LAMELLAR KERATOPLASTY USING FULL THICKNESS DONOR MATERIAL*

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WHEN DAMAGE TO THE CORNEA from degeneration, injury, or infection involves the endothelium, a state of progressive edema, epithelial erosion, and further degeneration develops which causes loss of vision and a painful eye. A limited classification of these cases would be:

A. Edema	with Fuch's endothelial-epithelial dystrophy
B. Edema	secondary to pressure, long-standing glaucoma
C. Edema	secondary to a touch of the endothelial surface by vitreous, iris
	secondary to products in the anterior chamber: multitudinous keratic precipitates, massive hemorrhage in the anterior chamber with blood staining of the cornea
D. Injury	endothelial, from operation: cataract extraction, corneal transplantation
	endothelial, from other trauma: ruptured Descemet's membrane, penetrating foreign bodies, lacerations
E. Infection	corneal, with ulcer or abscess: bacterial, fungal, or viral

A number of techniques have been described for treatment of edematous and vascularized corneas. Presuming that the persistence of disease is primarily due to loss of the anatomic and functional integrity of the posterior layers of the cornea and if the area of endothelial damage is small, a penetrating keratoplasty may be done, inserting a viable stretch of endothelium to re-establish the continuity of the posterior corneal surface.[1-2] When a penetrating graft is placed, if some of the affected area is not removed fluid will leak into the cornea, destroying the integrity of both the donor and recipient parts.[3-4] If the area of damage is large and a larger graft is used, the difficulties of penetrating keratoplasty increase and, when the whole cornea must be

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replaced by total penetrating keratoplasty, the hazards are large indeed.[5] Also, if the cornea is extensively scarred, a full thickness graft will become opaque. Finally, abnormality within the eye, such as vitreous in the anterior chamber, fibrous tissue across the back of the cornea, continuing uveitis, will spoil the result from penetrating keratoplasty.

In these more severe cases Stocker has used a large lamellar corneal graft—the purpose being to supply a large clear piece of cornea, protected from the aqueous by a line of scar at its posterior surface.[6] This is of value but in our experience the aqueous tends to find its way through the scar and the donor button tends to become edematous. Gundersen has suggested a total, thin, conjunctival flap.[7-8] This does supply a fresh surface but leaves a large edematous mass of cornea behind it. Paufique reported good results following curettage of the posterior corneal surface.[9] We have had no experience with this. Franceschetti has obtained good results using a mushroom graft, which we have not tried.[10]

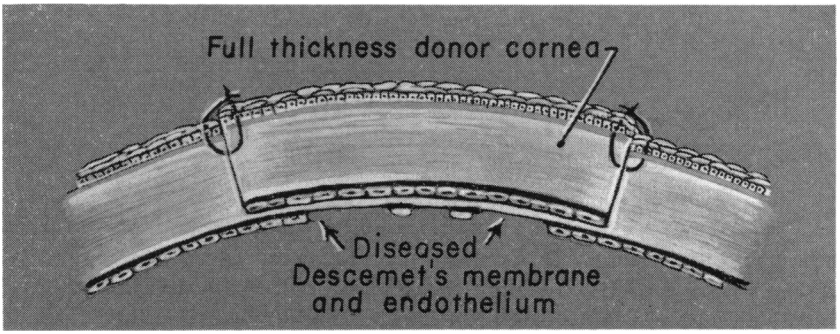

FIGURE 1. POSITIONING OF FULL THICKNESS GRAFT IN LAMELLAR BED

To meet the problem we have used a large, full thickness graft placed on a lamellar bed (Figure 1). If the lamellar bed be cut as deeply as possible little edematous cornea remains posterior to the graft. It was hoped that donor endothelium would be maintained and act as a barrier to aqueous entering the graft. Even if endothelium was lost from the graft, Descemet's membrane might hinder the movement of aqueous into the graft. Finally, a full thickness donor button has a smoother posterior surface than any split donor button and could give an improved optical result from that obtained with usual lamellar keratoplasty.

A. ANIMAL STUDIES

Grafting was done using albino rabbits. All grafts were round homografts, 8 mm. in diameter. The work can be set out as follows:

1. NORMAL HOST

LAMELLAR TECHNIQUE. Full thickness donor buttons were placed on deep lamellar beds and fixed in place using 6.0 interrupted silk sutures. The animals were sacrificed at various times and the eyes sectioned and studied histologically (see Table 1).

TABLE 1. NORMAL GROUP

Time from grafting to enucleation of host's eye	*Number of eyes*	
	Lamellar	*Interlamellar*
30 minutes	2	–
2 hours	1	1
4 hours	1	1
8 hours	–	1
1 day	2	2
2 days	2	3
3 days	–	1
4 days	–	2
8 days	–	1
14 days	–	1
21 days	–	1
28 days	–	1

INTERLAMELLAR TECHNIQUE. Full thickness donor buttons were taken, the epithelium removed, and the graft inserted interlamellarly. The animals were sacrificed at various times, the eyes sectioned and studied histologically (see Table 1).

To find if endothelium of blood vessels responds to this operation as does corneal endothelium, a few buttons taken from aortic wall were inserted interlamellarly and studied.

2. ABNORMAL HOST

A number of methods were tried to damage corneal endothelium without producing a severe reaction in the anterior chamber, without causing extensive necrosis of the corneal stroma, and without breaking Descemet's membrane. Finally a technique using acetic acid was chosen. Acetic acid 1% was irrigated into the anterior chamber for 5 minutes and then washed out with saline. Grafting was carried out, using the lamellar technique, and the animals were sacrificed at various intervals, the eyes sectioned and studied (see Table 2).

TABLE 2. ACETIC ACID GROUP

Interval between chamber injection and grafting	*Interval grafting to enucleation of host's eye*	*Number of eyes*
1 hour	4 hours	1
24 hours	1 hour	2
24 hours	2 hours	–
24 hours	4 hours	1
24 hours	5½ hours	1
24 hours	27 hours	3

3. TISSUE CULTURE STUDIES

Of the studies, three are pertinent.

a) A full thickness corneal button was placed endothelial side down on chicken plasma in a Carrell flask.

b) A button of aortic wall was placed endothelial side down on chicken plasma in a Carrell flask.

c) A full thickness corneal button was placed endothelium side up on chicken plasma, in a Carrell flask.

Results

1. NORMAL HOST

LAMELLAR TECHNIQUE. After grafting, the donor endothelial cells rapidly disappeared. This started at ½ hour (Figure 2), was advanced

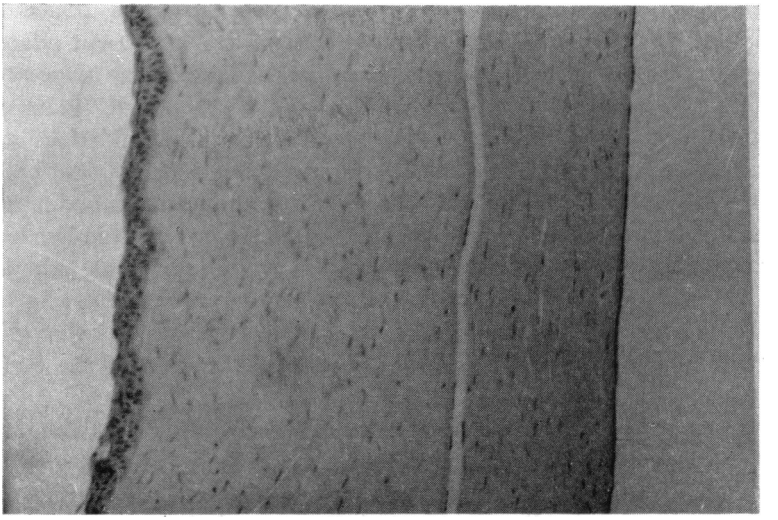

FIGURE 2. FULL THICKNESS GRAFT LYING IN A LAMELLAR BED ON NORMAL CORNEA FOR 30 MINUTES
Donor endothelium has partly disappeared.

