FULL-THICKNESS CORNEAL GRAFTS IN ADDIS ABABA, ETHIOPIA*†

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IN Ethiopia, as in many other African countries, blindness afflicts 4 per cent. of the population, with the partially-blind numbering up to 20 per cent. of the country's 20 million inhabitants. By far the most important cause of blindness in Africa is scarring of the cornea, not only because of its frequency (in European countries it accounts for less than 1 per cent. of the blind population, but in Kenya for 20 per cent.—Bisley, 1964) but also because such corneal scars normally develop in children who are otherwise quite healthy and have a full life-span ahead of them, whereas the other common blinding diseases (cataract, dystrophies, glaucoma, etc.) normally affect the aged when they have completed a lifetime of useful work. The source of this corneal scarring is manifold, but trachoma is generally a major factor, with an incidence in Ethiopia of between 30 and 100 per cent., 16 per cent. of whom have severe visual impairment in consequence (Guerra, 1951, 1965; Feitelberg, 1964; Voza, Renna, and Felici, 1964).

Thus, while vigorous measures have already been taken to control tuberculosis, malaria, and other major causes of disablement, about one million Ethiopians are either blind or partially blind, and remain an economic drain on the country's resources. The Ethiopian government, aided by the United Nations International Children's Emergency Fund is at present campaigning against trachoma and planning further preventive measures against this and other eye diseases, while the Haile Selassie I Foundation seriously endeavours to assist the blind Ethiopians to become productive members of the community.

For those who are already blind, the only effective treatment is keratoplasty, which in the large majority entails replacing the scarred cornea by a full-thickness graft. The ocular damage is usually so extensive that the prognosis is poor even with the best donor material. Furthermore, while keratoplasties on carefully selected patients and performed under high hygienic standards in sterile operating conditions, and with well-trained personnel have a success rate of up to 88 per cent. (Ainslie, 1959; Leigh, 1966), such ideal conditions can hardly be expected in developing countries.

Nevertheless, it was felt that the visit of a small team, who would undertake a pilot series of grafts, would at least prepare the ground for further surgical forays.

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Truly fresh human donor material could be obtained for only a few cases in our two series in Ethiopia, and some donor tissue stored longer than 2 days had to be used. However, human corneal donor tissue which had been stored at -197°C . for several weeks was also available and gave very satisfactory results. (Mueller, O'Neill, Trevor-Roper, Reiter, and Ludeck, 1966).

In the whole of Africa, the number of corneal grafts performed each year is very small, and in most African countries no grafts have been attempted for all the obvious reasons—the lack of trained personnel, absent facilities, social and religious barriers to obtaining donor material, etc.—but somehow the isolated eye surgeons must be encouraged to persevere. The effect of our work upon the vast blind population in Ethiopia was necessarily small, but we hope in this account of it to provide some such encouragement.

Local Conditions

The town of Addis Ababa and the surrounding countryside is served by sixteen hospitals under the control of the Ministry of Health, by Mission Hospitals, and by Hospitals of the Haile Selassie I Foundation; the four Eye Departments are units of the four principal hospitals. It was in one of these—the Eye Department of the Haile Selassie I Hospital—that this series of full-thickness keratoplasties was carried out in the autumn of 1965 and the spring of 1966.

At this Unit the facilities for examination were indeed good—a slit lamp, keratometer, various ophthalmoscopes, and an indentation tonometer being at our disposal. Most of the patients were poor, so that standards of hygiene were low; they had frequently travelled for weeks over rough country to seek help, but the eye conditions had often advanced so far that little could be done for them (Fig. 1, p. 231). Male patients, and those over 40 years old, were in the majority; the under-forties, who are often the main supporters of large families and cannot afford the loss of work, rarely sought treatment.

The amenities of the wards were well below the standards of European Eye Units, partly because of the shortage of trained nursing staff and efficient ward-orderlies, and partly because of outdated or absent ward facilities. Without exception, the ward patients wore part of their outdoor clothing, ate with their fingers as is the local custom, and wiped them on bedclothes and towels. The patient undergoing operation was dressed partly in his own clothes and partly in those supplied by the hospital; although he had a bath before the operation, his hair remained unwashed (and had obviously been so for some time previously).

The operating theatre was kept clean. The instruments were either sterilized in a hot-air oven for 80 minutes at $+120^{\circ}\text{C}$. or boiled for 15 minutes before use. Towels and gowns were sterilized in the hospital autoclaving unit, and sutures and needles were kept in dry plastic screw-top jars containing a tablet of formalin. Gloves were not worn, but surgeons, assistant, and sister cleansed their hands in the usual surgical manner. Caps and masks were invariably worn in the theatre but not for changing dressings in the wards; here sterile swabs and eye pads were used, but other aseptic precautions at the bedside could not be observed.

The patients seemed unable to understand the need to leave undisturbed the dressings covering the operated eye; they frequently coughed without restraint, they turned to lie on the side of the operated eye and bent down to floor level, and many of them did not realize that any of these actions might prove disastrous to the operative result.

During the second trial, 6 months after the first series, the hygienic conditions in the wards had deteriorated. In spite of the efforts of the sisters-in-charge, a further shortage of staff made supervision of the patients practically impossible. Sisters, nurses, and

dressers had been trained locally, and only one sister, who had received 4 months' supplementary training at Moorfields Eye Hospital in London, had had experience in assisting during the operation and nursing patients after keratoplasty.

