Experience with Fresh Venous Allografts as an Arterial Substitute

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AUTOGENOUS vein is considered the ideal graft to bypass occluded arterial segments in the lower extremity. In the absence of an autogenous vein, prosthetic materials and heterologous tissue have been used as alternative conduits, but they have distinct limitations. These limitations are particularly crucial in reconstruction below the knee, for here a pliable substitute with an endothelial-lined lumen which can be anastomosed to small vessels appears essential to long-term patency.

When an autogenous vein is not available for lower limb bypass, a better substitute than those already mentioned is needed. Over the past 4 years we have used fresh venous allografts when autogenous veins were not available. This paper presents our experience with 22 such bypass grafts used in the treatment of arterial insufficiency of the lower extremities.

Clinical Material

Since November, 1966, 22 patients have undergone arterial reconstruction in the lower extremity with the use of fresh venous bypass allografts. The patients' ages ranged from 40 to 76 years of age, the majority being in the seventh and eighth decades of life. The fresh allografts were obtained from eighteen cadavers and four living donors. The latter consisted of two patients undergoing vein stripping procedures and two undergoing unrelated procedures. All grafts were used within 12 hours after death of the cadaveric donors, or removal from the living donors. All of the grafts were placed in antibiotic solution containing 0.2% cephalothin and 25,000 units of bacitracin in 500 cc. of normal saline. They were not stored in a preservative.

The indications for operation were intermittent claudication in six patients, pain at rest in ten, and gangrene in six. The claudication interfered with work in four patients and seriously interfered with normal living in two.

The sites for homograft vein bypass were far from ideal. Twelve of the 22 patients had undergone previous attempts at revascularization. Numerous anatomic and morphologic variations occurred in both the proximal and distal sites of anastomosis of the bypasses (Table 1). The proximal site, or take-off, was from the patient's own artery (either the common or superficial femoral) in 15 patients or from a graft (either an aorto-femoral dacron or femoropopliteal autogenous vein bypass) in seven patients. In four of the eight patients in whom superficial femoral arteries were used as proximal anastomoses, a portion of the superficial femoral artery provided a suitable vessel for anastomosis after endarterectomy. Where a previous femoropopliteal autogenous vein bypass was used as proximal anastomosis, the autogenous vein had thrombosed as a result of extended distal disease. Therefore, a thrombectomy of the autogenous graft was necessary in three of the four patients before it was anastomosed to the homologous vein graft.

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TABLE 1. *Anatomic Variations in Venous Allografts*

Proximal		Distal	# Pts.
Common femoral artery	→	Proximal popliteal	2
		Distal popliteal	2
		Posterior tibial	2
		Peroneal	1
Superficial femoral artery	→	Posterior tibial	3
		Anterior tibial	3
		Peroneal	2
Aorto-femoral dacron by-pass	→	Distal popliteal	2
		Anterior tibial	1
Femoro-popliteal autogenous vein by-pass	→	Distal popliteal	1
		Posterior tibial	2
		Anterior tibial	1
			22

The distal sites of anastomoses were the proximal popliteal in two patients, the distal popliteal in five patients, the posterior tibial in seven, the anterior tibial in five, and the peroneal artery in three patients.

In 20 of the 22 transplants ABO blood groups of the donor and the recipient were known. Thirteen patients received veins from major ABO-compatible donors; in seven cases there was major ABO incompatibility. The blood groups of two donors were not known. No HL-A leukocytic typing was performed.

Results

The patients in this series have been followed from 3 months to 4 years. Eleven grafts (50%) have occluded and one became aneurysmal. The overall failure rate is 55%. The results of these homologous vein grafts cannot be accurately compared with the results of other grafts because most of the patients in this series either had undergone previous revascularization or the distal anastomosis was to a small vessel with poor run-off or both. The homograft vein in many was used as a last resort, often in a desperate situation.

