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REINFORCED COLLAGEN TUBES FOR THE MANAGEMENT OF PERIPHERAL VASCULAR INJURY

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Allograft and xenograft collagen tubes were prepared and evaluated by implantation into the circulatory system of mongrel dogs. Femoral interposition grafts, aortoiliac grafts, and carotid-to-jugular shunts were utilized. A variety of preservation methods were evaluated after it became evident that "fresh" graft material would not remain patent.

Different techniques for storage and preservation of the collagen tubes resulted in a graded patency rate but that fresh, autogenous vein grafts remained superior for the management of peripheral vascular injury.

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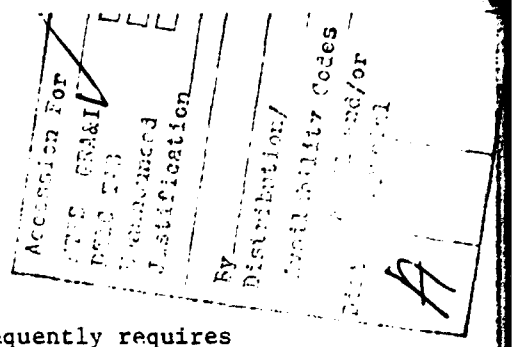

Summary

The management of peripheral vascular injury frequently requires rapid correction of the problem in order to prevent irreversible damage and severe blood loss. The availability of an "off-the-shelf" small diameter vascular prosthesis, with proven clinical use, will greatly improve this situation.

The most satisfactory prosthesis is often one that closely resembles the structure it is intended to replace. In replacement of blood vessels, synthetic fabric tubes are similar to the host vessel only in general shape and strength but not in basic structure, viability, flexibility, and the property of remaining free of thrombus. These differences become obvious in using synthetic grafts in vessels of small caliber in man where in a short time virtually all grafts smaller than 6 mm in diameter will thrombose.

A major concept in this study was to construct collagen tubes into which a loose fabric was incorporated that imparts strength to the stucture. Autograft tubes of this material for large vessels have demonstrated qualities superior to fabric grafts in that they remain thin and flexible over the years. If feasible for small diameter vessels, this material would then be a readily stored, immediately useable, off-the-shelf vascular prosthesis.

Allograft and xenograft collagen tubes were prepared and evaluated by implanting them into the circulatory system of mongrel dogs. Femoral interposition grafts, aorto-iliac grafts and carotid-to-jugular shunts were utilized. A variety of preservation methods were evaluated after it became evident that freshly excised graft material, without any other preparation, would not remain patent. In addition, these materials were compared with other non-biologic graft materials.

The results of this program were to show that different techniques for storage and preservation of the collagen tubes resulted in a graded patency rate but that fresh, autogenous vein grafts remained superior to all other materials for the management of peripheral vascular injury.

Objective

This was a feasibility study on the use of an off-the-shelf biologic material for the management of peripheral vascular injury.

Background

The autogenous saphenous vein is the vascular prosthesis of choice in smaller vessels, but this vessel is unavailable or unusable in 15-20% of elective surgery cases. This is probably even higher in emergency situations where multiple sites of injury may have destroyed the available veins, and when the situation is not appropriate for excision of a suitable vein.

The ideal non-autogenous material for the small vessel graft has not as yet been found. Considerable effort has been centered around the use of non-biologic synthetic materials. A satisfactory prosthesis should have the following qualities:

a. Availability - A graft should be readily available, preferable a stock item.

b. Porosity - There should be minimum porosity to prevent bleeding at the time of surgery.

c. Flexibility - The material should be flexible enough so that it will not buckle across joints.

d. Strength - The material should be strong enough to withstand arterial pressures to prevent dilatation or disruption.

e. Mechanical handling properties - The material should be non-fragile and easily handled by the surgeon.

f. Non-thrombogenic - The grafts should not tend to produce thrombosis.

g. The material should be non-degradable, non-carcinogenic, and non-antigenic.

h. The graft should match the dimensions of the vessels to which it will be joined.