Selection and Assessment of Patients

A reliable history of onset and of the cause of the eye condition could rarely be elicited. The visual acuity and the projection of light were tested with care. Patients with vision of 6/24 or better in the better eye were discouraged from operation, unless the affected eye was endangered. Uniocular patients with visual acuity of 6/60 were admitted for operation only when good donor material was available. Uniocular patients with dense corneal scars and cataracts were admitted, in spite of inaccurate projection of light; in some of them the corneal condition was complicated by nystagmus and several of these were later admitted in the hope of improving their sight from perception of light to counting fingers. A digital estimation of the intra-ocular pressure normally sufficed, because indentation tonometry over extensive scars and thin corneae was too unreliable and an applanation tonometer was not available. All but two patients with raised intra-ocular pressure were rejected; however, in these two cases emergency corneal grafting with iris inclusion was performed simply in the hope of salvaging a little of the sight that remained.

All suitable patients, who had an associated conjunctival, lid, or lacrimal infection, were referred for operation at a later date; nevertheless, six patients with blocked tear-ducts, but without obvious infection, underwent operation forthwith. Finally 48 patients were selected and admitted for full-thickness graft operation.

Procedure

Pre-operative Treatment and Anaesthesia

An oily suspension of a 1 per cent. tetracycline hydrochloride was instilled three times daily into both eyes for at least 3 consecutive days before operation. Blood, urine, and stools were examined to exclude specific tropical diseases, the patients were given 250 mg. ascorbic acid and 25 mg. vitamin B-complex tablets daily until discharged from hospital. On the day of operation the treatment with oily suspension was replaced by guttae chloramphenicol 0.5 per cent., administered hourly for 6 hours before operation. Guttae pilocarpine 1 per cent. were added 2 hours before the operation. Neither premedication nor sedation was given; the patients walked from the wards to the operating theatre.

General anaesthesia was administered by a locally-trained "advanced dresser" (although he had never before had the opportunity to anaesthetize a patient for a corneal graft). Atropine sulphate 1/100 gr. was injected intravenously, and, after intravenous thiopentone and suxamethonium 50 mg., the patient was intubated. Halothane vapourized in a Boyle's ether bottle by oxygen at a flow-rate of 4 litres per minute and intermittent additional thiopentone maintained general anaesthesia throughout the operation, which lasted 30 to 45 minutes.

At the end of the operation 38 patients went into laryngeal spasm and coughed; the eyes of the first three patients in whom this accident occurred were examined as soon as the patients co-operated, but the air injected into the anterior chamber was still present, and we were satisfied that the suturing was adequate. After return to the wards all patients were given an intramuscular injection of chlorpromazine 50 mg. as soon as they responded to questions.

Operation

Fresh donor material which had been stored at 4°C. was given time to acquire room temperature and was examined under 10 times magnification. When it was found suitable, the patient was anaesthetized and prepared for the operation. Deep-frozen donor tissue stored at -196°C. was thawed out immediately before surgery. Friable and scarred bulbar conjunctivae made the insertion of superior and inferior rectus anchoring-sutures difficult, and in some cases lid sutures were employed instead. Strip peritomy and cautery to bleeding vessels was performed in 34 cases.

Full-thickness corneal grafts were cut either from fresh intact donor eyes or from fresh or thawed-out frozen material consisting only of the cornea with a rim of sclera. Details of preparing the graft have been described elsewhere (Mueller and others, 1966). The host cornea was trephined with the same-sized Franceschetti trephine, anterior synechiae were separated by blunt dissection or divided, and the corneal section was completed with scissors. Broad iridectomies were performed in all cases that lacked an intact iris sphincter. The host disc was exchanged for the donor disc and the transplant was sutured with Barraquer silk on a 6 mm. Dello needle. The graft was held in position by four meridional anchoring sutures, and multiple interrupted direct sutures sealed the host-graft junction. All sutures were placed close to Descemet's membrane and tied with equal tension, the knots and ends being drawn away from the actual host-graft junction. At the end of the operation, air was injected into the anterior chamber and tetracycline and atropine ointment was instilled into the fornices of both eyes. The lids were closed and the eyes were padded and bandaged.

Post-operative Period and Complications

The patients were allowed up 48 hours after the operation. Every third day the operated eye was examined with a torchlight and under 5 times magnification. The non-operated eye was uncovered at the beginning, and the operated eye at the end, of the second post-operative week. The direct sutures were removed during the fourth and fifth week after surgery in the operating theatre. In a few cases surface anaesthesia was adequate for this, but the majority of patients required intravenous anaesthesia. The patients were discharged during the sixth week after operation with the instruction to instil oculentum terracortyl twice daily into the operated eye. Patients of the first series were examined at monthly intervals for 6 months, and some again after 9 months. The patients of the second series were seen at regular intervals for only 3 months, because most of them had to return to their villages with the onset of the rainy season.

