The acceptance of a vitreous carbon alloplastic material, Proplast, in the rabbit eye

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Proplast, a vitreous, carbon-Teflon, fluorocarbon polymer, was tested in rabbits for corneal tolerance and acceptance. Toxicity, vascularization, epithelialization, infection, and extrusion were studied clinically and histologically. Four techniques were used: implantation of irregular-shaped pieces of material in an interlamellar corneal pocket, lamellar graft implantation with one exposed surface, full-thickness corneal implants in a manner similar to penetrating keratoplasty, and full-thickness implants covered by a conjunctival flap. Results showed that Proplast allows fibrovascular ingrowth and stabilization without a significant foreign body response or encapsulation for a period of observation from 6 weeks to 4 months. Evidence of epithelial coverage and epithelial ingrowth was also found. Coverage of the Proplast with conjunctiva or corneal tissue was essential to prevent extrusion and infection.

Key words: keratoprosthesis, cornea, Proplast, rabbit

The development of alloplastic materials has fostered development of new applications in ophthalmology. One particular application, keratoprosthesis, has stimulated research investigation and clinical interest for many years. Even with the increased success of corneal transplantation, a group of particularly devastating diseases remain difficult to treat. Alkali burns, severe dry eye syndromes, and severely vascularized corneas are among those conditions in which grafts repeatedly fail. An alternative mode of treatment has been the surgical application of a keratoprosthesis, or artificial cornea, to provide a small optical window for clear vision. Researchers have met with modest success, particularly with the Cardona prosthesis and its variations in designs and surgical techniques. Dramatic early successes, however, have been tempered with late failures. Long-term results have included many complications.

With a foreign body in the eye, usually partially exposed, the complications have been predictable: infection and subsequent endophthalmitis, epithelial downgrowth, development of retroprosthetic membranes, glaucoma, and corneal ulceration, with leakage of aqueous around the keratoprosthesis, which leads to choroidal detachments, retinal detachments, unseating of the keratoprosthesis, and eventual extrusion.

Prosthesis designs and surgical techniques have been successfully modified to reduce the number of complications and extrusions and increase long-term tolerance. The most common complication responsible for keratoprosthesis failure remains aseptic corneal necrosis or collagen dissolution around the...
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Fig. 1. Insertion of Proplast chip into lamellar corneal pocket.

keratoprosthesis, which has been little affected by advances in technology. This aseptic necrosis has been attributed to three pathologic processes: ulceration as a consequence of degradation of corneal tissue by the enzyme collagenase, which is released by the advancing edge of corneal epithelium; desiccation of corneal tissue because of continued drying and poor corneal nutrition; and immunologic rejection of graft material in those designs that use donor grafts. The problem therefore continues to be that of complete integration of the keratoprosthesis into the surrounding corneal tissue.

Proplast is a new material that may offer considerable promise in integrating prosthesis with tissue. Proplast is a vitreous, carbon-Teflon fluorocarbon polymer with pore sizes ranging from 100 to 500 μm. It is inert, nontoxic, and nonbiodegradable and can be sterilized by steam autoclave. It can easily be cut to any desired shape and can be laminated to plastics and metals. It allows fibrovascular ingrowth without encapsulation or significant foreign body response when embedded in soft tissue alone. The carbon components of the material make Proplast "wettable" by promoting serum protein deposition, which aids in fibrovascular ingrowth. Proplast has been used successfully in orthopedic, otolaryngologic, and maxillofacial surgery for fixation of prosthetic devices to surrounding tissue, even when the points of union are subjected to continuous stress. We designed a study to evaluate Proplast with regard to tissue ingrowth and corneal acceptance in rabbits.

Fig. 2. Disc of 0.3 mm thick Proplast sutured into lamellar corneal bed with surface exposed. Two weeks after implant.
Fig. 3. Disc of 0.6 mm thick Proplast sutured into the cornea as full-thickness implant.

Fig. 4. Disc of 0.6 mm thick Proplast to be placed in cornea as full-thickness implant under a conjunctival flap.

