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Homologous meniscus transplantation

Experimental and clinical results*

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Summary. *The increase in severe ligament injuries of the knee has led to consideration of the need for meniscal transplantation in reconstructive operations for chronic rotational instability. Transplantation of the medial meniscus was carried out in two groups of 15 sheep. In one group lyophilised, γ-sterilised allogenic menisci were transplanted and these underwent a complete remodelling in 48 weeks. In the other group, deep frozen allogenic menisci were used and these remained fully functional without remodelling. We then carried out meniscal transplantation in 22 patients who were followed-up for a mean of 14 months. Arthroscopy was possible in two-thirds of the cases at an average of 8 months after operation. Both types of transplanted menisci, lyophilised and deep frozen, decreased in size, as small as a regenerated meniscus in some cases. In general the deep frozen menisci showed better results.*

Résumé. *L'augmentation de fréquence des graves traumatismes ligamentaires du genou a conduit à envisager la transplantation méniscale dans les opérations reconstructrices pour instabilité rotatoire chronique. La transplantation du ménisque interne a été réalisée dans deux groupes de 15 moutons. Dans un groupe on a utilisé des ménisques allogènes lyophylisés et stérilisés aux rayons γ, qui ont présenté, à la 48ème semaine, une transformation complète. Dans l'autre groupe, on a transplanté des ménisques allogènes réfrigérés à −30° C et ceux-ci sont restés parfaitement fonctionnels, sans transformation. Nous avons réalisé une transplantation méniscale chez 22 malades, qui ont eté suivis 14 mois en moyenne. Dans les deux-tiers des cas une arthroscopie a été possible vers le 8ème mois après l'opération. Les deux types de ménisques, lyophylisés et réfrigérés, diminuent de volume pour devenir aussi grêles, dans quelques cas, qu'un ménisque régénéré. Dans l'ensemble les ménisques conservés au froid donnent les meilleurs résultats.*

Introduction

Meniscectomy leads to degenerative changes in the knee joint, and this has been demonstrated in clinical, experimental and biomechanical investigations [1, 13, 20, 26, 29, 31]. The results of partial meniscectomy are better than total meniscectomy [28, 38, 40]. Arthroscopic partial meniscectomy is a further advance [5]. Suture of both fresh and old meniscal tears is frequently carried out [4, 9, 12, 18, 19, 23, 35, 38, 39]. The menisci are important in load transmission, and also have a significant dynamic function in the stabilisation of the joint; for example, the posterior part of the medial meniscus acts synergistically with the anterior cruciate ligament [3, 8, 11, 14, 28, 36].

Many attempts have been made to replace or reconstruct the meniscus, but only occasional clinical or experimental observations have been made [10, 17, 24, 34, 35]. The need for replacement arises when the anterior cruciate ligament substitute lacks the protection of the posterior part of the medial meniscus which has often been removed previously. If this is not present, the substituted ligament may well become loose.

Animal experiments

Material and methods

Thirty merino sheep, aged one year, were divided into two equal groups. Undamaged sheep menisci were prepared by

* This work received the Müller-SICOT award in 1987
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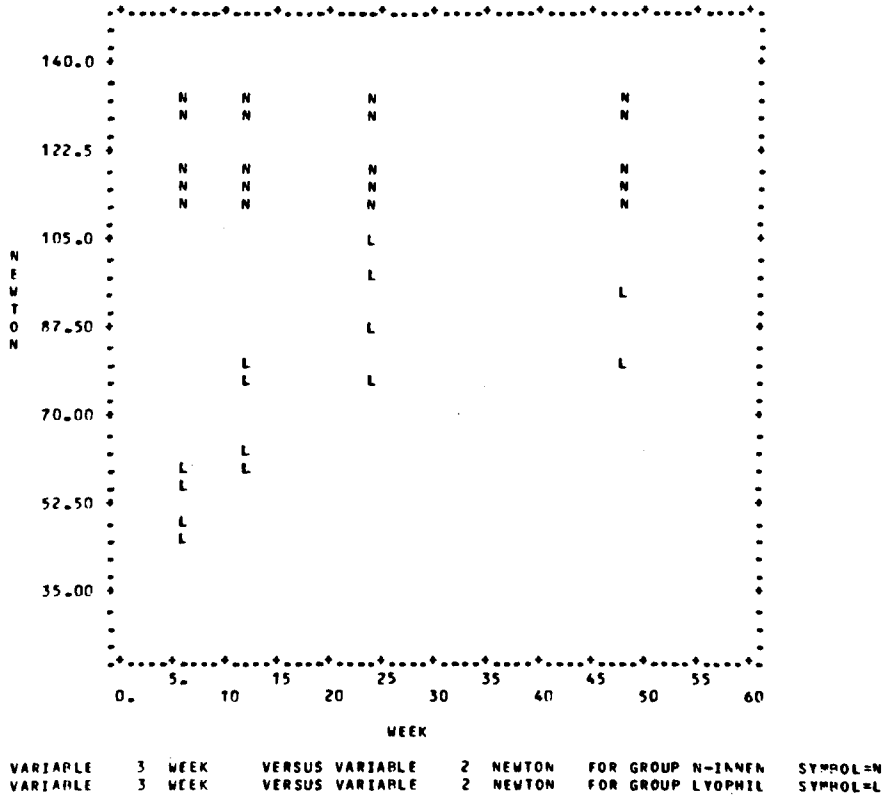


