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HOMOLOGOUS JOINT-TRANSPLANTATION IN MAN

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Complicated problems of reconstruction are involved in the resection of all or part of a joint. One solution is to replace the resultant defects with artificial material as is done, for instance, with a metal endoprosthesis in hip arthroplasty. The disadvantage here is that, since true union is ruled out, the mechanical stability will depend upon the extent to which the bone tissue tolerates the foreign material. In the case of a major resection, it may be difficult or impossible to design a functional endoprothesis to fill in the defect. This makes it desirable to look for a more biological solution. One possibility that presents itself is substitution with homologous tissue, *i.e.* with a homograft.

Experiments and clinical attempts to perform homologous joint transplantation have been performed ever since the turn of the century (for detailed historical surveys, see Chase & Herndon 1955, Woodruff 1960). Pinskij is thus quoted by Volkov (1966) as being the first to have performed such transplantations on sheep and dogs in 1893, though without obtaining stable union of the graft. A large number of whole and half-joint transplantations were performed by H. Judet (1908) and others, generally on the rabbit. The transplant was removed with or without the joint capsule and was implanted either subcutaneously or in its physiological location. Comparisons were made with autologous transplants moved in a similar way. The results proved contradictory. Some of the homografts united properly but most of them degenerated rapidly and were resorbed. Union was noted, on the other hand, for a large proportion of the autologous transplants and there was general agreement that these were preferable to the homograft. Herndon & Chase (1952) made extensive studies of whole knee-joint graft in the dog, using both autologous and homologous transplants. They found primary union of both types of graft with good functional results after observation times of up to two years but the

homografts subsequently degenerated and ultimately disintegrated entirely, putting an end to the joint function.

Homologous joint transplantation in man was first performed by Lexer in 1907. He transferred the graft straight from the donor without any special preservative measures. The grafts were obtained at amputation or from recently deceased individuals. In a summary published in 1925, Lexer reports having performed 23 whole-joint and 11 half-joint transplantations, most of them involving the knee-joint. He also reports a permanent cure in twelve of the whole-joint transplantations. However, the cases with a long observation time displayed degenerative changes and even though the joint function was good, the roentgenogram was reminiscent of osteoarthritis. Histological studies on two of Lexer's whole knee-joint transplantations were made by Bürkle de la Camp (1929) 14 and 16 years respectively after the operation. He found, for instance, that the normal articular cartilage had been entirely replaced by fibrous tissue and that the intra-articular ligaments and menisci had disappeared. The tissue in the articular end of the bones was viable and normal in appearance. All the half-joint transplantations united without complications according to Lexer and gave a satisfactory joint function, though in the long run mild osteoarthritis developed in the operated joint in these cases as well.

Lexer's work is truly epoch-making. Even though the clinical follow-up is not always clearly documented, several of his cases must unquestionably be described as functionally excellent. It is therefore surprising that the method was adopted by so few of his contemporaries and successors. Apart from a few isolated cases (May 1942, Capurro & Pedemonte 1953), it is only during the past decade that homologous joint transplantation has been taken up once more.

The modern method utilizes bone banks, the joint transplant being kept in a frozen state until it is to be implanted.

The conventional temperature for a bone bank is —15° to —20° C. Ottolenghi (1966) and Parrish (1966) have each reported seven cases of massive homologous half-joint transplantations in the reconstruction of defects after the resection of skeletal tumours. A complete femur was transplanted in one case. Bony union was noted in all cases but there were varying degrees of partial resorption of bone and/or necrosis of the articular cartilage. Large homografts have been used in similar cases by Merle d'Aubingné et al. (1966). In their reconstructions, however, these authors generally aimed at arthrodesis and consequently they have seldom used articular transplants.

Important contributions to the development of homologous joint transplantation have been made by Russian researchers in recent years. After extensive experimental studies on the dog, Imamaliev (1964) demonstrated that a transplantation was more likely to be successful if the transplant was pre-treated with a considerably lower temperature than that used in an ordinary bone bank. He found that the optimal conditions for storage of the homograft were —70° C for 24 hours followed by —20° C for one month.

This technique was adapted to clinical conditions by Volkov, who has reported (1966) the largest series of homologous joint transplantations in man to date, with a maximum observation time of 7 years. Half-joint transplantations had been performed in 80 cases, with an excellent result in 47, *ie.* complete anatomical restoration of the joint region as well as normal mobility and weight-bearing by the joint. Bony union was achieved in a further 24 cases but later there was arthrosis with impaired joint mobility. In the remaining 9 cases the result was poor, with disintegration of the transplant, which had to be resected in some cases.

Volkov's report also includes 25 homologous whole-joint transplantations (20 knee joints and 5 hip joints). Since these cases had been observed for less than 4 years, it was considered too early to present any conclusions. This group also clearly includes cases with "rapid bony union, satisfactory mobility and reossification of the graft without loss of shape".

After personal studies with Volkov (Nilsonne 1967), I was convinced that homologous joint transplantation represents a valuable method for the reconstruction of large bone-joint defects. The present paper reports four cases of my own in which the therapy has been based upon the Russian method.

