Clinical results of lyophilized human cadaver dura transplantation

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The clinical results of lyophilized human cadaver dura transplantation in 170 neurosurgical patients show that it is a safe and effective material for dural closure. It is associated with low complication rates and minimal cortical scarring and adhesions. The successful results have been attributed to the minimal foreign body reaction stimulated by freeze-dried tissue. These factors plus its capacity for safe and convenient long-term storage at room temperature make lyophilization the method of choice for preserving dura mater.

KEY WORDS  •  dura mater transplant  •  cadaver  •  lyophilization

It is now clear that the subdural space should be closed even after neurosurgical procedures in which dural removal has been necessary. Closure has been accomplished over the years by a wide variety of natural and synthetic materials including human dura mater procured from cadavers. In a previous report it was shown that human cadaver dura preserved by freeze-drying or lyophilization proved to be a satisfactory dural substitute for permanent implantation.

The functional characteristics of an ideal dura graft include successful performance of indicated function, no increase of infection rate, exclusion of existing or subsequent infection, a capacity for watertight closure of the cerebrospinal fluid spaces, and minimal foreign body reaction or cortical adhesion. This report examines these factors in a series of 170 patients who received lyophilized human cadaver dura from the U.S. Navy Tissue Bank.

Materials and Methods

The records of the U.S. Navy Tissue Bank Graft Registry were reviewed from January 1, 1953, to January 1, 1968. The materials and methods for this study have already been thoroughly described, but will be reviewed briefly. Dura mater obtained from cadavers from the U.S. Naval Hospital, Bethesda, Maryland, according to standardized criteria of donorship, was stored in −70°C freezers until sterility was ensured and suitability of the donor ascertained by diagnostic autopsy. Following this it was lyophilized to a residual moisture of less than 5% and stored in a vacuum at room temperature until use. Some of the dural grafts were sterilized with either liquid ethylene oxide, liquid betapropiolactone, or radiation prior to freeze-drying. Reconstitution was by immersion in sterile saline for 30 min.

The patient population was relatively uniform, and examples of most neurosurgical problems were represented. The cases were divided into three types: Class 1 included clean and uncontaminated cases that would run a normal risk of postoperative infection and other complications (elective tumor excisions). Class 2 cases were potentially contaminated (open trauma and cerebrospinal...
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fluid fistulas). Class 3 cases were those already contaminated (brain abscesses).

Results

The results are listed under each of the arbitrary categories set as characteristics of an ideal dural graft. The primary indication for grafting was to replace missing dura; this was successfully performed in 98% of the cases (Class 1, 100%; Class 2, 95%; and Class 3, 75%).

Infection. There was no instance of dural contamination at the time the graft was reconstituted. Among the 162 patients who had no infection before grafting, 10 (6.2%) developed infection. Table 1 shows that of the 121 clean cases in Class 1, two developed infection (1.7%). Of the 42 potentially contaminated Class 2 cases, eight developed infection (19%).

An important corollary to the consideration of infection rate is whether or not the graft localized existing or developing infections to the wound site, resisting penetration into the cerebrospinal fluid space. There were 18 cases in which this characteristic could be examined; in four (22%) the graft failed to keep the infection localized and meningitis or brain abscess developed. In the other 14 (78%) of these cases, the lyophilized dura graft satisfactorily excluded the infection.

CSF Leak. In one case out of the entire series of 170, reoperation was necessary to stop a cerebrospinal fluid (CSF) leak. Some information regarding this parameter may also be obtained from the 24 cases in which a lyophilized dural graft was used to close an existing cerebrospinal fluid fistula. In this group there were two failures (8%).

Biopsy and postmortem specimens were not often obtained, and histological evaluation of these was not always possible. Study of the 13 available specimens revealed a minimal nonspecific inflammatory cellular reaction that occurred over the first few weeks followed by gradual absorption and incorporation of the graft into the host dura. From 18 cases that came to reoperation for tumor recurrence or cranioplasty, it was observed that within several months the graft became virtually indistinguishable grossly and histologically from the patient's own dura except at the edges where there was some thickening and scar tissue remaining. Adhesion formation at this time was minimal.

Cortical scarring and adhesions are known to be related to focal seizure disorders. Indirect evidence as to incidence of adhesions was therefore sought through the frequency of postoperative seizure episodes. Fifty-one patients with intracerebral meningioma were chosen as the most uniform group for this evaluation. These patients usually had a single operative procedure, a minimum of postoperative complications, a fairly standard anticonvulsant program, and a relatively good long-term outlook. Of the 51 patients with intracranial meningiomas, there were 32 on whom there was good follow-up data for 1 year and who did not suffer tumor recurrence. Of these 32, only four were reported as having continuing seizure problems, which is a postoperative epilepsy rate of 12%.