The most satisfactory prosthesis is one that closely resembles the structure it is intended to replace. In replacement of blood vessels, synthetic fabric tubes are similar to the host vessel only in general shape and strength but not in basic structure, viability, flexibility, and the property of remaining free of thrombus. These differences cause synthetic grafts as small caliber to thrombose in a short time.

A major approach to this problem is to construct collagen tubes with an incorporated fabric which imparts strength to the structure. Autograft tubes of this material for large vessels have demonstrated qualities superior to fabric grafts in that they remain thin and flexible over long periods.

Military Significance

Replacement of diseased, obstructed or otherwise damaged arteries is one of the major techniques of modern vascular surgery. This is com-

monly accomplished by using a vein from one part of the body to repair or bypass the damaged artery. However, veins are not suitable or available in some patients, and this number will be much greater in the battle field where multiple injuries may also affect suitable veins. In addition, the pressure of time, due to either the patient's poor condition or the number of patients requiring attention, makes an off-the-shelf, immediately available vascular prosthesis very much needed in medical treatment centers. This program was directed toward developing such a material.

Methods and Material

The prosthesis was a mesh reinforced collagen tube. The material was formed in a host animal in the following manner (Figure 1):

1. A 20 cm long sleeve of very fine plastic mesh fabric (polypropelene or Dacron) was fitted about a silicone rubber rod. The 4 mm diameter of the sleeve material and the silicone rod were selected to ensure a tight fit.
2. The assembly was inserted under sterile conditions in subcutaneous tissue (panniculous carnosus) in the flank of the host. A small incision was made in the flank. The overlying tissue was separated by blunt dissection and the assembly was slipped into the space between tissue layers. The incision was then closed.
3. After ten weeks, the assembly was carefully dissected out from the surrounding tissue. The silicone rod was gently removed from the mesh sleeving and encapsulating fibrous tissue. The outer tube was then prepared for storage in the manner described below.

