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Meniscal replacement using a porous polymer prosthesis: a preliminary study in the dog

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A porous polyurethane prosthesis was used to replace the lateral meniscus in the dog. After an initial ingrowth of fibrous tissue, the prostheses became filled with tissue strongly resembling normal meniscal fibrocartilage. Although less severe than seen after total meniscectomy, cartilage degeneration was frequent, possibly because tissue ingrowth in the prostheses occurred too slowly. Porous polymers can be useful for replacement of the meniscus, provided that chemical and physical properties are optimized. Copyright © 1996 Elsevier Science Limited

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Nowadays there is an increasing understanding of the functional significance of the meniscus in load bearing[1], shock absorption[2], knee joint stability[3] and possibly joint lubrication[4]. Meniscectomy results in abnormal high concentrations of stress on the articular cartilage in the meniscectomized compartment[1] which, over time, results in degenerative changes. Such events have been demonstrated by long-term surveys of meniscectomized patients, as well as by experimental studies using laboratory animals[5–9].

The increasing awareness of the consequences of meniscectomy has induced a more conservative approach towards meniscal lesions. Since it has been shown that the degree of degenerative changes found after meniscectomy is directly proportional to the extent of meniscectomy[5], the basic principle is to preserve as much functional meniscal tissue as possible while addressing the clinical symptoms caused by tears. Although partial meniscectomy reduces degeneration of articular cartilage, lowers morbidity and improves earlier return to activity[9–11], the contact area within the joint still decreases when compared to normal and degeneration of cartilage is not prevented.

Therefore, repair of meniscal lesions preserving all meniscal tissue is a more preferable alternative. However, owing to the limited vascularity of the meniscus[12], the possibilities for repair are limited and only lesions limited to the vascular periphery can be repaired adequately[13–15]. No reliable methods exist for lesions situated in the avascular central part of the meniscus, although new experimental techniques are in development[16,17].

However, sometimes the extent of meniscus damage is so great that partial meniscectomy or repair are not appropriate and total meniscectomy is the only alternative. Considering its severe consequences, the use of allografts or protheses as meniscal substitutes may be justified. Fresh, freeze-dried or glutaraldehyde-fixed allografts provided poor results, with varying degrees of joint destruction[18,19]. Culture of allograft menisci before implantation provided satisfactory short-term results, but their long-term behaviour is unknown[18]. Cryopreserved allografts containing viable cells have been shown to be able to heal to host tissue, survive within the knee joint without immunological rejection and provide functional replacement for up to at least 6 months[19,20]. However, remodelling of the collagen structure and lack of cellular repopulation of the central part may comprise the long-term structural properties of the graft, thus limiting its functional behaviour[21]. Although reports exist describing normal biomechanical properties of transplanted allografts in dogs[20], others report inferior long-term behaviour concerning deformation and elasticity in the rabbit[22], sheep[23] and goat[24]. Degeneration of cartilage is seen more frequently than in control animals, although it appears to be less severe than seen after total meniscectomy[18,20,24]. Degeneration may also be attributable to the use of too small grafts[18,20].

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Biomaterial prostheses could have great potential. They are easy to produce and are available in unlimited numbers. Material composition, physical structure and size can be controlled, and immunological problems can be prevented. Prostheses have been made of reconstituted collagen[25], polyester–carbon fibre[26], fibre–Teflon[27] and Dacron® with polyurethane coating[28].

Up to now, results have been highly variable and healing with fibrocartilaginous tissue could not always be predicted. For several years we have performed experiments using porous polymers for repair of lesions in the avascular part of the meniscus of dogs and rabbits. It appeared that healing could be achieved in a substantial number of cases.

Furthermore, we observed that porous polymers predictably stimulate the transformation of fibrous repair tissue into fibrocartilage strongly resembling meniscal fibrocartilage[17,29]. The aim of the present study was to determine if the same polymer could be used as a prosthesis for the replacement of complete menisci by the formation of a fibrocartilaginous meniscal replica.