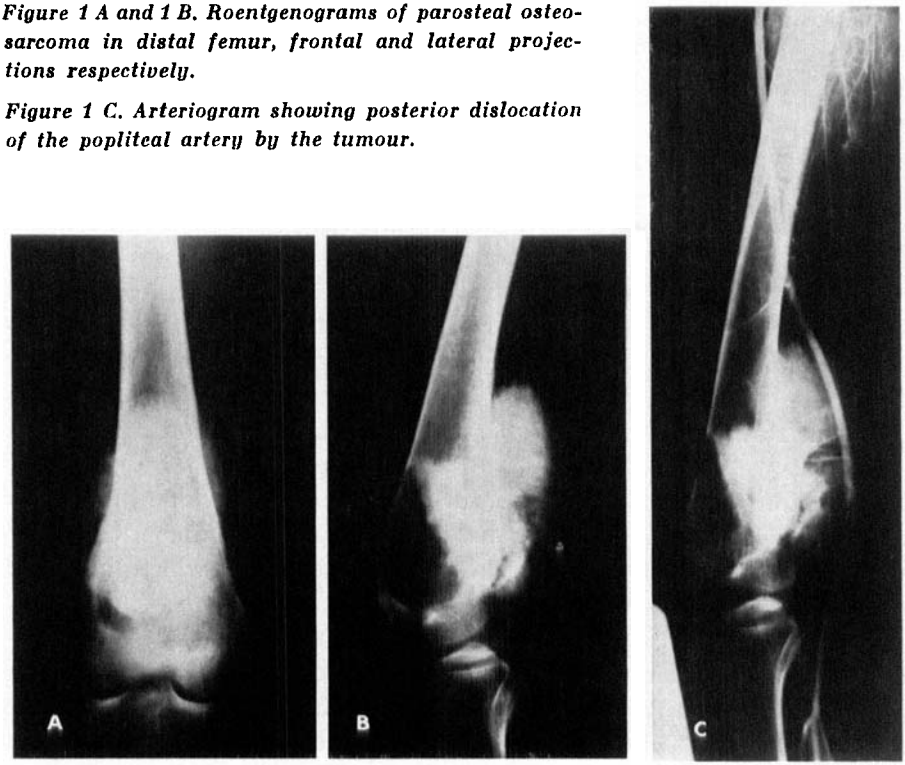
METHODS

The transplants were obtained from persons who had died of other causes than malignant tumour or an infectious disease. The suitable part of the skeleton (from the femur in all cases) was removed under normal, sterile surgical conditions less than 6 hours *post mortem*. Soft tissues were carefully scraped away from the diaphysis and the joint capsule was resected. The cruciate and collateral ligaments were retained in knee-joint grafts but not the round ligament in the case of grafts from the head of the femur.

The transplant used in Case 1 was sterilized in β-propiolactone immediately after it had been removed from the donor. It was then placed in the bone bank and stored at —20° C (no deep-freezer being available at that time). The transplants that were

Figure 1 A and 1 B. Roentgenograms of parosteal osteosarcoma in distal femur, frontal and lateral projections respectively.

Figure 1 C. Arteriogram showing posterior dislocation of the popliteal artery by the tumour.



taken later were placed in sterile plastic boxes, which were then sealed and placed in a deep-freezer (Industrial Products Laboratory Freezer IP–275) at —70° C and kept at this temperature for 24–48 hours. The temperature in the freezer was then raised to —20° C and the transplant was stored there for 1–4 weeks before use. The transplant was removed from the freezer about 1 hour before the calculated time of implantation and thawed in 37° C physiological saline solution to which a large dose of penicillin had been added. Bacteriological tests from the graft were negative both before and after the freeze treatment.

The surgical technique varied from case to case and is described in the following case reports.

MATERIAL AND RESULTS

Four cases of primary bone tumour were operated with homologous joint transplantation. In each case the conventional alternative to this reconstruction was amputation or exarticulation, in one case even hemipelvectomy.

Case 1

Woman, 20 years of age. Occasional slight pains in the right popliteal fossa for about one year, but it was only 14 days before admittance to the hospital that the

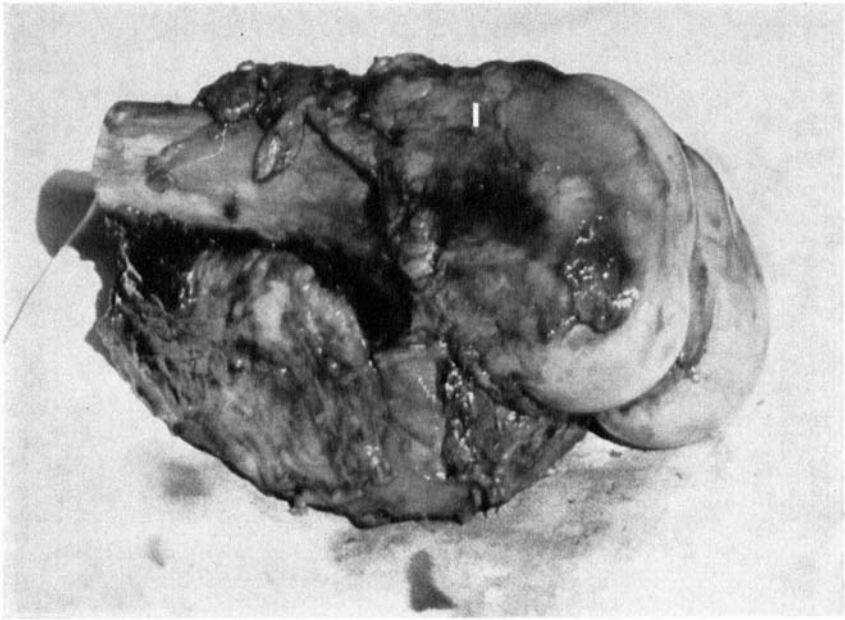


Figure 2. Resected distal femur, the tumour clearly visible behind and above the condyles.

patient had noticed a tumour there. At the clinical examination, a bony resistance the size of a tangarine was palpated in the right popliteal fossa. Roentgenography showed a well-defined, periostal tumour issuing from the popliteal surface of the femur. Osteolytic destruction was observed in the spongy bone of the femoral condyle, where the anterior cortex was thin. Angiography demonstrated dorsal dislocation of the popliteal artery by the tumour but no distinctly pathological vessels were seen (Figures 1a–1c). Biopsy showed that the tumour was a *parosteal osteosarcoma.*

Since the tumour was chiefly locally malignant, it was decided to avoid a femoral amputation and instead a radical, local resection was planned, followed by reconstruction with a homologous half-joint graft. At operation on 18 April 1966, the clearly encapsulated tumour was found to be growing expansively in the soft tissues. Vessels and nerves in the popliteal fossa were not engaged and could be moved to one side. After dissection, the femur was sawn through 16 cm proximal of the knee joint. The bone here was macroscopically tumour-free, and this was verified by frozen-section biopsy. The musculature was freed from the distal femur, the capsule of the knee-joint was cut ventrally and laterally at the level of the epicondyles but was extirpated dorsally, and the cruciate and collateral ligaments were severed at their attachments to the femur. The block resection of the distal femur, including the tumour, was completed after further soft-tissue dissection (Figure 2). The graft was now fitted into the defect and fixed to the patient's femur with two 6-hole plates (Figure 3a). The cruciate and collateral ligaments on the graft were sutured side-by-side to the corresponding structures in the patient.

