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# Glutaraldehyde-Preserved Venous Valve Transplantation in the Dog

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Transplantation of femoral vein grafts was performed on 33 mongrel dogs to assess graft patency and valvular function after storage in glutaraldehyde. The grafts were removed from the donor, flushed with room temperature heparinized lactated Ringer's solution, and then stored in a 0.2% glutaraldehyde solution for 16 hr. At the time of grafting, the veins were again flushed with lactated Ringer's and anastomosed orthotopically to the recipient. An arteriovenous fistula was also created. Postoperatively the animals received daily doses of aspirin (2 mg/kg) and dipyridamol (50 mg). The following groups were studied: Group I ($n$ = 10) served as controls and received fresh autografts. Group II ($n$ = 13) received autografts stored for 16 hr in 0.2% glutaraldehyde. Group III ($n$ = 10) received allografts stored similarly in glutaraldehyde for 16 hr. The grafts were monitored for evidence of patency. All grafts were removed for histological evaluation when patency was no longer detected or at the end of 7 weeks. Of the fresh and glutaraldehyde-preserved autografts (Group 1), 100% were patent at 7 weeks, and generally retained valve function. Patency of allografts was only slightly inferior but valve function was disappointingly poor at 7 weeks. 

## INTRODUCTION

There has been recent interest in direct reconstruction of venous valves for venous insufficiency syndromes. A variety of procedures, including valvuloplasty, autologous venous valve transplantation, and valve transposition procedures, have been utilized [1, 2]. A valve structure undamaged by previous phlebitis is usually available for direct reconstruction in congenital or developmental venous insufficiency syndromes [3–5]. In the postphlebitic variety in which the valvular apparatus has been destroyed, a valve transplantation from another site such as the axillary vein may be the only available option [5]. Frequently, the axillary vein valve may be unsatisfactory, however. A glutaraldehyde-preserved venous valve that is readily available from the "shelf" for use in these instances would greatly facilitate valve reconstruction surgery [6–9]. Valve insertions in multiple sites, a theoretically desirable goal, would also be facilitated with the availability of such preserved valve tissue. With these clinical goals in mind, glutaraldehyde preserved autografts and allografts were evaluated in dogs.

## MATERIALS AND METHODS

Thirty-three mongrel dogs weighing approximately 20 kg each were divided into three groups. Group I ($n$ = 10) received fresh autografts. Group II ($n$ = 13) received autografts which had been stored in glutaraldehyde (0.2%) for 16 hr and Group III ($n$ = 10) received allografts stored similarly in glutaraldehyde for 16 hr. In Group II and III animals, an adjunctive arteriovenous fistula was created to increase flow through the transplanted venous segment (Fig. 1).

*Surgical technique.* Animals were anesthetized with pentobarbital sodium and systemically heparinized with 3000 units of heparin. The left femoral vein was routinely used as the donor segment and the right femoral vein as the recipient site. The left femoral vein below the inguinal ligament was exposed through a longitudinal incision



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FIG. 1. Autografted vein valve and adjoining vein wall after glutaraldehyde preservation at 7 weeks after transplantation (H&E, 8.4×). Dog E-7. Valve cusp is intact.

and a 6-cm segment of the vein was excised with a valve when present. The right femoral vein was exposed through a similar incision and a 3-cm segment was removed. The valve containing left femoral venous segment was transposed to the right femoral area with appropriate orientation. End-to-end anastomosis with 6-O Prolene interrupted sutures was utilized. Fresh and stored grafts were washed with heparinized lactated Ringer's solution (at room temperature) before transplantation.

All animals were pretreated with aspirin (2 mg/kg) and dipyridamol (50 mg/daily) for 2 days prior to surgery, and this regimen was continued for 7 weeks postoperatively. All animals received antibiotics (Kanamycin) for 5 days postoperatively.

Patency of the grafts was monitored by daily Doppler examination with a hand-held Doppler (5 mHz). Retrograde reflux through the valve segment detected by Doppler during abdominal compression or distal compression release was indicative of valve failure. Ascending and descending venograms were selectively utilized to document patency and valve function. The transplanted venous segments were excised and submitted to light and electron microscopy. At the time of excision, valve function could be determined by stripping the venous segment empty caudad to the valve and observing reflux through the valve if present to fill the emptied segment.

## RESULTS

The transplanted venous segment remained patent in 100% of animals at 1 week postoperatively. At 7 weeks, similar patency rates were obtained in Groups I and II, and a slightly reduced patency rate in Group III (Table 1).

The status of valve function as monitored by Doppler probe examination or direct ex-

TABLE 2

OUTCOME OF TRANSPLANTED FEMORAL VALVE

| Group | No. of Dogs | Number of transplanted valves | Valve function at Postoperative Week | | | | | | | Functioning % |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | |
| I | 10 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 100 |
| II | 13 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 5 | 83.33 |
| III | 10 | 8 | 8 | 7 | 6 | 6 | 6 | 6 | 2 | 25 |

stances, a nearly intact valve histology was present even though the collagenous skeleton was thickened (Fig. 2).

## DISCUSSION

Even though a high degree of patency of the venous segment was observed with fresh and stored autografts as well as allografts at 7 weeks, valve function was disappointing in Group III (stored allografts). Only 25% of the transplanted valves could be confirmed to be functional *in situ* at 7 weeks (Table 2).

Reported experience with venous allograft segments, either fresh or stored, indicates gradual obliteration of the graft owing to either rejection or the storage method [2, 5, 10]. In the current study, a satisfactorily high patency rate of the vein segment was obtained at 7 weeks. However, the behavior of the transplanted valve contained within the venous segment was disappointing. There was absorption of the valve cusp due to unknown factors, rendering it nonfunctional. Factors possibly involved include the storage technique with glutaraldehyde [6–9], allograft rejection, and perhaps the arteriovenous fistula used as an adjunct to keep the venous segment patent. However, since 83% of the preserved autografts had functional valves at 7 weeks, the preservation technique and the arteriovenous fistula appear less likely mechanisms than a rejection-type phenomenon as the major explanation for the failure of stored allograft valves in this study.

Since glutaraldehyde-stored xenografts appear to function well for prolonged periods of time in high-pressure (aorta) as well as low-pressure (right ventricular outflow tract) environments [11], it should be feasible ultimately to develop a glutaraldehyde-preserved allograft or xenograft for use in the venous system. Attempts in this direction, that are reported herein, were not successful.

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