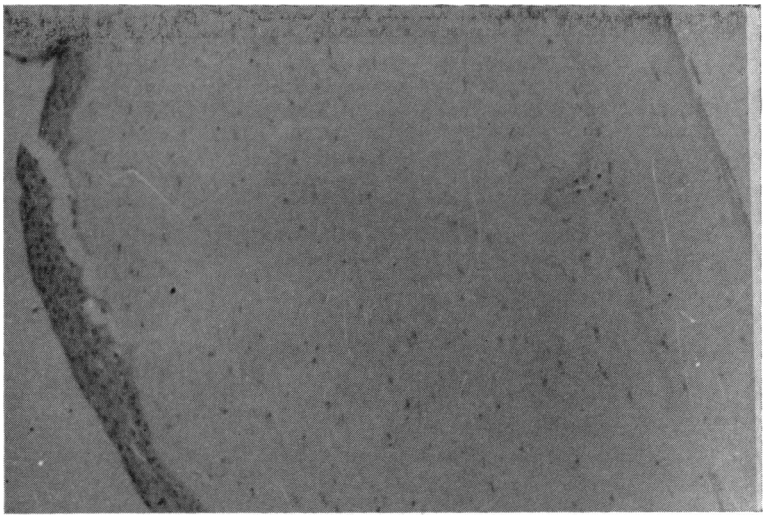

FIGURE 3. FULL THICKNESS GRAFT LYING IN A LAMELLAR BED ON NORMAL CORNEA FOR 24 HOURS
Donor endothelium has disappeared. Some inflammatory cells lie at the interface.

by six hours, and complete by 24 hours (Figure 3). A few inflammatory cells, polymorphonuclear, appeared in the adjacent recipient stroma starting about four hours after operation. By 24 hours after operation these were present at the posterior interface between donor and recipient, in the neighboring recipient cornea, and at the cut edges of the donor button. They were not present in the donor near its posterior surface. Descemet's membrane of the donor remained intact and showed normal reaction to routine stains but was wrinkled at some places. There was minimal edema; both the donor and recipient cornea and the stromal cells of the donor and of the recipient remained normal. Both the donor and recipient epithelium started to grow from five hours after operation but growth was present in the recipient side first. Epithelium from both the donor and the recipient formed a plug and filled the junction by 24 hours after operation. Where bulging of growing epithelium was present a slight erosion of the cells on the surface occurred.

INTERLAMELLAR TECHNIQUE. The appearances following the interlamellar operation were essentially the same as those seen after the lamellar procedure. There was no edema of either donor or recipient stroma, the stromal cells were normal. Donor endothelium disappeared rapidly, starting from ½ hour after operation (Figure 4). Some inflam-

FIGURE 4. INTERLAMELLAR GRAFT IN PLACE FOR 13 HOURS
Donor endothelium has disappeared. Host endothelium is intact.

matory cells were present at the interface between donor and recipient material and at the margins of the donor button but did not appear to penetrate donor Descemet's membrane. Endothelium of aortic wall, when a segment of vessel was placed interlamellarly in cornea, disappeared as rapidly as did corneal endothelium.

2. ABNORMAL HOST

Following irrigation of the anterior chamber with acetic acid the cornea rapidly became watery and opaque. The endothelial cells were immediately missing and the recipient stroma (Figure 5), on section, appeared edematous and acellular. After the donor button was inserted in the lamellar bed of the edematous recipient cornea, the donor endothelium rapidly disappeared, starting in ½ hour and being gone by 6 hours. Descemet's membrane of the donor remained intact, although slightly wrinkled. By 27 hours a few inflammatory cells were present at the interface between donor and recipient and in the neighboring recipient cornea. The stroma of the donor did not appear edematous, the stromal cells were present and there were only a few inflammatory cells at the margins of the donor button but none in front of Descemet's membrane (Figures 6, 7, and 8). This was the appearance whether

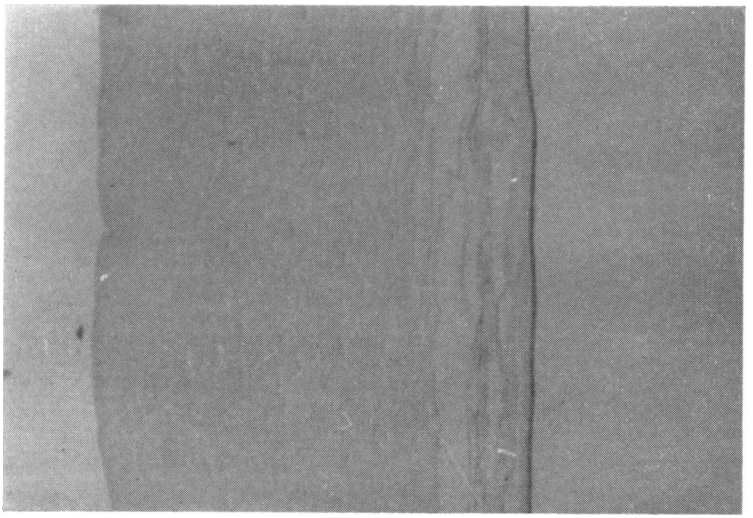

FIGURE 5. CORNEA 24 HOURS AFTER BURNING OF THE ENDOTHELIUM WITH ACETIC ACID

No endothelium is present. The stroma is edematous and no cells are present.

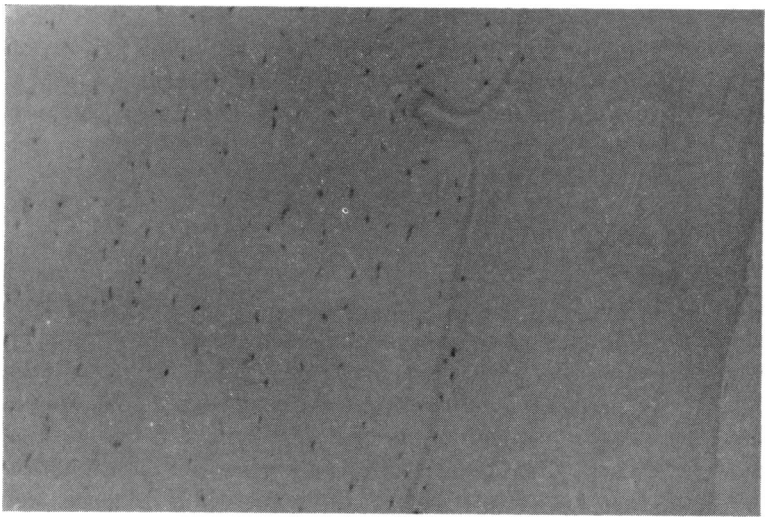

FIGURE 6. FULL THICKNESS GRAFT LYING FOR 1 HOUR IN LAMELLAR BED OF ACETIC ACID–TREATED CORNEA

The recipient bed is edematous. The donor endothelium is missing, Descemet's membrane is intact, stromal trabeculas are normal, and the stromal cells are present.