Two patients developed infection around the sutures during the second post-operative week, and this was treated successfully with neomycin drops. In seven of the 46 patients a secondary glaucoma was detected during the second and third post-operative months. Three of these eyes were treated successfully by iris inclusion, one by cyclodiathermy, and two were controlled with Daranide tablets, but one patient refused surgical treatment and his graft became oedematous. In two cases the host-graft junction ruptured during the removal of sutures; one of these grafts became and remained oedematous whereas the other remained clear.

Records and Assessments

The pre-operative, operative, and post-operative records were compared, and histological sections of host discs were prepared and examined. Donor material was examined under an operating microscope and the grafts were studied in the patients with a torch and under

5 times magnification or with the slit lamp. The clarity of the donor material and transplants were assessed and are recorded as follows:

○	Clear in all layers—Good result.	
○	Residual oedema	} Good result or partially successful.
○	Post graft membrane	
●	Diffuse minimal or maximal oedema—Failure.	

Donor Material

Fresh human donor material was obtained from the International Eye Bank at Colombo, from the Westminster-Moorfields Eye Bank, and from local donors in Addis Ababa. Deep-frozen donor tissue was air-freighted from London in a Linde liquid Nitrogen refrigerator. 27 whole donor eyes were received from Colombo, and fourteen suitable eyes were used for keratoplasty after an average of 74 hours after death of the donor. Sixteen whole fresh eyes came from London, and full-thickness grafts were cut from nine within 72 hours of death of the donor. They had arrived suspended in glass-bells and submerged in tissue-culture medium. 25 per cent. of the ice-cubes in the polystyrene transport boxes had melted, and the temperature of the suspending medium in the glass jars averaged 4.3°C. from Colombo and 4.4°C. from London. The average age of the Colombo donors was 51, of the London donors 62 years. Six eyes were used for endothelial viability tests and fourteen were discarded (Fig. 2).

FIG. 1.—Staphyloma with corneal ulceration in a glaucomatous eye. Vision: No perception of light.

FIG. 2.—Endothelial aspect of a discarded full-thickness corneal disc. Note stromal oedema and pigmentation.

Post-operative observations showed that graft oedema at and after operation does not indicate a non-viable endothelium. Two grafts which were clear at the end of operation became oedematous during the following 3 weeks and failed, whereas eighteen grafts diffusely oedematous during surgery cleared within 4 weeks and are still clear 12 and 24 weeks after surgery.

Nine anterior segments were obtained from local donors; four were discarded as unsuitable, one was examined for endothelial viability tests, and four were used for full-thickness keratoplasty within 36 hours of the death of the donor. The discarded material was non-transparent and its thickness had increased by 100 per cent. The transplanted material also showed severe oedema immediately after the operation, but three of the grafts gave good results later. It is our impression that the oedema which occurred in spite of such a short storage time might have been due to the fact that the tissue-culture medium, in which the anterior segments had been stored, had become alkaline.

Of the deep-frozen anterior segments, 23 were thawed out and full-thickness grafts were cut from 19 corneae. All corneae lost their epithelium, either during thawing or later during suturing. The material was of normal thickness, but its firmness made the insertion of the corneal needles more difficult than in fresh discs. Apart from marginal oedema where forceps gripped the edges, the discs remained clear during the operation. During the first four post-operative weeks either minimal oedema or folds in the deeper layers of the stroma appeared. Both changes, however, were transient, and the grafts cleared. Four anterior segments were used for endothelial viability tests.

The length of storage-time of the tissue frozen at -196°C . could not be related to the outcome of the grafts. However, two points seem to be of importance: the method of 4°C . storage and the length of time the fresh eyes were kept at 4°C . before they were cooled to and banked at -196°C . The clarity of a previously deep-frozen graft at the time of surgery does not indicate endothelial viability.

The analysis of fresh donor material reveals that the average age of donors was high in eyes received from London, whereas the time of storage was longest in those air-freighted from Colombo. The results suggest that the time of storage at 4°C . before grafting is more important for the final outcome of the grafting operation than the age of the donor. Tables I to V give the details of the donor material.

TABLE I
ANALYSIS OF DONOR MATERIAL

Source of Donor Material	Total Number of Donor Eyes	Suitable Donor Material	Average Age of Donor (yrs)	Average Storage Time (hrs)	Successful Clear Grafts (3-6 mths)						Total Successes
					10 mm.	9 mm.	8 mm.	7 mm.	6 mm.	5 mm.	
Colombo	27	14	51	74	0/1	0/1	2/3	3/4	3/4	0/1	8/14
London	16	9	62	69			1/1	4/6	1/1	1/1	7/9
Addis Ababa	9	4	23	24	0/1			2/2	1/1		3/4
Deep-frozen	23	19	42	607		0/1	1/1	9/12	5/5		15/19

Results

(1) Full-Thickness Corneal Grafts on Non-Perforated Eyes with Lesions of Trachoma Stage IV (11 cases)

Eleven patients showed clinical evidence of trachoma Stage IV and had received treatment for this condition as out-patients for many months before operation. Three of the eleven patients had had surgical correction of their entropion (e.g. Fig. 3). Fig. 3 shows one patient 9 months after an entropion operation and 3 months after right full-thickness corneal graft.