Fig. 1. Biomechanical investigation. Computer print-out of single values after transplantation of lyophilised menisci compared to normal values. (*N* normal meniscus, *L* lyophilised meniscus. *Ordinate*: force in Newtons, *abscissa*: time in weeks)

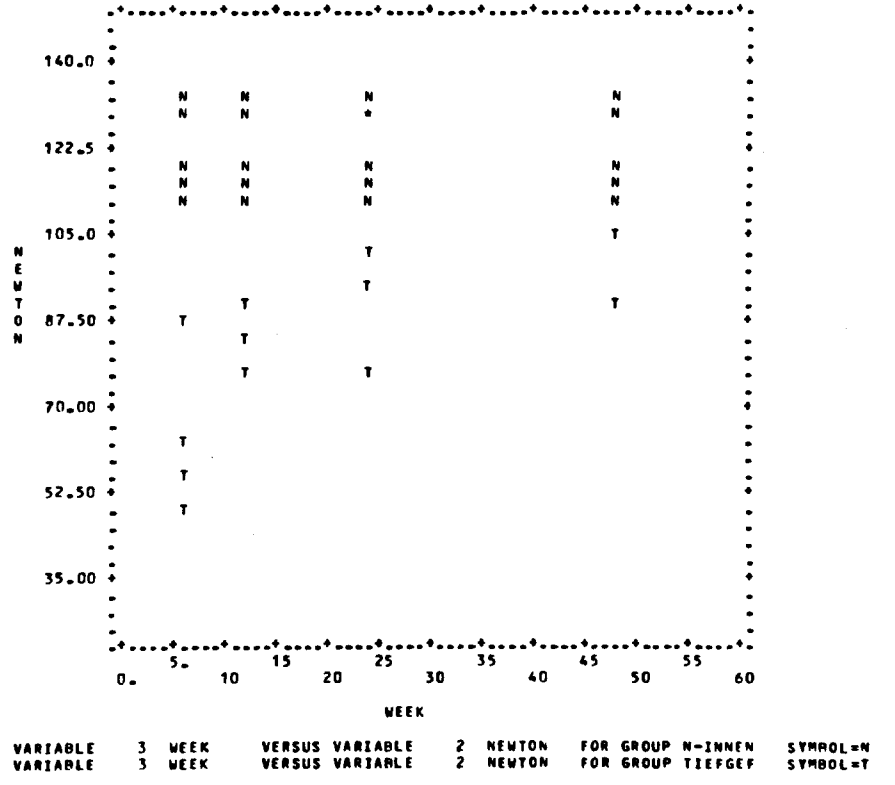
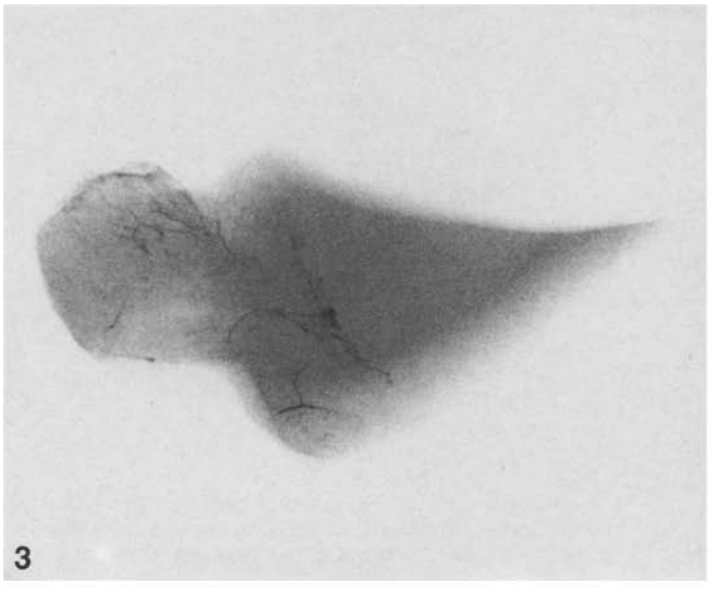


Fig. 2. Biomechanical investigation. Computer print-out of the single values after transplantation of deep frozen menisci compared to normal values. (*N* normal meniscus, *T* deep frozen transplant. *Ordinate*: force in Newtons, *abscissa*: time in weeks)



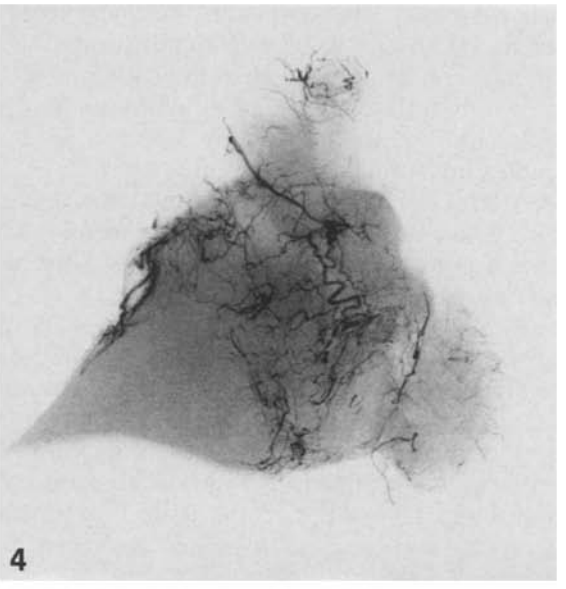


Fig. 3. Normal vascularisation of the medial meniscus of a sheep. As is the case with humans, vascularisation is present only in the capsular margin

Fig. 4. Microangiograph six weeks after transplantation of a lyophilised meniscus. Vessels have entered from the base and from the synovium

freeze-drying and γ-sterilisation (Braun-Dexon), and transplanted into the first group. Deep frozen (at −30° C) meniscal transplants were used in the second group. The menisci to be transplanted were removed under sterile conditions from the opposite knee when a previous experiment was being carried out (Fig. 3).

