implant or sham operations, as assessed by fluorescent tetracycline marker.

A thick layer of connective tissue between reactive bone and the pin surface was present at 10 days in all the specimens; its thickness was progressively reduced at 20 and 30 days.

The bony shell was not continuous and in some areas only a thin, connective membrane separated the metal from the bone marrow cells (Fig. 5). Where the bony shell surrounded the pin, bone had grown very close to the metal surface, but a direct bone–metal contact was never observed: a 10–20 μm thick membrane with flattened fibrocytes or an amorphous

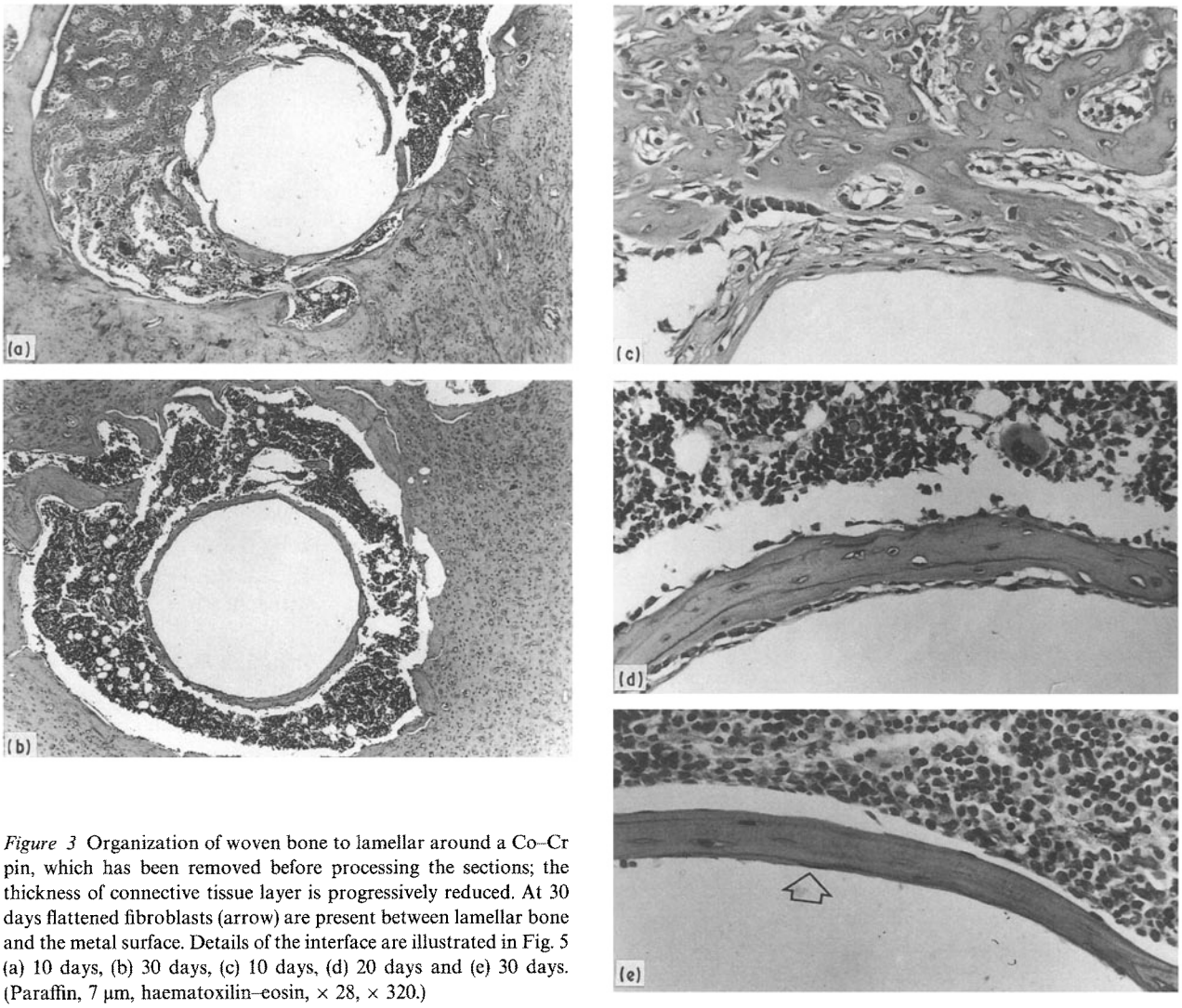

Figure 3 Organization of woven bone to lamellar around a Co–Cr pin, which has been removed before processing the sections; the thickness of connective tissue layer is progressively reduced. At 30 days flattened fibroblasts (arrow) are present between lamellar bone and the metal surface. Details of the interface are illustrated in Fig. 5 (a) 10 days, (b) 30 days, (c) 10 days, (d) 20 days and (e) 30 days. (Paraffin, 7 μm, haematoxilin–eosin, × 28, × 320.)