FIG. 3.—(See Figs 5 and 7). Patient 9 months after bilateral entropion operation and 3 months after right full-thickness corneal graft.

calibre reached the centre of the cornea in six cases. The stroma showed either diffuse minimal or single or confluent dense opacities (Figs 4 and 5). The corneae were irregular and in some areas they were reduced up to 50 per cent. of normal thickness.

Peritomy and cautery to the bleeding vessels did not prevent bleeding from the trephine cut; it was omitted in the last four cases. Post-operatively all eyes became severely injected, but vascularization of the grafts did not occur. Apart from superficial vascularization around the sutures, the vessels did not invade the grafts, and quickly regressed with the removal of the sutures.

Ten transplants were clear and remained clear from the fifth week onwards (Figs 6 and 7). Four of these were fresh and six were frozen grafts with an appearance indistinguishable from the fresh ones. We were able to observe six of them for 24 weeks, and four for 36 weeks after surgery, to confirm that they did not alter and remained clear. One deep-frozen disc of 9 mm. diameter had been transplanted into a corneal bed of about one-half its normal thickness; it became oedematous,

FIG. 4.—Minimal corneal opacification of a cornea with lesions of trachoma Stage IV. Vision: Counting fingers at 5 m.

FIG. 6.—(See Fig. 4) 6 mm. full-thickness corneal graft with fresh material 38 weeks after operation. Vision: 6/24.

FIG. 5.—Corneal opacification with superficial and mid-stromal vascularization of a trachomatous eye. Vision: Perception of light.

FIG. 7.—(See Fig. 5) 6 mm. full-thickness corneal grafts with fresh material 3 months after operation. Vision: 6/24.

and remained so for the 3 months observed. In our experience, the larger grafts have a lower success rate.

During the first two post-operative weeks the eyes were treated only with a tetracycline ointment. Hydrocortisone ointment was added at the beginning of the third week. The injected eyes whitened slowly; after 3 months they were still mildly inflamed, but those observed for 6 months were white.

Thus it is our impression that corneae with trachomatous scars and vascularization give good results after full-thickness corneal grafts. The results are demonstrated in Table II.

TABLE II
FULL-THICKNESS CORNEAL GRAFTS ON 11 NON-PERFORATED EYES WITH LESIONS OF TRACHOMA STAGE IV

Type of Donor Material	F	F	D.F	F	D.F	D.F	D.F	D.F	D.F	D.F	F
Size of Graft (mm.)	7	7	6	7	7	7	7	6	7	9	6
Clarity of Graft	After operation
	After 12 wks
	After 24 wks						*	*	*	*	*
Last Visual Results	6/12	6/12	6/12	6/12	6/6	6/60	6/24	6/36	6/18	2.0	6/24
Successes	Clear Fresh Grafts: 4/4; Clear Deep-frozen Grafts: 6/7										

* Observed 12 weeks

F = Fresh

D.F = Deep-frozen

(2) Full-Thickness Corneal Grafts on Eyes with Simple Corneal Scars (3 cases)

Three eyes showed no clinical evidence of trachoma, and two of the corneae were free from vascularization. In one case the central scar was the result of small-pox, but in the other two the aetiology of the corneal opacities was unknown.

Peritomy was not performed and the operation and post-operative progress were uneventful. Two grafts were clear 8 weeks and 12 weeks after surgery, and one of these which was observed for a longer period was still clear 24 weeks after the operation. One graft failed; the transplant was clear until the fifth post-operative week, but the host-graft junction separated when the sutures were removed and within 24 hours oedema of the graft was visible at the site of separation and this spread across the transplant within a few days. The transplant remained oedematous, but neither host nor graft had become vascularized by the 32nd post-operative week. The patient awaits repetition of the operation and transplantation of a graft of a larger diameter.

All three grafts were cut from fresh material. The minimal oedema present at first had dispersed after removal of sutures (Fig. 8, opposite). Because of the small number, these results cannot be compared with those of the previous group. All three grafts, however, showed minimal ocular injection after surgery, in which they differed from the eleven grafts in the first group. The results are shown in Table III (opposite).

FIG. 8.—6 mm. full-thickness corneal graft with fresh material 40 weeks after operation. Visual improvement from counting fingers to 6/60. Note senile cataract.

TABLE III
RESULTS OF GRAFTS ON 3 SIMPLE CORNEAL SCARS AND 6 OTHER THERAPEUTIC CASES

Type of Case	Simple Corneal Scars (3)			Therapeutic Grafts (6)					
				Staphyloma (2)		Descemetocele (2)		Corneal Rupture (2)	
Type of Donor Material	F	F	F	D.F	F	F	F	D.F	F
Size of Graft (mm.)	6	5	6	7	9	7	7	7	10
Clarity of Graft	After operation
	After 12 wks
	After 24 wks
Last Visual Results	6/60	3-0	6/18	1-0	0-5	6/60	6/12	2-0	1-0
Successes	Clear Fresh Grafts: 2/3			Clear Fresh Grafts: 2/4		Clear Deep-frozen Grafts: 1/2			

* Observed 12 weeks F = Fresh D.F = Deep-frozen

(3) Full-Thickness Corneal Grafts on Perforated Eyes with Lesions of Trachoma Stage IV (15 cases)

All fifteen patients showed scarred tarsal conjunctivae and extensive superficial and mid-stromal vascularization; in addition, trunk vessels reached the corneal scars in eight cases. Anterior synechiae were present in all fifteen eyes, and an anterior cortical cataract was present in five and a nuclear cataract in one. In two patients the lens was firmly adherent to the cornea. Three eyes were aphakic; the strands of capsule in one eye were attached to the centre of the opaque cornea.