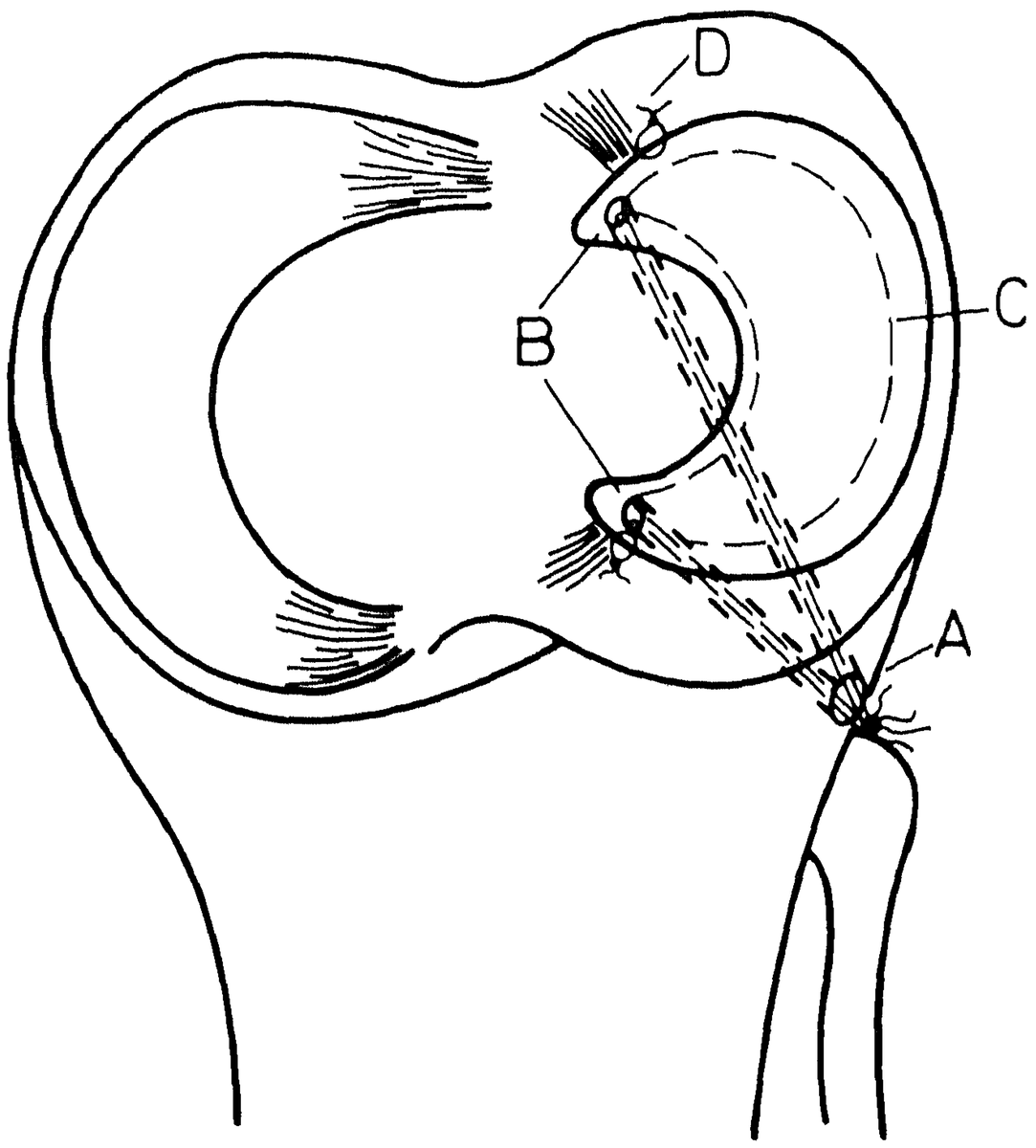

Figure 1 Operative procedure. After separating the meniscus from its attachments, drill holes were made starting from the proximal lateral tibia (**A**) and ending on the anterior and posterior areas of the intercondylar eminentia (**B**). Two sutures were pulled longitudinally through the prosthesis (dotted lines, **C**) and attached to the proximal tibia. The remains of the anterior and posterior meniscal attachments (**D**) were sutured to the appropriate meniscal horn.

