Eye (1991) **5**, 265–278

THE MONTGOMERY LECTURE

Some Factors Which Affect the Visual Outcome of Corneal Transplantation

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Summary
Corneal transplantation, which began in Dublin early in the nineteenth century, is now widely practised. Most grafts are done for visual reasons, some to manage corneal destructive disease. The factors associated with allograft rejection are well known, but a clear graft does not mean that the transplantation procedure has been successful. Successful corneal grafts enable patients to improve their life-style. To achieve this, the graft must be transparent and free of optical aberrations, the eye must be capable of achieving good vision, and the patient must have a life-style which would benefit from a successful functioning graft. A study of patients who have had corneal grafts identified the presence of a functioning graft, the lack of need for a contact lens, and the achievement of visual acuity in the operated eye which exceeds that of the contralateral eye, as requirements for patient satisfaction.

In accepting the invitation to deliver the 1990 Montgomery lecture, I am aware of the great honour bestowed upon me. The list of previous lecturers contains the names of famous men who have made great contributions to ophthalmology over many years. My only distinguishing characteristic is that I come from further away from Ireland than anybody else who has had the honour of delivering this prestigious lecture. Although Australia is the most remote continent, this does not mean that Australian society has escaped the influence of Irish culture, science and medicine.

Two of my major interests, corneal transplantation and Australian Rules Football, had their beginnings in Ireland.

Australian Rules Football is the most popular of the 5 major codes played in Australia, and the origins of the game go back to the 1850s in Victoria, when the Irish population of the colony was the largest outside Ireland.[1] From humble beginnings in the paddocks around Melbourne, the game has grown to its dominant position in Australian sport, drawing crowds of 100,000 people to major games. Although Australian Rules football is slightly different from the Gaelic football played in Ireland, the two countries play each other from time to time.

Corneal transplantation had its beginnings in Ireland. In the late 18th century, there was considerable interest in the prospect of corneal transplantation overcoming the ravages of Egyptian ophthalmia. This serious eye

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disease, which produced a great deal of blindness and disability as a consequence of corneal inflammation, was brought back to Europe from Egypt at the end of the 18th century. It led to the development of ophthalmology as a separate branch of surgery and created a great deal of interest in the potential of corneal transplantation, even at a public level. Erasmus Darwin, Charles Darwin's grandfather, was the first in the English-speaking world to suggest a strategy for corneal transplantation. In 1797 he wrote,

> "Could not a small piece of the cornea be cut out by a kind of trephine, about the size of a thick bristle, or a small crow quill, and would it not heal with a transparent scar?"[2]

As Darwin suggested, there were two important questions about the biology of corneal transplantation that needed to be answered. Firstly, would a graft heal, and secondly would the resultant scar be transparent?

Amongst the first practical contributions to the science of corneal transplantation were those of Samuel Bigger, an Irish ophthalmologist.[3] In 1831 he travelled to Germany, where there was already some interest in the subject. In particular, Reisinger had commenced experiments with rabbits after becoming interested in the early skin grafting work of Astley Cooper in London. Reisinger seemed to be more interested in the healing process than the visual result. He reported a partially successful graft in the Bavarian Annals of 1824. This partial success in one animal was all that was recorded, despite experiments being carried out in animals in a number of centres at that time. After his visit to Germany, Bigger visited Egypt, " . . . a country noted for the prevalence of destructive ophthalmia." Somehow, in 1835 he became " . . . a prisoner with a nomadic tribe of Arabs, about 12 or 14 days journey from Grand Cairo." It was under these circumstances that he carried out the first corneal graft to result in improved vision.

"The subject of the operation was a pet gazelle, who had lost one eye from inflammation and the power of seeing with the other, from a wound to the cornea. The replacement cornea was taken from another animal of the same species, brought in wounded, but not quite dead; adhesion took place, and 10 days after the operation the animal gave unequivocal signs of vision. The upper part of the transplant remaining perfectly transparent."

