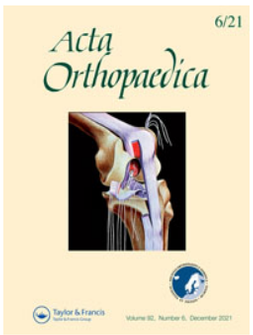

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HISTOLOGICAL CHANGES IN CLINICAL HALF-JOINT ALLOGRAFT REPLACEMENTS

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Fourteen biopsies of cartilage and subchondral bone were taken from nine half-joint knee allografts 10 weeks to 8 years after the transplantation. Deep-frozen cadaver grafts were used to replace the defective half-joint after resection for bone tumour. The biopsies revealed a slow substitution of the dead grafted bone and cartilage. Subchondrally, signs of incorporation could be seen from 12 months on. The dead cartilage matrix degraded gradually and slow simultaneous regeneration was observed. Thus, fibrocartilage was seen on the articular surface of the graft at 12 months, chondrocytes were present at 18 months, but islands of hyaline cartilage were not seen earlier than 7 years after the transplantation. In accordance with the earlier clinical findings, the histological signs of rejection were minimal. The long-term result of half-joint allograft transplantation is obviously dependent on the cartilage component.

Key words: alloimplant; bone grafting; cartilage grafting; joint transplantation

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Half-joint allograft transplantation is indicated after the resection of large, aggressive, low-grade malignant bone tumours. The viability of the cartilage becomes the limiting factor in the long-term results. Although the chondrocytes – like the osteocytes – of the graft lose their viability during the preservation procedure currently used, the clinical results of grafting have been reasonably good (Parrish 1973, Koskinen et al. 1979). We have performed nine half-joint allograft replacements in the knee region, the longest follow-up being 10 years. The present histological report is based on 14 biopsies which elucidate the incorporation of the graft in the host bone.

PATIENTS AND METHODS

Half-joint allograft replacement of the knee region was performed in 9 patients, 7 males and 2 females. The age range was from 17 to 42 years. The tumours were as follows: giant cell tumour – 5, parosteal osteosarcoma – 2, chondroblastoma – 1, and chondrosarcoma – 1. Seven operations were distal femoral and two were proximal tibial graft transplantations.

Before the transplantation the grafts were preserved at –70°C for 48 hours and at –20°C for 30–180 days. The operative procedure consisted of a local radical resection of the tumour, fixation of the graft by stable osteosynthesis, surrounding of the graft-host junction with autogeneic iliac chips, and reconstruction of the knee ligaments (Koskinen et al. 1979).

The biopsies were taken partly to determine the right time for weight-bearing and partly in connection with otherwise-indicated operative procedures, removals of metal implant etc. (Table 1). The formalin-fixed biopsy material was decalcified and processed by routine methods, and histological sections were stained with haematoxylin and eosin.

RESULTS

Fourteen biopsies were taken at various time intervals after the operation. Up to 12 months, no

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Table 1. Histological findings at various time intervals after half-joint allotransplantation of the knee

No.	Patient[1]	Follow-up in months	Histological finding
1	9	2½ mo	Dead bone
2	8	3 mo	Dead bone and cartilage. Living connective tissue cells
3	10	3 mo	Dead bone
4	9	4 mo	Dead cartilage and bone
5	10	5½ mo	Dead cartilage and bone
6	9	6 mo	Dead cartilage and bone
7	7	7½ mo	Dead cartilage
8	10	8 mo	Dead bone. Resorption. Osteoblast activity
9c	11	12 mo	Living fibrocartilage. Living bone
10	6	18 mo	Living bone
10	5	30 mo	Living bone. Living cells in cartilage
12	9	36 mo	Living cells in cartilage. Living bone
13	1	83 mo	Living hyaline cartilage. All bone living
14	1	96 mo	Living bone

[1] Patient numbers refer to the numbering used in Koskinen et al. (1979).

