Biologically inert synthetic dural substitutes

Appraisal of a medical-grade aliphatic polyurethane and a polysiloxane-carbonate block copolymer

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Two types of artificial membranes, a medical-grade aliphatic polyurethane and a polysiloxane-carbonate block copolymer, were tested as substitutes for dura in 24 and 12 rabbits, respectively. The films were placed either epidurally, subdurally, or as dural grafts in equal subgroups of animals. The postoperative course was uneventful with no manifestations of convulsive disorder or cerebrospinal fluid leak. The animals were sacrificed 3, 6, or 9 months after implantation of the artificial membranes. Both types of artificial membranes were easily removed from the underlying nervous and the other surrounding tissues. The histological examination failed to reveal adhesions, neomembrane formations, or any type of foreign body reactions to the polyurethane film. The implantation of the polysiloxane-carbonate film caused no reaction when it was applied epidurally. As a dural graft, the polysiloxane-carbonate copolymer induced the formation of a thin neomembrane of one to two layers of fibroblasts which formed a watertight seal of the dural defect. A similar thin neomembrane was found to encase this artificial membrane in the group of animals in which it was implanted subdurally. There was no foreign body reaction to the polysiloxane-carbonate film. The authors conclude that these materials hold promise as dural substitutes or in the prevention of spinal dural scarring, and should be evaluated clinically.

KEY WORDS • dura mater • dural substitute • synthetic membrane • polyurethane • polysiloxane-carbonate block copolymer

As one of the investing layers of the brain, the dura mater offers not only insulation but also mechanical support, protection, and containment of cerebrospinal fluid (CSF). Duraplasty is an absolute necessity whenever the surgeon faces problems such as a dural defect due to congenital anomalies, cranial base fractures, or excision of a meningioma. Neurosurgeons continue to seek the ideal dural substitute, but most tested materials have been abandoned because of serious disadvantages such as the formation of adhesions, poor physical and mechanical properties, high cost, and difficulty in obtaining, storing, and processing these materials. The growing number of complications caused by artificial dural substitutes now in use justifies an evaluation of new biomaterials.

Tecoflex EG-85 resin,* an elastomeric material, is a medical-grade aliphatic polyurethane. The biocompatibility of this polymer is well established, more extensively in artificial heart-related research. L. R. Resin† is a polysiloxane-carbonate block copolymer. Its ingredients and structure are also expected to make it biocompatible and, as a membrane, it can be manufactured in various strengths and degrees of flexibility. The principal objective of our study was to determine whether either material could reduce adhesions to brain that form even when autologous dura is retained, as in most neurosurgical procedures, and if either could prevent the intra- and extradural scarring that so often develops following lumbar disc surgery. Furthermore, this study was designed to help determine if either material could form an effective but inert barrier.

Materials and Methods

Artificial Dural Substitutes

Tecoflex. Tecoflex resin is a medical-grade thermoplastic aliphatic polyurethane synthesized of methy-

* Tecoflex resin manufactured by Thermedics Inc., Woburn, Massachusetts.

† L. R. Resin, Model 3320, manufactured by General Electric Co., Pittsfield, Massachusetts.
Artificial dural substitutes

diene bis-(cyclohexyl) diisocyanate, poly-(tetramethylene ether glycol), and 1,4-butane diol chain extender. It is available in a wide durometer hardness range from 80 shore A to 72 shore D. Tecoflex EG-85 is in a membrane form of 72 shore A durometer hardness; a 2-mil thickness was used for this study.

L. R. Resin. The copolymer L. R. Resin 3320 belongs to the family of thermoplastic elastomers. It is a block copolymer of polycarbonate and polydimethyl siloxane. Any one block copolymer of the family can be explicitly described by the formula of the type (DMS)ₙ(BPAC)ₘ, where n and m represent the sizes of the dimethylsiloxane (DMS) and bisphenol (BPAC) blocks, respectively. These materials can be produced in the form of clear film and vary in character from strong rubber to tough plastic depending on the bisphenol-A carbonate content. A film of 8-mil thickness was used in these experiments.