MATERIALS AND METHODS

Animals

Experiments were performed under aseptic conditions on 24 lateral menisci of 13 adult mongrel dogs weighing 25 kg or more. Anaesthesia was accomplished by intravenous administration of penthotal (30 mg kg^{-1}) and maintained after intubation with nitrous oxide and halothane.

The right or left lateral meniscus (chosen at random) was approached by a lateral incision of the knee joint capsule without detachment of any ligaments. Using a Beaver eyeblade (Waltham, MA, USA) the meniscus was separated from its anterior and posterior attachments. Two drill holes were made in the lateral aspects of the proximal tibia, ending in the anterior and posterior area of the intercondylar eminentia. Two 4-0 mersilene sutures were attached to a properly sized prosthesis and were pulled through the drill holes (*Figure 1*). In the first six prostheses the sutures were attached to both prosthesis horns. This resulted in tearing-out and subsequent dislocation of the prosthesis. Therefore, in the remaining 12 prostheses the sutures were applied longitudinally through the entire prosthesis, running parallel to the central and peripheral border. The remains of the meniscal attachments were sutured to the appropriate prosthesis horn. The prosthesis' periphery was sutured to the perimeniscal capsular and synovial tissues using dexon sutures. The capsule and skin were then closed in layers. The dogs were not immobilized and walking was allowed.

In six control knees the same procedure was performed without implantation of a prosthesis.

Follow-up periods ranged from 8 to 28 weeks for both control and prosthesis groups. The animals were killed at intervals of 2 and 4 weeks, respectively.

Polymer

Prosthesis material consisted of an aliphatic polyurethane, as described before[30]. Pores were created using the salt-casting–freeze-drying technique. Total porosity was 86%, consisting of 43% macropores of 150–300 μm and 57% micropores smaller than 90 μm. Its compression modulus was 150 kPa. Earlier morphometrical analysis has shown that the material had a 1 year degradation rate of 50%.

Histology

After killing the disarticulated knees were photographed and inspected for gross degenerative changes. The prostheses were cut into transverse slices covering anterior, antero-medial, medial, medio-posterior and posterior regions. From each of these regions adjacent slices were taken for routine histology and immunohistochemistry. For histology slices were fixed in acetone at −20°C, infiltrated in glycol methacrylate and embedded at 4°C. They were cut into 2 μm sections and stained with Toluidine Blue and Giemsa.

For immunohistochemistry, frozen sections were cut in a cryostat at 8 μm and pretreated with trypsine and hyaluronidase (Sigma, St. Louis, MO, USA) for 30 min. Then they were incubated with a monoclonal anti-collagen I antibody and a monoclonal anti-collagen II antibody, the characterization of which has been published before[31,32].

After washing and treatment with heat-inactivated normal rabbit serum, antibodies were applied and incubated overnight at 4°C. Sections were incubated with peroxidase-conjugated rabbit anti-goat immunoglubulin G (Dakopatts, Glostrup, Denmark) for 1 h at room temperature. Sections were then incubated with peroxidase–3,3′-diaminobenzidine tetrahydrochloride (Sigma) for 8 min at room temperature. Control sections were taken through the same procedure, except that either the first or second antibody was applied. They were all negative.

Articular cartilage

Femoral condyles and tibial plateaux were removed and studied for gross degenerative changes. They were pencilled with India ink and studied by stereomicroscopy according to Meachim[33].

