Study and clinical application of a porcine biomembrane for the repair of dural defects

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A biomembrane was developed from pig peritoneum treated with 0.65% glutaraldehyde. This was evaluated for use as a dural substitute in an animal model and in a patient population. After being treated with the glutaraldehyde solution, the biomembrane lost its antigenicity while its collagen underwent an irreversible cross-linking reaction, causing it to become a stable nonviable polymer resistant to absorption by the host. The biomembrane was used experimentally in 43 procedures on 20 dogs and was applied clinically in 614 patients. The results demonstrated that it is an acceptable material for the repair of dural defects, with the following advantages: 1) it is nontoxic to the body and brain tissues, with minimal tissue reaction; 2) its biophysical properties facilitate watertight closure with sutures; 3) its distensibility makes it suitable for decompressive surgical dural repair; and 4) its visceral surface is extremely smooth, causing virtually no adhesions with the brain tissue while the outer surface readily heals with the subcutaneous tissue.

Key Words • dural substitute • peritoneal membrane • biomembrane

An evaluation of the repair of dural defects with nylon silica gel was begun in 1976 because of problems with watertight closure. As a result, a biomembrane dural substitute prepared from pig peritoneum was developed. A literature search has revealed no reports of similar preparations. The current report discusses the method of preparation, and presents the results of animal experiments and clinical application of this biomembrane.

Materials and Methods

The biomembrane was obtained from the peritoneum of healthy pigs, harvested within 30 minutes of sacrifice. The selected peritoneum was taken to the laboratory in a sterile container and processed. The tissue was first washed thoroughly with distilled water, then the residual fatty tissue was removed. After being stretched on a spreader, the peritoneum was soaked in a solution of 0.65% glutaraldehyde for 1 week. The resulting biomembrane was free of fatty tissue, uniform in thickness, and clean. The tissue was cut under sterile conditions into pieces from 6 × 6 cm to 8 × 11 cm. Each piece was then stored in a sealed ampule containing the same glutaraldehyde solution. Ten percent of the samples were chosen at random for bacterial culture; only when all cultures were negative was the remainder of the lot considered acceptable for use.

Animal Experiments

During the period from June, 1980, to August, 1981, a total of 43 craniotomies involving the right frontal temporoparietal areas were carried out under general anesthesia in 20 healthy mongrel dogs. Dura was removed from an area measuring 2.5 × 2.5 cm and was replaced with a biomembrane of the same size and a thickness of 0.2 mm. The dural substitute was sutured into position with either interrupted or continuous sutures. No cerebrospinal fluid leak was detected at the time of repair. The implanted membrane had a strong resemblance to normal dura

Results of Animal Experiments

Observation of the tissues removed during the second craniotomy revealed the outer surfaces of the implanted membrane to be tightly adherent to the temporalis muscle, although easily separable from it. The outer surface of the membrane retained its original smooth-
ness with some scattered capillary oozing. The thickness of the membrane varied from 0.2 to 0.4 mm. In general, the implanted biomembrane was thicker, less elastic, and stiffer than before implantation. There were no or very slight fibrous adhesions between the inner surface of the implants and the brain tissue. As a rule, the longer the period of implantation, the less were the fibrous adhesions; no adhesions were found in connection with implantation for longer than 6 months (Fig. 1). The appearance of the cerebral cortex under the implants was normal. In two dogs with postoperative infection, the implanted biomembrane was thickened and adherent to the brain tissue.

The postoperative observation period varied from 62 to 124 days; the average was 102 days after the first operation in the original group of 20 dogs, from 210 to 300 days for the 15 dogs undergoing a second craniotomy between 62 and 124 days after original implantation of the tissue. The biomembrane consisted mainly of fibrous connective tissue (Fig. 2). Vascularization of the tissue was found in eight cases, osteotrabeculae in two, and slight infiltration of chronic inflammatory cells in three. A large number of phagocytes were found in the specimens from the two dogs with incisional infections. The cerebral cortex was normal in 13 dogs (Fig. 3) and showed mild infiltration of inflammatory cells with astrocytic proliferation in two dogs.

Electron microscopy with a Model DXA 4-10 electron microscope showed the biomembrane to consist of collagenous and elastic fibers prior to implantation (Fig. 4). The dura mater of the normal dog consists mainly of regularly arranged collagenous fibers with a

FIG. 1. Photomicrograph showing the interface between the inner surface of a biomembrane implant and brain tissue. There are no adhesions. H & E, × 225.

FIG. 2. Photomicrograph of a sample of biomembrane. The field shows mainly fibrous connective tissue. H & E, × 225.

FIG. 3. Photomicrograph of the cerebral cortex of a dog with biomembrane implants showing a normal appearance. H & E, × 225.

FIG. 4. Electron micrograph of the biomembrane before implantation showing collagenous and elastic fibers. × 7600.
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FIG. 5. Electron micrograph of the dura mater of normal dog, which consists mainly of regularly arranged collagenous fibers with a structure similar to that of the biomembrane. × 10,100.

FIG. 6. Electron micrograph of the biomembrane removed after implantation showing a large amount of collagenous fiber. × 5290.

structure similar to that of the biomembrane, containing a few fibrocytes with intact cell membranes and a small amount of cytoplasm with a few rough endoplasmic reticula and mitochondria inside (Fig. 5). The biomembrane removed after implantation consisted mainly of collagenous fibers (Fig. 6); a few fibroblasts, white cells, and lymphocytes were also present. The arrangement of collagenous fibers was regular in some areas and irregular in others. There were a few spindle-shaped fibroblasts with slender processes rich in cytoplasm in which more rough-surfaced endoplasmic reticula and mitochondria were seen than had been observed in the normal dura. Normal canine brain tissue consists mainly of neurons and glia (Fig. 7 left). In the experimental animals, a few neurons became swollen and there was a decrease in the amount of endoplasmic reticulum, ribosomes, and mitochondria. The brain tissue under the implant consisted mainly of normal neurons and glia (Fig. 7 right). A few neurons were either contracted or swollen.