Animal Preparation

The experiments were performed on 36 New Zealand White rabbits weighing 2.5 to 3.0 kg each. All animals were anesthetized with 4% halothane, intubated, and allowed to respire spontaneously a mixture of oxygen and 2% halothane. Twenty-four rabbits were used for the Tecoflex film study and 12 rabbits for the L. R. Resin film study. For implantation of the artificial membranes, all sutures involving dura alone or dura and either type of film were made with a 10-0 nylon suture. The other layers of the surgical wounds were closed with a silk suture. All animals were observed on a day-to-day basis, and were sacrificed with sodium pentobarbital overdose at 3, 6, or 9 months following implantation.

Implantation of Tecoflex

The Tecoflex film was tested with either intracranial or intraspinal implantation in rabbits. Intracranial Studies. A frontotemporal craniotomy was performed on 12 rabbits, and a piece of Tecoflex film was either placed epidurally or sewn in place,

Intraspinal Studies. A lumbar (L3-5) microsurgical laminectomy was performed on 12 rabbits and the Tecoflex was either placed epidurally or sown in place

as a dural graft, in subgroups of six animals each. For epidural implantation, a 3 x 10-mm strip of Tecoflex was placed over the dura following an L3-5 laminectomy. In the implantation of Tecoflex as a dural graft, an elliptical 3 x 10-mm strip of dura was removed and the synthetic material was sutured to the edges of the dural defect in a watertight fashion.

Implantation of L. R. Resin

The L. R. Resin film was implanted intracranially in only 12 rabbits, and the experimental procedures were performed as for Tecoflex. The film was implanted either epidurally, subdurally, or as a dural graft, in subgroups of four animals each. Due to the greater thickness of the L. R. Resin film, a 7 x 7-mm size of sheet was used.

Histological Technique

The head or the part of spinal column containing the dural substitute was placed in 10% formalin. The specimens with Tecoflex were decalcified with 5% nitric acid and the specimens with L. R. Resin and HCl ethylenediaminetetra-acetic acid (EDTA). They were then embedded in paraffin, sectioned with a microtome, and stained with hematoxylin and eosin.

Results

Table 1 summarizes the reactions observed in the tests of both Tecoflex and L. R. Resin in the various modes of implantation.

Implantation of Tecoflex Film

Intracranial Studies. In rabbits undergoing either epidural or subdural implantation, except for rare loose connective tissue surrounding the implant, the artificial film could easily be detached and slipped out from the neighboring tissue. The material is extremely thin and pliable and retained these characteristics as well as its filmy quality. In rabbits with implantation as a dural graft, there was some proliferation of connective tissue limited to the epidural face of the Tecoflex film.

No adhesions were found between the Tecoflex film and the brain or dura in any of the three subgroups. The brain beneath the Tecoflex film was normal. Histological examination failed to reveal any collagen, fibrous bands, or areas of infiltration of the brain or dura by lymphocytes or macrophages (Fig. 1 left).

Intraspinal Studies. No adhesions were found between the Tecoflex film and the dura in any animal receiving epidural implantation or implantation as a dural graft. There was only some loose connective tissue limited to the epidural space over the dorsal surface of the graft. The Tecoflex retained its filmy quality and could be easily detached and slipped out from the surrounding tissues. No foreign body reactions or adhesions were found and the underlying spinal cord had a normal appearance. The film thus prevented scarring

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Table 1 summarizes the reactions observed in the tests of both Tecoflex and L. R. Resin in the various modes of implantation.
FIG. 1. Photomicrographs of tissue obtained from rabbits after implantation of Tecoflex film as a dural draft. Left: Specimen showing normal brain (parenchyma and arachnoid membrane) below the site where the Tecoflex membrane was implanted. There is no gliosis or foreign body reaction to the artificial membrane. H & E, × 38. Right: Specimen showing spinal cord (dorsal surface) below the site where the Tecoflex membrane was implanted (A). There is no gliosis below the artifact space (B) (the artificial membrane dissolved during preparation for histological examination) or any indication of foreign body reaction. There is a moderate degree of fibrosis (C) above the artifact space but no adhesions. H & E, × 23.