Total peritomy and cautery to bleeding vessels were performed in ten cases; in the other five only trunk vessels were cauterized. At operation, more complications were revealed; in one case of aphakia the posterior capsule was found to be damaged and in two others the lens had been either extruded during the perforation or dislocated following trauma; in both cases some vitreous was lost.

Nine grafts were clear 4 weeks after surgery, three were clear over their upper

third, and three transplants were severely oedematous; at 12 weeks eight, and at 24 weeks six, remained successful.

Two grafts clear until the eleventh and thirteenth week respectively, developed a secondary glaucoma; the transplants became oedematous and the ocular tensions remained uncontrolled for 3 months in spite of treatment with acetazolamide 500 mg. daily. When iris inclusion operations were performed both grafts cleared within days; one regained complete transparency, whereas a small paracentral nebula remained visible in the other (Fig. 9).

FIG. 9.—Full-thickness graft with material stored at -196°C . 39 weeks after operation. Eye developed closed-angle glaucoma 13 weeks after operation, and iris inclusion was performed 24 weeks after graft surgery. Note anterior cortical cataract.

Two grafts partially clear at 4 weeks improved so that after 12 weeks only the lower half of the transplants showed oedema; in one of them, observed for 24 weeks, the oedema regressed further to take up only a sickle-shaped section over the lower host-graft junction. Deep to it a post-graft membrane could be seen.

Three grafts remained oedematous 12 and 24 weeks after operation. A reduction of the oedema became noticeable in one of them at 12 weeks, when iris and lens could be seen, and the patient's vision improved. A secondary glaucoma occurred in another graft 7 weeks after operation; acetazolamide therapy was commenced at maximal dosage, but the oedema remained unaltered and deep vascularization soon invaded the transplant. The patient refused anti-glaucomatous surgery.

In this group fresh donor material was transplanted in ten and deep-frozen corneal tissue in five cases. Five of the fresh and four of the frozen gave good results at the end of the varying periods of observation. In this group several transplants were of large diameter; four eyes received transplants of 8 to 10 mm. diameter, of which two failed, one is only partially clear, and one (of 8 mm.) is successful.

The failures of this group probably derived from a variety of factors. First of all, secondary pathological changes of the host-cornea seemed to have influenced the final outcome of the graft. Secondly, other intra-ocular complications were quite frequently encountered, and a number of grafts had to be of very large size. The success rate would probably have been improved by shorter storage-time of the fresh donor material. The results are given in Table IV (opposite).

(4) *Full-Thickness Grafts on Perforated Eyes with Ocular Lesions of Unknown Aetiology (11 cases)*

The eleven eyes in this group showed superficial large-calibre vessels which

TABLE IV

FULL-THICKNESS CORNEAL GRAFTS ON 15 PERFORATED EYES WITH LESION OF TRACHOMA STAGE IV

Type of Donor Material	F	F	F	F	D.F	F	F	D.F	F	F	F	D.F	D.F	D.F	F
Size of Graft (mm.)	6	8	7	7	7	6	8	8	10	7	6	7	7	7	7
Clarity of Graft	After operation														
	After 12 wks														
	After 24 wks											*	*	*	*
Last Visual Result	3-0	2-0	0-5	2-0	6/60	0-5	0-5	6/9	3-0	6/24	6/24	6/60	5-0	5-0	0-5
Successes	Clear Fresh Grafts: 5/10; Clear Deep-frozen Grafts: 4/5														

* Observed 12 weeks F = Fresh D.F = Deep-frozen

extended into the corneal scars and also fine deep-stromal vascularization in sections of the cornea. Anterior synechiae were present in all cases and anterior cortical cataracts in three. Two eyes were aphakic.

Peritomy was performed in only six cases; in the remaining five the superficial trunk-vessels were cauterized and the operation was completed without complication.

Eight of the eleven grafts were clear 12 weeks after the operation; seven of these were observed for 24 weeks and remained clear. Secondary glaucoma occurred in one of these cases 6 weeks after surgery, but the tension remains controlled by dichlorophenamide and the graft is still clear; the patient awaits further surgery. Three grafts were only partially clear at the twelfth week after operation because of fine diffuse oedema over part of the grafts; by the 24th week one had cleared in all layers, the second showed only residual oedema over the lower half and a post-graft membrane deep to the stromal oedema, and the third could not be observed any further.

Of interest is the result in one uniocular patient. Skin and cartilage of his nose had been destroyed completely by lupus vulgaris and ulcers were present over the skin of the nasal bones and cheeks (Fig. 10, overleaf). An 8 mm. full-thickness corneal graft cut from fresh donor tissue was performed and the operated eye was uncovered at the end of the first post-operative week to allow treatment of the eye and skin condition. The post-operative period was uneventful; the graft, now 9 months after operation, is clear in all layers and the skin ulcers have healed. Figs 11 and 12 (overleaf) show the patient's eye before and 9 months after the operation.