For the transplantation, an incision was made over the medial side of the knee and the joint opened in front and behind the medial collateral ligament. The normal meniscus was removed. The transplant was shaped with a scalpel and sutured in position by interrupted nonabsorbable stitches. The medial ligament was never severed. The calcaneal tendon was resected to prevent weight-bearing and prophylactic antibiotics were given. The animals limped until about the 12th week, but they walked and jumped normally as the calcaneal tendon regenerated.

In each group, observations were made at the 6th, 12th, 24th and 48th week. Three animals had to be sacrificed earlier. In two the wound broke down, and in the other there was necrosis at the medial side of the knee. The transplanted menisci were examined by vital staining, microangiography, scanning electron microscopy, and biomechanically.

Results

Lyophilised γ-sterilised menisci. After six weeks these menisci were completely healed around

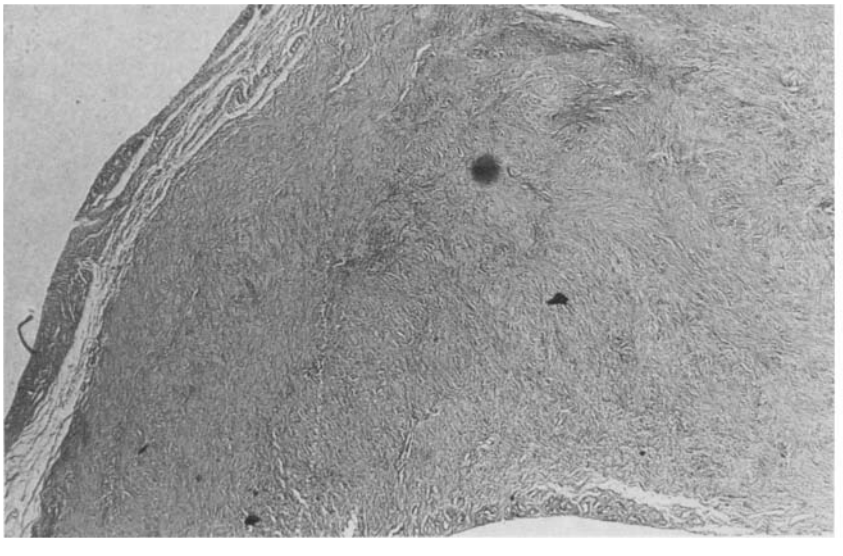


Fig. 5. Cross-section of a lyophilised meniscus 48 weeks after transplantation showing remodelling and replacement by undifferentiated collagenous tissue (H & E ×12)

their periphery, the synovium was hypertrophied and ingrowth of vessels was demonstrated by microangiography (Fig. 4). Histologically, the meniscus was completely covered by synovium and was occasionally vascularised by connective tissue penetrating from the synovium.

After 12 weeks, a newly formed vascular network could be demonstrated in the meniscus and there was an increased infiltration of fibroblasts and capillaries.

After 24 weeks, vascularisation had progressed and at 48 weeks the transplant had completely healed macroscopically. The synovium remained hypertrophied and microangiography showed almost complete revascularisation. The meniscus was almost fully remodelled progressing from the surface to the centre, with fibroblast proliferation and a newly formed collagen fibre structure (Fig. 5).

Over the whole period, there were no signs of cellular inflammation or rejection. Occasional plasma cells were found near the suture material.

Deep frozen menisci. In general, these menisci were incorporated in a similar way to those in the first group. At 48 weeks there was complete healing, but revascularisation was only slight and remodelling did not occur. There were no signs of inflammation or rejection (Figs. 6 and 7).

Biomechanical investigation. It was carried out using a special standardised traction device in a universal test machine. Analysis used the BMDP programme at the Institute of Statistics and Biomathematics, University of Munich. The tensile strength of the deep frozen transplant corresponded to that of lyophilised transplant at 6 weeks ($p = 0.27$), 12 weeks ($p = 0.09$) and 24 weeks ($p = 0.49$). The tensile strength of the normal was not reached even after 48 weeks (Figs. 1 and 2).

Clinical investigation

Replacement of the medial meniscus is indicated when the anterior cruciate ligament has to be replaced because both these structures act synergistically [29, 38] as a block which prevents anterior subluxation of the tibia.

Methods

In some cases we obtained menisci from donors of vital organs in accordance with conditions laid down for deep frozen bone transplantation ($-70°$ C). We also used cadaveric menisci which were lyophilised and γ-sterilised; these menisci are stored in sterile packs and rehydration before operation takes half an hour.