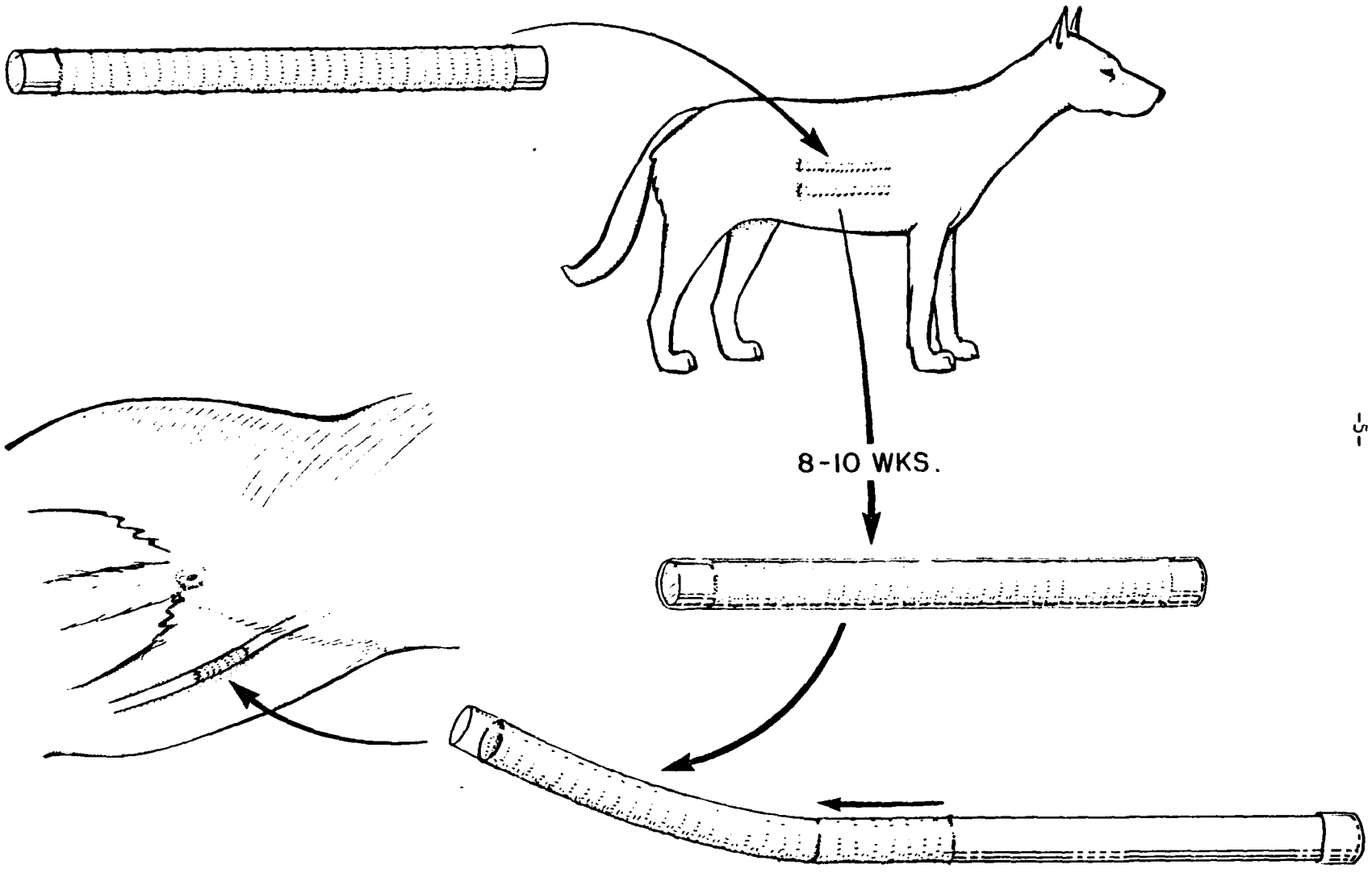

FIGURE 1

4. Preservation was by freezing in Ringer's lactate or by immersion in 2% glutaraldehyde followed by storage at 40° F. The material was stored in individual sealed glass containers. Each container was marked to indicate the host animal number, dates of insertion, and removal from the host and vendor lot number of the mesh sleeve material.

Graft materials (eg, autogenous vein, biologic prosthesis commercially available graft materials) were then utilized as bypass interposition grafts of the carotid or femoral artery in the dog. The animal was anesthetized with Nembutol (.2 cc/kgm) and placed on positive pressure assisted respiration. The vessel to be bypassed was exposed. In the case of femoral and carotid interposition grafts, the vessel was cross-clamped and divided at the sites of anastomosis. Aortoiliac grafts were prepared using an side-to-end anastomosis to the aorta and an end-to-end anastomosis to the distal vessel. Micro-surgical techniques were used throughout. After ascertaining that the graft was patent and the anastomoses were not "leaking," the wound was closed.

Patency was determined by palpation, ausculation, selective angiography, and Doppler sounds.

Prior Investigations by Others

An ideal non-autogenous material for small vessel grafts has never been found despite considerable effort in the use of non-biologic synthetic materials. In addition to "standard" prostheses of Dacron and Teflon,

efforts to use viable and non-biologic tubes included the placement of negative charges on a prosthetic surface[1,2,3,4], the use of electronegative materials[5,6,7], the use of grafts coated with electronegative materials[5,6,7], such as graphite-benzolkonium-heparin.[8-14] Other workers have used tissue cultures of fetal endothelial cells.[15,16] Another approach has been to use tubular structures from other individuals or species, such as the human umbilical vein, venous allografts, and modified bovine carotid arteries.[17,18] None of these investigations have resulted in a useful small diameter vascular prosthesis.