Fresh donor material was used in six cases, and frozen tissue in five; apart from one frozen and one fresh graft all transplants were clear. The success rate in this non-trachomatous group (Table V, overleaf) is higher than in trachomatous eyes. In the trachomatous group, however, larger grafts were frequently transplanted and complications were more frequently encountered. Vascularization of grafts in both groups was transient. Eyes on which peritomy had been performed were more injected than those without peritomy and cautery.

FIG. 10.—(See Figs 11 and 12). Uniocular patient 9 months after full-thickness keratoplasty. Note scars of lupus vulgaris.

FIG. 11.—Large para-central corneal scar with vascularization of unknown origin. Vision: Counting fingers at 5m.

FIG. 12.—8 mm. full-thickness corneal graft with frozen material 40 weeks after operation. Vision: Counting fingers at 5m. Note anterior polar cataract.

TABLE V
FULL-THICKNESS CORNEAL GRAFTS ON 11 PERFORATED EYES WITH LESIONS OF UNKNOWN AETIOLOGY

Type of Donor Material	F	F	F	D.F	F	D.F	F	F	D.F	D.F	D.F
Size of Graft (mm.)	7	7	8	6	7	6	7	5	7	6	6
Clarity of Graft	After operation										
	After 12 wks										
	After 24 wks										
Last Visual Results	4.0	2.0	3.0	6/6	6/6	6/12	6/12	6/60	6/24	6/60	3.0
Successes	Clear Fresh Grafts: 5/6; Clear Deep-frozen Grafts: 4/5										

* Observed 12 weeks F = Fresh D.F = Deep-frozen

The results in all these groups show that corneal grafts on non-perforated eyes have a higher success rate. The failures in all perforated eyes may have been due partly to the multiplicity of intra-ocular complications and partly to the larger size of the transplants (see Discussion).

(5) *Therapeutic Grafts* (6 cases)

CORNEAL STAPHYLOMATA.—These were present in the only eyes of two unioocular girls aged 10 and 11 years. Both ectatic corneae were densely vascularized and in some areas reduced to about 25 per cent. of their thickness; multiple anterior synechiae and anterior cortical cataracts were present. The lens of one eye was adherent to the staphylomatous cornea. One cornea was replaced by a fresh, and the other by a frozen corneal disc.

The fresh transplant was clear 4 and 8 weeks after the operation, but secondary glaucoma gave rise to a peripheral oedema of the transplant at the beginning of the third post-operative month. A cyclodiathermy was performed and the tension returned to normal; the graft, however, remained ectatic and oedematous in its periphery.

The frozen full-thickness corneal graft was clear 4 and 12 weeks after the operation and the intra-ocular pressure remained normal throughout the time of observation.

DESCEMETOCELE.—Two patients were operated on for a leaking descemetocele (Fig. 13). In both instances fresh grafts were transplanted.

One graft remained clear throughout the 24 weeks of observation, but the other became oedematous 4 weeks after surgery because of secondary glaucoma. Oral treatment with Daranide brought the ocular tension down to normal and the graft, having been oedematous for 3 weeks, regained complete clarity (Fig. 14). This patient awaits anti-glaucomatous surgery.

FIG. 13.—Corneal scar with leaking descemetocele. Vision: Perception of light.

FIG. 14.—(See Fig. 13). 24 weeks after operation. Ocular tension controlled. Vision: 6/12.

CORNEAL RUPTURE.—Two patients were admitted with corneal rupture and absent anterior chambers. Both corneae showed heavy vascularization and severe reduction of corneal thickness. The ectatic cornea of one eye had ruptured in its centre and the cornea of the other at the limbus. Scarred and friable conjunctiva prevented wound closure by a conjunctival flap and the corneae were replaced by partial and total corneal grafts. One graft was cut from a fresh, and the other from a frozen donor eye, and the first operation was completed by an iris inclusion.

Both grafts were oedematous after surgery, the intra-ocular pressure in the eye that had received the deep-frozen disc was and remained raised in spite of treatment with dichlorphenamide. The oedema over the upper cornea cleared slowly, but that over the lower half persisted, and 32 weeks after the operation a post-graft membrane had formed deep to this oedematous section of the graft. The patient refused further surgery.

The intra-ocular pressure of the eye with the fresh graft remained normal, but the graft remained oedematous throughout the post-operative observation, the conjunctiva over the iris inclusion showing a well-formed drainage bleb.

The results in this group are shown in Table III (above).

Visual Results

Fourteen patients with pre-operative projection of light are compared with 32 patients with vision of at least counting fingers.

The results in the first group are less satisfactory, intra-ocular complications being very frequent. One patient improved to 6/12, and another to 6/36, and two patients with cataracts gained 6/60 vision. The sight of the remaining ten patients improved to "counting fingers"; nine of them show either cortical or nuclear cataracts and in addition four have nystagmus. The large grafts of two patients were oedematous, but both showed visual improvement 24 weeks after the operation.

The results in the second group with pre-operative vision of at least "counting fingers" are encouraging; 22 improved to 6/60 and better, and eight improved their acuity in "counting fingers", but the other two experienced some loss of sight. Two of the 32 eyes are complicated by cataracts but improved to 6/60. Two eyes have nystagmus, but nevertheless improved, one to 6/60. Partial amblyopia in three cases and oedematous grafts in four cases improved their vision to a limited extent; nevertheless, one achieved 6/60. The results are given in Tables II to V (above) and in Table VI.