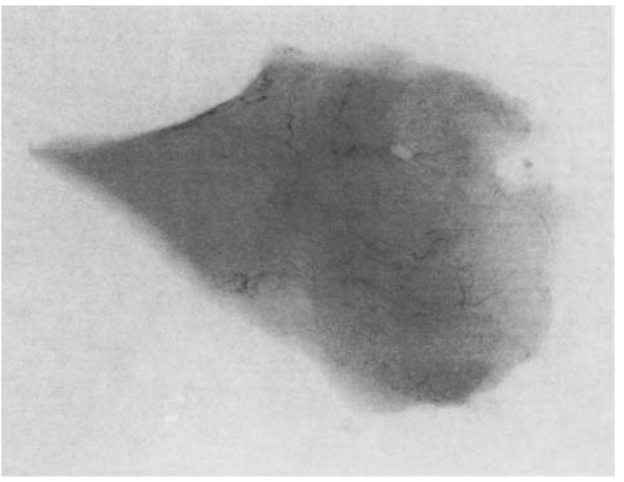


Fig. 6. Cross-section of a deep frozen meniscus 12 weeks after transplantation. Healing is complete with synovial hypertrophy and invasion of new blood vessels near to the base

Surgical technique. We used the same approach as in our usual technique for replacement of the anterior cruciate ligament [38, 39] with a medial hockey stick incision. In grade II anteromedial instability, the medial collateral ligament was split longitudinally, whereas in grade III cases the tibial insertion was detached with a chisel. Any meniscal remnants were trimmed. The allogenic meniscus to be transplanted was shaped with a scalpel and then placed on the tibial plateau. The knee was carefully moved to allow the meniscus to slide into position. The posterior part was either attached to the remnant of the original meniscus or fixed by a stitch through the bone in the intercondylar area. An additional attachment was also made to the posterior cruciate ligament. The meniscus was then attached with interrupted stitches (Vicryl USP 3–0 at 5 mm intervals) which were inserted from posterior to anterior along the trimmed peripheral margin. Reconstruction of the anterior cruciate ligament was then carried out using the middle one third of the patellar ligament, with any further measures that were necessary. Continuous passive movement was started and the patient discharged after two weeks. Full weight-bearing was allowed after 14 weeks [38].

Immunology. There have been many investigations into the antigenicity of lyophilised and deep frozen connective tissue, cartilage and bone transplants [6, 7, 15, 16, 22, 25]. Our tests for possible antigen-antibody reactions were based on the

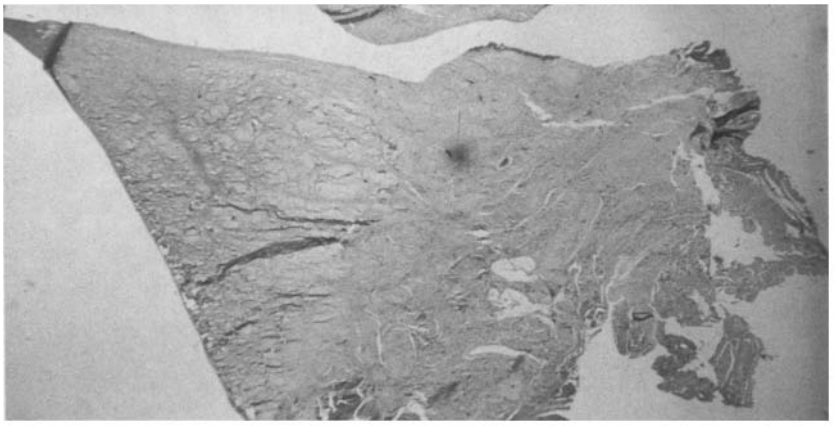


Fig. 7. Cross-section of a deep frozen meniscus after 48 weeks showing complete healing and slight synovial hypertrophy (Alcian-PAS, × 12)

HLA system [32, 33]. The test is positive with a reaction of 30% antibodies.

Patients

The first meniscal transplantation at the Munich-Großhadern University Hospital was carried out on May, 24, 1984. Between then and September 25, 1986, a further 21 homologous medial menisci have been transplanted.

There were 19 men and 3 women with an average age of 29.6 years (youngest 21 and oldest 45 years). The number of right and left knees was the same.

Nineteen patients had chronic grade III antero-medial instability and 3 had grade II. The injury had taken place between 11 months and 8 years previously, with an average of 2.5 years. The medial meniscus had already been removed in 17 patients.

The operative findings in the 22 knees can be summarised as follows:

Medial meniscus completely removed	11 knees
Regenerate menisci	3 knees
Presence of a marginal meniscal border	3 knees
Medial meniscus totally disrupted and irreparable	5 knees
Articular cartilage smooth on the medial femoral and tibial condyles	6 knees
Chondromalacia in the load-bearing area of the medial femoral condyle	6 knees
Foci of chondromalacia on medial femoral and tibial condyles	12 knees
Retropatellar chondromalacia (grades II and III)	21 knees
Absent anterior cruciate ligament	21 knees
Loose anterior cruciate after operation	1 knee

Table 1. Clinical details and operation in deep frozen meniscal transplants

Nr.	Name	Age (years)	M/F	L/R	Diagnosis	Op-date	Additional operation	Type of transplant
5	S. R.	25	M	L	AMRI III° Chon. mal.	10. 09. 84	L.C.A.P. L.C.M.A.	Med., l.
6	S. J.	25	M	L	AMRI II°	09. 10. 84	L.C.A.P.	Lat., r.
7	G. E.	25	M	R	AMRI III° Chon. mal.	08. 11. 84	L.C.A.P. L.C.M.A.	Med., r.
12	M. M.	26	M	R	AMRI III° Chon. mal.	16. 07. 85	L.C.A.P. L.C.M.A.	Med., r.
14	R. M.	24	F	L	AMRI III° Chon. mal.	29. 07. 85	L.C.A.P. L.C.M.A.	Lat., r.
18	K. A.	45	M	R	AMRI II° Chon. mal.	04. 04. 86	L.C.A.P. L.C.M.A.	Lat., l.