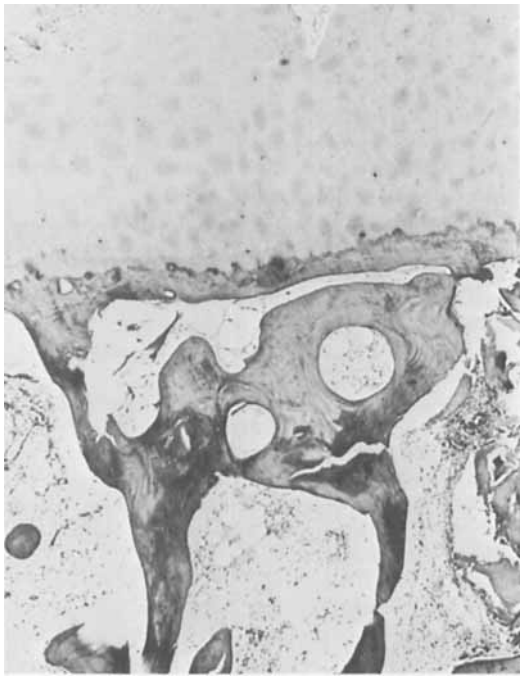

Figure 1. Dead cartilage and subchondral bone in the graft biopsy at 6 months. H & E.

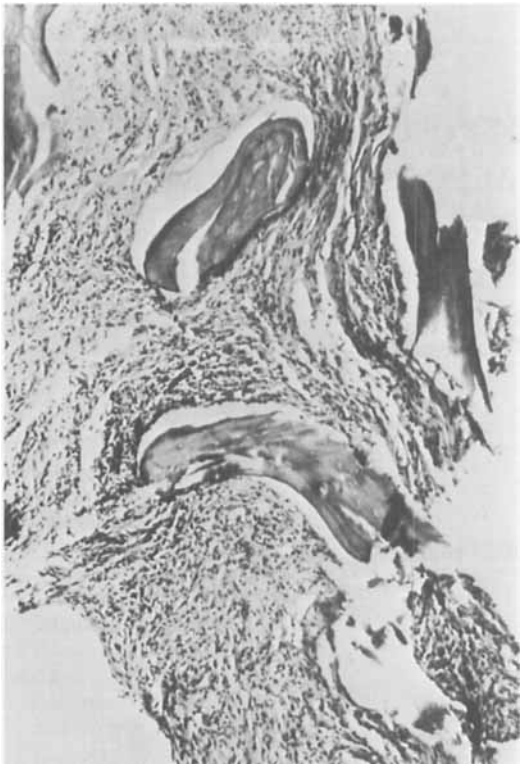

Figure 2. Established blood circulation and viable connective tissue were present between the dead bone trabeculae of the graft at 3 months. H & E.

living osteocytes were seen in the subchondral part of the graft, and the chondrocytes of the joint cartilage were also found to be dead (Figure 1). On the other hand, established blood circulation and viable connective tissue between the dead bone trabeculae could be seen as early as at 3 months (Figure 2); some lymphocytes were also present. The first sign of regeneration was seen in the 12-month specimen as new bone adjacent to dead bone trabeculae, but the cartilage was still inactive. At 18 months, the substitution of bone was well advanced subchondrally, but only a few living chondrocytes could be seen at the osteocartilaginous border (Figure 3). Deeper in the grafted bone (Figure 4) there was active formation of new osteons, with both mature and immature bone adjacent to dead bone trabeculae. The medullary stroma was loose connective tissue with some lymphocytes.