The results obtained from these animal experiments suggested that the biomembrane is satisfactory for the repair of dural defects. The study was therefore continued in the clinical setting.

Clinical Applications

The biomembrane was used to repair dural defects in 614 patients between December, 1980, and October, 1986. The series included 416 males and 198 females ranging in age from 7 to 62 years, with an average age of 35 years. There were 221 cases involving brain tumor, 393 cases of acute cranioencephalic trauma, two cases each of spontaneous intracerebral hematoma and posterior fossa lesions, and one case each of rhinorrhea,

FIG. 7. Left: Electron micrograph of the brain tissue of a normal dog, showing normal neurons and glia. × 4100. Right: Electron micrograph of brain tissue underneath a biomembrane implant showing mostly normal neurons and glia. × 5285.
spinal canal stenosis, and spinal tumor. In total, 612 procedures for dura mater repair were carried out, 300 for repair of dural defects and 312 for repair of surgical decompression. Spinal dura was repaired in two cases. The location of implantation was frontal in 212, frontotemporal in 222, temporoparietal in 137, at the posterior fossa in 41, and over the thoracic spine in two. The size of biomembrane used varied from 1.5 • 2.0 cm to 8 • 11 cm. In general, a larger size of biomembrane segment was needed for decompression procedures.

**Technique**

During the operation, the biomembrane was removed from the sealed ampule containing glutaraldehyde solution and washed three times, 3 to 5 minutes for each wash, in sterile saline. It was then trimmed to the size and shape corresponding to the defect. With the smooth surface toward the brain and the rough surface facing out, the biomembrane was sewn to the dura with interrupted sutures, except in the cases of rhinorrhea and spinal defect repairs.

**Clinical Observations**

In early cases, the patients were noted to be mildly febrile for 3 to 6 days after implantation. In three patients high fevers occurred after implantation, but bacterial cultures were negative. The patients' fever gradually defervesced. Retrospectively, it was noted that the biomembrane used in these patients was given only a short wash prior to implantation. Hyperthermic reaction caused by irritation with glutaraldehyde was suspected. No similar pyrexic responses were observed after the three-wash procedure was strictly followed. There were no remarkable changes in blood pressure, pulse, or respiratory rate after implantation. No subcutaneous fluid collection was observed in any of the cases.

All except one of the 613 patients were discharged with uncomplicated wound healing. The follow-up period ranged from 3 months to 5 years. Two patients had a secondary exploration 8 days and 13 months after implantation because of the suspicion of other secondary lesions. No adhesions were found between the implants and brain tissue in either patient, and the brain surface appeared normal in both instances (Fig. 8). In patients who had undergone electroencephalography pre- and postoperatively, there were no notable changes. The one exception was a patient with a severe head injury who died 12 hours after admission. No adverse reaction to the biomembrane was observed.

**Discussion**

Dural defects are often associated with head injury, intracranial tumor, and a wide variety of processes requiring neurosurgical intervention. They require prompt repair for the reestablishment of the anatomic barrier. Various strategies for dural substitution have been tried for nearly a century. In 1895, a rubber membrane was used by Abbe to repair dural defects in two traumatic epileptic patients after excision of dura and cerebral scars. In 1898, rubber membrane and silver foil were used by McCosh in 14 patients. Tissue reactions of these patients were so severe that muscle membrane and cadaveric dura were subsequently suggested by Kirschner and Finsterer, respectively. In 1940, dried human amnion was introduced by Chao, and this technique was widely accepted. Polyethylene and silicone rubber-coated fibers were utilized by Ingraham, et al., and Campbell, et al., considered human freeze-dried dura to be more beneficial.

Since 1974, experimental and clinical studies of various dural substitutes have been carried out in China. These studies concluded that polyester fiber and silicone rubber-coated nylon were better substitutes than simple silicone rubber, and that freeze-dried dura was a better material than pressurized polyethylene and dried amnion. In 1980, the authors developed a biomembrane from pig peritoneum that was treated with 0.65% glutaraldehyde solution. Glutaraldehyde provides relatively good sterilization, and in studies with porcine heart valve, it has been shown that these tissues lose antigenicity and the collagen undergoes irreversible changes in cross-linking. Presumably, similar changes occur in porcine peritoneum. The resulting substance has been found to be relatively nontoxic with adequate washing. After implantation, no adverse reactions of surrounding tissues have been observed. The tissue reaction is minimal and no subcutaneous fluid collection has been found. Its biophysical properties permit simple dural repair with watertight closure. The extremely smooth visceral surface appears to prevent scar formation between the membrane and cerebrum. While the potential of transmission of disease from the donor animal to humans does exist, this would appear to be quite uncommon.

**FIG. 8.** Photograph at a second exploration operation in a patient 13 months after implantation of biomembrane dural substitute. No adhesion was found between the implant and brain tissue, and the cerebrum appeared normal.
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and unlikely. Conversely, human-to-human transmission of fatal slow viral disease has been reported several times in the use of human dura. Such disease transmission has not occurred in the vast experience with porcine heart valves or in the current study. Therefore, the authors consider this biomembrane to be an ideal dural substitute.

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