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Leader

Articular tissue grafts

The dilemma of how best to treat a patient with articular cartilage damage, whether it be early, from trauma, osteochondritis, or tumour, or late, from primary or secondary osteoarthritis, has taxed orthopaedic surgeons for generations. Although late osteoarthritis can be successfully treated for 10 to 15 years in major joints such as the hip or knee by replacement prostheses, these have a finite life owing to wear, loosening, and material failure and are thus of little value to young patients.

As a result many patients with early cartilage damage due to trauma, osteochondritis, avascular necrosis, chondromalacia, and early osteoarthritis are at present untreatable. Attempts to promote joint surface healing by fibrocartilage of denuded areas of articular cartilage following drilling were first described by Pridie¹ and, although the results were promising in these patients reported by Insall,² the clinical experience of this method has proved disappointing. Similarly, although juxta-articular osteotomy of the femur has been reported to produce repair in some cases by stimulating proliferation of fibrocartilage from the surface of the hip joint,³⁻⁵ this is an unpredictable phenomenon. Furthermore, in no other joint has repair of articular surfaces been stimulated in such a way as to be clinically useful. As a result many attempts have been made to replace articular surfaces with allografts and in some instances xenografts.

Partial joint allografts

In 1908 Judet transplanted osteochondral allografts of half joints and whole knee joints in rabbits beneath the skin and in two cases into physiological sites.⁶ He concluded that joint transplantation was more successful when the capsule was transplanted with the joint, and the best results were obtained if the capsule and the joint surface formed a physiological entity. Coworkers, however, found superior results with joints in which the capsule was excised.^{7,8} In 1913 Pucci introduced a further factor by carrying out a total of 21 whole joint and half joint elbow allografts, some of which were fresh and some after preservation from one to eight days at 0°C.⁹ He reported 18 good results out of 21. Following this, numerous comparisons of autografts and allografts were carried out and also allografts which were composed of differing amounts of articular cartilage and subchondral bone. These varied from a small osteochondral shell allograft to a total joint allograft (fig 1). In general, the autografts were successful provided that sepsis was avoided and allografts had a high proportion of failures due to rejection.

Total joint allografts

Total joint allografts have been studied in animals with and without vascular anastomoses. When transplantation was carried out without vascular anastomoses in dogs by Herndon and Chase¹⁰ they achieved uniformly good results in 120 autografts, but the 19 allografts showed slow degenerative change and even after two years, replacement of the bony component of the graft was not complete. When vascular anastomoses were carried out by Reeves in 1968 rejection occurred in all cases unless the recipients were treated with azathioprine as an immunosuppressive drug.¹¹ It became obvious that for an allograft to survive the articular cartilage should be healthy, but that rejection occurred through the medium of the marrow component of the bone which was transplanted with the cartilage. As there was no method for achieving adhesion of cartilage alone to host bone this method raised a fundamental problem. In 1968 Chesterman and Smith reported 50% of successes with 24 femoral head shell allografts over five and a half years in dogs.¹² They thought that the failures were due to inadequate fixation and not to rejection and as a result, Burwell devised a precisely fitting graft for transplantation in sheep to try to overcome this problem.¹³ Over a longer period of time, however, gradual destruction of the allografts occurred in about 60% of cases.

Articular cartilage allografts

Since the first allografts of cartilage were transplanted by Leopold¹⁴ in 1881 into the anterior chamber of the eye, where they increased in size, it was known that cartilage alone was less likely to undergo rejection. Several authors, in particular Bacsich and Wyburn, reported prolonged survival of costal cartilage allografts implanted subcutaneously in guinea pigs and rabbits.¹⁵ In 1971 McKibben

Figure 1 Types of osteochondral allograft.

transplanted immature sheep articular cartilage into femoral condyles of mature and immature recipients.¹⁶ The grafts survived and it became apparent that articular cartilage itself with its avascularity and protective matrix could survive as an allograft alone. Furthermore, there was a suggestion that immature articular cartilage had greater powers of resistance to the allograft reaction.

The second approach avoiding the use of bone has been to transplant chondrocytes in the hope that they would proliferate in the articular defect and effect repair. Thus in 1971 Bentley and Greer transplanted chondrocytes, which had been isolated from the matrix by enzymatic digestion, into the articular surfaces of rabbit knees.¹⁷ They found that both isolated epiphyseal and articular cartilage chondrocytes transplanted into articular surfaces were incorporated without rejection (fig 2).