Abbreviations to Tables 1–4: *M* male; *F* female; *L* left; *R* right; *AMRI* antero-medial rotation instability; *II/III* grade II/III; *Chon. mal.* chondromalacia medial compartment; *Med.* medial; *Lat.* lateral; *L.C.A.P.* anterior cruciate ligament – plastic; *L.C.M.A.* medial collateral ligament – approximation; *Tractopex.* tractopexy; *PR.d.* Pridie drilling; *H.* healed; *P.h.* paritally healed; *N.h.* not healed; *Reduc.* reduced; *AB* antibody; *Clin.* only clinical follow up examination

The following types of menisci were used for transplantation

Allogenic lyophilised medial meniscus	8
Allogenic lyophilised contralateral lateral meniscus	8
Deep frozen homologous medial meniscus	3
Deep frozen contralateral lateral meniscus	3

Three knees developed effusions after operation and a fourth patient had a fever from the 5th to the 12th day. In these four patients the knees had settled by the time of discharge from hospital. A more serious complication occurred in a 45 year old man who had had two previous operations on the knee. There were signs of infection after the 4th day and staphylococcus aureus was cultured from the wound. Arthroscopic lavage was sterile and there was no intra-articular abnormality. A further case had a soft tissue infection which settled with antibiotics. The remaining 17 knees healed satisfactorily and were able to start early movement in a knee brace.

Follow-up. All the patients were seen regularly in our clinic and the average follow-up was 13 months with a range of 4 months to 2½ years. Results were not available for the two patients who had been operated only 4 months previously. The remaining 20 patients were reviewed as follows:

By clinical examination only	4
By arthrography	6
By arthroscopy	16

In all, 23 arthroscopies were carried out.

Results

Individual results are shown in Tables 1–4.

Deep frozen meniscal transplants. Results were known in five of the six patients, but one was only followed-up clinically.

Two patients had arthrography 4 and 6 months after operation, respectively, and showed the appearance of a normal meniscus.

Arthroscopy was carried out in five patients at from 5 to 24 months from the operation. In four cases the meniscus was normal in size, but in two cases it was smaller, by 2/3rds in one patient at nine months. In the latter patient the knee was arthroscoped later and the appearance was the same.

Complete healing of the meniscus was confirmed by arthroscopy or arthrography in five patients, and in the other clinical examination was satisfactory.

A moderate synovial reaction was demonstrated at 5 months in one case. The state of the articular cartilage was generally improved. There was grade III chondromalacia on the medial side of the joint in three cases, and grade I changes in one case.

Table 2. Results of deep frozen meniscal transplants

Nr.	Follow up post. op. (months)	Arthrographical findings	Arthroscopical findings				Immunology	Lachman-sign	Meniscus sign med.	Subj. judgment	Comments
			Size of meniscus	Healing	Synov. reaction	Cartilage med.					
5	5	–	Normal	H	Moderate	II	–	Negative	–	Satisfied	Chon. mal.
	9	–	1/3 reduc.	H	None	I	–	Negative	–	Very satisfied	
6	9	–	2/3 reduc.	H	None	Normal	–	Negative	–	Very satisfied	Traum. rupt. lat. men.
	24	–	2/3 reduc.	H	None						Chon. mal.
7	12	–	Normal	H	None	Normal	44% AB	(+)	–	Very satisfied	
	15	–	Normal	H	None	Normal	0% AB	(+)	–	Very satisfied	
12	4	H	–	–	–	–	0% AB	Negative	–	Satisfied	Chon. mal.
	14	–	Normal	H	None	II	–	Negative	–	Satisfied	
14	6	H	–	–	–	–	–	Negative	–	Satisfied	Chon. mal.
	12	–	Normal	H	None	II		Negative	–	Satisfied	
18	8 (Clin.)	–	–	–	–	–	0% AB	(+)	–	Not satisfied	Infection