On his return to Dublin, Bigger carried out a number of experiments, and reported the results of corneal transplantation in 18 rabbits. These experiments included various combinations of allografts and autografts. Of the 18 grafts he reported, 16 recovered imperfect vision. He almost certainly observed the corneal allograft response, although of course he did not understand its significance. "On the 30th day, violent inflammation occurred in one of the rabbits, without any evident cause, and terminated in a copious deposition of puriform lymph in the anterior chamber. At the end of 10 days it subsided."

Bigger recognised the potential importance of corneal transplantation and correctly predicted that the technical aspects of surgery, the main thrust of his work, would be easier in humans because the eye was larger and the subject was likely to be more co-operative. He was also concerned about the source of donor material. He suggested the cornea of the pig was likely to be the most useful, and his advice was taken up by others interested in the subject with, at least with hindsight, predictable results.

Bigger was also concerned about the use of human donor tissue. "In a spirit of just and humane feeling, he deprecates the removal of the cornea from the human eye, even when permitted for gain by the possessor; but thinks that a person affected with incurable amaurosis might be prevailed upon to part with his pellucid cornea, which might be replaced with one taken from some inferior animal." In his conclusion, Bigger attempted to predict the patients who were most likely to benefit from corneal transplantation. He was "of the opinion that cases of blindness caused by smallpox, ulcers on the cornea, and ophthalmia not affecting the deeper structures of the eye, would be the most favourable for operation." In his paper of 1837, he concluded, with a plea to his colleagues " . . . imploring hospital surgeons to give the matter their attentive consideration, particularly as experiments and analogy have shown the feasibility of the operation." Bigger pursued corneal trans-

plantation because of its potential as a treatment for blindness and disability and he was largely responsible for initiating the line of researchers who have maintained the assault on corneal transplantation for the last 150 years.

Great advances have been made since Bigger made his seminal contributions to corneal transplantation. Anaesthesia, asepsis, and effective antimicrobial and anti-inflammatory therapy have been introduced into surgical practice. So too have microsurgical techniques and materials, and the nature and significance of the allograft response have been elucidated. Despite these giant strides in medical science, not all of the problems of corneal transplantation have been solved. Although the procedure has the potential to restore vision to those who are blind or visually disabled as a result of corneal disease, there is a very wide spectrum of corneal disorders and some patients gain more from transplantation than others. Bigger recognised that the major question was how to decide who would be helped by corneal transplantation, and 150 years on this still remains a major question.

Corneal transplantation: Choosing the appropriate outcome measurement

Choosing an appropriate and quantifiable end point is a critical consideration in all scientific assessment. The choice of an end-point depends on an understanding of the aim of the exercise. In surgery, this can be complicated because one procedure is often done for more than one indication, and because the measurable aspects of a result may not correlate well with what the patient considers to be an appropriate outcome. Deciding on an appropriate outcome for corneal transplantation involves some difficult considerations along these lines.

Corneal transplantation is the most widely practised form of clinical transplantation. It is generally perceived as being the most successful. This is so if the same criteria are used to assess the outcome of corneal transplantation as are applied to other forms of clinical allografting, such as kidney, liver, bone marrow and heart and lung transplantation. For these forms of essential organ transplantation, survival of the patient correlates with graft survival. These grafts are done to overcome diseases which are inevitably fatal without successful transplantation.

Corneal transplantation is not done to preserve life but to overcome disability, or to preserve the integrity of the eyeball. Sometimes the procedure is carried out to reduce pain. There is, therefore, the need to invoke a range of outcome measurements to correlate with the indications. Reduction of pain and preservation of the globe are relatively easy to judge and count. An assessment of the impact of corneal transplantation on visual disability is a more complex consideration.

When considering the outcome of the procedure done for reduction of visual disability, it is appropriate to consider a number of objective measurements. Corneal graft function is one important consideration. A corneal graft must be thin and transparent if the patient is to see through the cornea. This is not particularly useful information in itself. A failed graft will always result in poor vision but a functioning graft may not necessarily deliver good vision. A measure of visual function is to be preferred, but which clinical measure is appropriate?