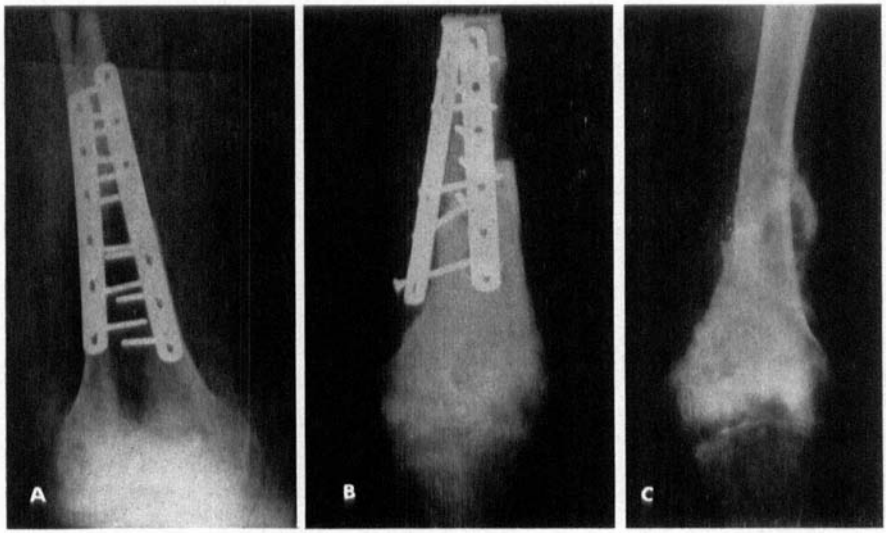


Figure 3. Roentgenograms at different stages after the transplantation.
Figure 3 A. Immediately after the operation.

Figure 3 B. 10 months later, infection and disintegration of osteosynthesis.

Figure 3 C. 21 months later, osteomyelitis of the transplant, no bony healing, signs of arthritis in the knee joint.

After this the knee-joint was found to be completely stable. The remains of the joint capsule were sutured to the graft and the musculature was placed loosely around it. After the operation the patient was placed in a large hip plaster and given prophylactic antibiotic therapy with penicillin and streptomycin.

The postoperative course was uncomplicated to start with but a rise in temperature and signs of wound infection appeared after 3 weeks. Cultures of the wound secretion showed the presence of *B. proteus*. The infection could not be arrested in spite of intensive, prolonged general and local treatment with antibiotics combined with repeated incisions and fistulatomies. X-ray examination showed destructive changes in the graft and loosening of the material used for the osteosynthesis (Figure 3b). Some periostal callus formation was seen from the patient's femur towards the graft but no true bone union.

At operation on 11 May 1967, the screws and plates were removed. The graft was found to be fairly firmly anchored to the femur with a hard fibrous callus. Bone samples were chiseled from the graft for histological examination. The presence of vital osteoid tissue was demonstrated and even the formation of new bone in the graft, besides the expected signs of chronic unspecific inflammation. The treatment with antibiotics was consequently continued as for an ordinary osteomyelitis, but without result.

In an attempt to drain the infection, a wide opening was chiseled along the lateral part of the graft on 28 September 1967 and the wound was left open. The graft could now be moved in relation to the femur. A further biopsy showed that

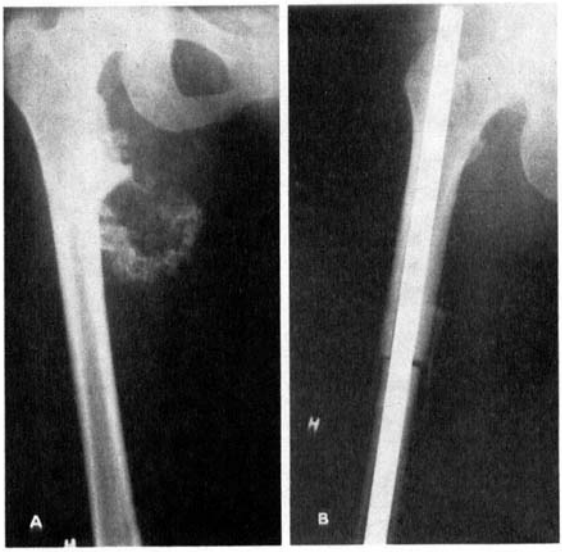


Figure 4 A. Chondrosarcoma in the region of the lesser femoral trochanter.

Figure 4 B. After resection of the proximal 20.5 cm of the femur. The transplant is fixed to the host femur by a Küntscher nail. Good fitting of the head of the transplant to the host acetabulum.

there was still vital bone in the graft. The infection persisted in spite of these measures, and X-ray examination on 1 February 1968 showed increasing destruction of the graft and no bony union (Figure 3c).

The infection has not had any effect on the patient's general clinical state. Apart from the rise in temperature at the onset of the infection, she has been sub- or afebrile. The sedimentation rate was about 70 mm/h to start with but more recently it has remained around 30 mm/h. There was a slight anaemia early in the follow-up period but not later. Total proteins in serum have been within normal values since the operation. The albumin fraction has remained low (minimum 44.6 per cent) and consequently albumin (albumin 20 per cent, Kabi) has been given intravenously on several occasions. Electrophoresis has also demonstrated elevated α_2- and γ-globulin fractions, the highest levels being 12.3 per cent and 24.1 per cent, respectively. The most recent examination, 1 February 1968, gave albumin 57.4 per cent, α_2-globulin 9.5 per cent, and γ-globulin 19.4 per cent.