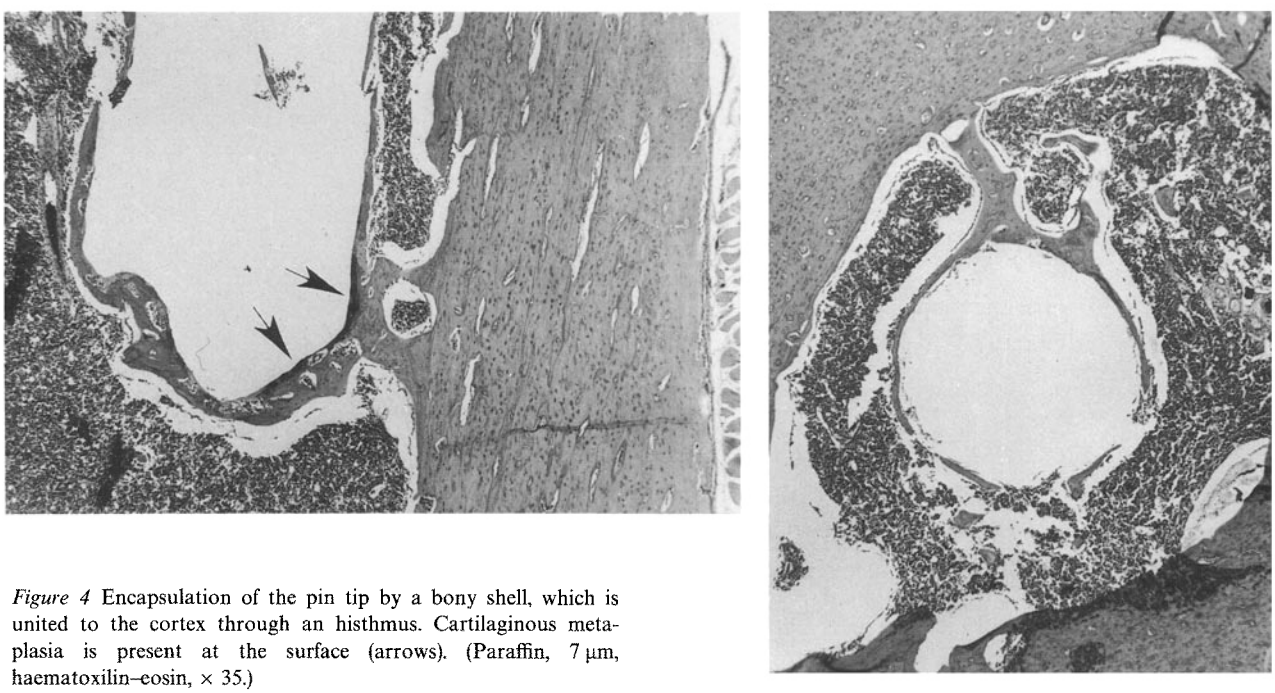

Figure 4 Encapsulation of the pin tip by a bony shell, which is united to the cortex through an histhmus. Cartilaginous metaplasia is present at the surface (arrows). (Paraffin, 7 μm, haematoxilin–eosin, × 35.)

material layer of about 1–2 μm (Fig. 5) was present between bone matrix and metal.

As far as bone–metal contact is concerned, no differences were observed among implants of stainless steel, Co–Cr and titanium. Cartilaginous metaplasia was present at the interface in proximity to the distal and proximal ends of the pins (Fig. 4), but never in the intermediate part.