Visual acuity measured with a Snellen chart is very widely used and has gained almost universal acceptance. Snellen acuity is not a useful or complete measure of visual function when used alone or without stipulation. Quite apart from the well known limitations of acuity testing, considerations such as the time after surgery that the vision is measured, and the optical correction used during the test, are important in the context of corneal transplantation. The final refraction cannot be achieved until all the sutures have been removed. This is often not until well into the second year after surgery. Furthermore, the form of optical correction which yields the best visual acuity may not be acceptable to the patient, who may have to function on a day-to-day basis with something quite inferior. Visual acuity should be tested with the patient using his everyday or socially-acceptable correction. Even when these requirements are met, the Snellen acuity measurement provides a far from complete picture of a patient's visual performance. Many grafts are done for

patients whose vision in the contralateral eye is good. Presumably, the purpose of the procedure is to provide improved binocular function, better field, and perhaps improved stereopsis. Any improvement in binocular function is not assessible using acuity measurements alone. The acuity measurement may be quite misleading. Anisometropia in one form or another is relatively common after corneal transplantation. A high level of acuity may be achieved only with an anisometropic correction. To assess the true meaning of an acuity reading requires a knowledge of the vision in the other eye and the refraction of both eyes.

Another approach is to disregard the results of psychophysical tests such as acuity and refraction, and to assess visual disability directly. This approach takes surgeons out of the area of the objective measurements with which they are familiar, into the more subjective, consumer-directed, approach of the market surveyor or sociologist. The process is time-consuming, the results can be difficult to interpret, and, perhaps more importantly, the results must be interpreted individually for each patient because the expectations of patients having surgery for disability vary greatly. Social, economic, psychological and cultural factors interact with physiological factors to determine how a patient expects to benefit from surgery. If we are to accept the patients' judgement of whether our surgery has reduced disability, we must make a careful assessment of their perceptions of their preoperative disability and post-operative expectations. Matching the patients' expectations and the surgeons' expectations is a well-recognised pillar of the act of medicine, but it is notoriously difficult to achieve with some patients.

When deciding upon the criteria to be used to assess the outcome of corneal transplantation, it is not enough to consider the patient and the surgeon. There are interested third-parties. Increasingly, medicine is coming under the watchful eye and guiding hand of those who finance health services. Government agencies and insurance companies are increasingly interested in the outcome of medicine in relation to resources consumed. More and more, we can expect increasingly precious resources to be allocated on the basis of benefits derived for money spent. We live in the age of "Outcomology".[4] It behoves us to come up with a range of objective measurements and consumer-based criteria for evaluating the success of our procedures, including corneal transplantation.

The need to develop appropriate measures of outcome for corneal transplantation has prompted us to establish two data bases, the Australian Corneal Graft Register, and the Flinders Medical Centre data base, in order to evaluate relationships between the various factors which influence outcome.

Australian Corneal Graft Register

The Australian Corneal Graft Register was established in 1985. Ophthalmologists from all states of Australia contribute prospective data about their patients.[5] They provide data on standard forms at the time of surgery and follow-up data at regular prescribed intervals. More than 2,200 grafts are now being followed. The data is analysed using customised software and a report is published each year.

The Register provides very useful information because of its size and the breadth of practice it describes. However, the deficiencies of such a data base must be acknowledged. About 80% of the grafts done in Australia are included, so the material contributed is not entirely comprehensive. There may be differences in the way observers report observations despite everyone's best attempts to standardise observations and recording procedures. Of course, facilities and conditions vary from centre to centre and this may be particularly important when making psychophysical measurements such as visual acuity.