Case 2

Woman, 36 years of age. After 6 months of slight pain in the right groin, the patient noticed a resistance proximal and medial on the right thigh 14 days before admittance. A bony tumour the size of a grapefruit was found on palpation. X-ray examination showed a highly calcified, round tumour issuing from the region of the lesser trochanter (Figure 4a). Chondrosarcoma was the probable diagnosis. No clinical or roentgenological signs of metastasis.

The conventional treatment in such a case would have been exarticulation at the hip or possibly hemipelvectomy. However, local resection of the tumour together with the proximal femur seemed to be feasible and was not contra-indicated for tumour-biological reasons. Treatment was accordingly planned as a major local

block resection with replacement of the defect by a homologous half-joint transplant.

At operation on 19 January 1967 the tumour was found to be growing expansively with a well-defined capsule. A Smith-Petersen incision was made and prolonged laterally to the distal femur. The proximal border of the tumour lay close to the ischial tuberosity but had not invalided this. The femoral vessels were moved to one side without difficulty. The iliopsoas muscle was severed about 5 cm proximal to the upper border of the tumour, after which the femur was sawn through transversely 20.5 cm distal of the tip of the greater trochanter. The capsule of the hip-joint was cut along the fibres on the ventral side; and after the round ligament had been severed, it was possible to dislocate the head of the femur. The gluteal musculature was removed from the greater trochanter and the block resection was completed after further soft-tissue dissection (Figures 5a and b). The defect was filled with a homograft. After reaming of the medullary cavities, the graft and the host femur were carefully aligned and fastened to one another with a Küntscher nail 40 cm long and 15 mm in diameter (Figures 4b and 5c). After reposition good congruence was noted between the head of the graft femur and the host acetabulum and movements in the joint harmonized. The capsule of the hip-joint was reconstructed by suturing it to the graft. The gluteal musculature was sutured anatomically to the greater trochanter of the graft. Some autologous bone grafts from the

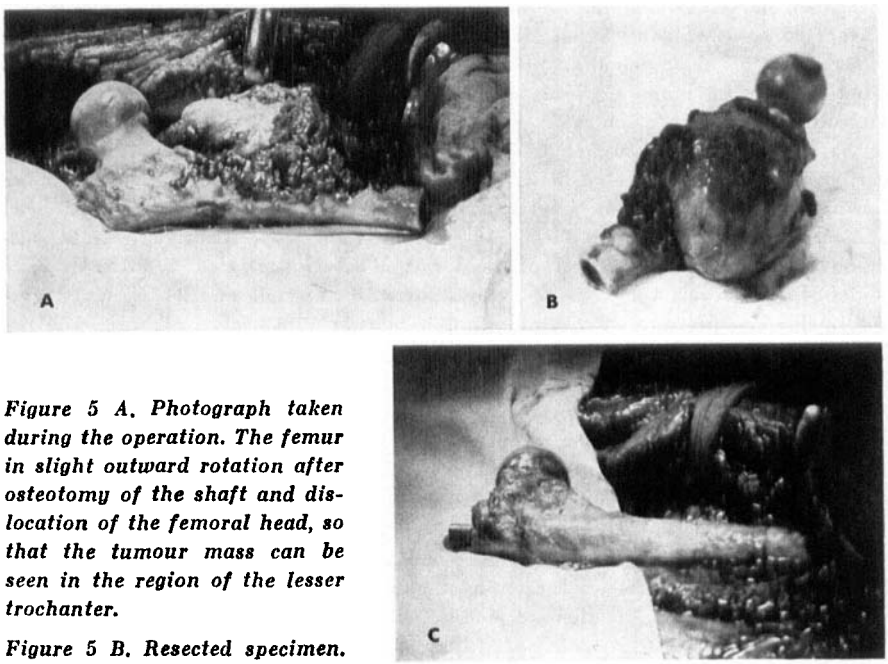


Figure 5 A. Photograph taken during the operation. The femur in slight outward rotation after osteotomy of the shaft and dislocation of the femoral head, so that the tumour mass can be seen in the region of the lesser trochanter.

Figure 5 B. Resected specimen.

Figure 5 C. The homograft is fixed to the host femur by a Küntscher nail, the head of the transplant has not yet been placed in the acetabulum.

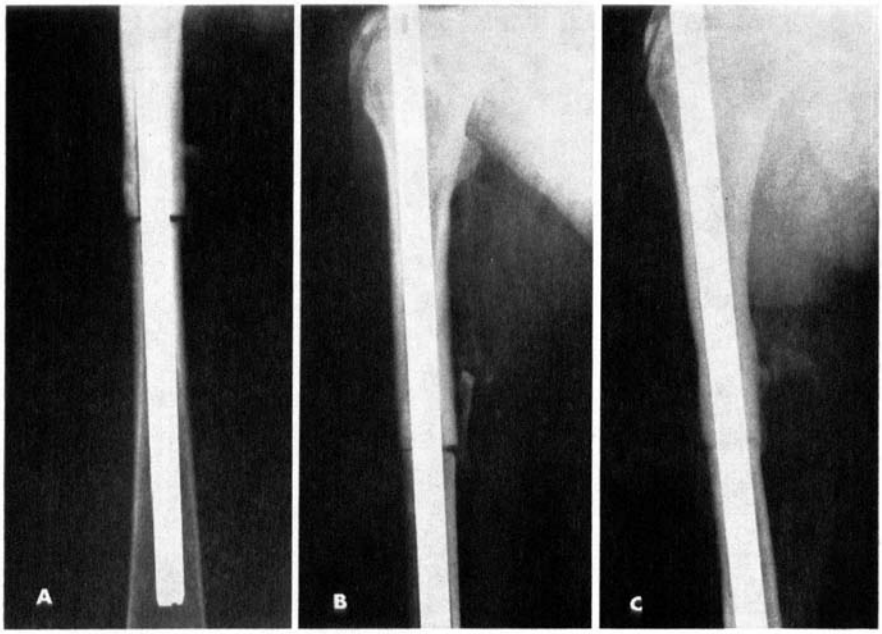


Figure 6. Roentgenograms at different stages after the transplantation.

Figure 6 A. After 4 months.

Figure 6 B. After 6 months.