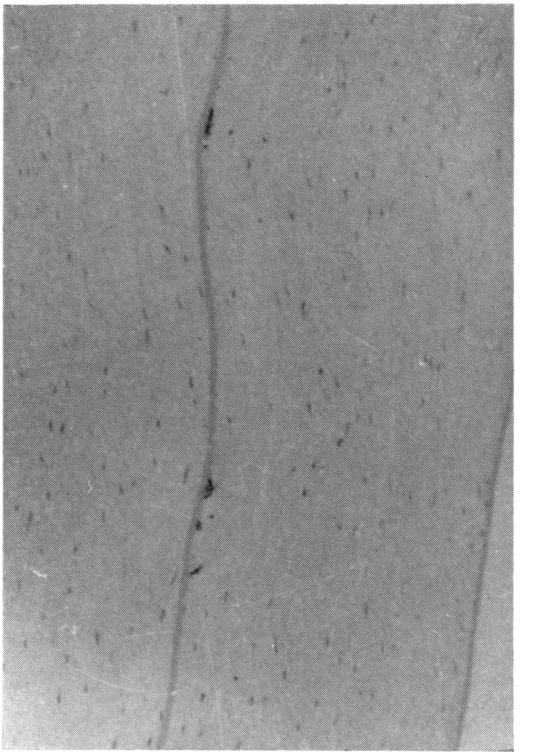

FIGURE 7. FULL THICKNESS GRAFT LYING FOR 5½ HOURS IN LAMELLAR BED OF ACETIC ACID–TREATED CORNEA

Recipient cornea is edematous and contains inflammatory cells; there is no endothelium. There is some nuclear material posterior to donor Descemet's membrane but no endothelium. Donor stroma is normal.

grafting was done immediately following burning of recipient endothelium by acetic acid or up to 24 hours later.

3. TISSUE CULTURE STUDIES

Corneal endothelium lying on chicken plasma in a Carrell flask disappeared rapidly, starting at ½ hour and being gone by six hours.[11] Aortic endothelium, lying similarly, disappeared in the same period. Corneal endothelium, lying face up in a Carrell flask, survived beyond 24 hours.

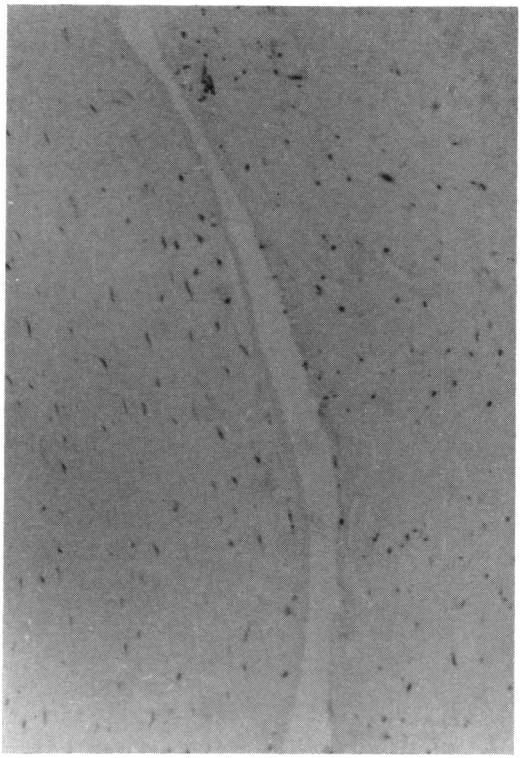

FIGURE 8. FULL THICKNESS GRAFT LYING FOR 27 HOURS IN BED IN ACETIC ACID–TREATED CORNEA Inflammatory cells in donor stroma; recipient stroma still contains fixed cells and regular lamellas.

B. CLINICAL CASES

Table 3 gives the history of the donor materials and of the recipient tissues.

CASE 1

This man, who was 71 years old in October, 1962, had a cataract extraction done on the right eye in 1947 and a needling for secondary membrane in the pupillary area done in 1948. In 1949, he was treated in the hospital for iridocyclitis in the right eye. In 1950, he had a cataract extraction done on the left eye. In September, 1959, he developed bullous keratopathy in the right eye and a month later in the left eye. In February, 1962, a hole was formed in the updrawn iris of the right eye, using the light coagulator.

TABLE 3

Recipient			*Donor*		*Interval between death and enucleation*	*Storage time*
Case	*Sex*	*Age*	*Sex*	*Age*		
1	M	71	F	17	1 hour	24 hours
2	F	77	M	49	17 hours	6 hours
3	F	75	M	57	6 hours	24 hours
4	F	56	M	47	3 hours	24 hours
5	M	43	M	72	13 hours	2 hours
6	M	44	M	70	9 hours	48 hours
7	M	54	F	72	2 hours	48 hours
8	M	45	M	25	3 hours	4 hours
9	M	32	M	75	8 hours	24 hours
10	M	84	F	79	3 hours	6 hours

In October, 1962, his visual acuity was O.D. 10/300, O.S. C.F. at 6 feet. The right eye was red and painful, there was diffuse corneal edema, epithelial bullas, an updrawn iris with fibrous tissue in the small pupillary area, a hole in the iris which had been produced by the light coagulator, and a tension of 30 mm. of mercury. Light projection was good. The left eye was red; there were epithelial bullas and diffuse corneal edema. A complete iridectomy had been done and the pupillary area was clean. The tension was 22 mm. of mercury, light projection was good. The Wassermann reaction was negative. Culture from the eyes contained a number of saprophytes but no pathogenic organisms.

On October 8 a 9-mm. full thickness button was put in a deep lamellar corneal bed in the left eye, and affixed with 12, 7.0 silk sutures. This graft healed: in January, 1963, the visual acuity was 20/400 with a +13.00 lens. The graft was firmly in position but hazy due to a moderate amount of edema. The eye was white and comfortable (Figure 9). In May, 1963, the graft was similar but a thin clear cleft could be seen between donor and recipient tissue, about 3 mm. across, near the lower margin of the graft (Figure 10). The patient stated that during the spring the eye would clear and he would be able to read print but then it would cloud over again. This had happened several times.

The button removed from the recipient showed loose and relatively acellular stroma. There was no epithelium.

CASE 2

This lady was 77 years of age in 1963. She had a cataract extraction done on the left eye in January, 1961, the right eye in December of the same year. Following the second operation she developed bilateral corneal edema, worse in the left eye. The tension of the left eye rose to 60 mm. of mercury, that of the right eye remained normal. Vision improved with correction to O.D. 20/400 O.S. 20/80 but fell as the corneal edema increased. Cultures showed no growth; the Wassermann reaction was negative.