Table I. Test results of Proplast material implants

<table>
<thead>
<tr>
<th>Series</th>
<th>No. of eyes</th>
<th>Implant size</th>
<th>Position of implant</th>
<th>Duration</th>
<th>% retained</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8</td>
<td>2 by 3 by 0.3 mm</td>
<td>Interlamellar</td>
<td>4 mo</td>
<td>37.5</td>
</tr>
<tr>
<td>2</td>
<td>6</td>
<td>7 mm round by 0.3 mm thick</td>
<td>Superficial lamellar</td>
<td>4 wk</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>6</td>
<td>7 mm round by 0.65 mm thick</td>
<td>Penetrating button</td>
<td>4 wk</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>6</td>
<td>7 mm round by 0.65 mm thick</td>
<td>Penetrating button with conjunctival flap</td>
<td>6 wk</td>
<td>100</td>
</tr>
</tbody>
</table>

Material and methods

Proplast material was tested in rabbit corneas by four different techniques (Table I). Albinorabbits weighing from 1.75 to 5.0 kg were used. Ketamine (given intramuscularly) or urethane (given intraperitoneally) was used as the anesthetic agent. An additional retrobulbar injection of 2% lidocaine, with epinephrine 1/100,000, was given in the last two surgical procedures.

In the first series, in order to determine the reaction and tolerance of the cornea to Proplast, pieces of Proplast of various sizes and shapes were embedded in the cornea of one eye of each of eight rabbits. The pieces were placed at approximately...
Fig. 5. Rabbit eye in which a full-thickness button of Proplast was implanted and covered with conjunctival flap.

Fig. 6. Rabbit eye 4 months after insertion of Proplast into intralamellar corneal pocket, showing segmental vascularization from limbus closest to the implant.

Fig. 7. Rabbit eye 4 weeks following insertion of Proplast into intralamellar corneal pocket, with local inflammatory response and impending extrusion of the implant.
half the corneal depth through an interlamellar pocket formed by making a perilimbal incision and an interlamellar dissection toward the center of the cornea (Fig. 1). The incision was sutured with 10-0 nylon suture. The eyes were then observed for signs of inflammation, fibrovascular ingrowth, and rejection. Histologic studies were performed on enucleated globes over a 4-month period.

Further studies were performed in order to determine the potential for epithelialization of Proplast material. A second series of six rabbits underwent a lamellar keratectomy and implantation of a 7 mm round Proplast button, 0.3 mm thick. The Proplast was sewn into position in the lamellar bed by means of 10-0 nylon interrupted sutures, with the anterior surface of Proplast left exposed (Fig. 2).

In a third series of six rabbits, a complete penetrating keratectomy and implantation were performed, in a fashion similar to penetrating keratoplasty, with running 8-0 nylon suture (Fig. 3). No antibiotics were given postoperatively. The rabbits were observed for evidence of inflammation, vascularization, epithelialization, infection, and extrusion. Histologic examinations were performed on all eyes in both series.

A fourth series of six rabbits received implants similar to those of the third series, except that the suture used for implantation was changed to either 8-0 silk or 7-0 polyglycolic acid and the Proplast implants (Fig. 4) were completely covered with a conjunctival flap (Fig. 5). The rabbits were observed for signs of vascularization, epithelialization, infection, and extrusion. Histologic sections
were studied by using hematoxylin and eosin (H&E) stain for cell type and tissue invasion and Masson trichrome stain for presence and distribution of collagen.

Results

The first series of rabbits that received interlamellar implantation of Proplast all showed conjunctival injection and discharge during the first several days following implantation, which subsequently subsided. Segmental vascularization of the cornea and apparent fibrous ingrowth into the implants could be seen by the third to fifth weeks after implantation (Fig. 6). Over a 4-month period, partial extrusion of the implants began in five of the eight eyes. The eyes in which the implant developed erosion and extrusion had several characteristics in common. Any extrusion that did occur happened relatively soon after implantation, between the second and sixth weeks. The area where extrusion developed was generally in an area of the cornea over a sharp edge or point of Proplast. The eyes were quiet and the Proplast appeared free of exudate during the first day or two of partial erosion, but signs of ocular inflammation and mucopurulent exudate appeared on the areas of extruded Proplast, and complete erosion occurred gradually in four of the five cases (Fig. 7). In the remaining three cases, the Proplast was tolerated without being extruded for 4 months.

The nonextruded implants were found to contain pores filled with fibrovascular tissue and varying amounts of collagen. Chronic inflammatory cells were present but were rare or moderate in number and tended to have an inverse relationship to the amount of collagen present. No foreign body giant cells were seen. The extruded implants also had ingrowth of fibrovascular tissue, but in addition, they contained large numbers of inflammatory cells and fibrin. The surrounding cornea showed large dilated vessels, and the corneal stroma contained inflammatory infiltrates.