Figure 6 C. After 13 months. Consolidation achieved in the region of osteosynthesis. No degenerative changes visible in the hip joint.

iliac crest were placed around the region of osteosynthesis on the shaft of the femur. The other muscles were positioned around the femur and the skin was sutured. A histological examination of the specimen confirmed the diagnosis of a well-differentiated *chondrosarcoma.*

After the operation the patient was placed in a hip plaster, which was removed after 2 months. Balanced traction was then applied to train knee mobility. After 4 months the patient was allowed up with no weight-bearing on the operated leg. Periostal ossification was already evident from X-ray examination, both between the homograft and the host femur and between the autologous grafts and the other components in the region of osteosynthesis (Figures 6a–6c). The ossification continued unabated, and after 10 months the osteosynthesis was judged to be sufficiently stable to permit careful weight-bearing. The clinical assessment 13 months after the operation is that bony union has been achieved. The roentgenological structure of the graft is normal throughout its length, including the head of the femur, and there are no signs of degeneration of the joint. Full weight-bearing is now permitted (15 February 1968) and is not painful. Active extension-flexion on the operated side is 180–90° in both the hip and the knee joint. The quadriceps muscle is weak but the patient can lift the leg in the supine position. There is good

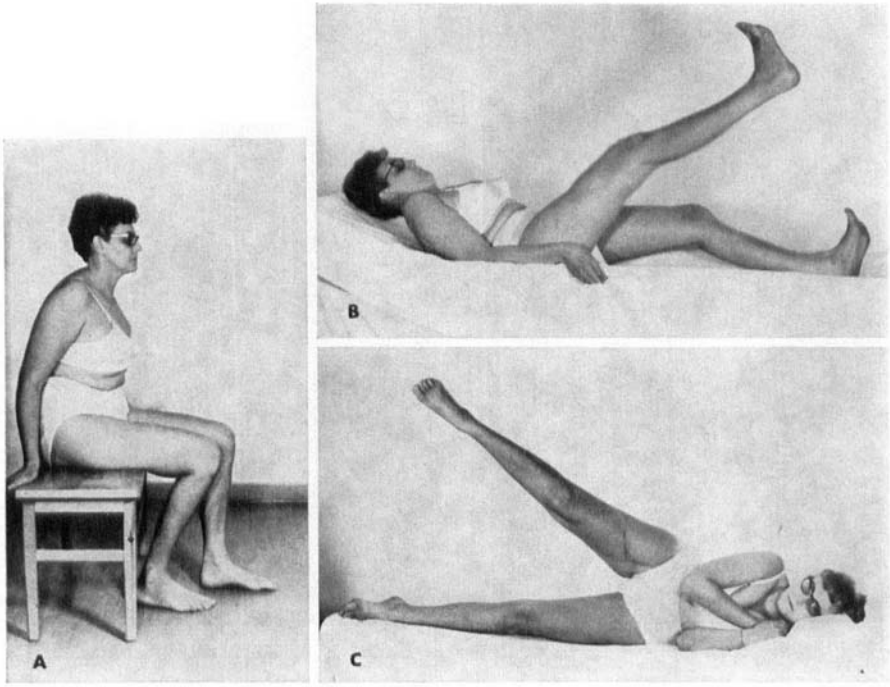


Figure 7. Case 2. Photographs showing the ranges of active and passive mobility in the hip and knee joint of the operated leg (right) 13 months after the operation.

active abduction in the hip-joint and the passive rotational mobility is normal (Figure 7).

A subfebrile temperature characterized the first two postoperative weeks, after which the temperature has been normal. The sedimentation rate has been normal throughout. During the first two weeks there was also an anaemia as well as reduction of total proteins in serum to 5.5 per cent and the albumin fraction to 44.3 per cent. These parameters soon returned to normal after blood transfusions and intravenous administration of albumin and they have subsequently remained within normal limits. Electrophoretic controls showed elevated α_2-globulins during the first weeks followed by a return to normal levels. There was no rise in the γ-globulin fraction. The patient's general condition has been entirely unaffected throughout the follow-up period.

Case 3

Woman, 42 years of age. Pains and a swelling in the left knee that gradually grew in the 3 months before admission. X-ray examination showed a cystic, well-defined destruction in the lateral femoral condyle (Figure 8a). Biopsy gave the diagnosis *giant cell tumour grade II–III*. After treatment with curettage, the cavity was filled with heterologous bone transplants (Kieler-Knochenspan) (Figure 8b). Bony union seemed to be taking place at first but after about one year there were roentgenological signs of local recurrence of the tumour (Figure 8c). Another biopsy

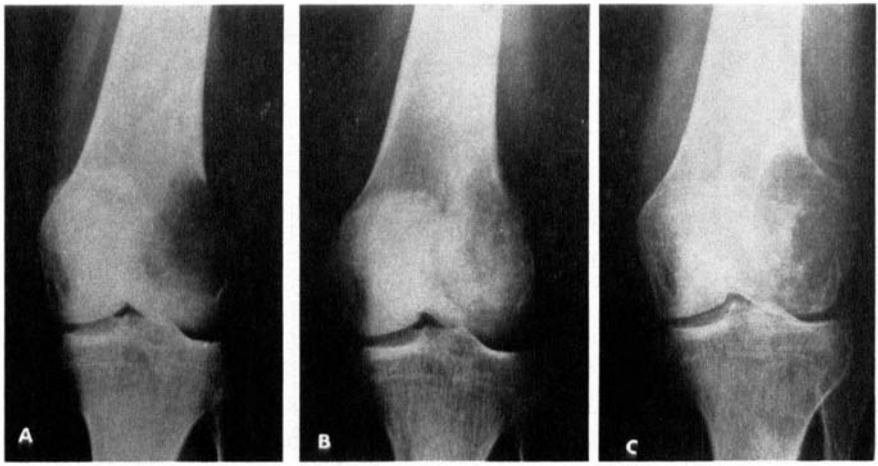


Figure 8 A. Giant-cell tumour in the lateral condyle of the femur.
Figure 8 B. After curettage and filling of the cavity with heterologous bone.
Figure 8 C. Recurrence of tumour 1 year later.