RESULTS

After wound dehiscention, two knees showed infection within 2 weeks after operation. These knees were not included in the present study, leaving 22 knees for assessment (16 prosthesis and six control knees). The dogs favoured the unaffected limb for 2–3 weeks, after which they regained a normal gait pattern and no longer seemed to be hindered by the operation. In the first six knees the prostheses were secured using single sutures which were only pulled through anterior and posterior prosthesis horns. After killing four of these prostheses appeared to be dislocated due to a tearing-out of the sutures. Therefore, the following prostheses were secured using two sutures running longitudinally through the entire prosthesis. Of the remaining 10 prostheses, only one dislocated.

Macroscopy

The short-term implants had a connective tissue appearance, similar to dislocated implants. They were light brown in colour and had a soft consistency. After 3 months the prosthesis had a yellowish glistening appearance, and had a firm consistency. A rim of hyaline-like neocartilage had formed at the prosthesis' inner margin (*Figure 2*).

Microscopy

Tissue ingrowth into the prosthesis was incomplete until 18 weeks. From 8 to 18 weeks ingrowth of tissue was seen in the prosthesis' periphery adjacent to the capsular tissues and at its superior and inferior surface, enveloping an empty centre. After 18 weeks the central areas also became filled and ingrowth was complete. The histology of the tissue filling the prosthesis was essentially identical to the tissue seen in small polyurethane implants used for meniscal repair[17,29].

Initially, the prosthesis became filled with vascular fibrous tissue. A moderate foreign body reaction was seen, consisting of giant cells, macrophages and some lymphocytes. Labelling with anti-collagen type I antibodies showed a diffuse labelling, whereas

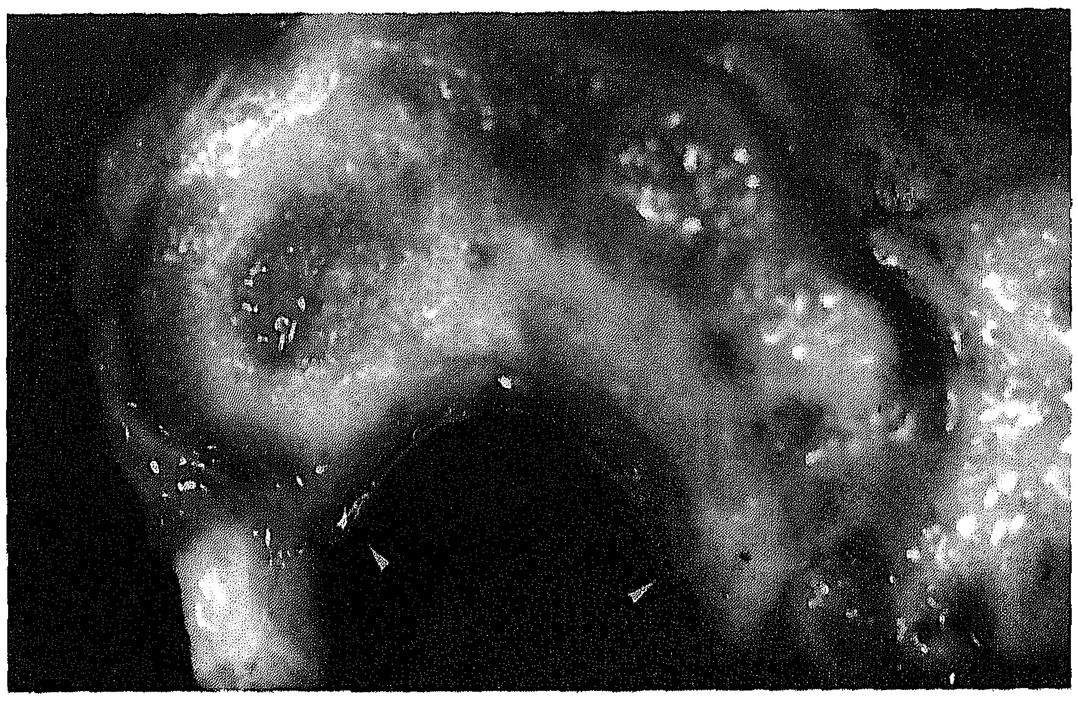

Figure 2 Meniscal prosthesis after 16 weeks. The prosthesis has a firm consistency and has a cartilaginous, glistening appearance. A small rim of hyaline cartilage has formed at its inner margin (white arrowheads). Original magnification ×5.