Sterile procurement of cadaver dura is costly and elaborate. Considerable economy of time and cost could be accomplished with post-procurement sterilization. We have used this method somewhat empirically since 1958. Table 2 shows how the 228 pieces of dural graft were handled during the 15-year period reported. Since a sterile dural product can be obtained with any of these methods, the clinical data were analyzed to see if the functional characteristics had been altered after sterilization. The results with sterilized dura were compared to those with steriley procured dura (Table 3). Sterilization was certainly not harmful and may actually have exerted some benefit. In potentially contaminated (Class 2) cases, it appeared that the sterilized grafts may have enhanced resistance to the subsequent development of infection. Sterilely procured grafts excluded in-

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**TABLE 1**

Infection rate of dural grafts related to the degree of original contamination

<table>
<thead>
<tr>
<th>Class of Contamination</th>
<th>No. of Cases</th>
<th>Infections No., %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class 1 (clean)</td>
<td>120</td>
<td>2 (1.7%)</td>
</tr>
<tr>
<td>Class 2 (potentially contami-</td>
<td>42</td>
<td>8 (19%)</td>
</tr>
<tr>
<td>nated)</td>
<td>162</td>
<td>10 (6.6%)</td>
</tr>
</tbody>
</table>

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TABLE 2
Methods of processing 228 dural specimens from cadavers

<table>
<thead>
<tr>
<th>Dural Specimens</th>
<th>Sterile Procurement</th>
<th>Nonsterile Procurement and Sterilization by:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Ethylene Oxide</td>
</tr>
<tr>
<td>No., % processed</td>
<td>83 (36%)</td>
<td>103 (45%)</td>
</tr>
</tbody>
</table>

Infection in 37% of the cases and failed in 50%, whereas the sterilized grafts excluded infection in 83% of the cases and failed in 8%.

Discussion

Although a substantial post-grafting infection rate of 6.2% was noted, division of the cases into those that should have low as contrasted to high infection rates showed that in both instances the infection rate was comparable to several series of ungrafted recipients. Although the development of infection influences the outcome of cases in which dura grafts have been used, the data suggest that there will be a good chance for a satisfactory result in spite of the infection.

The results regarding the exclusion of infection and adequate closure of the cerebrospinal fluid space are reassuring but not conclusive. Although this and other information is helpful in determining that lyophilized dura is safe and effective, the evidence suggesting a minimal foreign body reactivity is probably most critical. The relative inertness of these dura grafts is possibly the major factor in the generally excellent results with the use of this material. This conclusion was predicted from Rosomoff’s animal studies in this laboratory which were followed by a successful clinical trial in 60 patients, and is further suggested by the histological evaluation of the clinical material and the lower seizure rate (12%) compared to that of other series.

Other lyophilized tissues have also been associated with minimal foreign body reaction; studies of orthotopic grafts of lyophilized skin have revealed that it is the graft itself that is nonreactive. This nonreactivity seems peculiar to freeze-dried tissue and is not yet completely understood. Although nonviable tissues have long been considered to be less reactive than viable ones, it now appears that something specific occurs with lyophilization over and above its killing effect which makes the product particularly inert.

The finding that sterilized lyophilized dura may give superior results is surprising. This is, however, a retrospective study, and each method of processing represents a different period of time. Patients in the sterile procurement group were generally grafted earlier since sterile procurement ended in 1958, and improvements in operative techniques, postoperative care, and infection control may have influenced the better results seen in the more recent cases. The age of the donor may also influence the success or failure of the graft, and the age of the donors in this study varied considerably. A more extensive evaluation might indicate, for example, that exclusion of infection is impaired in dura taken from older donors, which tends to be thinner. Since it appears, however, that the post-procurement sterilized grafts are at least as satisfactory as the steriley procured ones, the betapropiolactone sterilization method currently used may be safely continued until laboratory studies now in progress de-
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... demonstrate which means of sterilization is most advantageous.

Conclusions

This study was initiated by inquiries from military neurosurgeons as to whether the dura they were using in combat casualties could possibly be responsible for infectious complications. The answer returned was that almost certainly the dura was not a contributing factor, that in a significant number of patients it has provided safe closure of the cerebrospinal fluid space, and that lyophilized human cadaver dura may be the graft of choice where autogenous material from the operative site is not available.

References


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