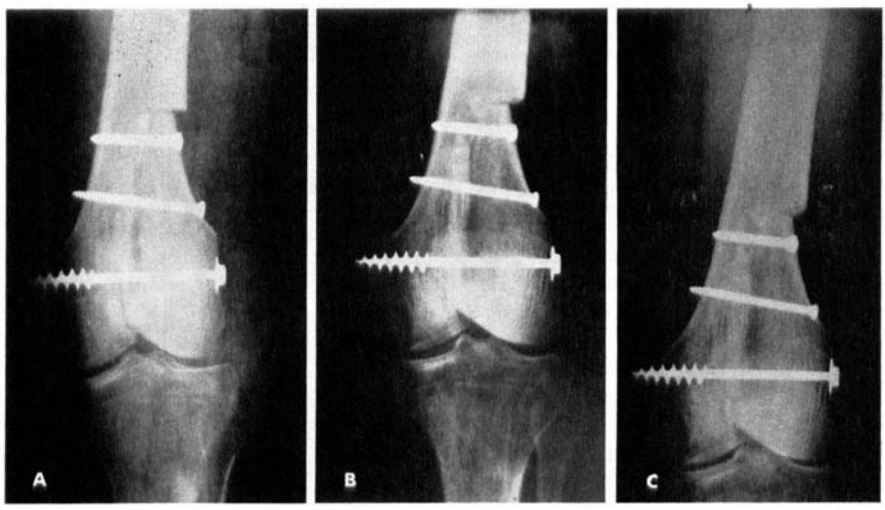


Figure 9 A. After resection of the lateral, distal part of the femur, the homograft being fixed in its bed.
Figure 9 B. 4 months after the transplantation.
Figure 9 C. Consolidation 10 months after the transplantation.

indicated that the giant cell tumour still belonged to grade II–III. It was therefore considered justifiable to treat the tumour by local resection.

At operation on 25 April 1967, it was found that the tumour had penetrated the cortex dorsally and laterally but that it was growing expansively with a well-

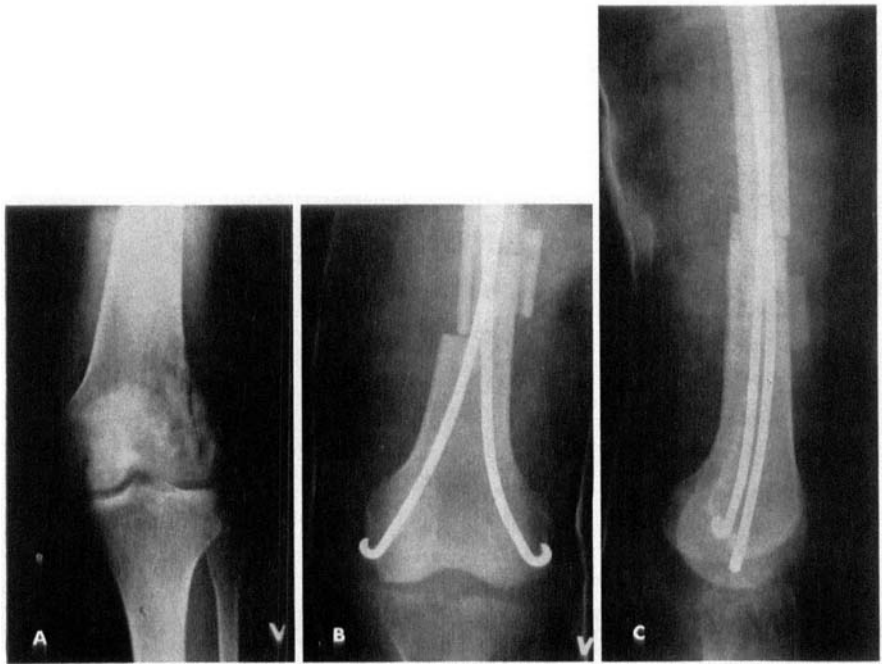


Figure 10 A. Central fibrosarcoma in the distal femur.

Figure 10 B and C. The distal femur has been resected and a homograft put in place. The transplant is fixed to the host femur by Rush pins, stability in the region of osteosynthesis also being secured by step-cut osteotomies.

defined capsule. This made it feasible to resect the whole of the lateral femoral condyle including the tumour. The medial plane of resection was placed next to the attachment of the cruciate ligament, the proximal 10 cm from the articular surface of the condyle. The posterior cruciate ligament and the lateral collateral ligament were sacrificed. The defect was filled with a homograft, which was fixed with screws (Figures 9a). It was not possible to reconstruct the joint capsule.

Postoperatively the entire leg was kept in plaster for 4.5 months, after which knee mobility was exercised without weight-bearing. X-ray examinations showed progressive bony union of the graft. After ten months the union appeared to have consolidated (Figures 9b and c) and weight-bearing was started. The knee joint is completely stable with an active range of movement of 175–140°. There is no pain on weight-bearing.

The immediate postoperative reaction was moderate with a slight temporary rise in temperature and an increase in the sedimentation rate. Total proteins in serum were normal but the albumin fraction fell to 54.7 per cent, and α_2- and γ-globulin rose to 10.0 per cent and 20.3 per cent respectively during the first weeks. All these parameters subsequently returned to normal spontaneously. The patient's general condition was excellent throughout.

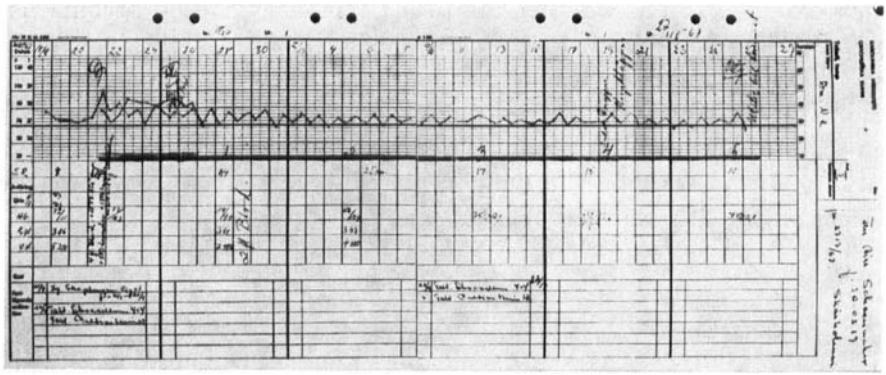


Figure 11. Temperature chart showing the mild reaction after homografting.