In the second series, rapid vascularization of the corneas occurred toward the implants. Mucopurulent material was adherent to the exposed Proplast surface within 48 hr, which suggested infection. Hypopyon ulcers and corneal perforation occurred within 3 weeks in four of the eyes. Extrusion occurred in all six of the implants in this series. On histologic examination, these grafts were similar to the extruded interlamellar implants, again with fibrovascular ingrowth and large numbers of acute inflammatory cells. Epithelialization over the Proplast surface did not occur.

In the third series, with full-thickness non-covered implants, a moderate amount of exudate could be seen on the anterior surface, but no hypopyon ulcers or corneal perforations developed. By the third week, however, all rabbits showed evidence of impending extrusion with poor apposition be-
Fig. 11A. Photomicrograph of cornea with full-thickness Proplast implant, which demonstrates the prominent fibrovascular tissue invasion into the Proplast. (H&E; ×100.)

between Proplast button and cornea (Fig. 8). Extrusion occurred first in areas where lid and nictitating membrane crossed the implanted material. These animals had shallow or flat chambers throughout the study. On histologic examination of these enucleated specimens, a moderate polymorphonuclear exudate was visible on the surface, and early evidence of ingrowth of fibrovascular tissue could be seen. Some cases showed definite early epithelial ingrowth. No stromal ulceration or foreign body reaction was observed, except focally in areas of sutures.

In the fourth series, the implants were well tolerated without infection or extrusion for an observation period of 6 weeks. Conjunctival flaps showed various degrees of retraction, which ranged from essentially none at all in five cases (Fig. 9) to almost complete retraction in one case in which a buttonhole had been made at the time of surgery. The gross appearance of the bisected enucleated eyes showed that apposition between cornea and button varied with the status of the overlying conjunctival flap. When the flap was intact, the apposition was good (Fig. 10). When the flap was retracted, however, apposition was less exact. Grossly, all anterior chambers were observed to be shallow or flat, with the iris adhering to the corneas and Proplast implant. Histologic examination showed definite ingrowth of fibrovascular tissue in all cases (Figs. 11A and 11B). The ingrowth contained a component from both the conjunctival flap and the corneal edge. Definite evidence of epithelial ingrowth was apparent in some cases where little or no substantia propria remained beneath the epithelium (Fig. 12). In no case did epithelial invasion extend below the anterior third of the implant. Epithelium did not appear to invade the fibrovascular layer but remained above it. Epithelial invasion of the wound and anterior chamber was seen only in eyes with extruding implants. Evidence of epithelial coverage of the implant surface was also consistent,
even in areas where there was little subepithelial tissue between the epithelium and the Proplast material. In no case with good conjunctival flap coverage was any significant inflammation observed. All cases showed focal areas of foreign body giant cell reaction in areas of sutures. No stromal ulceration was seen in any case.

Discussion

These studies showed that Proplast implanted in the rabbit cornea does allow ingrowth of fibrovascular and epithelial tissue and epithelialization. It can be tolerated in the rabbit cornea for periods of at least 4 months when covered by a conjunctival flap or intact corneal tissue. The extrusion of the implants in the first series was probably the result of aseptic or pressure necrosis or simple mechanical erosion. Stone has shown that in any implantation of material into the cornea, it is important to contour the implanted material to the anatomical shape of surrounding tissue in order to prevent pressure necrosis and extrusion of the implant. The finding that Proplast is tolerated in the cornea without toxic reaction, along with histologic evidence of invasion of fibrovascular tissue, is consistent with previous reports of its use in other surgical specialties. This is the first report of epithelial ingrowth and coverage of Proplast material. Our experience of rapid infection and extrusion of exposed Proplast is consistent with that of others. We found no evidence of encapsulation, which has occasionally been reported with Proplast in other applications. The presence of flat anterior chambers in all animals receiving full-thickness Proplast buttons (series 3 and 4) is related to the porosity of the Proplast, which allows percolation of aqueous fluid from the anterior chamber.

With clear evidence of fibrovascular ingrowth, epithelial coverage, and ingrowth, Proplast could conceivably be integrated even more rapidly in very densely vascu-
Fig. 12. Photomicrograph of superficial implant and covering tissue near center of implant. Epithelium is continuous on the surface with areas of localized invasion of epithelium into the Proplast. (H&E; ×250.)

larized tissue, the very tissue in which corneal transplantation failure is common. The rapid fibrovascular ingrowth could also, conceivably, bring in alpha1-antitrypsin and alpha2-macroglobulin, which may promote corneal healing and decrease the incidence of corneal ulceration.17

We believe the findings of fibrovascular and epithelial ingrowth are encouraging and warrant further study on Proplast with respect to its potential use for keratoprostheses-tissue stabilization.

REFERENCES

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