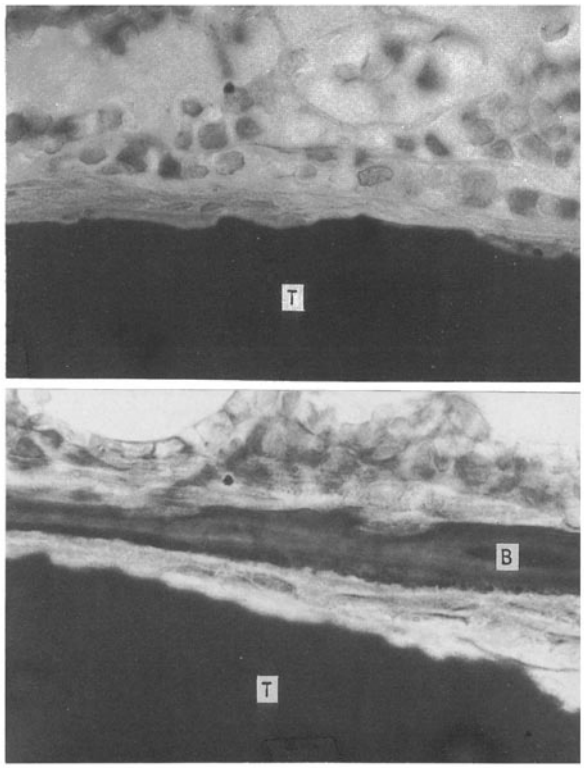

Figure 5 A thin connective membrane around a titanium pin separates the metal from bone marrow or lamellar bone; B = bone, T = titanium. (Resin, 15 μm, haematoxilin–eosin, × 800.)

The reaction in the metaphysis did not differ in quality: less woven bone was formed between the implant and the original trabeculae; this new bone was remodelled on the shape of the implant and cartilaginous metaplasia was also observed at this distal site (Fig. 6).

4. Discussion

Reaming of the medullary canal and filling it with a large nail or acrylic cement destroys the medullary vascular supply of the bone and induces consequent changes, which represent an adjustment to the new situation. Revascularization of necrotic bone begins from the intact periosteal and metaphyseal system 10, 11, 17, 18, and remodelling takes place following the pattern of revascularization [17, 19]. Reactive, periosteal apposition has been constantly observed and different explanations for this phenomenon have been given [6, 15, 20–22]; the endosteum shows the same response as the periosteum, namely activation of osteogenesis; qualitatively it does not differ from the normal repair process of diaphyseal fractures.

Endosteal reaction has been observed in a similar experimental model by Schaberg *et al.* [23] with both metal and plastic wires; however, the absence of osteogenetic phenomena in surgically treated controls reported by these authors, may be explained by the fact that after 2 weeks, reactive woven bone has been already completely resorbed.

Little attention has been paid so far to the fact that early endosteal apposition is also present in experimental animals after reaming and nailing of the diaphysis. The early appearance of endosteal apposition suggests that some endosteal cells can survive the procedures which destroy marrow and medullary vessels but also that revascularization takes place in a short time. This issue is relevant for several aspects concerning fixation of cementless prosthetic stems, which seldom completely fit the medullary canal.

However, major damage to the medullary vascular supply is not the determinant factor of endosteal reaction, because it was also observed to occur when most of the radial branches of the central vessels were spared by the surgical procedure.

Endosteal bone apposition should be interpreted as a reaction either to mechanical trauma or to an irritative factor represented by the foreign body inside the medullary canal. On the contrary, periosteal activation and increased remodelling of cortical bone were not observed in this experiment and they seem to relate directly to extensive damage of medullary vascular supply produced by reaming. The new endosteal bone has the same features of bone callus and undergoes the same evolution, namely remodelling out of existence in a short time.

The presence of the intramedullary implant has a relevant effect on remodelling because lamellar bone is formed near the surface of the implant.

Through the remodelling process mechanical forces are known to influence bone architecture; in this model, because both ends of the pins were encapsulated by bone, strains originated from the different coefficient of elasticity of the bony cylinder and the pin. It is therefore possible to speculate that these strains were the controlling factors in remodelling of woven bone around the pin. Cartilaginous metaplasia has been observed at the interface between bone and cement in total hip replacement and it has been interpreted as evidence for stress transfer from the implant to the bone [24]; the presence of similar findings at the ends of the pins confirms the view that the implant is not mechanically neutral. The connective membrane or the layer of amorphous material between the implant and the bony shell may be associated with micromovements at the interface rather than to a lack of bone binding properties of the metal examined. Strains at interface and micromovements are difficult to quantify in biological models; however, in this experiment they should have been over a wide range, due to different moduli of elasticity of the pins, length and positions inside the femur; nevertheless, no significant differences of endosteal response and morphology of interface were observed in pins cast in stainless steel, Co–Cr and titanium. This could suggest a threshold phenomenon with an "all or nothing" tissue response.