Implantation of L. R. Resin Film

In rabbits with epidural implantation, no adhesions, encapsulation, or other type of reaction were found and the L. R. Resin membrane could be easily detached from the surrounding tissues. In rabbits that underwent subdural implantation, the L. R. Resin film caused the formation of a thin pseudomembrane with which it was encapsulated (Fig. 2 left). Implantation of the L. R. Resin film as a dural graft led to the formation of a similar thin pseudomembrane which made a watertight seal with the dural edges (Fig. 2 right).

In both dural grafting and subdural implantation, the pseudomembrane was composed of one to two layers of fibroblasts and was not adherent to the brain or to the L. R. Resin film. Furthermore, it did not have any of the characteristics of neomembranes such as excessive proliferation of cells, sprouting of capillaries, or extracellular space filled with collagen and elastic fibers. There was no inflammatory cellular reaction such as proliferation of lymphocytes. The cortex beneath the film had a normal appearance. There was no proliferation of astrocytes or increase of glial fibers (Fig. 2). By contrast, foreign body reaction was obvious in areas surrounding the sutures with which the L. R. Resin film was secured in position as a dural graft.

Discussion

A variety of artificial products have been tested as substitutes of dura.

<table>
<thead>
<tr>
<th>Type of Implantation</th>
<th>Tecoflex</th>
<th>L. R. Resin</th>
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<tbody>
<tr>
<td></td>
<td>loose connective tissue</td>
<td>no neomembrane formation</td>
</tr>
<tr>
<td></td>
<td>surrounding outer side of</td>
<td></td>
</tr>
<tr>
<td></td>
<td>film</td>
<td></td>
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<tr>
<td>epidural</td>
<td>minimal connective tissue</td>
<td>thin pseudomembrane composed of</td>
</tr>
<tr>
<td></td>
<td>over film</td>
<td>1 or 2 layers of fibroblasts</td>
</tr>
<tr>
<td></td>
<td></td>
<td>surrounding film, watertight</td>
</tr>
<tr>
<td></td>
<td></td>
<td>seal of dural defect</td>
</tr>
<tr>
<td></td>
<td>loose connective tissue</td>
<td>thin pseudomembrane composed of</td>
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<td></td>
<td>surrounding film</td>
<td>1 or 2 layers of fibroblasts</td>
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<tr>
<td></td>
<td></td>
<td>surrounding film</td>
</tr>
<tr>
<td>subdural</td>
<td>loose connective tissue</td>
<td>not implanted</td>
</tr>
<tr>
<td></td>
<td>limited epidurally</td>
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<tr>
<td>intraspinal</td>
<td>loose connective tissue</td>
<td>not implanted</td>
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<td></td>
<td>limited over film</td>
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* In all animals the membrane could be easily detached from the surrounding tissues, the brain under the film was normal, and there were no adhesions or foreign body reactions.
Artificial dural substitutes

The present state of the art in biomaterials research fails to qualify most of these materials as potential dural substitutes and few, if any, are regularly used in neurosurgery. Silicone-coated Dacron and Teflon are the materials most extensively tested as dural substitutes in humans. Initial reports about the former were promising, but its wider use has revealed significant complications. As a highly electrostatic material, it can accumulate dust, lint, and powder on its surface and it requires extremely careful handling. It provokes the formation of a neomembrane and encapsulation of sufficient thickness to cause compression of the central nervous system and even cervical myelopathy, or it can simulate recurrent tumor. Subdural hematomas or recurrent subarachnoid hemorrhage have been also reported to develop in the space between the neomembrane and the silicone-coated Dacron. Teflon gave satisfactory results as a dural substitute in humans but in animals caused the formation of a thick neomembrane firmly adherent to the brain and has not gained the acceptance in neurosurgery that it has acquired in other surgical specialties. More recently, a Marlex-mesh duraplasty was shown to induce an inflammatory response with formation of thick fibrous tissue, simulating recurrent brain tumor.