TABLE VI
VISUAL RESULTS AFTER FULL-THICKNESS CORNEAL GRAFTING

Pre-operative Vision	Perception of Light						Counting Fingers†					
	No. of Cases	Nystagmus	Cataract	Amblyopia	Glaucoma	Oedema of Graft	No. of Cases	Nystagmus	Cataract	Amblyopia	Glaucoma	Oedema of Graft
Counting Fingers	10	4	9		2*	2	8	1		2	2*	4
6/60-6/9	4		2				22	1	2	1	2*	
Deterioration of Vision							2				1‡	2

* Glaucoma controlled † 2 cases with pre-operative vision 6/60 ‡ Glaucoma not controlled

A comparison of the visual results of grafts on non-perforated eyes with those on perforated eyes shows that in the former group twelve out of fourteen patients, and in the latter only fourteen of 32, improved their vision to at least 6/60. This is because all the cases of nystagmus or amblyopia and twelve of the thirteen cataracts occurred in patients belonging to the perforating group.

Grafts up to 7 mm. diameter gave the best visual results and 24 of the 37 improved their vision to 6/60 and better; here again a higher incidence of improvement was

observed in the non-perforated eyes. Two grafts of 8 mm. gave an improvement of vision to at least 6/60, whereas grafts of 9 and 10 mm. failed to do so. The results are shown in Tables II to V (above).

Histological Appearances of Corneal Discs

Histological sections from all host discs were prepared and examined; typical and unusual findings are here reported.

Epidermalization of the disc epithelium was seen in three sections. Two of the transplanted discs are clear, but one showed re-epidermalization over its lower half. The condition was treated with subconjunctival injection of hydrocortisone with some success.

Epithelial degeneration, destruction of Bowman's membrane, calcification of scarred stroma, and superficial or midstromal vascularization was present in numerous discs, and the typical picture of trachoma Stage IV in eleven discs (Figs 15 and 16).

FIG. 15.—Typical corneal lesion of trachoma Stage IV. $\times 625$.

FIG. 16.—Destruction of Bowman's membrane and midstromal vascularization in trachoma Stage IV. $\times 140$.

Partial destruction of Descemet's membrane was detected in all discs with perforating corneal lesions. Its reduplication was present in five discs and a retrocorneal membrane was present in six. One case of duplicated Descemet's membrane and one post-corneal membrane extended to the disc margin and most likely on to the remaining host cornea (Fig. 17, overleaf). Both grafts are clear in spite of having been grafted into abnormal host corneae.

In one case, destruction of endothelium and Descemet's membrane with pigmentation over the entire disc was present (Fig. 18, overleaf). This graft failed and it is suggested that the endothelium was most likely also absent over the remaining host cornea.

Endothelium and Descemet's membrane were found to be destroyed over disc areas where anterior synechiae had been separated by blunt dissection (Fig. 19, overleaf).

FIG. 17.—Retrocorneal membrane extending to edge of host disc. $\times 140$.

FIG. 18.—Destroyed endothelium and Descemet's membrane of host disc. Uveal pigment adherent to stroma. $\times 140$.

This suggests that anterior synechiae to the remaining host cornea should be left undisturbed. The host cornea denuded of its endothelium and with a destroyed Descemet's membrane is likely to give rise to host oedema and possible post-graft membrane formation. This was observed in one case with certainty.

Discussion

The purpose of corneal grafting was to enable the patients to become independent and to give them the opportunity to earn their living. Visual improvement from perception of light to "counting fingers" and from "counting fingers" to 6/60 vision and better was greatly appreciated. High degrees of visual acuity, essential in other communities, were usually not required, as the majority of patients were farm-workers and craftsmen, and they were not therefore generally tested for glasses. The patients were poor and the purchase of spectacles would have been an expense they could ill afford.

Grafting the full thickness of the cornea did not present special difficulties, in particular as general anaesthesia was employed. Ectasia and rupture of the host-graft junction was prevented by inserting an adequate number of deeply-placed sutures, tied under an equal tension. In our experience ectasia is more common in small grafts, which require relatively more sutures than transplants of larger diameters. Mathematical calculation shows that the number of sutures is inversely related to the diameter of the transplant. Suture marks upon the transplant are more obvious

FIG. 19.—Anterior synechiae at edge of host disc. Note absence of endothelium and destroyed Descemet's membrane. $\times 140$.

in small grafts. We believe that the intra-ocular pressure acting on the graft and the sutures is of greater force over small areas than over larger ones. The sutures of a small graft have to resist this relatively greater force and tend to be buried more deeply into the upper stroma of the graft, thus giving rise to linear scars (Figs 9 and 10; and Mueller and others, 1966). Despite a high incidence of post-anaesthetic coughing and straining, anterior synechiae did not occur and the host-graft junction did not rupture. The separation of two junctions is the result of too early removal of sutures. Single sutures cut out, which is not unusual; however, contrary to the findings of Dhanda (1963), it was not noticed that in trachomatous cases the corneae are more friable and sutures cut out more readily, nor did we observe post-operative ulcers of the grafts.