At 2½ years, the cartilage had a clearly fibrous

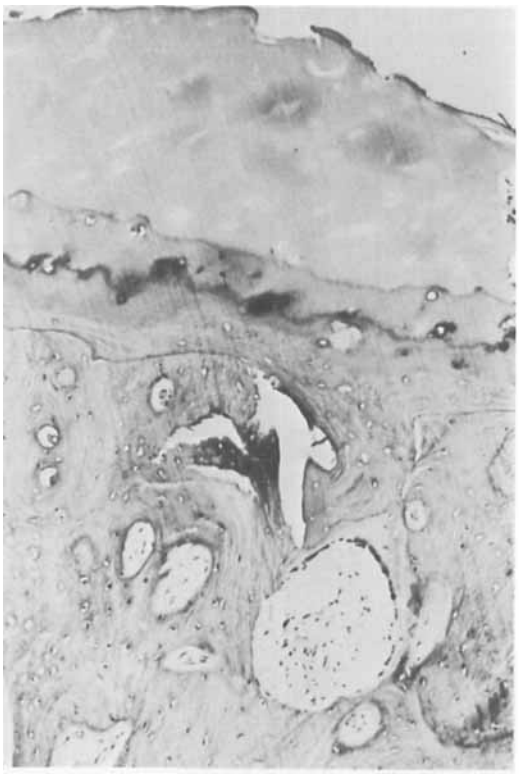

Figure 3. Photomicrograph of histologic section at 18 months. The cartilage is dead, but some living chondrocytes are seen in the vicinity of the osseous part of the graft where creeping substitution is fairly advanced. H & E.

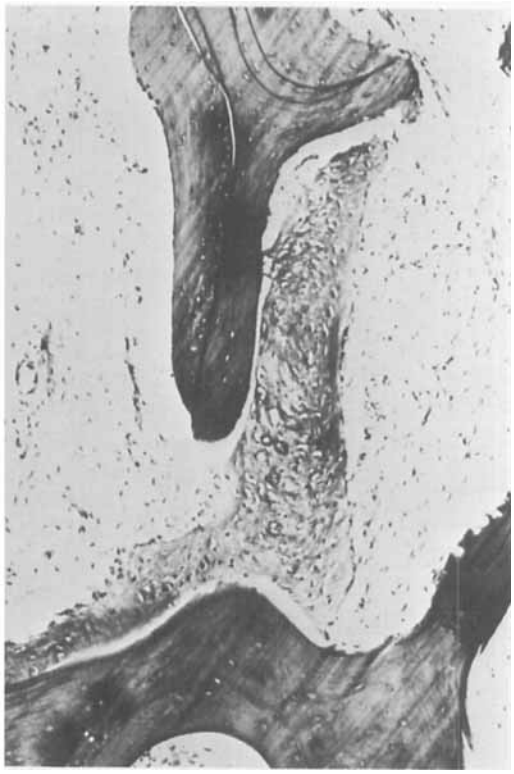

Figure 4. Deeper part of biopsy in Figure 3. The creeping substitution process is very active with immature bone in addition to dense trabecular bone attached to dead grafted-bone trabeculae. H & E.

character (Figure 5), but some of the cells were of chondrocyte type and showed clustering. At 7 years, islands of hyaline cartilage could be seen in peripheral non-weight-bearing parts of the graft (Figure 6). At 7 and 8 years, almost total substitution of the underlying bone had taken place, although some patches of grafted bone were observed.

DISCUSSION

The incorporation of deep-frozen allograft to host bone presented no major problems clinically. As indicated by scintigraphic studies using ^{99m}Tc diphosphonate (Koskinen et al. 1979), the rate of incorporation was very slow.

These findings are corroborated by the present histological observations, where newly-formed bone was not seen subchondrally earlier than at 12 months. The increased uptake of ^{99m}Tc diphosphonate in the subchondral region at 3 months in some grafts corresponds with an established blood circulation and early formation of connective tissue (Figure 2). Only the oldest case, with an 8 year scintigraphic follow-up, was found to be inactive, an indication that incorporation was complete. A detailed report of the scintigraphic studies will be published later.