The series is too small and the follow-up too short to determine the true long-term patency rate of homologous vein grafts. However, they obviously do not maintain the patency of autogenous veins. In our institution the 2-year patency rate for femoro-popliteal autogenous vein bypass grafts is 80% and for grafts to vessels below the knee, 65%. One patient had an autogenous vein in one extremity and a homologous vein in the other as a femoro-popliteal bypass under similar conditions. The homologous vein occluded at 5 months and the autogenous vein is still open at 2 years.

Although one would expect that grafting into more proximal vessels would have better results, this was not the case. There did not appear to be any correlation between the distal site of anastomosis and the long-term patency. The most common point of occlusion of the homograft veins was in the proximal portion of the implanted graft. Here the lumen is the narrowest and we suspect occlusion at this point occurs secondary to contraction of the vessel by fibrosis and periadventitial reaction. In three instances we have resected the proximal occluded segment, thrombectomized the distal homograft with Fogarty catheters, and replaced the resected segment with another homograft or prosthetic graft. Two of these remained patent up to 3 months and then re-occluded, and a third is still patent 6 months following the secondary reconstruction.

A microscopic section of one of the excised occluded vein grafts (Fig. 1) shows complete replacement of the normal preexisting vein wall by dense sclerotic tissue. There is partially hyalinized fibrous tissue present throughout a markedly thickened wall, with extension well into the periadventitial adipose tissue. All traces of normal media and adventitia have been obliterated by the fibrosis.