Results

1) Preserved Allograft and Xenograft Collagen Tube for Aorto-Iliac Segment (= 4.5 mm I.D.)

A total of 42 preserved allografts and 17 preserved xenografts were compared to 14 control bypasses using the autogenous jugular vein in the contralateral position. Tables I and II show the results. The aortoiliac data showed that heparin-saline was the most effective preservation technique. Graft materials were then evaluated in the more difficult femoral interposition graft position.

TABLE I: AORTOILIAC BYPASS ALLOGRAFTS

Preservative	Storage	Total	Number Patent	Patent at Sacrifice Range(days)
Heparin-saline	frozen	8	6	44-258
90% ethyl alcohol	40°F	7	3	30-121
10% formalin	40°F	7	4	68-105
2% glutaraldehyde	40°F	6	2	6- 21
Methyl prednisolone given systemically	fresh			
None (autografts)	fresh	7	7	90
		35	22	

TABLE II: AORTOILIAC BYPASS XENOGRAFTS

Preservative	Donor	Number	Patency Data
None (fresh)	pig	1	patent at 166 days
None (fresh)	goat	2	closed at 82/patent at 126
None (fresh)	sheep	1	patent at 150 days
Freezing heparin-saline	goat	1	patent at 90 days
Freezing in heparin-saline	pig	1	patent at 91 days
Freezing in heparin-saline	sheep	1	patent at 106 days
Freezing in heparin-saline	rabbit	2	closed at 71/patent at 253
90% ethyl alcohol	goat	1	closed at 16 days
90% ethyl alcohol	pig	1	closed at 88 days
90% ethyl alcohol	sheep	1	closed at 106 days
10% formalin	pig	1	closed
10% formalin	sheep	1	closed at 118 days
Systemic solu-medrol	pig	1	closed
Systemic solu-medrol	goat	1	closed at 92 days
Systemic solu-medrol	sheep	1	closed
		17	7 patent, 90-253 days

2) Preserved Collagen Tube for Femoral Interposition Graft

A total of 29 preserved allografts and 13 preserved 4 mm xenografts from a goat donor were made in the dog. Eleven control autografts were made using the autogenous jugular vein in the contralateral femoral. Animals were sacrificed after 90 days if the graft was patent. In addition, grafts were examined immediately if the animal died from unrelated causes. The results are detailed in Tables III and IV below.

TABLE III: FEMORAL INTERPOSITION ALLOGRAFTS

Preservative	Storage	Number	Patent at Sacri. Number	Avg.	Range	Patency Less Than 90 Days Number	Avg.	Range (days)
Ringer's Lactate	frozen	8	3	80	62-94	5	46	26-75
2% glutaraldehyde	40 F	7	3	84	65-96	4	57	52-62
Methyl prednisolone given systemically pre- and post-op	fresh	10	4	55	45-74	6	51	42-62
Autogenous vein (control)	fresh	10	10	93	85-100	-	-	-
		35	20			15		

TABLE IV: FEMORAL INTERPOSITION XENOGRAFTS

Preservative	Storage	Total Number	Patency Less Than 90 Days Number	Avg.	Range
Ringer's Lactate	frozen	3	3	66	62-69
2% glutaraldehyde	40 F	6	6	37	15-55
Methyl prednisolone given systemically pre- and post-op	fresh	4	4	53	42-65
		13	13		

3) Treated Umbilical Vein

In order to evaluate new experimental materials, the human umbilical vein was evaluated as a vascular conduit. This material was used for 28 aortoiliac bypass procedures in 20 dogs.

The table below (Table V) summarizes our results. We concluded that neither freezing nor 2% glutaraldehyde provided preservation treatment conducive to a successful graft, and that the biologic collagen tube was a superior prosthesis.