The rate of incorporation by creeping substitution appears to be proportional to the size of the transplant. Using 5 to 10 mm thick subchondral bone plate in articular cartilage transplantation, Pritzker and coworkers (1977) observed complete bone replacement in 16 months. Our transplants consisting of the whole condylar region

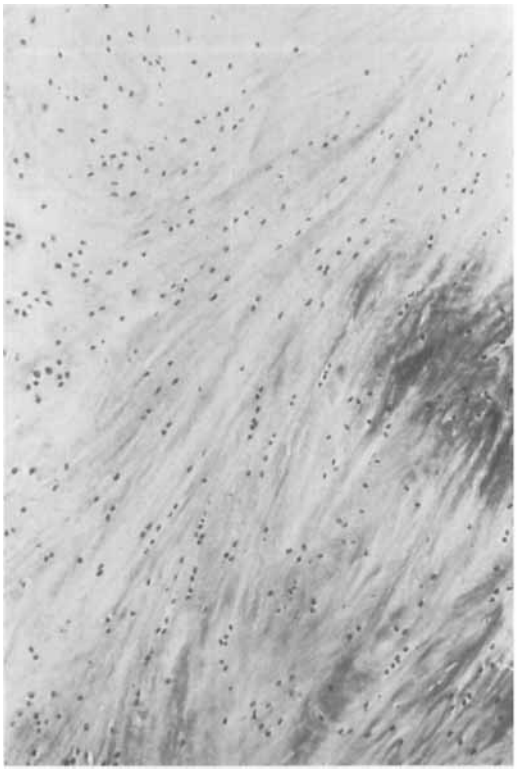

Figure 5. Cartilage at 2 1/2 years. The general appearance is fibrous, with chondrocytes in small clusters. H & E.

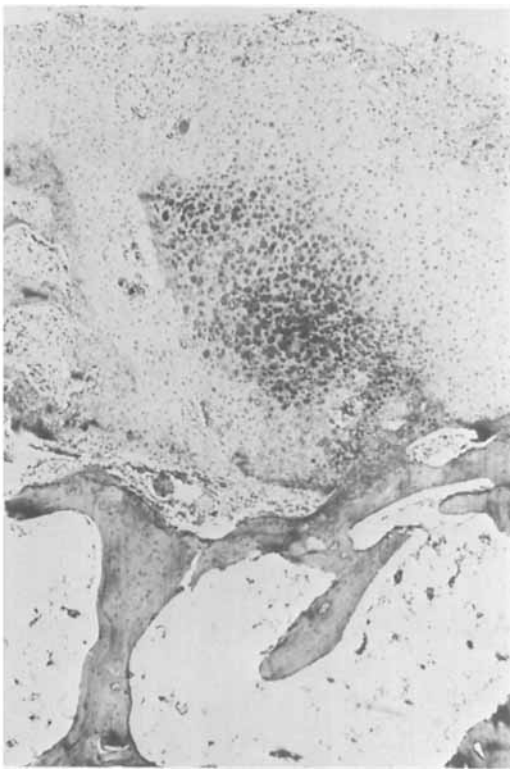

Figure 6. Islands of hyaline cartilage at 7 years. H & E.

with metaphysial bone obviously had a much larger bone mass for substitution by host bone.

Although no efforts were made to match the grafts immunologically, only a few signs of rejection were experienced (Koskinen et al. 1979). In two cases, (at 3 and 18 months), the biopsy revealed some lymphocyte infiltration.

The long-term functional result of a half-joint allograft transplantation is obviously dependent on the viability and regeneration of the joint cartilage. The chondrocytes will die due to preservation by freezing, as evidenced also by the present histological studies. The integrity of the cartilage component was obviously maintained by the cartilage matrix for some years. Pritzker and coworkers (1977) reported survival of the chondrocytes in transplants which were refrigerated at 4°C and inserted 15 to 72 hours after death of the donor. We found it necessary to use a deep-freezing preservation procedure to reduce the immunogenicity of the massive bone component of the graft (Koskinen et al. 1979).

Survival of the chondrocytes can obviously be improved during a preservation procedure. Mankin and associates (1976) suggested impregnation of the cartilage with glycerol before deep-freezing to improve the viability of the chondrocytes. Experimentally, both glycerol and dimethyl sulphoxide have been used for the same purpose (Söndenaa 1980).

The present observations indicate that regenerative processes occur in the transplanted and primarily dead cartilage. These processes apparently begin in the peripheral non-weight-bearing parts. Whether the regeneration can overcome the competing degradation of the cartilage and take on clinical importance remains an open question.

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