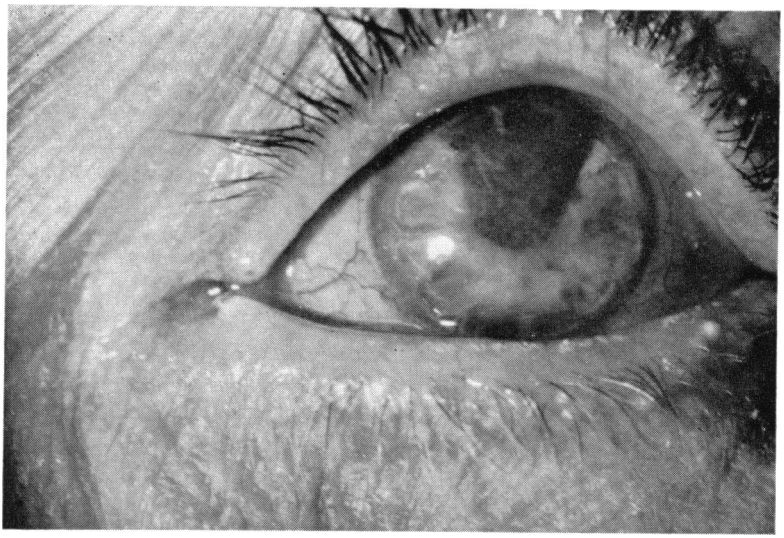

FIGURE 9. CASE 1 AFTER GRAFTING FOR BULLOUS KERATOPATHY

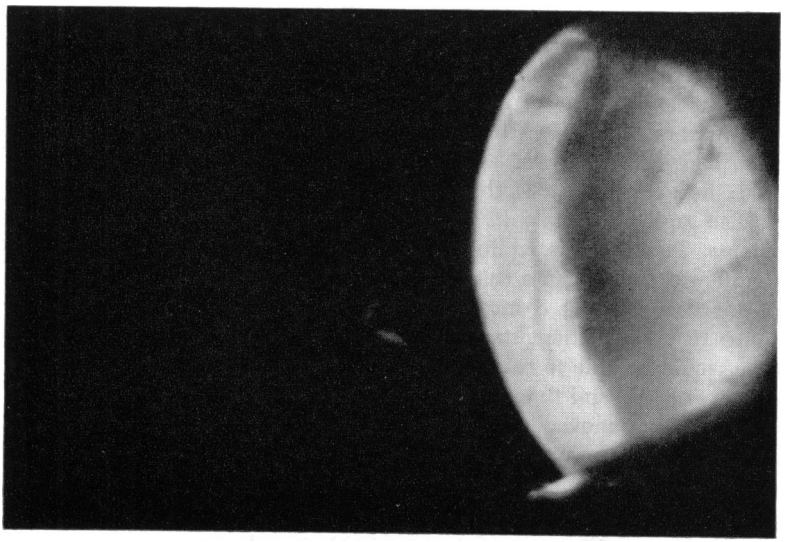

FIGURE 10. CASE 1 AFTER GRAFTING FOR BULLOUS KERATOPATHY
A clear cleft can be seen between the graft and the recipient cornea.

On September 13, 1962, an 8-mm. full thickness button was placed on a deep lamellar bed and affixed with 12, 7.0 silk sutures in the left eye. The graft healed at first and seemed to be healthy. However, gradually it became edematous and opaque and retracted at its lower margin. By January, 1963,

a very thin area was present below the graft in the lamellar bed, and Descemet's membrane was bulging (Figure 11). On January 31, a 9-mm. full thickness graft was placed on a lamellar bed, dissecting out the old button and to fresh recipient cornea about the old bed. This new graft was fixed with 12, 7.0 silk sutures. On April 6, 1963, it was healed but slightly edematous. There were a few vessels lying in recipient tissue at its posterior surface leading to a round plaque of fibrous tissue behind the center of the graft. Vision was H.M. at 1 foot with good projection. There was no sensation over the graft. Keratometer readings were: horizontal 42.50, vertical 40.50.

FIGURE 11. CASE 2 AFTER GRAFTING FOR BULLOUS KERATOPATHY
Edema of graft, retraction of its lower edge from the bed in the recipient cornea.

The tissue taken from the recipient at the first operation showed loss of epithelium and Bowman's membrane in many places. There was some subepithelial edema. The posterior stroma was filled with chronic inflammatory cells and blood vessels.

The tissue taken from the recipient at the second operation was divided into two parts. The upper part, containing the healed border of graft, was sectioned. Epithelium was present lying on a thin layer of subepithelial fibrous tissue. There was some edema of the anterior portion of the stroma. The donor and recipient areas were firmly healed together. Descemet's membrane was intact at the posterior surface of the graft; there was no donor endothelium present.

The lower part, containing the retracted border of the graft, was cultured

in tissue culture. *Candida albicans* was grown. Stromal cells were grown and by sex chromatin study were found to be male cells, indicating survival of the cells of the first graft for four months.

CASE 3

This lady was 75 years of age in 1962. She had a cataract extraction done on the right eye in 1951, on the left eye in 1960. Following the second operation bullous keratopathy developed in both eyes. This became progressively worse and in November, 1962, she was admitted requesting enucleation of the right eye.

Vision of the right eye was H.M. at 1 foot with good projection. The cornea was grossly edematous and there were large blebs under the epithelium. Descemet's membrane was wrinkled; there was loose vitreous in the anterior chamber. The tension was normal. The left eye showed a similar picture. Besides the corneal edema, there were some fine vessels growing down from the wound above and a secondary membrane in the pupillary area. Vision was 20/200 with good projection. Cultures grew nonpathogenic staphylococci and *B. proteus*. The Wassermann reaction was negative.

On November 14, a 9-mm. full thickness donor button was placed in a deep lamellar bed and affixed with 12, 7.0 silk sutures in the right eye. The graft healed well and remained clear. Fibrous tissue and some fine vessels were present in the donor tissue behind the graft (Figure 12). On April 6, 1963, acuity was $+9.00\ +4.00 \times 120 = 20/400$ although her ability to get about using the eye suggested better vision than that.

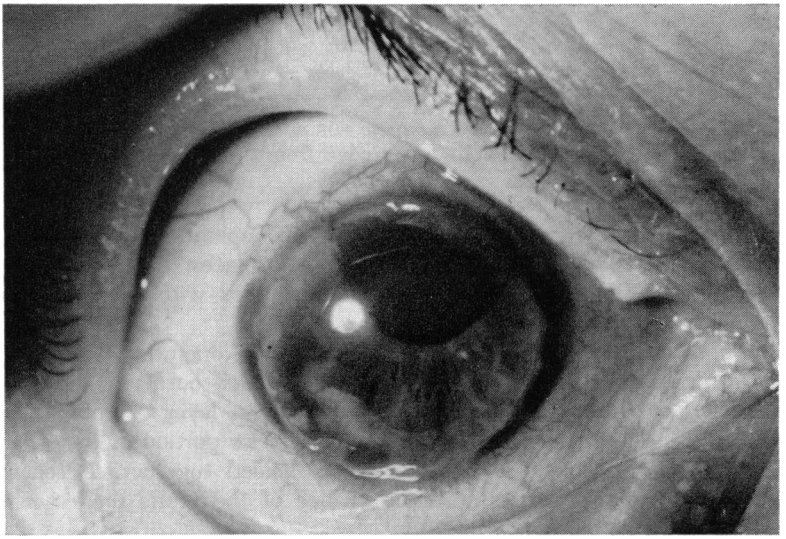

FIGURE 12. CASE 3 AFTER GRAFTING FOR BULLOUS KERATOPATHY

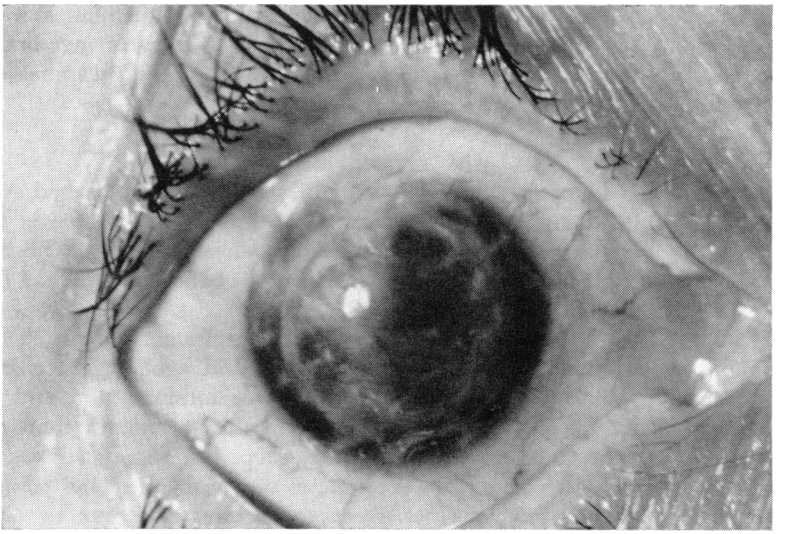

FIGURE 13. CASE 4 AFTER GRAFTING FOR BULLOUS KERATOPATHY
The scar tissue lies at the interface between donor and recipient cornea.