In the initial experiments of Bentley and Greer the allografts of chondrocytes are thought to have failed in some instances not because of rejection but because of dislodgement from the grafted area. In view of this Aston and Bentley carried out a series of experiments in which articular cartilage and epiphyseal cells were cultured for periods of up to six weeks.¹⁸ The aim of this technique was twofold: (a) to produce cultures which were physically firmer, were easy to handle and therefore able to be placed into a defect; and (b) to endeavour to produce a material which had normal matrix constituents, particularly type II collagen, which is unique to articular cartilage.

Aston and Bentley found that after six weeks in culture, articular cartilage cells produced a matrix which was similar in most respects to hyaline cartilage and, in particular, was positive for type II collagen. Also, 30 times the number of cells were produced in six weeks, which opened up the possibility of a cartilage 'bank'. Further experiments were carried out in which this cultured material and whole plugs of articular cartilage were transplanted into adult rabbit knees.¹⁹ Examination of the grafts at the end of one year showed 84% successful incorporation with the solid plugs and 64% using cultured chondrocytes. In a further series of experiments in which early arthritis was produced by injections of the enzyme papain into rabbit joints, similar survival figures were achieved. There was no evidence of rejection and failures all seemed to be due to mechanical loosening of the graft at an early stage (fig 3).

Human allografts

The application of allografts in humans was sporadic after Tuffier's half joint autograft in 1901 of the femoral head in a

Figure 2 Section of rabbit articular surface six weeks after implantation of isolated chondrocytes. Total filling of the defect by cartilage which is incorporated into the host without rejection is seen. (Toluidine blue.)

Figure 3 Section of rabbit articular surface 12 months after implantation of a whole plug of articular cartilage showing incorporation of the allograft. (Toluidine blue.)

patient who had had a fractured humerus.²⁰ A report at four months suggested that the graft was surviving but no long term follow up was reported. In 1908 Lexer reported the results of five whole joint and four half joint allografts in man.²¹ The whole joints were four knees and one elbow all taken from fresh amputations. He reported three excellent results in knee joint transplantations, but again progressive deterioration of the articular surfaces occurred, though function remained good over two years. By 1925 Lexer had performed a total of 25 whole joint allografts²² and he claimed 12 or 13 permanent cures in nine knee joints and three finger joints. Bürkle-de-la-Camp examined two of Lexer's whole joint allografts 14 and 16 years after operation.²³ He found that fibrocartilage had replaced the destroyed articular cartilage, but otherwise the tissues were viable. Apart from a few remnants of cruciate ligaments, the intra-articular ligaments and menisci disappeared. This suggested that the bony component could be replaced but that the prospects of achieving good results from this technique were low.

Whole joint allografts

The largest experience with whole joint allografts was reported by Volkov in 1970, who had performed 15 of the knee, three of the hip, and two of the elbow.²⁴ In 14 knees partial destruction of one surface was seen after 18 months, especially in the tibial portion, and the failure was attributed to tissue incompatibility. Rejection was reported in 12% overall, but long term results were not reported.

Osteochondral allografts

In recent years most osteochondral allografts have been frozen in an attempt to reduce their antigenicity. Merle D'Aubigné and Dejouany used frozen massive osteochondral allografts to replace bone and joint surfaces resected for tumour at the knee in nine patients, with reported successful incorporation of the grafts.²⁵ This method has been continued by other workers—notably, Ottolenghi²⁶ and, more recently, by Mankin *et al*²⁷ in Boston. The antigenicity of bone has been diminished by freeze drying, but the process destroys some if not all of the articular cartilage and attempts have been made to find methods of preserving the articular cartilage by using such substances as glycerol and dimethyl sulphoxide. Also, this method theoretically requires the incorporation or replacement of large amounts of allograft bone, which calls for prolonged splintage of the affected limb. Fracture of the bony component of the graft and infection rates of over 20% with this technique have been reported. Thus the complications are considerable and only worthwhile in limb preservation for tumours where the alternative is amputation.

It is apparent that the less bone that is used in a transplant, the better the chance of success. This has led to the increasing use of small grafts (shell allografts) in which only 1 cm or less of bone with the overlying articular cartilage is used as a transplant. This method has been pioneered by Langer and Gross²⁸ based on the work of Chesterman and Smith¹² and successful results in up to 69% of patients have been achieved over 10 years when used for replacing articular surfaces at the knee damaged by osteochondritis dissecans, osteochondral fracture, avascular necrosis, and early osteoarthritis.

Clinical applications of allografts

For the past 10 years clinical applications have been progressing in parallel with the use of freeze dried massive osteochondral allografts for replacement of tumours, where death of articular cartilage is not so important. For replacing articular surface damage, living cartilage has been used: (a) with a minimum of bone as shell osteochondral grafts or (b) with living intact cartilage plugs or (c) with chondrocyte cultures.