Topical treatment with hydrocortisone preparations was commenced in most cases at the beginning of the third post-operative week, and in a few cases earlier. Reactivation of trachoma was not observed and vascularization of the transplant grafted into heavily vascularized corneae was not noticed, unless the grafts became severely oedematous. We repudiate the idea that vascularization, in particular trachomatous vascularization of host cornea, is likely to be the cause of failures of full-thickness grafts (Kamel, 1965). Heavy vascularization was present in at least eighteen host corneae, but oedema developed in only three of the eighteen cases and partially cleared in one of them.

The cause of failure of transplants is most likely a non-viable endothelium of transplant and/or host cornea. The failures of large diameter grafts in particular are due to loss of endothelial viability; the mechanical trauma, and therefore the endothelial damage is greater. Vital staining of whole corneae shows a greater number of pathological cells in the periphery of the cornea which would be included into larger transplants.

Results of full-thickness keratoplasty on trachomatous patients have been reported by previous authors. Visual improvement to at least 6/60 was obtained in six out of 22 cases (Dhanda, 1963) and in fifteen out of 35 cases (Paufigue and Charleux, 1964). Our results of fifteen improved out of 26 trachomatous grafts compare favourably with theirs. Improvements in non-trachomatous eyes have been reported by Dhanda; his good results in 34 out of 74 patients and our findings of nine out of fourteen clear grafts with visual improvement to 6/60 confirm that the success rate in trachomatous eyes is comparable to that in non-trachomatous eyes (Farnarier, Guillot, and Bona, 1951).

The results of fresh and frozen transplants cannot be compared if fresh material stored at +4°C. for more than 48 hours is regarded as less successful for full-thickness corneal grafts. This, however, implies that the export of fresh donor tissue to far-away countries is not practical, and stresses the need for the long-term preservation of corneal donor tissue. The successful storage of corneae with a rim of sclera in one medium at -196°C. is an important factor in establishing a practical method for long-term preservation.

The selection of fresh donor material was made after macroscopical examination of the cornea and on several occasions after biological tests on the second cornea of a pair of donor eyes. No attempts were made to remove the epithelium of fresh donor eyes. Its removal may injure Bowman's membrane and may later give rise

to superficial opacities, but if left *in situ* it will be shed without causing damage. The epithelium is replaced within days and is discharged with tears; the likelihood of its giving rise to antibody formation is minimal. The epithelium of all the frozen donor discs was lost by the end of the operation but opacities in the region of Bowman's membrane were not observed. The loss of the epithelium confirms the findings of Smith, Ashwood-Smith, and Young (1963) that dimethyl-sulphoxide (DMSO), the only protective agent used in this series, has a loosening effect upon the intercellular cement substance. This loss, however, did not affect the outcome of the frozen grafts and fifteen of the nineteen transplanted discs gave good results. Material stored up to 37 days was transplanted. No attempt was made to establish an optimum banking period, which can be estimated in animal experiments. Storage times of 6 months at -196°C . are likely to be reached and would be sufficient for all practical purposes.

Recent reports state that DMSO gives rise to lens opacifications. In our experience of grafting frozen material protected by DMSO, the clarity of either animal or human lenses was unaffected. DMSO was always washed out of the disc before it was placed into the host and sutured.

The purpose of our visits to Addis Ababa was to study the possibility of full-thickness corneal grafting of fresh and frozen corneal donor tissue, and to teach the technique to the resident ophthalmic surgeons. The studies were undertaken at considerable expense unacceptable to the Ministry of Health of any developing country. The World Health Organization and the United Nations International Children's Emergency Fund support work in preventive and curative medicine in Ethiopia and in other developing countries. Local medical schools in Africa make all efforts to train their doctors to meet the needs of the African medical practitioner and general surgeon; they cannot allow more than 10 per cent. of their graduates to specialize while Africa remains "doctor hungry", and visiting specialists should continue to stimulate teaching and research (*Lancet*, 1966). Raising the necessary funds must of necessity be the responsibility of more fortunate countries and we gratefully acknowledge the assistance we received which made this work possible.

Summary

A series of 48 full-thickness corneal grafts performed in Addis Ababa is described, using fresh and frozen human donor material. In spite of difficult local conditions, the patients were observed for periods varying between 3 and 9 months after operation, and 73 per cent. of all grafts gave good functional results, the percentage being slightly higher when donor material that had been stored at -197°C . was used.

The visual results are analysed, and in 26 out of 46 patients the sight improved to at least 6/60, and eighteen improved to counting fingers. Only two patients lost part of their pre-operative sight. 50 per cent. of all the cases grafted had the corneal lesions of trachoma Stage IV; in nineteen out of 26 the grafts were successful, and the results compare well with those in non-trachomatous eyes. Corneae which had not suffered perforation showed a higher success rate, in particular when the transplants were of 7 mm. or less in diameter. The presence of nystagmus and cataract did not contraindicate grafting. Improvement even only to counting fingers was of great value to those who had been practically blind before surgery.

The operative technique adopted prevented rupture of the host-graft junction, and the pre- and post-operative procedures used succeeded in avoiding ocular infection in spite of the patients' lack of intelligent co-operation and the low standards of hygiene that prevailed.

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