Corneal sensation over the graft was absent. Keratometer readings were horizontal 46.25, vertical 50.25; the image was slightly irregular. She wished to have the operation performed on the left eye.

CASE 4

This lady was 56 years of age in 1962. She had a cataract extraction done on her right eye in 1960. Following that she had an epithelial downgrowth which was scraped off the back of her cornea. Bullous keratopathy then developed and in 1962 her vision was reduced to C.F. at 1 foot. In November, 1962, the right eye showed an edematous cornea, the anterior chamber was deep, there was a complete iridectomy, the pupillary area was clear, tension was 21 mm. of mercury. Cultures from the eye and nose showed non-pathogenic staphylococci; the Kahn test was negative. The left eye had been blind and glaucomatous from 1951 and was removed in 1962 because of pain.

On November 26, 1962, an 8-mm. full thickness donor button was placed on a deep lamellar bed and affixed with 8, 7.0 silk sutures. The graft healed well and the eye cleared continuously after operation. On April 6, 1963, acuity was C.F. at 3 feet with good projection. The graft itself was clear; however, there were many fine vessels at the interface between donor and recipient cornea (Figure 13). There was one, small, circular, clear cleft, about 1 mm. across, at this interface. There was no sensation over the graft. Keratometer readings were: horizontal 52, vertical 51.

The tissue taken from the recipient showed loss of epithelium in some areas. Fibrous tissue was present on both sides of Bowman's membrane, which was absent in many places. Blood vessels and chronic inflammatory cells were present in the stroma.

CASE 5

This man was 43 years of age in 1962. In January, 1961, he had Ajax cleaner spilled in his right eye. This produced a large necrotic area in the centre of the cornea, which then had little tendency to heal. On two occasions dendritic figures were seen at the margin of the eroded area. The patient was an alcoholic.

In December, 1961, the left eye was normal, visual acuity being 20/15. The right eye, orbit and lids, were grossly injected and swollen. The cornea was insensitive, thick, and edematous. There were erosions at 5 and 12 o'clock and about the central area, circumferentially, 4 mm. in from the limbus, was a ring of scarring. There were deep and superficial vessels coming in from all sides and large precipitates on the back of the cornea. The pupil was dilated, did not react. Deeper structures could not be seen. Visual acuity was hand movements at two feet. Culture grew non-pathogenic staphylococci. The Wassermann reaction was negative.

On December 18, a 10-mm. full thickness donor button was placed in a deep lamellar bed and affixed with 12, 7.0 silk sutures. The graft healed but about a month after operation the lower part of the anterior face of the graft broke down and then healed with vascularization. On April 6, 1963, the graft was thick and clear, although not protruding. There were some fine vessels in its lower part and some large vessels at its posterior surface. Acuity was H.M. at 3 feet with good projection. Corneal sensation was absent. The eye was white, comfortable.

The tissue taken from the recipient showed loss of epithelium in many places. There was edema, round cells, hyaloid bodies, giant cells containing pigment under the epithelium. Bowman's membrane was largely absent. The anterior stroma was edematous; posteriorly, the stroma contained a few blood vessels and deposits of pigment.

CASE 6

This man was 34 years of age in 1962. In June of 1960, a foreign body, probably aluminum, became embedded in the right cornea. No particle could be seen but an abscess formed in the depth of the cornea at its center and large vessels grew into the area from below. There were many precipitates on the back of the cornea, the anterior chamber contained some cells, the pupil was active, the tension was normal. Culture from the eye showed no growth; the Wassermann reaction was negative. Visual acuity was C.F. at 10 feet. This abscess continued to increase in size. The left eye remained normal.

On November 2, 1960, a 7-mm. full thickness graft was placed on a deep

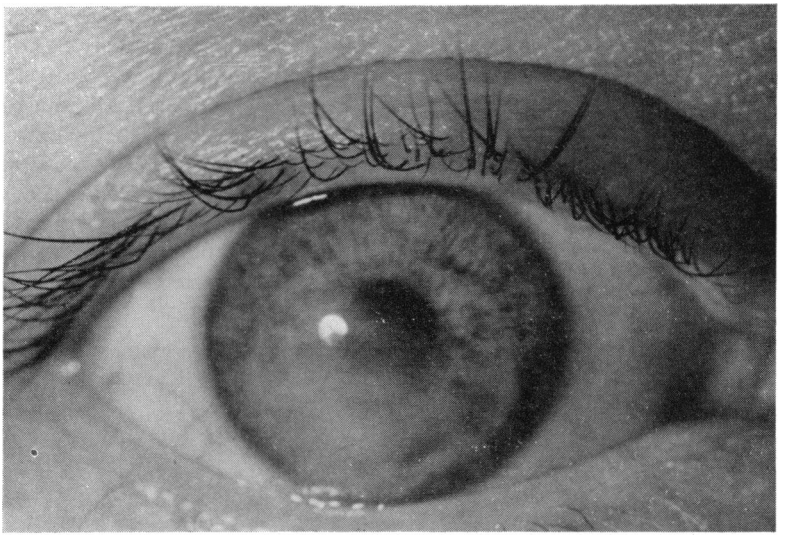

FIGURE 14. CASE 6 AFTER GRAFTING FOR CORNEAL ABSCESS DUE TO RETAINED ALUMINUM
The scar represents the site of the abscess and is behind the graft.

lamellar bed. On dissecting into the abscess it was found to communicate with the anterior chamber. The graft was affixed with 8, 6.0 silk sutures. Culture from the abscess gave no growth.

The graft healed but scar formed between the posterior surface of the graft and the recipient bed. The graft remained clear but at the area of the abscess a grayish infiltrate formed in the posterior recipient tissues, producing a plaque about 4 mm. across. Gradually this area of scarring decreased and vessels and scar at the posterior surface of the graft became less marked. The upper part of the graft was clear (Figure 14). Vision on March 26, 1963, was $+4.00 \times 180 = 20/300$. Sensation was absent over the graft; keratometer readings were horizontal 44.00, vertical 53.00.

CASE 7

This man was 53 years of age in 1962. In 1957, a flake of steel entered the left cornea. It remained there three weeks and was extruded spontaneously. Following that he had many recurrent erosions of the cornea. In 1961, for a few months, his ocular tension was elevated. His right eye remained unaffected.

In January, 1962, the right eye was normal, acuity was 20/30. The left eye was injected. The upper part of the cornea was thickened, edematous, vascularized. There was a deep erosion in the center of this area and a small knuckle of Descemet's membrane was protruding. Vision was 20/200

which was obtained through cornea below the affected area. Culture grew a non-pathogenic staphylococcus. The Wassermann reaction was negative.

On January 10, 1962, a 8-mm. full thickness graft was placed in a lamellar bed and affixed with 12, 7.0 silk sutures. In March he was back at work, his visual acuity was 20/200 with a +2.00 correction. In June his eyes, face, and shoulders were burned by a toluol fluid. This necessitated skin grafting and there was considerable conjunctival injection of the affected eye. The corneal graft clouded slightly but then cleared and by April, 1963, acuity was 20/60 with −2.00 +4.00 × 65 correction (Figure 15). Sensation was absent over the graft. Keratometer readings were: vertical 42.00, horizontal 46.25.