In order to take advantage of the strengths of the Register and to minimise the weaknesses, contributing surgeons can have their own results analysed separately and confidentially. They can also include information related to their particular interests in addition to the core material which is standard for all contributors. This source of information is very important when dealing with highly specific outcomes such as visual acuity, where standard observations are so critical. To look at more specific aspects of corneal transplan-

tation requires detailed analysis of cases. This is difficult to do in the Register because of its size, the far-flung geographic distribution of contributors and the different approaches to care in the different institutions. To overcome this, some centres keep their own data, concentrating on aspects of care and outcome that they are interested in, or think they might become interested in, in the future. The Australian Corneal Graft Register is happy to manage this data on behalf of individual contributors. At Flinders Medical Centre, more than 300 corneal grafts have been carried out by the author and followed for nearly ten years in some cases. Using data from this source, a number of questions can be addressed that are difficult to answer with data from the Register.

Indications for corneal transplantation

As previously mentioned, any assessment of outcome must bear a direct relationship to the indication for surgery, and the indications for corneal transplantation vary markedly from one setting to another. The indications for corneal transplantation as recorded in the Australian Corneal Graft Register are set out in Table I. It is clear that the major indication for surgery is to reduce visual disability, with the control of focal inflammatory processes or pain less frequent indications.

Improvement in vision is the usual indication for corneal transplantation and will now be considered more thoroughly. There will be no further discussion of the factors which are associated with the outcome of grafts done to control focal destructive disease or pain. For the purpose of this discussion, it is appropriate to look at all patients having corneal grafts, even if the primary indication was not visual. By being "all-inclusive" we can look at a more heterogeneous group and get a better idea of the crude factors which influence corneal transplantation in the general sense.

Table I. *Australian Corneal Graft Register Report 1989. Indications for graft in the Australian Corneal Graft Register*

Indication	*Per cent*
Keratoconus	33%
Bullous keratopathy	23%
Failed previous graft	13%
Corneal scars	12%
Corneal dystrophies	6%
Corneal ulcers	3%
HSV and HZO	3%
Miscellaneous	7%

Visual acuity

The results of surgery, expressed in terms of visual acuity, are set out in Table II and Fig. 1. In view of the heterogeneity of the group, the results are surprisingly good. Approximately 50% of grafted eyes achieved an acuity of 6/18 or better with appropriate optical correction (not pinhole).

Of course this means that 50% of patients do not achieve this level of vision. Approximately 20% of the latter patients had a failed graft and therefore had no chance of achieving an excellent visual result. Of the remainder, 40% had co-existing ocular disease, such as retinal disease or glaucoma, and 40% had an optical problem, such as astigmatism, to account for their poor vision. The co-morbidities and complications recorded as contributory to a poor result are set out in Table III.

Visual disability

Although Snellen acuity is the most widely accepted measure of visual performance, and notwithstanding the difficulties discussed above, the relationship between visual acuity and visual disability is not straightforward. Visual acuity measurement has all of the problems associated with psychophysical tests. The measurement of disability is even more complicated. It is not just a person's disability which affects his day-to-day functioning, it is his perception of his disability which is critical. If the patient cannot do more after surgery than he could before, then the effort has been wasted. With this bald judgement in mind, the limitations of visual acuity as a measure of the outcome of corneal transplantation become even more obvious. The lifestyle of the patient, the expectations of the patient which are likely to be affected by the pre-operative vision, and the attitude of the patient to life in general and vision in particular, are all factors which will affect the perceived outcome. An analysis of the results of corneal transplantation in terms of the visual

Table II. *Australian Corneal Graft Register Report 1989. The results of corneal transplantation expressed in terms of visual acuity*

	Number of patients			
	Surviving grafts		*Failed grafts*	
Best corrected visual acuity	*−PH**	*+PH*	*−PH*	*+PH*
6/4	9	—	—	—
6/5	38	—	—	—
6/6	171	12	—	—
6/9	155	19	1**	—
6/12	75	34	—	—
6/15	—	1	—	—
6/18	63	32	4	—
6/24	32	16	—	1
6/30	—	2	—	—
6/36	31	14	3	1
6/60	30	20	6	6
6/120	3	—	1	1
Count fingers at 3 feet	35	13	30	7
Hand movements	14	4	31	—
Light perception only	1	2	7	—
No light perception	2	—	10	—
Unknown/not recorded	97	—	30	—
TOTAL	756	169	123	16

*−PH: minus pinhole; +PH: plus pinhole; **: IOL touch to cornea

acuity achieved in the eye after surgery, neglects these considerations.