Case 4

Woman, 37 years of age. Diffuse, moderate ache in the left knee for about 5 months. More severe pains after a fall from a bicyle led to an X-ray examination. An irregular, patchy destruction was observed in the distal femur, most pronounced in the lateral condyle (Figure 10a). Biopsy showed that the change was due to a *central fibrosarcoma* of low malignancy (tissue resembling that in desmoplastic fibroma of bone was demonstrated in parts of the tumour).

At operation on 21 September 1967, block resection of the distal femur was performed 16.5 cm proximal of the articular surfaces of the femoral condyle. The resection was macroscopically radical, and this was verified by histopathological examination. The defect was filled with a homologous half-joint transplant that was fixed to the host femur with two Rush pins (Figures 10b and c). The surfaces of the osteosynthesis were shaped as for a Z-shaped osteotomy. Autologous cortical bone grafts from the femur were placed next to the region of osteosynthesis. In the knee joint, the cruciate and collateral ligaments on the graft were sutured side-by-side to those of the host. The joint capsule was sutured to the transplant. The entire leg was encased in plaster after the operation, and this treatment is still in progress. An X-ray examination 1 February 1968 showed signs of a periostal callus.

The postoperative course was entirely uneventful. There was hardly any rise in either the body temperature or in the sedimentation rate (Figure 11). There was no anaemia and total proteins in serum were normal. The albumin fraction dropped temporarily to 51.2 per cent at the same time as α_2-globulin rose to 11.0 per cent and γ-globulin to 19.0 per cent after which normal values were recorded. The patient's general condition was entirely unaffected.

IMMUNOLOGIC STUDIES

Immunologic tests were conducted in Cases 1 and 2 nineteen and ten months respectively after the transplantation in collaboration with the Research Laboratory Surgical Clinic at Serafimerlasarettet. The test

was designed to tell whether the host's lymphocytes had become immune to the homograft. Using a method reported by Coulson & Chalmers (1964), lymphocytes were isolated from peripheral venous blood from the patients. The lymphocytes were then placed on monolayer cultures of five different human fibroblasts according to Möller et al. (1967). In no case did the lymphocytes appear to have any cytotoxic effect on the different fibroblasts.

DISCUSSION

The results in these cases of homologous joint transplantation must be regarded as preliminary because the observation time is still so short. The favourable findings to date nevertheless make it worth reporting the observations of a theoretical and practical nature that are associated with the method employed.

The essential innovation in the procedure concerns the pre-treatment of the homograft. The deep-freeze technique seems to be a prerequisite for a successful transplantation. Lexer and his contemporaries, who generally performed direct transplantation between donor and host, admittedly achieved surprisingly good bony union in some cases. Degenerative changes in the graft frequently appeared quite soon, however, which is probably why the method was abandoned. In contrast to this, the Russian technique, by which the transplant is frozen at —70°, has resulted in good union between the homograft and the host bone in a majority of both the experimental (Imamaliev) and the clinical (Volkov) cases. The transplants in Cases 2, 3, and 4 in the present series were pre-treated according to the Russian technique and the absence of any postoperative reaction was analogous to the results of the authors cited.

Theoretically, too, a temperature of —70° should be suitable for preserving massive bone-joint transplants. It has thus been shown that at —70° the tissue fluids form ice crystal *intracellularly* whereas at —20° they chiefly form *extracellular* ice crystals (Meryman 1957). The shorter the time taken to freeze the specimen, the more the intracellular reaction will predominate. The capacity of the present freezing unit is such that the specimen are calculated to have been frozen to a homogenous temperature of —70° in about one hour. This treatment probably resulted in the definite destruction of all the cells in the transplant.

This assumption is supported by the immunologic studies, which

showed that the host's lymphocytes had no cytotoxic effect on the fibroblasts tested. It must be admitted, however, that these tests could not be made with fibroblasts from the specific donor of the graft. On the other hand, it seems reasonable to draw a parallel with patients receiving homologous skin grafts. These patients' lymphocytes thus have a cytotoxic effect on most of the fibroblasts tested, which suggests that there is a high incidence of cross-reactivity. One would expect to find the same high incidence of cross-reactions regardless of the type of tissue transplanted since the transplantation antigens are probably represented on all nucleated cells. The negative results in Cases 1 and 2 suggest that the patients had not become immune, probably because the graft did not contain viable cells at the time of the operation.

Another consequence of freezing the transplants is an effective sterilization of them. This was confirmed by the negative bacteriological tests after the transplants had thawed as well as by the aseptic course in Cases 2, 3, and 4. Intensive postoperative antibiotic treatment is nevertheless called for in view of the length of the operation, which was about 6 hours for the most massive transplantation. The conservation technique employed in Case 1 (sterilization with β-propriolactone and storage at —20°) must be considered in connection with the postoperative infection. Sterilization of vascular grafts, heart valves, bone grafts, etc. with β-propriolactone is recommended by Lo Grippo et al. (1957). Investigations concerning this clinic's conventional bone bank, which is run at —20° (Hult 1950, Nilsonne 1963), have not revealed any appreciable complications in the form of infection. It is thus unlikely that the bone-bank technique was responsible for the local infection in Case 1. Contamination of the wound in some other way was probably responsible for this.

The surgical trauma involved in a joint transplantation can be classified as moderate. The general condition of all the patients was thus very little affected in the postoperative phase. The typical postoperative effect comprised slight anaemia, moderately elevated sedimentation rate, depressed albumin level, and a rise in α_2-globulin and γ-globulin. These reactions were transient in Cases 2, 3, and 4, the value returning to normal a few weeks after the operation. These findings are similar to the results reported by Åsén et al. (1965) for surgical trauma in the treatment of fractures and non-union of the lower leg. The metabolic reactions in the present cases are thus not specific for homologous joint transplantations. The more prolonged disturbances registered in Case 1 are ascribable to the infection.