TABLE V: AORTOILIAC BYPASS GRAFTS USING TREATED UMBILICAL VEIN

		RESULTS		
Technique	Total	1 wk. postop.	3 wks. postop.	3 mos. postop.
Autogenous Jugular Vein	12	--	--	11 patent
Fresh umbilical vein, cannulated, stored frozen in Ringer's	10	4 patent*	0 patent	--
Glutaraldehyde treated umbilical vein, cannulated, stored frozen in Ringer's	10	4 patent	1 patent	1 patent
Glutaraldehyde treated umbilical vein, non-cannulated, stored frozen in Ringer's	4	--	0 patent	--
Fresh umbilical vein, cannulated, stored frozen in Ringer's Imuran administered	4	--	0 patent	--
	40	8	1	1

*One dog died during the first postoperative week. Autopsy revealed the umbilical vein graft to be patent.

Conclusion

The results of this program were to show that different techniques for storage and preservation of the collagen tubes resulted in a graded patency rate but that fresh, autogenous vein grafts remained superior to all other biologic freshly preserved or modified prostheses. These results are shown in Figure 2 and Figure 3.

ARTERIAL INTERPOSITION GRAFTS (CAROTID AND FEMORAL)

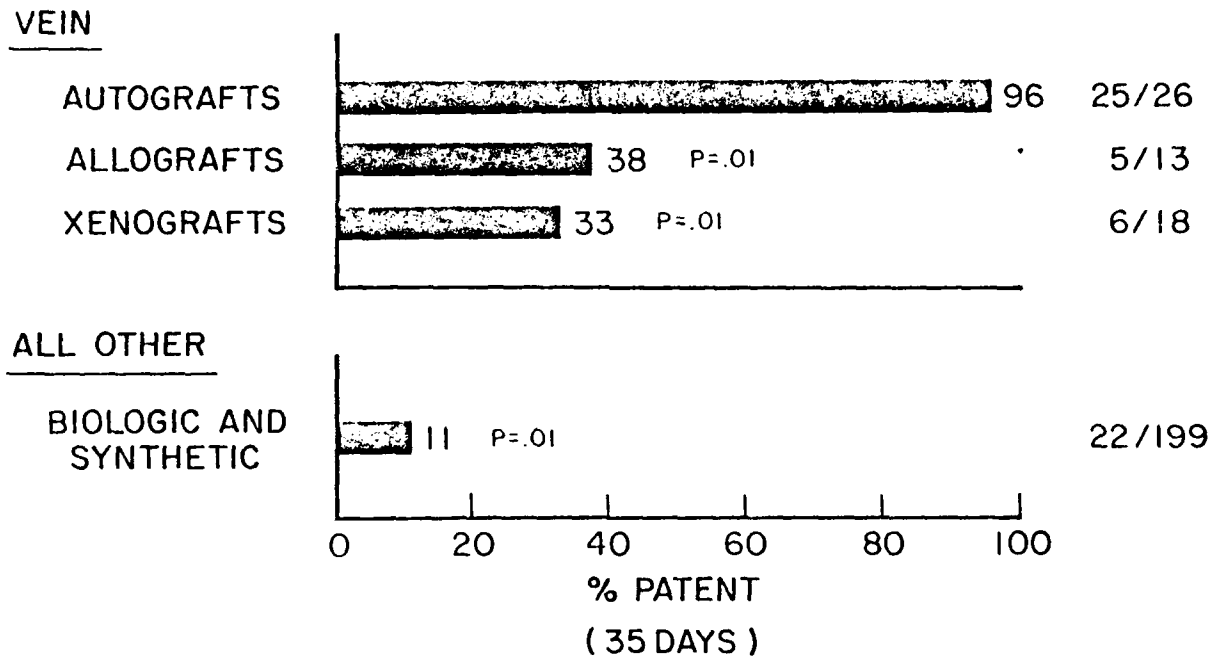

FIGURE 2

ARTERIAL INTERPOSITION GRAFTS (CAROTID AND FEMORAL)