This is not to say that the achievement of a clear functioning graft with good acuity is not a high priority. It does, however, suggest that achieving a clear graft, or even a good visual acuity, is not the whole story. To have any chance of improving the patients' lot, a graft must function, and with minimal optical aberrations, and the eye with the graft must be free of any other disorder which could limit visual potential. Furthermore, the patients' lifestyle must be capable of benefiting from the improved vision.

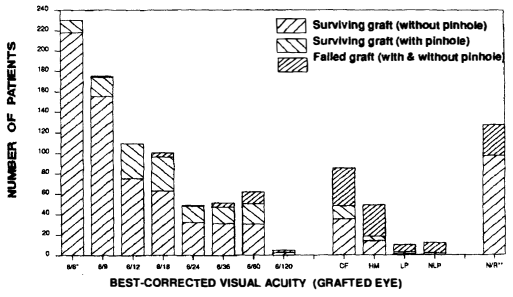

Fig. 1. *Australian Corneal Graft Register 1989. The results of corneal transplantation expressed in terms of visual acuity.*

With the aim of uncovering some of the factors affecting the visual outcome of corneal transplantation in the broader sense, we have looked at a group of patients under our own care at Flinders Medical Centre. A group of patients who had received grafts were recalled and the status of their grafts, visual acuity and refraction, visual disability and attitudes to the surgery, were evaluated. This evaluation was carried out on patients who had been operated on more than two years previously, in the expectation that their refraction and rehabilitation would be complete. The study will be reported elsewhere,[6] but some of the more important features are relevant to this discussion.

A consecutive series of 209 cases fulfilled the criteria with respect to time. However,

Table III. *Australian Corneal Graft Register Report 1989. Ocular decrease contributing to visual acuities less than 6/18 in patients with clear grafts*

Factor affecting visual outcome	*Number*	*(%)*
Cataract	36	(3%)
Amblyopia	24	(2%)
Aphakia	50	(5%)
Retinal detachment	12	(1%)
Cystoid macular oedema/maculopathy	120	(11%)

patients who lived more than 500 kilometres away were excused, as were those who were infirm, unable to travel to the clinic, or who had died in the interim. This left a group of 60 patients to study. They were evaluated by a person from outside the clinical team, a medical student on elective secondment. Patients were re-assessed with a clinical examination, including Snellen acuity, reading-line test and keratometry, and were given a standard questionnaire aimed at discovering their level of visual disability and their attitude to the corneal transplantation procedure. Because the study was a preliminary to more extensive outcome studies, no attempt was made to limit the indications for surgery. About half the patients (48%) had surgery for keratoconus. Nine patients (15%) were operated on for a previously failed graft. The remainder had the sequelae of inflammatory disease and two cases were operated on for impending perforations.

Approximately 65% achieved 6/18 vision or better in the grafted eye (Fig. 2). In 52% of patients, the level of vision achieved was better than in the contralateral eye. In 13% of patients, the grafts had failed. Of those that were clear and functioning, 22% had more than 5 diopters of spherocylindrical astigmatism. A further 13% had irregular astigmatism (Fig. 3). Spectacles were used by 52% of patients to achieve their best vision and 17% used contact lenses on the grafted eye, with a further 20% using both spectacles and contact lenses. Only 8 (13%) had required keratorefractive surgery to reduce spherocylindrical astigmatism.

The questionnaire was directed towards evaluating the level of disability patients had following surgery and their attitude to their corneal transplantation. Approximately 75% of graft recipients reported that they were managing their day-to-day activities well. However, some patients commented that lighting conditions affected their ability to function and that glare was a particular problem. Forty per cent of patients felt restricted with respect to hobbies and pastimes. Although the overwhelming majority (93%) believed that the graft had been "worth the trouble" and they would be prepared to go through the procedure again, less than half believed that the outcome had matched their expectations.