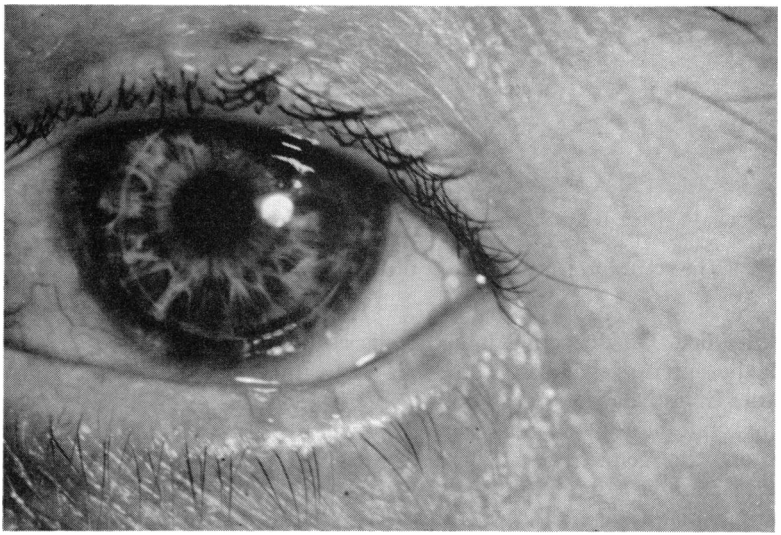

FIGURE 15. CASE 7 AFTER GRAFTING FOR RECURRENT BREAKDOWN OF THE CORNEA INITIATED BY RETAINED STEEL

CASE 8

This man was 22 years of age in 1962. In 1943 he had almost continuous herpetic inflammation of the left cornea. Following that year he had many bouts of keratitis extending to August, 1961, when his eye became continuously inflamed. During all this time his right eye remained unaffected.

In February, 1962, the right eye was normal in appearance and corrected to 20/20 acuity. Acuity of the left eye was count fingers at 10 feet. The whole of the lower part of the cornea was affected—the tissue was thick, vascularized, and edematous. Below the center point was an erosion about 3 mm. across and Descemet's membrane was protruding. Routine cultures and cultures for fungus showed no growth. The Wassermann reaction was negative.

On February 2, 1962, a 9-mm. full thickness graft was placed in a deep lamellar bed, and fixed in place with 12, 7.0 silk sutures. Care was taken in dissecting the corneal tissue about the descemetocele and the anterior chamber was not entered.

The graft healed but a hemorrhage occurred between the donor and recipient cornea, which gradually vascularized. The graft itself remained free of vessels but slightly edematous. The eye as a whole stood the operation well and gradually cleared. In September, 1962, the eye was white and comfortable, the graft was clear but lay on a firm underlying bed of pink scar. He could see hand movements at 3 feet and projection was good.

The tissue removed from the recipient showed irregular loss of Bowman's membrane, subepithelial edema, and scarring of stroma.

CASE 9

This man was 32 years of age in 1962. In 1953, he had a herpetic infection of the left cornea. In March, 1956, he had a 10-mm. lamellar graft placed on the left cornea. This graft healed but scarred extensively and he had many bouts of pain and photophobia with decreasing vision. During 1961 the eye was a continual problem due to pain and photophobia. The right eye remained unaffected.

In January, 1962, the right eye was clear and acuity was 20/20; the left eye had light perception with good projection. The whole of the cornea was an immense, thick scar. Vessels were coming in from all sides and in the lower nasal quadrant a large fibrous pannus was extending into the central corneal area, completely hiding the limbus. The pressure felt normal. Cultures grew pathogenic staphylococci. The Wassermann reaction was negative.

On January 15, a 9-mm. full thickness donor button was placed on a deep lamellar bed and affixed with 10, 7.0 silk sutures. When the scar was dissected away the central, posterior tissue of the recipient cornea was found to be like a sieve, with many points of leakage from the anterior chamber. A watertight wound was obtained at the edge of the graft and the eye at the end of operation felt normally firm.

The graft healed and remained clear, the eye whitened. The donor and recipient tissues adhered at the margins of the graft and in a ring about 3 mm. wide between the posterior surface of the graft and the recipient bed. This left a 3–4-mm. wide central area where there was a small, second, anterior chamber. This space appeared clear in its upper part but a collection of gelatinous material formed a level, like a hypopyon, across its lower third. Fibrous tissue gradually obliterated the space and by July, 1962, the area was a dense scar. In May, 1963, the eye was white and comfortable. The graft was clear and lying on a white fibrous bed (Figure 16). Vessels came into the bed from the limbus below and medially. The anterior chamber was clear. The pupil was responsive. Light projection was

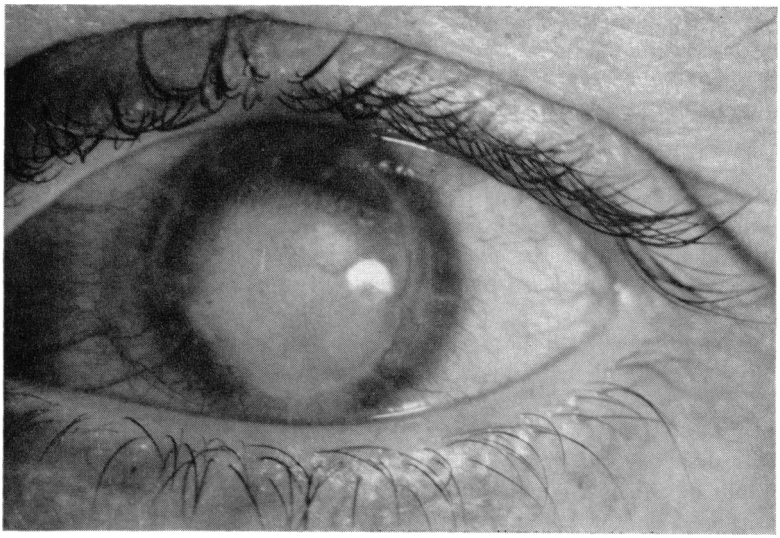

FIGURE 16. CASE 9 AFTER GRAFTING FOR A DIFFUSELY ERODED CORNEA, ORIGINALLY AN HERPETIC INFECTION
The graft lies on the dense scar.

good; he could count fingers laterally, to the side of the scar. Tension was 20 mm. of mercury Schiotz, taken on the graft. Keratometer readings were: horizontal 37.50, vertical 43.75.

CASE 10

This man was 84 years of age in 1962. He was seen in April, 1962, when he stated that his right eye had been sore for an indefinite time. He had a spastic entropion with epithelial abrasions of the right eye, and a Wheeler type procedure was performed. This improved the position of the lid but in May an irregular serpentine ulcer appeared in the cornea. This was indolent and steadily progressed. The left eye was unaffected.

In September, 1962, the left eye was healthy, acuity was 20/40 with pinhole, and tension was 18 mm. of mercury. The right eye had light perception only, but the projection was good. The right lower lid was slightly notched near its center, but there was no entropion. The eyeball was injected. There was considerable stromal edema of the cornea and vessels were entering from the limbus on all sides. At the center was a large erosion with Descemet's membrane bulging over an area 3 mm. across. Culture from the eye grew non-pathogenic staphylococci; the Wassermann reaction was negative. He had arteriosclerotic heart disease with congestive failure.