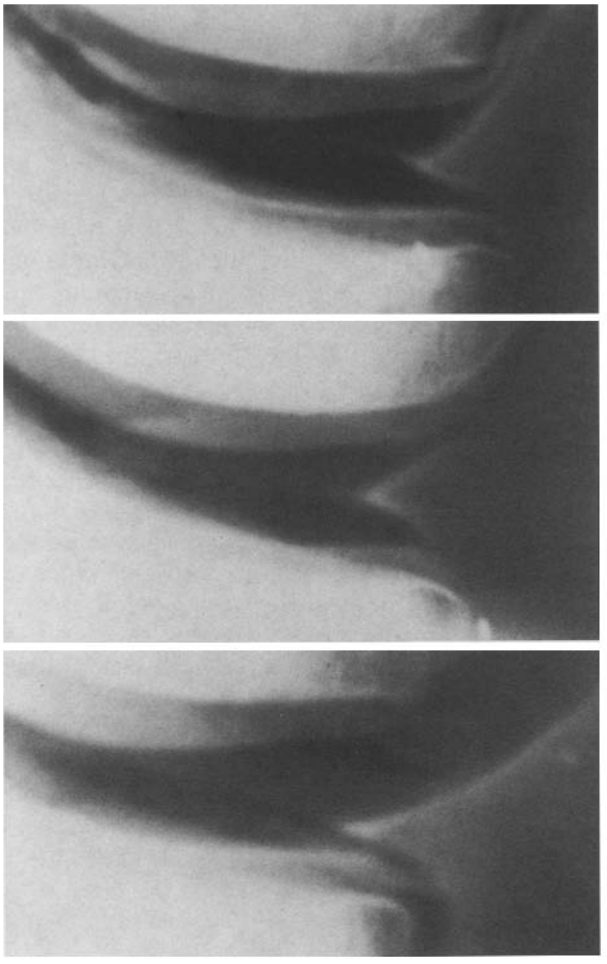


Fig. 8. Arthrograph three months after transplantation of a lyophilised meniscus showing complete healing (case 13)

No antibodies were found, except in one patient who showed 44% antibodies, but this finding had become normal at a later follow-up.

All six patients had a stable knee. The Lachman was either negative (4) or single positive (2). There were no meniscal signs on clinical examination. Three of the patients were very satisfied with the result, two were satisfied and one was not satisfied (this was the patient who had had an infection).

Lyophilised meniscal transplants. Fourteen of the 16 cases were followed up for at least six months. Ten patients were arthroscoped a total of 15 times, and four others had arthrography (Tables 3 and 4); two patients were followed up by clinical examination alone.

In the first patient the meniscus was reduced by 1/3rd of its size at 10 months; at 23 months the transplant was completely destroyed. In the other cases, arthroscopy showed that the meniscus had become smaller, particularly after a long period.

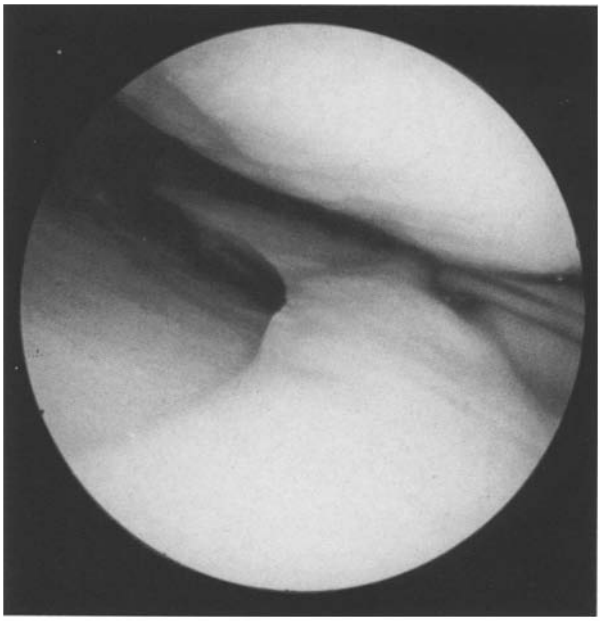


Fig. 9. Arthroscopy two months after transplantation of a lyophilised meniscus showing complete healing (case 8)

In four cases in this group the transplanted meniscus was reduced in size by 2/3rds after more than 5 months, and in a further four it was reduced by 1/3rd. Arthroscopy showed a normal appearance of the meniscus in only one patient.

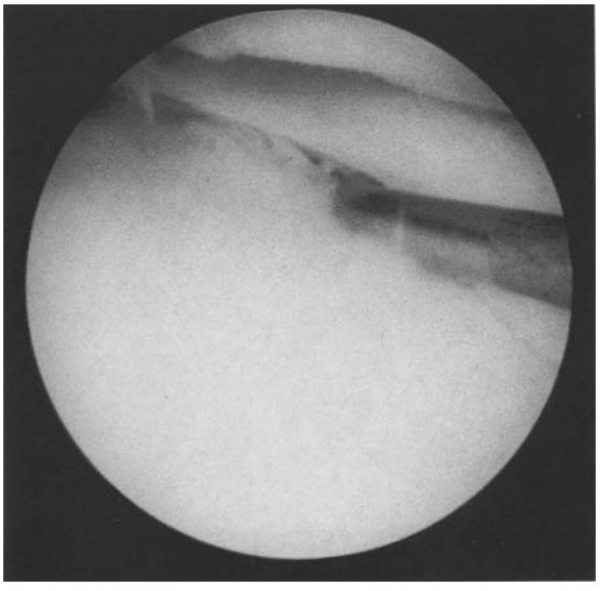


Fig. 10. Arthroscopy 13 months after transplantation of a deep frozen meniscus. The posterior horn is slightly reduced in size, but there is complete healing (case 12)