labelling for type II collagen was negative. Starting at 10 weeks, areas of metachromasia were observed throughout the implant, indicative of the formation of a cartilaginous matrix (*Figure 3*). In these cartilaginous areas chondrocytes could be observed lying in a metachromatic matrix with course collagen bundles devoid of blood vessels and inflammatory cells (*Figure 4*). Morphologically, this tissue strongly resembled normal meniscal fibrocartilage. Type I antibodies showed a diffuse labelling of both fibrous tissue and metachromatic fibrocartilage. Type II antibodies showed positive labelling of fibrocartilaginous areas only, whereas surrounding fibrous tissue was negative (*Figure 5a–c*). Subsequently, more fibrous tissue transformed into fibrocartilage and after 18 weeks the prostheses contained fibrocartilage only.

Six of seven dislocated prostheses were located subcutaneously outside of the joint capsule, whereas one had become a loose body lying in the intercondylar groove. Remarkably, all dislocated prostheses

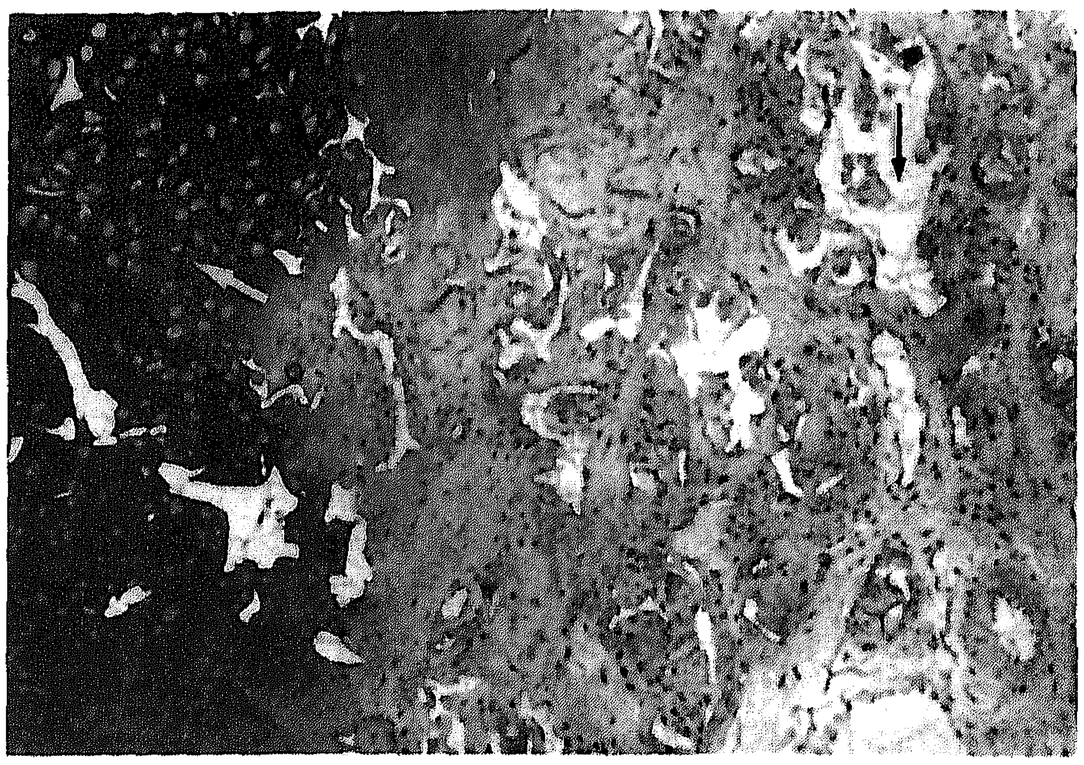

Figure 3 Repair tissue filling the prosthesis pores after 12 weeks. Transformation of vascular fibrous tissue (light tissue, right) into metachromatic fibrocartilage (dark tissue, left) containing chondrocytes (white arrow). White areas represent the polymer (black arrow). Toluidine Blue stain. Original magnification ×200.