On October 2, a 9-mm. full thickness graft was placed on a deep lamellar bed and affixed with 12, 7.0 silk sutures. There was considerable difficulty

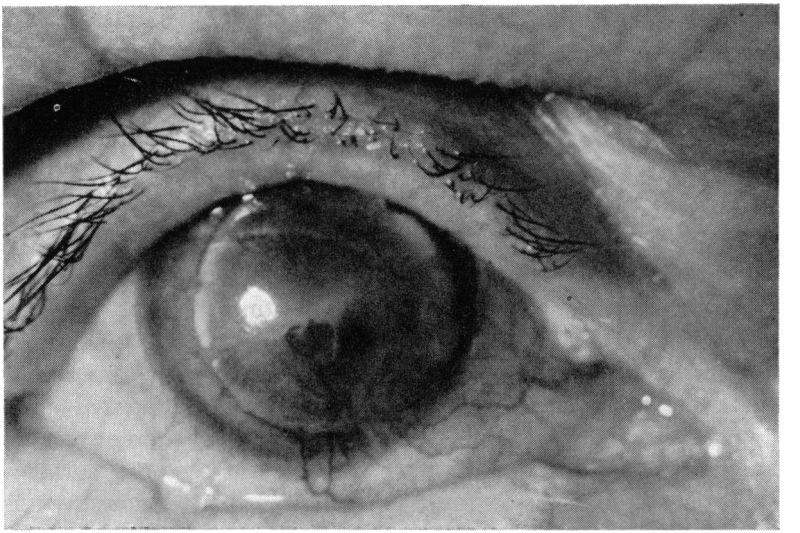

FIGURE 17. CASE 10 AFTER GRAFTING FOR DIFFUSE SENILE EROSION OF THE CORNEA

dissecting the bed about the descemetocele but this was done without entering the anterior chamber.

The graft healed and the eye gradually whitened. On April 6, 1963, vision was light perception with accurate projection. The graft was raised in its bed, being thicker than the surrounding cornea. There was a layer of vessels lying along the posterior surface of the graft and a few fine vessels growing into the graft from its lower margin. Just below the center of the graft and over the site of the former descemetocele, the surface had eroded but had re-epithelialized. The rest of the graft was clear (Figure 17). Sensation was absent over the graft. Keratometer readings were: horizontal 42.25, vertical 42.50, the mires appearing irregular.

The tissue taken from the recipient showed a single layer of flat epithelial cells with loss in a number of places. Bowman's membrane was missing in most areas and replaced by hyaloid deposits and round cells. The anterior stroma was edematous. Chronic inflammatory cells and blood vessels were present, particularly in the deeper stroma.

DISCUSSION

A. EXPERIMENTAL

From these experiments, both on rabbits and using tissue culture, it is apparent that corneal endothelium dies rapidly when placed on a lamellar recipient bed. This, probably, is a property of all endothelium,

as illustrated by the rapid death of aortic endothelium. Also, a minimum of inflammatory cells appears at the interface between donor and recipient and in the neighbouring recipient stroma. It would seem that death of donor endothelium does not call forth a significant inflammatory response from the host. The fact that donor endothelium was grafted would appear to be no factor in the subsequent health of the donor material.

Following the placing of a full thickness button on a lamellar bed, donor Descemet's membrane remained intact. It was slightly wrinkled but did not change its appearance with routine stains. It may be a factor in keeping the donor button clear of edema for, when grafting is done on an edematous cornea, on one side of donor Descemet's membrane is edematous, recipient stroma, on the other side normal-appearing, donor stroma. Certainly, donor Descemet's membrane prevents inflammatory cells from penetrating through the posterior surface of the button, for they are not found in the neighboring donor stroma.

It is encouraging that in every rabbit the donor material healed to the host. There was no indication of rejection of donor by host although the time limits of our experiments were too short to know if a late reaction to the graft would take place.

B. CLINICAL

The ten eyes on which this procedure was done were severely diseased and originally were considered lost. While the final visual results were not good all the eyes have been saved and several interesting observations can be made.

After ten out of the eleven operations the full thickness graft healed firmly upon the lamellar bed. In the one case in which the graft retracted sex chromatin studies demonstrated that the donor tissue was still viable after four months. Since infection with *Candida albicans* was probably present it is remarkable that the graft survived as well as it did. In all the cases this acceptance to the recipient area took place under adverse circumstances, particularly gross leakage from the anterior chamber. It would seem established that healing of a full thickness graft on a lamellar bed can be obtained in a high percentage of cases.

The grafts, although usually lying on vascularized scar tissue, tended to remain free of vessels. Some vessels came in from the sides, but they did not extend through Descemet's membrane into the back of the graft.

Also, the grafts scarred little. Only in case 9 and after the first

operation in case 2 did the graft grossly scar or degenerate. In case 10 some erosion of the graft occurred but this rehealed and the main substance of the button remained free of scar. In most cases either a clear or a slightly edematous graft rested on underlying scar tissue. In view of the fact that the grafts were lying on severely diseased corneas they maintained their integrity surprisingly well.

It was our impression that the longer these cases were followed the better the grafts appeared. The majority have been followed somewhat more than a year. The oldest graft, which has been in place two and one-half years, has continually become clearer.

Finally all these patients experienced relief of their severe symptoms. Case 3 who originally requested enucleation of the right eye is now insisting that a keratoplasty be done on the other eye.

C. OVER-ALL

Experience from the animal experiments and the clinical cases shows that a full thickness corneal homograft placed on a lamellar bed will heal to its host. Endothelium of the donor dies rapidly and for the purpose of healing the graft can be considered full thickness, without endothelium. Donor Descemet's membrane appears to prevent inflammatory cells and blood vessels from extending through the posterior face of the graft into its stroma. It also appears to limit the flow of fluid from an edematous recipient stroma into the graft. This quality, in any measure, would give it value in treatment of the wet cornea.

In the clinical use of a full thickness button the donor may be thicker than the recipient and protrude as a flat disc at the anterior corneal surface. This inequality in thickness is not as distressing as one might think. The recipient cornea is often thicker than normal and there is plenty of depth for the donor to settle fully into position. Also it is our impression that with time the junction between donor and recipient smooths out. An epithelial plug forms at the wound and may level the transition. There may be erosion of either the donor or recipient edge, whichever is protruding, leading to alignment. Finally, a vertical scar forms between donor and recipient and with time this seems to contract, drawing back and leveling the edges of both donor and recipient.

SUMMARY

In both clinical cases and animal experiments it has been found that a full thickness corneal homograft placed on a lamellar bed will heal to its host. Endothelium is rapidly lost but Descemet's membrane

remains and appears to have valuable properties. It limits the spread of inflammatory cells into the graft, prevents invasion of the graft by blood vessels through its posterior surface and has some effect in keeping fluid out of the graft.

Experience with a small series of severely diseased eyes operated on by this procedure shows that there may be clinical indications for such grafts.

ACKNOWLEDGMENT

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DISCUSSION

DR. FREDERICK W. STOCKER. While probably several ophthalmologists have occasionally tried to use a full thickness donor cornea in a lamellar bed of the recipient's cornea, the first comprehensive report on this technique was by the German ophthalmologist, Hallermann, in 1959 (Klin. Monatsbl. Augenh., 135:252–9, 1959). This author pointed to the advantages of this as compared with the standard technique which uses lamellar sections of donor corneas which do not contain Descemet's membrane and endothelium. He emphasized that for bullous keratopathy the full thickness lamellar graft was in his opinion the method of choice.

Inspired by Hallermann's well-written article, my associate, Dr. S. D. McPherson, Jr., and I embarked on an evaluation of this method. In this discussion, I shall confine myself to the clinical aspects and hope that Dr. McPherson will add something about the experimental work which was done. A preliminary report on our experience was given at the meeting of the Southern Medical Association in November, 1962.

Of the eight cases in which we have used full thickness lamellar grafts five were done for aphakic bullous keratopathy, one for metaherpetic bullous keratopathy, one for recurrent metaherpetic keratitis without bullas, and one on an eye on which a conjunctival flap procedure had been performed elsewhere which had developed an almost perforating ulcer in the center. Except for the traumatic cases reported by the essayists, this represents a similar group of patients to theirs.