Titanium is known to have better bone-binding properties than stainless steel or Co–Cr alloy; the finding of a connective layer between titanium and reactive endosteal bone supports the view that mechanical load and micromovement at the interface are the critical factors which determine the type of bonding between biological matrix and the metallic substrate.

In clinical applications a thin layer of bone is often observed around hip cementless prosthetic stems;

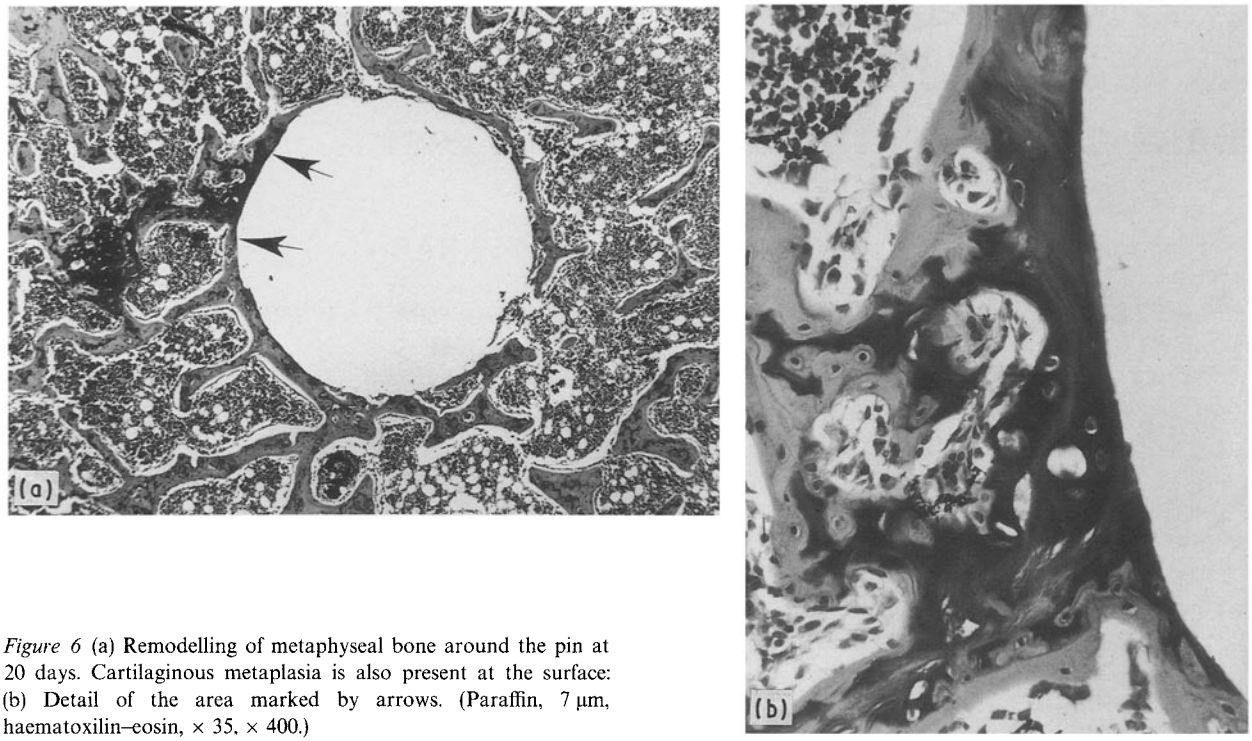

Figure 6 (a) Remodelling of metaphyseal bone around the pin at 20 days. Cartilaginous metaplasia is also present at the surface: (b) Detail of the area marked by arrows. (Paraffin, 7 μm, haematoxilin–eosin, × 35, × 400.)

evidence of fibrous ingrowth with obliquely oriented collagen fibres between the bone shell and the surface of the stem has been presented [25, 26]. There is a striking similarity between the findings in cementless stems and those of the experimental model; in both, the bony shell may be related to the endosteal reaction and to mechanical strains at the interface, which seem capable of orienting bone remodelling around the implant.

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