Figure 4 Typical fibrocartilage formation in a 20-week prosthesis showing chondrocytes (white arrow, right) lying in a metachromatic matrix with coarse collagen bundles (black arrow, left). White areas represent the polymer. Polarized light photograph. Original magnification ×280.

(follow-up periods 8–20 weeks) were completely filled with tissue. Cartilage had formed only in the prosthesis located intra-articularly. The other implants were filled with fibrous tissue only. A partially regenerated meniscal rim was noticed in one 24-week meniscectomy control knee. Microscopically, it consisted of non-metachromatic fibrous tissue not containing any chondrocytes.

Articular cartilage

Degenerative changes of articular cartilage were present in all meniscectomized control knees. Moderate fibrillation of cartilage seen at 8 weeks progressed to severe destruction exposing the subchondral bone after 20 weeks. Degeneration in association with a dislocated prosthesis was comparable to meniscectomy and was more severe when follow-up periods were longer. Degeneration associated with well incorporated prostheses was frequent, although less severe than seen after meniscectomy or dislocation. Intact cartilage was seen in five knees. In the remaining six knees, varying degrees of cartilage destruction were seen, although exposure of the subchondral bone did not occur. In two of these six knees it appeared that the drill holes were located in the central part of the tibial cartilage instead of in the eminentia. This surgical error may have contributed to the cartilage damage. Cartilage degeneration was not related to the length of follow-up or formation of fibrocartilage inside of the prosthesis.

Tibial plateaux were more frequently and more severely affected than femoral condyles.

DISCUSSION

Several meniscal prostheses have been applied in animal studies in an attempt to slow down or prevent postmeniscectomy cartilage degeneration. Until now, none has met with uniform success. A quickly degradable collagen prosthesis in the dog is reported to be transformed into a meniscus replica containing fibrochondrocytes, thus providing protection to the articular cartilage. Without providing any data, it is concluded that both pore structure and resorption rate