The bullous keratopathy was stopped in all cases with postoperative observation from six to seventeen months, and all eyes were made comfortable. Visual improvement in general was modest but quite dramatic in one case of metaherpetic keratitis in which vision improved from 20/400 to 20/40. In three cases, fresh donor corneas were used, in five corneas preserved either by glycerol dehydration or by silica dessication. It was found that preserved corneas did just as well as fresh ones; in some respects they may be even preferable.

We can confirm the observation of the essayists that the full thickness graft, although thicker than the defect in the recipient's cornea, adapts itself well. The edges smooth out gradually and after a while, the cornea does not appear thicker than normal. If the keratectomy has been made deep enough, it may be difficult to distinguish the donor from the recipient cornea after the cleft between the two has subsided.

The following complications were observed:

1. In one case of bullous keratopathy, the cleft between donor and recipient persisted and is still present after one year. There is, however, no bullous keratopathy of the graft, the patient is comfortable, and vision is somewhat better than before. The possibility of survival of the endothelium leading to a second anterior chamber may be considered in this case, as viable cornea was used for the graft.

2. Vascularization between the two corneal layers occurred in heavily vascularized corneas. The blood vessels, however, did not have the tendency to invade the graft, as remarked by the authors.

3. Hemorrhages between the layers occurred in two cases and were very slow in being absorbed. [Slide]

4. Pneumococcic infection in one case, and probably fungus infection in another, occurred but healed, leaving a scar, of course.

5. In one case, partial necrosis occurred in the graft which gradually regenerated again.

The main question is why does a full thickness lamellar graft constitute a better barrier against the penetration of the aqueous than a lamellar graft?

Certainly, the endothelium cannot be responsible since we obtained at least as good results with non-viable donor material. Descemet's membrane as such does not constitute a barrier as we know from clinical observations and from the fundamental experiments by Leber in 1873 (Graefe's Arch. f. Ophth., 19:Abt. 2:87–185, 1873). Possibly Descemet's membrane provides for a smoother line of separation between donor and recipient which may encourage the formation of a thin solid connective tissue barrier which would act as a barrier to the aqueous humor.

The following slides may illustrate these remarks.

The first slide shows the eye on which a conjunctival flap had been done by a prominent member of this society. The cornea had the appearance of an egg white which was cosmetically very disturbing. The ulcer which had developed in the center of the flap is not well seen in this photograph. The next slide shows the same eye one year after a full thickness graft with preserved material. While far from a perfect result, the eye looks more natural from a distance and vision has improved from light projection to counting fingers.

The next slide shows the case of bullous keratopathy mentioned before. The patient was so uncomfortable as to demand the removal of the eye. The next slide shows the eye one year after the operation. The patient is comfortable, and vision has improved from finger movement to 5/70.

The next case is our prize case. The poor preoperative picture shown in the next slide does not demonstrate well the deep vascularized scar and bullous keratopathy which was present. Vision was 20/400. The next slide shows the same eye after the full thickness graft with preserved material. Vision 1½ years after the operation is 20/40.

In conclusion, it may be said that full thickness lamellar grafts seem to be the method of choice in bullous keratopathy. They are also suitable for other cases in which a deep keratectomy has to be done. For very superficial lamellar grafts the customary partial thickness lamellar grafts may still be preferable.

It was a pleasure to read and discuss this excellent paper, and the authors have to be commended for having brought this timely subject up for discussion.

DR. SAMUEL D. MCPHERSON, JR. As Dr. Stocker told you, we first became interested in the possibility of implanting full thickness corneal grafts in lamellar beds some 18 months ago when we read Hallermann's report of the clinical use of this technique. Our initial evaluation was undertaken in rabbits. We used 7.5-mm. penetrating grafts from freshly sacrificed animals. These were implanted in lamellar corneal beds of animals of a similar strain and sutured into place with direct sutures. Animals were sacrificed at monthly periods for six months. Their eyes were removed, sectioned, and examined histologically. The usual number of grafts were lost from infection, and a small number disappeared either from graft rejection or absorption of

donor material. Those in which the grafts took healed nicely, and the grafts were essentially clear. The first slide is that of an eye from an animal sacrificed four weeks after operation and shows that approximately one-half of the total thickness is composed of donor and one-half of recipient cornea. Descemet's membrane is irregularly folded, and there is a peculiar difference in staining density of donor and recipient material. The second slide is a high power of the same cornea and shows an irregular line of fibroblasts along donor Descemet's membrane. The next slide is that of a cornea removed six weeks after operation. Descemet's membrane is less folded, and there is less fibroblastic proliferation and less staining differential. The next slide is from a cornea removed five weeks after grafting, and you will see that there are several cystoid spaces along the graft interface. The next slide is a higher power of one of these cystoid spaces and shows cells which may well be endothelial cells lining this space. We paid little attention to this in the laboratory; however, in our clinical experiences and using the same technique we encountered certain difficulties at the graft interface which are probably due to the persistence of similar cystoid spaces. The next slide is that of an eye of a patient with progressive Fuchs's dystrophy following cataract extraction. Using fresh donor material, a full thickness graft in lamellar bed was done on this patient. Sixteen days postoperatively the patient developed a pneumococcal infection at the graft interface. This slide shows the grey, smooth dense opacity which has occurred at this point. The patient was placed on chloromycetin to which his organism was found to be sensitive, and the next slide shows the appearance of the eye three months after operation. The opacity has cleared, and both donor and recipient corneas are reasonably clear. The last slide is of the same eye nine months after operation. The bullous keratitis is relieved, and both donor and recipient corneas are clear.

These findings suggest that in the application of this procedure, the best results may be obtained using donor material which is non-viable and does not contain endothelium to form cystoid spaces at the graft interface. I would like to congratulate the authors on their excellent paper. I am glad that we are able to confirm and supplement their findings. Although we have seen quite a few complications, both with the experimental and clinical use of this procedure, it seems to have a definite place in the surgical treatment of chronic bullous keratitis.

DR. A. GERARD DEVOE. We, too, have used the full thickness grafts both with and without endothelium in a number of patients. The exact number I do not recall, but it is certainly a dozen or fifteen. We can confirm that there is no difficulty at all with these grafts taking and remaining clear when the endothelium is normal. However, we have not been successful with these when the host endothelium is defective, and this was the type of case in which we particularly wanted to use the graft.

In bullous keratopathy, for instance, on the supposition that perhaps the

donor endothelium is able to live and persist on the graft, we hoped possibly this might prevent fluid from entering the graft. However, in all cases which we have done, failure has occurred, with edema as commonly found in other types of graft.

In several instances in which we have had occasion to re-examine the tissue pathologically the endothelial cells have been dead as the essayists indicated.

The matter of blood vessels is another problem. We have used these full thickness grafts in conjunction with buried keratoplasties which Cardona has described. This, to me, makes rather good sense. If one can get down deeply in the cornea so that only a thin scarred layer is left, then put in the buried prosthesis, and cover that with a fresh, full thickness graft, it might remain clear. This would be ideal. However, our most difficult cases have been these heavily vascularized cases one gets with ammonia or live burns. We cannot confirm that full thickness grafts remain unusually resistant to blood vessels. They too have become vascularized.

DR. JOHN HARRY KING, JR. We have also used this type of graft, and I would like to re-emphasize the point that Dr. DeVoe brought out, and that is that the lamellar section must be very deep. In some of the cases shown here, there is much opportunity for edema and scar formation between the large amount of host cornea remaining and the new graft.

We do not agree that this is the best technique. It is another method and there is as yet no uniformly satisfactory technique for treating bullous keratopathy. A full-thickness graft in a lamellar bed is simply the formation of a barrier, and whether or not that barrier is posterior or anterior does not seem to make much difference. We still rely very heavily on the thin conjunctival flap advocated by Dr. T. Gundersen, and when the cornea becomes quiet, one can do a deep lamellar graft later to improve the vision.