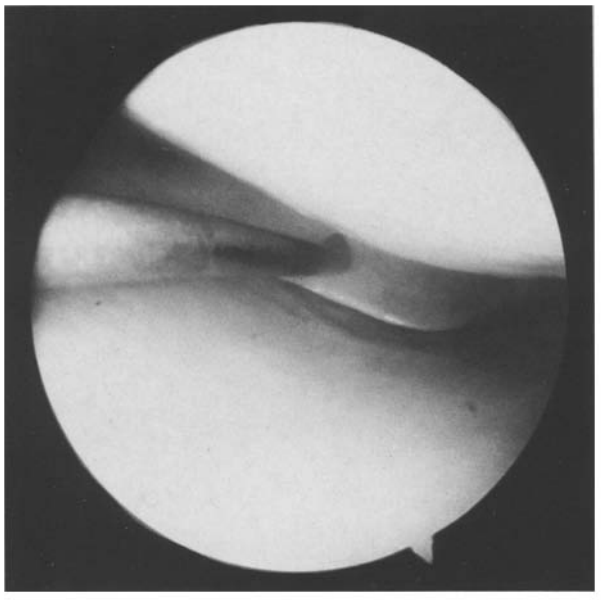


Fig. 11. Arthroscopy 25 months after transplantation of a lyophilised meniscus. The meniscus is reduced in size, but there is complete healing (case 9)

In the first patient there was no healing of the posterior part at 22 months, and the second had a small meniscus with detachment of the anterior and posterior parts at 24 months. The third patient was found to have a one centimetre gap in the region of the collateral ligament, but this did not cause symptoms.

Synovial reaction was more pronounced than in the deep frozen transplants, and in four there was an intense synovitis. The articular cartilage was altered to a greater degree with grade II chondromalacia (Figs. 8–11).

The immunological findings were the same in the two groups; 4% antibodies were detected in one patient in whom arthroscopy was normal and this does not indicate an immunological reaction [33, 34].

Testing stability showed a dorsal double Lachman sign in one patient; a single positive with a hard endpoint in seven, and in six the test was negative. These patients did not have symptoms.

In two patients there were meniscal signs but in one of them arthroscopy showed no abnormality. The other had sustained a rotational injury while playing football, and arthroscopy 19 months after the meniscal transplant revealed a hypermobile posterior part which could be folded forwards into the joint with a hook. There was also a lobular rupture 3 mm wide and 1 cm long in the posterior part. The flap was removed and the meniscus was resutured to the capsule. The flap and the base of the transplanted meniscus were examined histologically and the findings are illustrated in Fig. 12. The patient has had no further symptoms.

In this group, five patients were very satisfied with their result, seven were satisfied and two dissatisfied. The cause of the dissatisfaction was not attributable to the transplant: one of the two patients had persistent posteromedial rotational instability; the other had chronic synovitis, with pain and swelling after exercise, but arthroscopy did not reveal a lesion of the meniscus.

Although the numbers are too small for statistical analysis, the transplanted meniscus seems to get smaller as time passes, and this is much more obvious in the lyophilised group in which there is more evidence of synovitis and cartilage damage.

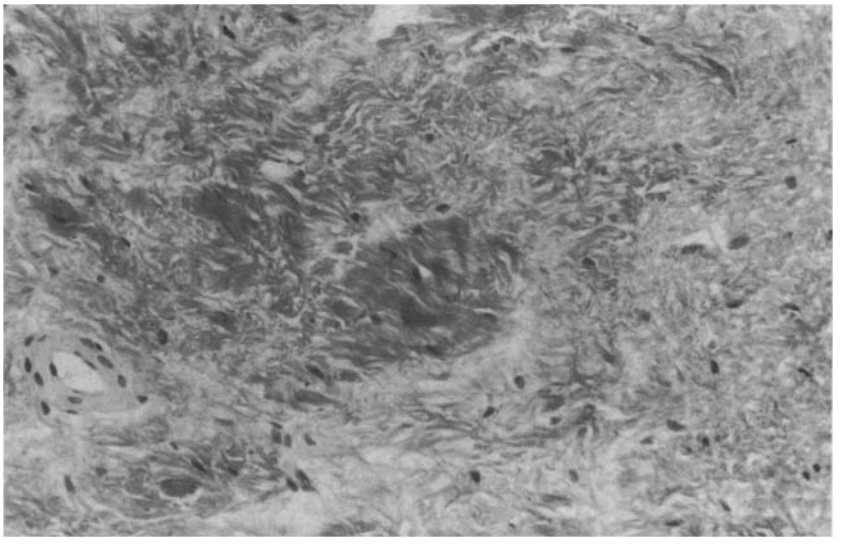


Fig. 12. Lyophilised meniscus transplanted 19 months previously and followed by a further injury. Photomicrograph of the base of the meniscus showing revitalised meniscal tissue with capillaries and fibroblastic proliferation (Elastica-Van Gieson, × 50) (case 11)