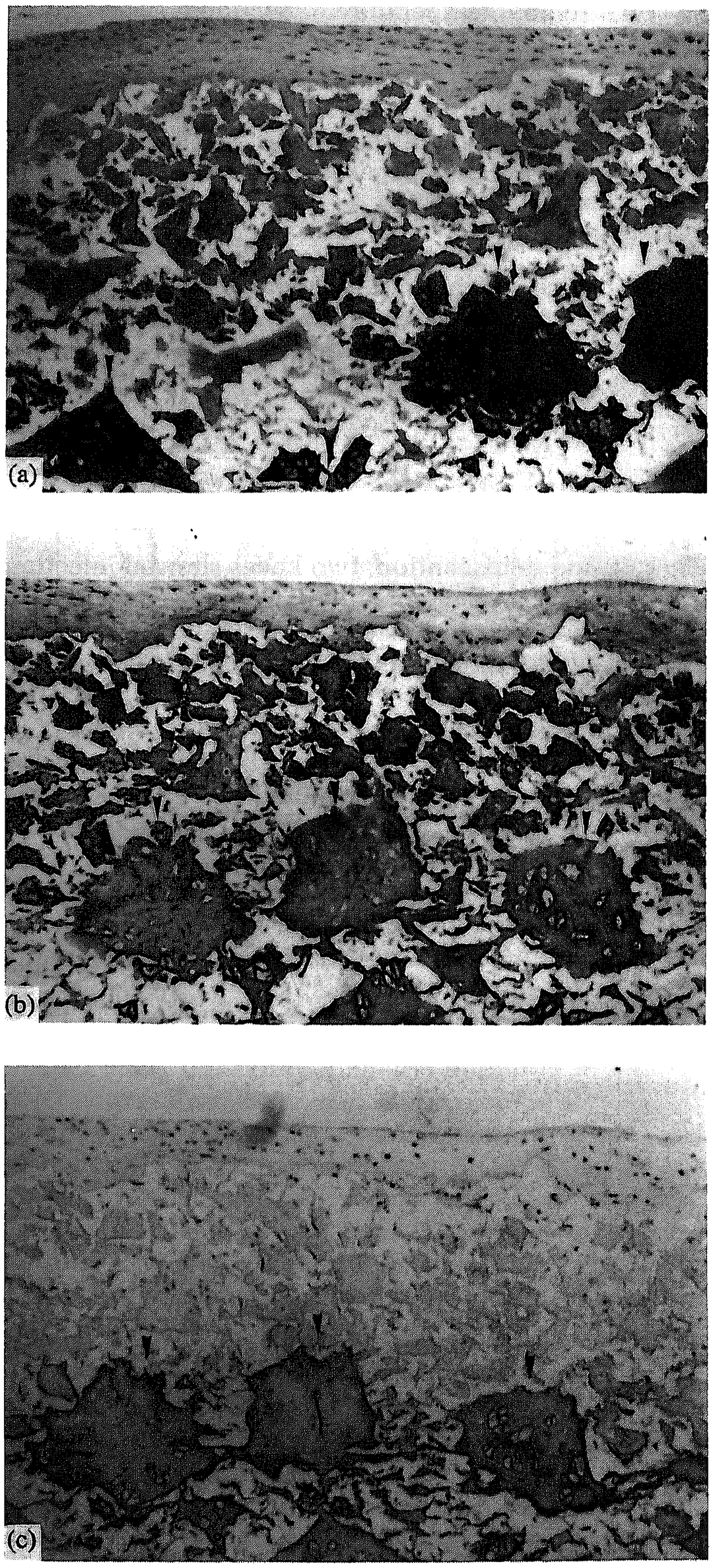

Figure 5 **a,** Repair tissue after 12 weeks. The surface layer consists of fibrous tissue. In the deeper zone metachromatic fibrocartilage has formed (arrowheads). Toluidine blue stain. Original magnification ×125. **b,** Adjacent section after labelling with anti-collagen type I antibody. Diffuse distributions are seen in both fibrous areas (superficial zone) and fibrocartilaginous areas (arrowheads). **c,** Adjacent section after labelling with anti-collagen type II antibody. Type II collagen is present only in the fibrocartilaginous areas in the deeper zone (arrowheads). The fibrous tissue in the superficial zone shows negative staining.

of the material used are important[25]. Cartilage protection up to 1 year postoperation can also be achieved by implantation of a fibre–Teflon prosthesis. After an initial response of inflammatory cells and fibroblasts, fibrocartilage formed after 9 months. In some animals degeneration of the tibial condyle was seen within 3 months after operation and was attributed to lack of early tissue ingrowth into the prosthesis, causing absent prosthetic function[27]. A minor cartilage-protective effect could be achieved after implantation of a polyester–carbon fibre prosthesis in the rabbit. No ingrowth of tissue was seen, biological regeneration was poor and the inflammatory response was severe. Again, pore structure was not clearly defined[26]. Implantation of a prosthesis made of Dacron with polyurethane coating and limited porosity gave results similar to meniscectomy in terms of biomechanical behaviour and effect on the articular cartilage. Failure was often caused by insufficient incorporation[28]. The conclusion may be that, although meniscal prosthesis may provide protection to the articular cartilage, results are highly variable.

This may be due to the fact that in every instance both material and structural properties of the prosthesis were different. In most cases ingrowth of tissue was lacking, insufficient or occurred too slowly. The structure of prostheses was never clearly defined.