As pointed out above, the homograft consists of dead tissue. There is no viability to start with either in the osteoid tissue or in the articular hyaline cartilage. The graft must be absorbed, reconstructed, and incorporated by the invasion of host tissue. This process was followed on the X-ray from the callus formation in the region of osteosynthesis. At the same time, it is remarkable how well the homograft in Cases 2, 3, and 4 retained not only its outer shape throughout the process but also the typical trabecular bone structure in the meta- and epiphyses. It has not been considered necessary to make bone biopsies for histological checks in these cases because the X-rays indicate that creeping substitution of the graft's osteoid component is taking place. Neither have histological studies been made on the cartilaginous component, the articular cartilage, for fear of disturbing the intra-articular adaption. No roentgenological change has been observed in the structure of the transplanted joint components, nor are there any signs of osteoarthritis (except in Case 1, in which osteomyelitis and septic-arthritis have developed). The observation time in Cases 2, 3, and 4 is still short (max. 13 months), however, and more definite conclusions must await the result of prolonged functional utilization of the homograft.

The most noteworthy bone-biological reaction occurred in Case 1. Callus formation was poor and a clinically manifest osteomyelitis developed with pronounced macroscopic destruction of the graft. Even so, biopsies from the graft 12 and 16 months after the transplantation showed histological signs of vital bone tissue. In spite of the osteomyelitis and the non-union between the host bone and the graft, the latter was being transformed in a viable direction. This was most probably the result of the graft being invaded by vessels from surrounding tissue, which thereby created channels for osteoid tissue. A healing mechanism of this type has been demonstrated in experimental fractures by Göthman (1961). The observation emphasizes the importance of further studies on the induction of osteogenesis.

In choosing a method of fixation to promote osteosynthesis between the graft and the host bone, consideration must be paid to the need for stability as well as the creation of optimal conditions for callus formation. In Case 2 this problem was resolved by reaming the medullary cavity until its circumference was exactly the same in the host bone and the graft; exceedingly rigid fixation was then achieved with the medullary nail. In the other cases, compression was achieved with screws or Rush pins. The importance of good internal fixation is also heavily emphasized by Volkov, who recommends step-cut osteotomies

in the region of osteosynthesis as an extra precaution against lateral dislocation. This was done in Case 4. The contact surfaces are larger with this type of osteotomy and callus formation is accordingly facilitated. The addition of autologous bone grafts to the region of osteosynthesis in Cases 2 and 4 should theoretically stimulate callus formation still further.

Stable internal fixation is also essential for early exercise of the operated and the neighbouring joints. It may be possible to start such exercises sooner after the operation than has been attempted to date. A good muscle pump improves the local circulation, which is important for incorporation of the homograft. Restitution of the graft takes a long time and the union must be sufficiently stable before weight-bearing can be permitted. Volkov and Ottolenghi recommend total non-weight-bearing for 10–12 months. This practice has been adopted in the present cases with good results to date.

It is still too early to assess the importance of reconstructing the ligamentary apparatus. This was done in the knee joint in Cases 1 and 4. If normal or almost normal joint mobility is achieved postoperatively, however, some ligamentary function will presumably be required to ensure stability in the joint.

A central question in the discussion of homologous joint transplantation concerns the indication for this operation. From a simple mechanical point of view, the indication is a desire to substitute a bone-joint defect. In other words, it is a question of performing an arthroplasty with biological material in order to achieve true bony union. Defects that can be treated in this way may arise, for instance, after radical resection of primary skeletal tumours located close to a joint. Five of Ottolenghi's seven cases thus concerned giant cell tumours and Volkov also regards skeletal tumours as one of the main indications for homologous joint transplantation. Volkov's other indications include skeletal defects after osteomyelitis, tuberculosis, or trauma as well as dysplasia of joint components. Merle d'Aubigné et al. recommended massive homografts in the surgical treatment of giant cell tumours, parosteal osteosarcoma, and certain types of chondrosarcoma.

In the present series of homologous joint transplantation, Case 1 had a parosteal osteosarcoma, Case 2 a well-differentiated chondrosarcoma, Case 3 a giant cell tumour, and Case 4 a central fibrosarcoma.

In the case of parosteal osteosarcoma, it seems to be agreed that radical resection is the method of choice (Copeland 1965, McKenna et al. 1966). The present case of chondrosarcoma most closely represented

a well-differentiated peripheral chondrosarcoma, for which radical resection is also justified (Lichtenstein 1965, McKenna et al., Dahlin 1967). Local resection has been recommended if possible in cases of giant cell tumour (Sherman 1965, Lichtenstein 1965). The proximity of a joint, however, often leads to curettage being tried first, but the frequency of recurrence is high. The possibility of joint transplantation makes resection a considerably more adequate measure. In the case of central fibrosarcoma, it is not certain whether amputation is necessary or whether local resection is sufficient. In Case 4 the fibrosarcoma was well differentated, which justified the treatment with block resection (Jaffe 1965, McKenna et al. 1966).

There were thus clear indications for local surgery in these four cases. Such cases would previously have been treated with amputation for want of suitable substitution material. The use of a homologous joint transplantation makes it possible to avoid disfiguring measures without endangering the biological principles for treatment of the tumour. This opens up new possibilities for the treatment of primary bone tumours.

SUMMARY

Four cases of homologous joint transplantation in man are presented. The indication for this surgical treatment was the presence of a primary bone tumour, which was resected together with the articular end and part of the shaft, in one case of the proximal femur, in three cases of the distal. The observation time is still short. In two cases there was complete roentgenological and clinical union within 10–12 months. The patients are allowed full weight-bearing, which is not painful and is performed with good active and passive mobility in the operated joints. The theoretical, technical, and surgical problems in homografting of bone and joint components are described and discussed.

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