The angiographic appearance of the homograft vein bypass is similar to that

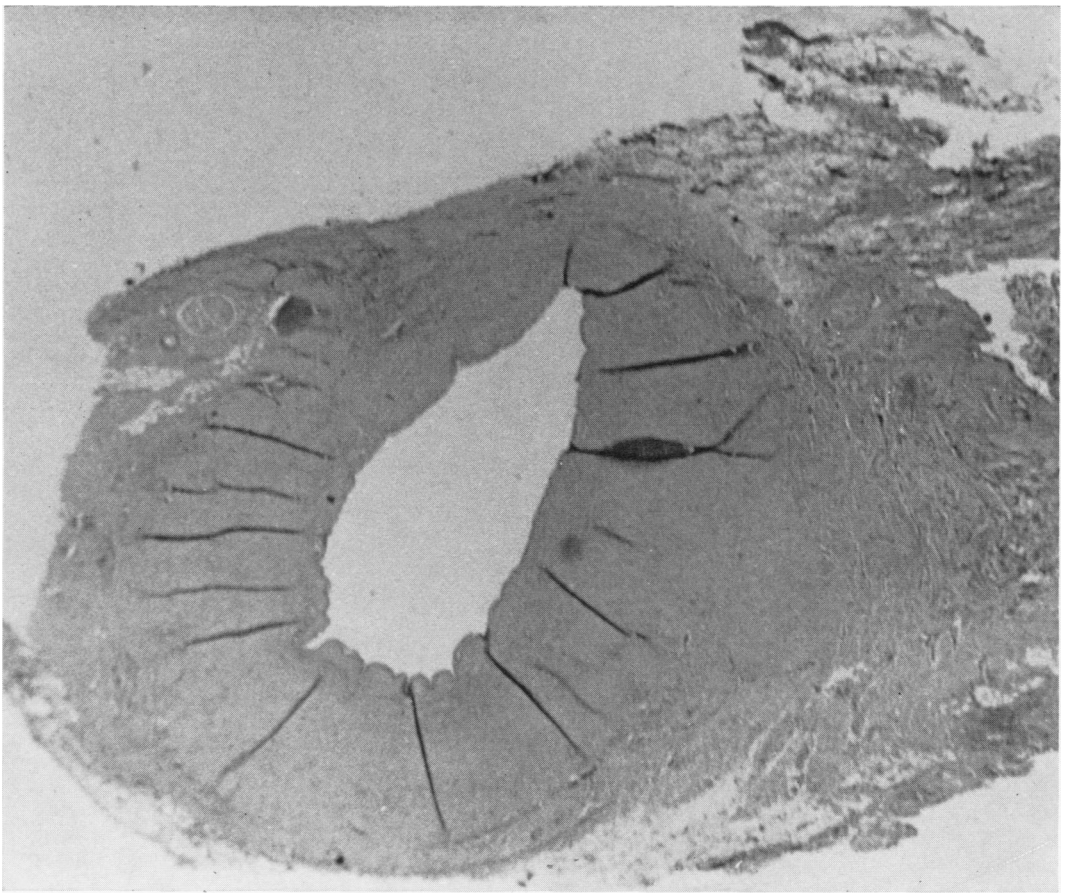

FIG. 1. Transverse section of homologous vein graft removed from patient 6 months following insertion. Dense fibrosis has replaced the normal vein wall, which is markedly thickened. H&E ×11.

seen in an autogenous vein bypass (Fig. 2). However, one would expect a roughened lumen because of the increased atheromatous changes which occur in the intima of homologous veins (Fig. 3).

Of particular interest in this series is the role which cell typing may play. Of the six grafts that remained patent for one year or more, all had compatible ABO blood groups. In contrast, of those with major ABO incompatibility, none were patent longer than 6 months (Tables 2 and 3). The true significance of this factor is difficult to assess because of the small series and the possible influence of technical factors in these complicated cases. Despite this uncertainty, there appears to be a definite correlation between long-term patency and ABO compatibility.

Discussion

The experimental evaluation of homologous veins as a vascular substitute began in Alexis Carrel's[3] second experiment of aortic replacement when a homograft vein from one dog's jugular to another dog's thoracic aorta was left in place for 2 years

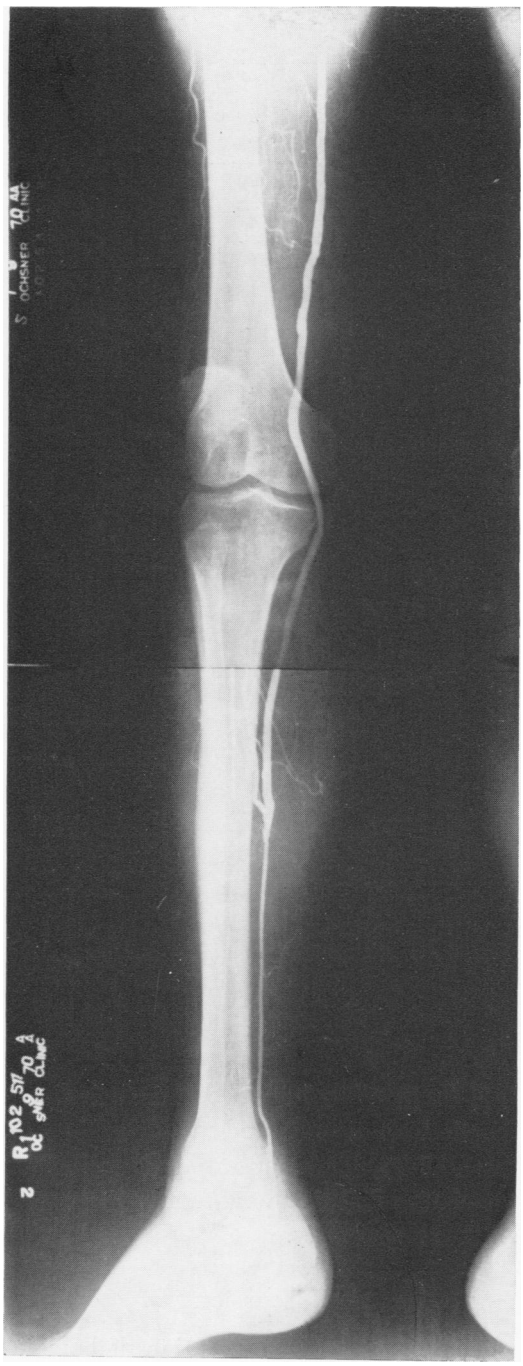

FIG. 2. Arteriogram of femoro-posterior tibial bypass with homologous vein graft. Graft has been functioning 3½ years. Note very little roughening of lumen.