The clinical situation has been brought into focus because of the increasing incidence of early articular cartilage damage recognised by the use of arthroscopy and magnetic resonance imaging. Thus a new group of patients with sports injuries and early osteoarthritis is being recognised in whom early cartilage damage is seen. Thus far osteochondral allografts have been used with considerable success by Langer and Gross, who discovered that acceptable results could be achieved with small osteochondral allografts without matching the donor and the recipient of the osteochondral graft.²⁸ These pioneers established criteria for harvesting articular cartilage allografts from renal transplant donors and for the precautions required to prevent transmission of infection. Their results for established osteoarthritis were in the order of 60% over a five

Figure 4 Lateral radiograph of the knee of a 16 year old girl who had sustained a compression fracture of the lateral femoral condyle five years previously.

Figure 5 Lateral radiograph of the knee of the same patient showing a well incorporated osteochondral allograft three years later.

year period, but the series was complicated by a low but definite infection rate of about 5–10%. Bentley *et al* (unpublished data) carried out transplants in seven carefully selected patients with osteochondritis, old osteochondral fractures, and early osteoarthritis of the knee, with success in five over a three to five year period (figs 4 and 5). It appears essential, however, to replace the whole of the damaged area of cartilage and, furthermore, to correct any angular deformity of the joint before transplantation by osteotomy to avoid excessive loading of the graft, which may lead to fracture of the bony component.

Composite grafts

In recent years Muckle and Minns have developed the concept of replacing defects in articular surface with a woven carbon insert with the idea of supporting the repair fibrocartilage formed from the subchondral bone.²⁹ This method has some appeal in the sense that the carbon fibre may act as a matrix for the fibrocartilage forming in defects of articular surfaces in much the same way as collagen does in normal hyaline cartilage. A recent independent clinical review of this technique used in patients with early osteoarthritis, chondromalacia, and osteochondritis dissecans indicated that the clinical result was satisfactory in 70%.³⁰ A prospective study of patients randomly allocated to this method and to the control drilling method is presently being carried out in this unit, in which all patients undergo check arthroscopy of the knee one year after the implantation. Preliminary results in eight of 11 patients have shown good clinical results with formation of a good healing surface seen on arthroscopy (fig 6).

This raises the interesting question of whether carbon fibre could be used to support chondrocyte allografts in humans. As a result in the articular cartilage laboratory at Stanmore experiments have been performed which show that animal chondrocytes can be grown in woven carbon and produce normal matrix constituents of proteoglycan and

type II collagen as demonstrated by fluorescent antibody techniques³¹ (fig 7). Thus there is a possibility of a composite graft of carbon fibre or some other material in which living chondrocytes are grown which can then be used to replace and fill defects in articular surfaces.

Conclusion

It appears that the use of osteochondral allografts to replace defects in articular surfaces of the knee and some other joints caused by osteochondritis, traumatic chondromalacia, osteochondral fractures, and avascular necrosis of the femoral condyles gives successful results in 80% or more of

Figure 6 Arthroscopic appearance of woven fibre mesh implanted into the femoral articular surface for osteochondritis dissecans one year previously. The incorporation of the mesh, which is covered with smooth fibrocartilage, is apparent.

Figure 7 Section of preparation of woven carbon with living chondrocytes after six weeks in culture. The fluorescence indicates the presence of type II collagen.

cases over five to 10 years. The recognition of transmissible viruses, particularly hepatitis B, cytomegalovirus, and HIV, however, has led to concern about the possibility of transmission of these diseases by such grafts. In the case of bone allografts it is now accepted practice not to carry out allotransplantation until at least 90 days from the harvesting of the graft. This gives an opportunity to recheck the donor of the graft or the recipient of an organ such as the kidney, heart, lung, etc. Therefore studies are continuing to assess the cellular viability and matrix integrity using radioactive isotope methods of human articular cartilage stored in nutrient tissue culture medium over periods of three months. The hope is that articular cartilage will be stored in a satisfactory condition for three months or more in the cartilage bank and thus be available as and when necessary without the risk of transmission of virus diseases.

Woven carbon mesh used alone has given good symptomatic relief of pain in 70% of patients over five years and is a worthwhile and innocuous procedure for small defects of 3 cm in diameter or less.

The use of intact cartilage plugs countersunk into the articular surface, of cultures of chondrocytes alone and cultures of chondrocytes within a supporting woven carbon matrix meshwork, appears very promising in animals. These methods have exciting possibilities for the control of symptoms from painful disabling conditions in young patients who have joint surface injuries and in the long term prevention of progressive joint breakdown and disabling osteoarthritis in many patients.

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