The tissue reaction is not only dependent on material composition[34,35], but also on the implant's physical framework[35–37]. It has been shown for several tissues that this not only alters the rate of tissue ingrowth but also the degree and type of differentiation of ingrowing tissue, thus determining the ultimate type of tissue formed. It seems likely that the same applies for ingrowth of meniscal fibrocartilage or differentiation of mesenchymal tissue into fibrocartilage.

Preliminary results have shown that fibrocartilage formation inside of a porous implant is highly dependent on the type of polymer used. When a slowly degradable rigid polyurethane (compression modulus 150 kPa) was used for meniscal repair, abundant fibrocartilage formation could be observed. However, after using a less rigid (compression modulus 40 kPa), quickly degrading copolymer of poly(lactic acid) and caprolactone, fibrocartilage formation was rare. Material composition *per se* does not seem to be the explanation for this phenomenon, since fibrocartilage can be observed in polymer implants with varying chemical composition[17,29]. Also, the implant's structure *per se* does not seem to be essential, since preliminary studies have shown that fibrocartilage can be formed in implants with pore sizes varying from 50 to 500 μm. Most likely, the biomechanical properties of an implant are the most critical factor, determined by material composition, its degradation rate and possibly its total porosity.

An ideal prosthesis should induce the formation of a meniscal replica providing more or less identical biomechanical properties as a normal meniscus. The implant should last long enough to establish the essential structural framework, it should not evoke an inflammatory reaction that leads to eventual destruction of the graft or joint, it should provide for the stability of the normal meniscus and, most importantly, the implant should prevent or retard osteoarthritis[25]. It seems logical that normal meniscal fibrocartilage should be formed, since this tissue can be expected to fulfil these demands.

From the present study it appeared that complete polymer prostheses can predictably stimulate the formation of repair tissue strongly resembling normal meniscal fibrocartilage. This is based on morphological grounds as well as on the fact that labelling with antibodies showed that the repair tissue contained the two most important meniscal collagens, type I and type II. Biochemical analysis of repair tissue in polymer implants used for meniscal repair[29] has confirmed this transition of fibrous tissue into fibrocartilage.

A differentiation must be made concerning the inner and outer parts of the meniscus. Histologically, the inner one-third of the meniscus more closely resembles hyaline cartilage, whereas the outer two-thirds are more fibrous in appearance[38]. The major collagen type of this inner rim is type II, whereas the peripheral part of the meniscus is almost completely composed of type I collagen. In addition, small amounts of type III, V and VI are detectable[39–42]. Using antibodies, we could not observe this varying collagen distribution and biochemical analysis of inner and outer prosthesis areas seems to be necessary.

It may be possible that prolonged follow-up periods result in rearrangement of the collagen types, since compression is thought to influence the collagen type formed in the fibrocartilaginous intervertebral disc, thus enhancing the content of type II collagen[40].

Degeneration of cartilage was frequent after meniscectomy in control knees or dislocation of inserted prostheses. In knees with well incorporated prostheses, cartilage destruction was less severe but was still present in 50% of the knees. It cannot be excluded that these results will become worse with increasing follow-up periods.

The reason for prosthesis failure regarding protection of the cartilage may be the slow ingrowth of its centre, resulting in too long a period before the prosthesis begins to function. Alteration of pore sizes and porosity, which can easily be done in polymers, may solve this problem. The observation that osteoarthritic changes were more prominent in the tibial plateaux than in the femoral condyles may be explained by the fact that frictional forces are larger in the tibia[43].

CONCLUSIONS

The present study showed that a meniscal replica can develop after implantation of a porous polymer prosthesis. Formation of fibrocartilage which strongly resembled normal meniscal fibrocartilage took place predictably. Cartilage degeneration decreased when compared to meniscectomy. Improvement of implantation technique improved the results. Thus, porous polymers may be used for meniscal replacement providing that their physical structure is optimal.

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