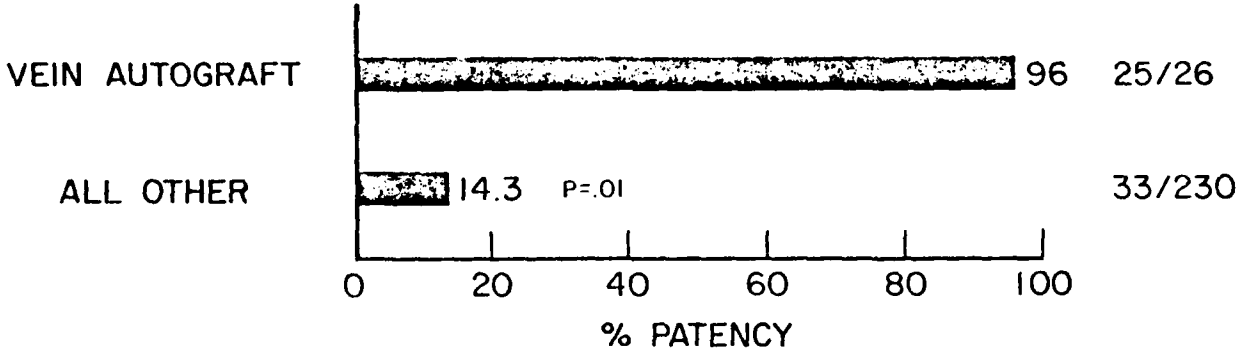

FIGURE 3

References

1. Sawyers PN and Deutch B: Use of electrical currents to delay intravascular thrombosis in experimental animals. Amer J Physiol 187:473, 1956.

2. Schwartz SI: Prevention and production of thrombosis by alterations in the electric environment. Surg 108:533, 1959.

3. Richardson JW and Schwartz EI: Prevention of thrombosis with the use of negative electric current. Surg 53:636, 1962.

4. Driller J: Unpublished data.

5. Murphy PV, LaCroix A, Merchant S, and Bernhard W: Development of blood compatible polymers using the electric effect. J Biomed Mat Res Sympos 1:59, 1971.

6. Sawyer PN, et al: Electrochemistry of thrombosis - an aid in the selection of prosthetic materials. J Biomed Mat Res 4:43, 1970.

7. Sharp WV, et al: Experience with negatively charged polyurethane-backed velous. J Biomed Mat Res Sympos 1:75, 1971.

8. Whiffen JD, et al: Vessel patency following non-suture anastomosis with intravascular rings. Arch Surg 91:939, 1965.

9. Gott VL, et al: GBH coatings on plastics and metals. Ann NY Acad Sci 146:Art, 1:21, 1968.

10. Wright JS, et al: The retardation of intravascular thrombosis by sulphatated surfaces. Surg 61:744, 1967.

11. Salzman EW, et al: New anti-thrombotic surface. Surg 61:1, 1967.

12. Kramer RS, et al: Stability of GBH surfaces. J Thor Cardiovasc Surg 53:130, 1967.

13. Milligan HL, et al: The search for correlation between electrokinetic phenomena and blood thrombus formation on implant materials. J Biomed Mat Res 2:51, 1968.

14. Leininger RI, et al: The Zeta potential of some selected solids in respect to plasma and plasma fractions. Trans ASAIO 10:237, 1964.

15. Bernhard HF, et al: Fetal fibroblasts as a sub stratum for pseudoendothelial development of prosthetic surfaces. Surg 66:284, 1969.

16. Manfield PB, et al: Endothelial cells versus fibroblasts for prelining vascular prostheses. Circ Suppl 45, 11:187, 1972.

17. Dardick and Dardick: The fate of human umbilical cord vessels used as interposition arterial grafts in the Baboon. Syrg Gyn Obstet 4:567, 1975.

18. Gupte P, et al: Umbilical vein as a small diameter vascular prosthesis. 28th ACEMB, 1975.

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