The medical-grade polyurethanes belong to the chemical class of thermoplastic elastomers. They have been used extensively for various medical applications such as heart ventricular assist devices, insulators for pacemaker leads, intra-aortic balloons, blood-containing tubes, and small-caliber vascular prostheses. It is well established that carcinogenesis does not result from their long-term implantation in humans. Specifically, the mechanical and physicochemical properties of Tecoflex have been studied extensively in vitro and in vivo. These studies demonstrated that this material does not provoke any adverse reaction, and is suitable for implantation in a variety of natural environments such as the genitourinary and intestinal tracts, biliary duct, and cardiovascular system with great potential as a component of artificial hearts.

A variety of criteria have been proposed to define the ideal dural substitute. Tecoflex film, a biomedical-grade polymer, meets the characteristics of an ideal dural substitute. It can be extruded into film and molecularly varied to create a range of products from soft and flexible to hard and rigid. Due to its very good mechanical properties such as strength and endurance, it can be produced in a form with physical and mechanical characteristics (consistency, flexibility, and tensile strength) very similar to dura. Furthermore, it does not degrade when placed in long-term contact with body fluids and it resists blood clotting, is noncarcinogenic, and contains no toxic components that can leach into the body. Our experience suggests that it is waterproof, holds sutures securely, and is easily handled, stored, and sterilized. Histological examination of the tissue-material interface did not reveal any cellular damage caused by surface adhesion. Furthermore, the clinical observation of animals failed to indicate convulsive disorder, brain injury, or CSF leakage.

A thin film of Tecoflex could also be used in spinal surgery to coat nerve roots after a lumbar laminectomy, thus preventing future adhesions between dura and...
paraspinal muscles. In this application, it appears to hold the potential to form a sliding surface or, at least, to reduce scarring. Processed natural membranes have not been shown to offer such an advantage and the risk of infection is a consideration which thus far has not been encountered with Tecoflex or other medical-grade aliphatic polyurethanes in various bioimplantable devices. 5,10,11,19,23,32,33,35,38,40,41,49

The L. R. Resin film belongs to a family of materials which utilize the (DMS)ₙ(BPAC)ₘ copolymer structure. These materials have surface properties of silicones and the mechanical strength and fabrication characteristics of thermoplastics. We are not aware of any other study on L. R. Resin regarding either its use as a substitute for human or animal tissues or its biocompatibility. However, the long period of implantation and observation of L. R. Resin film in our study allows us to conclude that this material does not induce excessive fibroplasia and that the likelihood of thick neomembrane formation is minimal.

Based on the properties of the materials we tested, the long period of observation, and the results of the histological examination, we conclude that these artificial membranes have inert properties suitable for use in neurosurgery. Since they can be manufactured in every thickness, tensile strength, and flexibility, they could be used in the following situations: 1) to repair a dural defect following excision of a brain or spinal tumor, and to offer containment and mechanical support of the nervous tissue; 2) to provide an adhesion-free plane for repair certain dural defects due to congenital anomalies, such as cranial synostosis, craniofacial encephalomeningocele, or spinal dysraphic states. Of the two artificial membranes we tested, Tecoflex is the more promising for clinical use in neurosurgery. It is more inert than L. R. Resin, and its biocompatibility, as well as that of other medical-grade polyurethanes, is well established in a great variety of implantable devices in other parts of the body. 5,10,11,19,23,32,33,35,38,40,41,49

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J. Neurosurg. / Volume 73 / December, 1990

D. E. Sakas, et al.
Artificial dural substitutes


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