and 2 months. In his experiment, the vein maintained the same size as the aorta, but its wall was replaced with connective tissue. Since that time, numerous experiments have been performed to evaluate the efficacy of homologous veins as arterial substitutes.[1, 8, 11, 13, 14, 18, 20] In early experiments comparison was made between homologous veins and homologous arteries in regard to their efficacy as arterial conduits. Because the voluminous clinical use of homologous arteries showed frequent degeneration with aneurysmal formation, studies were performed to see if homologous veins acted in the same or a different manner. Experimental studies performed by us,[2] as well as those of others,[1, 6] have shown that the homograft vein becomes aneurysmal less frequently than the homograft artery. There are two possible explanations for this. First, the media of the artery is much thicker than that of a vein of comparable size. The large fibromuscular layer in the artery undergoes ischemic degeneration, becoming a hypocellular pale-staining layer of homogeneous tissue showing no evidence of fibrosis. In contrast to this, the small fibromuscular layer in the vein usually shows marked proliferation of fibroblasts with collagen deposition leading to complete fibrous replacement of the vein wall. Not only may the mass of the media be responsible for the difference in histological reaction, but also the relative blood supply of the vessel wall may be pertinent. In the artery the wall of the vessel obtains its nourishment mainly from vasa vasorum which penetrate only into the media. In contrast, the vasa vasorum of the vein often penetrates into the lumen of the vessel. Thereby, the vein actually receives some of its blood supply from its own lumen; whereas the artery relies on its blood supply through the vasa vasorum from without. The vascular supply in the intima of

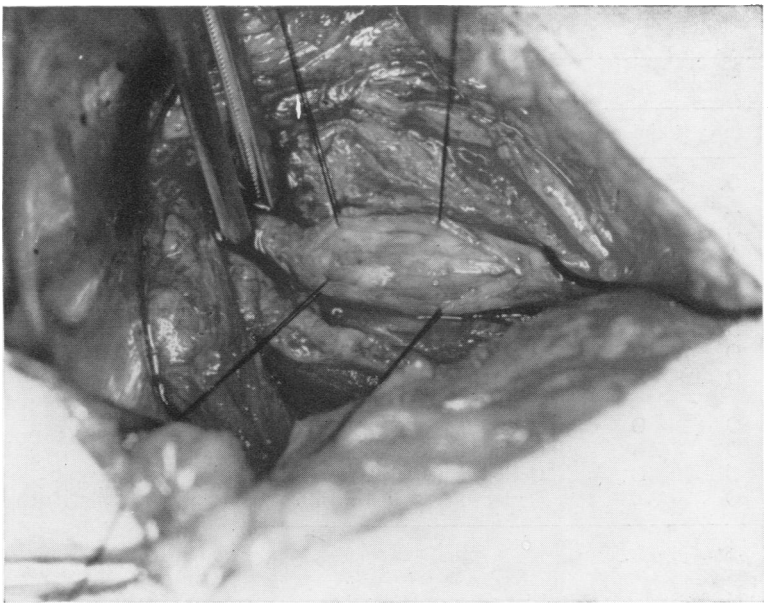

FIG. 3. Photograph of proximal portion of femoro-peroneal bypass with homologous vein graft. Longitudinal incision in anterior wall of graft reveals atheromatous changes within lumen. The graft has been in place for 6 months.

the vein can encourage cellular proliferation and progressive thickening of the tunica intima. The artery wall, on the other hand, is poorly vascularized and degeneration occurs without remarkable concomitant fibrous proliferation.

Another difference between arteries and veins may be related to a differing antigenicity of the two structures. Although mass *per se* does not significantly alter the antigenicity of a structure, cellularity is indeed an important factor. Should the highly cellular muscle layer of the artery be one of increased antigenicity, then this in itself would cause greater destruction than a vein. The strength of a homograft vein is due to the early and active proliferative process leading to extensive fibrous displacement of the vein wall, which, combined with periadventitial fibrosis, gives reasonable strength. In contrast, the strength of the homograft artery is dependent primarily upon whatever structural elements of the original artery wall remain intact.