Table 3. Clinical details and operation in lyophilised meniscal transplants

Nr.	Name	Age (years)	M/F	L/R	Diagnosis	Op-date	Additional operation	Type of transplant
1	S. G.	36	M	L	AMRI III° Chon. mal.	25. 05. 84	L.C.A.P.	Med., l.
2	D. C.	26	M	R	AMRI III° Chon. mal.	30. 05. 84	L.C.A.P. L.C.M.A. P R.d.	Med., r.
3	S. U.	21	F	L	AMRI III° Chon. mal.	07. 06. 84	L.C.A.P. L.C.M.A.	Med., l.
4	H. J.	34	M	L	AMRI III° Chon. mal.	18. 07. 84	L.C.A.P. L.C.M.A. P R.d.	Lat., r.
8	S. G.	39	M	R	AMRI III° Chon. mal.	10. 12. 84	L.C.A.P. L.C.M.A. P R.d.	Med., r.
9	L. E.	23	M	L	AMRI III° Chon. mal.	28. 02. 85	L.C.A.P. L.C.M.A.	Lat., r.
10	R. J.	40	M	R	AMRI III°	07. 02. 85	L.C.A.P. L.C.M.A.	Lat., l.
11	W. H.	28	M	R	AMRI III°	04. 02. 85	L.C.A.P. L.C.M.A.	Lat., l.
13	E. R.	26	M	L	AMRI III° Chon. mal.	15. 10. 85	L.C.A.P.	Lat., r.
15	W. W.	31	M	R	AMRI III° Chon. mal.	11. 02. 86	L.C.A.P. L.C.M.A.	Med., r.
16	G. H.	28	M	R	AMRI III° Chon. mal.	27. 02. 86	L.C.A.P. L.C.M.A.	Med., r.
17	W. M.	21	M	L	AMRI II° Chon. mal.	24. 03. 86	L.C.A.P.	Lat., r.
19	V. H.	25	M	L	AMRI III° Chon. mal.	10. 04. 86	L.C.A.P. L.C.M.A. Tractopex.	Med., l.
20	R. H.	40	M	R	AMRI III°	28. 05. 86	L.C.A.P. L.C.M.A.	Lat., l.
21	S. M.	25	F	L	AMRI III°	12. 08. 86	L.C.A.P.	Med., l.
22	E. W.	39	M	R	AMRI III°	25. 09. 86	L.C.A.P. L.C.M.A.	Lat., l.

The deep frozen transplants in general showed better results.

Discussion

In 1916, Lexer attempted autologous fat flap interpositional arthroplasty and in 1933 his colleague Gebhard caried out similar operations in animals [17]. Replacement of dog's menisci with a teflon net produced substantial adhesions [34], and bridging meniscal defects with carbon net were also unsatisfactory [35]. Locht et al. [24] replaced the tibial plateau with fresh homologous transplants, including the meniscus.

Müller [29] believes that the posterior part of the meniscus functions synergistically with the anterior cruciate ligament by way of the posterior oblique ligament which is attached to it. This suggests that replacement of the anterior cruciate ligament should be accompanied by meniscal transplantation in order to achieve long-term stability.

Our animal experiments and early clinical experience indicate that meniscal transplantation is a reasonable procedure, especially when a deep frozen meniscus is used, and will restore stability to a knee in which there is chronic anteromedial instability and an absent meniscus. No adverse immunological reactions have been demonstrated.

Table 4. Results of lyophilised meniscal transplants

Nr.	Follow up examination post. op. (months)	Arthrographical findings	Arthroscopical findings				Immunology	Lachman-sign	Menis-cussign med.	Subj. judgment	Comments
			Size of meniscus	Healing	Synov. reaction	Cartilage med.					
1	10	–	1/3 reduc.	P.h. (post. norm)	Heavy	II	0% AB	(+)	–	Satisfied	
	22	–	3/3 reduc.	No	Heavy	II		(+)	–	Satisfied	
2	6	–	Normal	H	Heavy	Normal		(+)	–	Satisfied	Chon. mal. insuffic. suture ant. + post. part
	14	–	1/3 reduc.	P.h.	None	II		(+)	–	Satisfied	
3	8	–	1/3 reduc.	H	Heavy	II		(+)	–	Satisfied	Chon. mal.
	14		2/3 reduc.	H	Heavy			(+)			
4	8	–	1/3 reduc.	H	Heavy	II		(+)	+	Not satisfied	Effusion, pain
8	2	–	Normal	H	Mode-rate	Normal		Neg.	–	Very satisfied	Chon. mal.
	14	–	2/3 reduc.	H	None	Normal	0% AB		–	Very satisfied	
9	9 (Clin.)	–						+ + post.	–	Not satisfied	Deficiency of extension 15° posterior instability
10	20	H					0% AB	Neg.	–	Very satisfied	
11	11	–	Normal	H	None	Normal	0% AB	(+)	–	Very satisfied	
	19	–	1/3 reduc.	P.h.	Mode-rate	II		(+)	+	Very satisfied	New injuri, post. part
13	3	H	–	–	–	–	0% AB	Neg.	–	Very satisfied	
	12	–	2/3 reduc.	H	None	Normal		Neg.	–	Very satisfied	
15	3	H transpl. reduced to a rim					0% AB	Neg.	–	Satisfied	Chon. mal.
	7	–	2/3 reduc.	H	None	III	–	Neg.	–	Satisfied	
16	3	P.h.	–	P.h.	–	–	4% AB	(+)	–	Very satisfied	
	7		Normal	P.h. Med.	Mode-rate	I		(+)	–	Very satisfied	Chon. mal. insuffic. suture of 1 cm length
17	8 (Clin.)							Neg.	–	Satisfied	
19	5	–	3/3 reduc.	H	Heavy	II	0% AB	(+)	–	Satisfied	Chon. mal. transplant reduced to a rim
20	8 (Clin.)						0% AB	Neg.	–	Very satisfied	
21	4 (Clin.)						0% AB				
22	4 (Clin.)						0% AB				

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