There have been a number of studies [1, 13] to compare patency between fresh and preserved homologous vein grafts. Some investigators have felt that there is no difference; whereas others support one or the other as the preferred method of procurement and processing.

Studies [8, 13, 18] have shown that the autogenous vein is distinctly superior to the homologous vein. In general, an autogenous vein transplant survives as a living structure; whereas homologous veins are largely replaced by fibrous tissue from the host. The experimental work of Barner *et al.*[1] seems to support the difference in homologous veins and autogenous veins on an immunologic basis. Support for this thesis is found in the fact that the majority of thrombi in homologous veins occur before 30 days and the medial degeneration and inflammation seen at 20 to 45 days may well be the morphologic expression of an immunologic reaction, a basis for thrombosis. Schwartz *et al.*[15] have demonstrated that homograft canine veins are only weakly antigenic. Degenerative changes occur first in the adventitia and subjacent media. Cellular reaction may be mild or moder-

TABLE 2. *Venous Allografts with Major ABO Compatibility*

Blood Types			
Donor	Recipient	Status	Duration Patency
O	O	Patent	4 years
A	A	Patent	2 years
O	O	Patent	2 years
A	A	Patent	1½ years
A	A	Patent	1 year
O	O	Patent	9 months
B	B	Patent	8 months
O	O	Patent	6 months
O	B	Patent	3 months
O	O	Occluded	2½ years
O	AB	Occluded	6 months
O	O	Occluded	2 months
O	AB	Occluded	1 month

ately severe. Viable muscle cells were identified in many cases 119 days after homografting. We consider it significant that experimental and clinical studies of venous homografting have demonstrated that failure, when it occurs, is usually due to vessel occlusion, presumably from the combined effects of fibrotic stenosis and thrombosis. The latter has been a prominent feature and is a recognized characteristic of severe tissue rejection. A prominent feature of severe immunoreaction to renal homografts [12] is thrombotic occlusion of medium and large blood vessels. These changes occurred in spite of appropriate immunosuppressive measures.

TABLE 3. *Venous Allografts with Major ABO Incompatibility*

Blood Types			
Donor	Recipient	Status	Duration Patency
B	A	Patent	4 months
B	A	Occluded	6 months
A	O	Aneurysm	4 months
A	O	Occluded	4 months
B	O	Occluded	3 months
B	A	Occluded	3 months
B	A	Occluded	2 months

As far as we know, homografting of large vessels, both arteries and veins, has previously been done with total disregard of tissue compatibility and/or immunosuppression. Our experience suggests that, with the simple expedient of appropriate ABO matching, results may be significantly improved. How much more might be accomplished by more sophisticated tissue matching or by the exhibition of modest immunosuppression is a matter of conjecture.

There has been limited clinical experience with the use of allograft veins as arterial substitute, and no one person has substantial experience. Review reveals that fifty such operations [4, 7, 9, 10, 16, 19] have been performed and that the patency rate among these is 48%. The follow-up on the majority of these patients has been short, although it varies from immediate post-transplantation to 4½ years. There has also been a much higher incidence of aneurysmal formation than in our series for which the reason is not apparent. There has not been much enthusiasm for the use of homologous veins as arterial substitute, and it is possible that follow-up on these preliminary reports has proven a higher occlusion rate with time. This we would expect knowing the histological changes which do occur.

Summary

Twenty-two homologous veins have been used as bypass grafts for arterial reconstruction in the lower extremity where autogenous veins were not available. Eleven of the 22 later were shown to be occluded. Patency of the allografts appeared to be enhanced by compatible ABO matching. Our limited clinical experience suggests that homologous veins can be used as arterial substitutes for limb salvage when donor and recipient have compatible matching of the ABO system.

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