There was a significant correlation between a patient's level of satisfaction and whether the visual acuity in the grafted eye matched or exceeded the contralateral eye. Furthermore, satisfied patients tended to report that their preoperative expectations were met.

It is usually accepted that improvement in medicine can come from a close evaluation of failures and the identification of the reason behind the failure. It was considered that

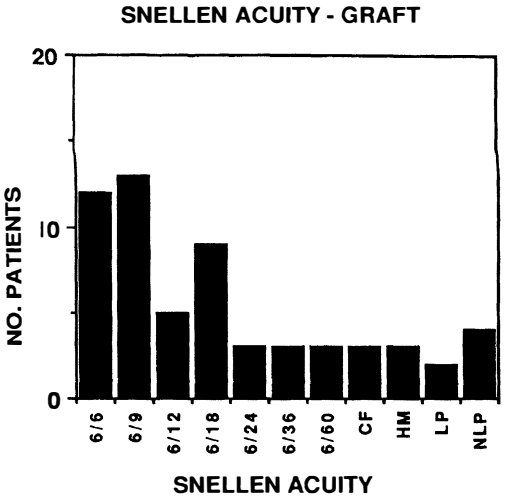

Fig. 2. *Flinders Medical Centre Data. The results of corneal transplantation in sixty patients expressed in terms of visual acuity.*

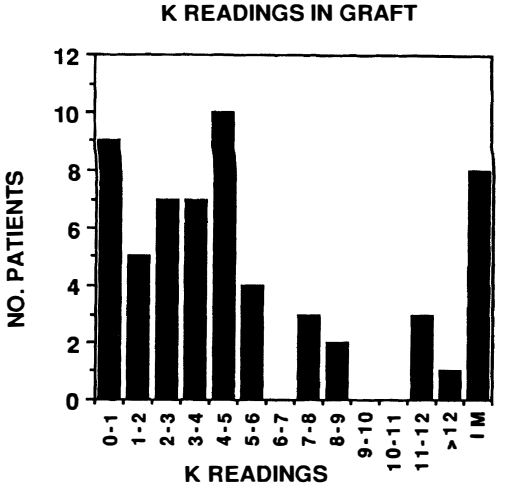

Fig. 3. *Flinders Medical Centre Data. The results of corneal transplantation in sixty patients expressed in terms of keratometry readings.*

eight patients indicated that they were significantly dissatisfied with the outcome of the procedure. Three of these patients had failed grafts. Of the other five, the Snellen acuities with correction were remarkably good. Four of them had vision of 6/12 or better and one had vision of count fingers which was attributable to astigmatism and an inability to cope with any form of correction. All of these five patients reported that they disliked wearing contact lenses and indeed this factor appeared to be the major source of their unhappiness.

Strategies for improving the visual outcome of corneal transplantation

For a patient to benefit from corneal transplantation, the graft must function in the metabolic sense; it must be optically clear with minimal aberrations, the eye should be free of co-existing disease which might reduce the visual potential below what would otherwise be expected, and there needs to be room for improvement in the patient's lifestyle. Therefore, the outcome of corneal transplantation can be improved by reducing the impact of corneal graft failure, reducing the impact of post-operative aberrations and co-existing ocular disease, and ensuring that the procedure is restricted to those who, because of their disability, are likely to benefit from the surgery.

Measures to reduce the impact of allograft rejection

Corneal allograft rejection is the most common cause of corneal graft failure. The factors influencing the survival of corneal grafts have received considerable attention in recent years. At a clinical level, vascularisation of the recipient bed and inflammation, or a history of inflammation, are well established factors affecting corneal graft survival.[7] At a histological level, survival is influenced by the number of interstitial dendritic cells in the recipient's corneal bed.[8] As with most other forms of allograft rejection, the degree of major histocompatability antigen mismatch between donor and recipient influences graft survival.[9] Although a discussion of the cytokinetics of the corneal allograft response is beyond the scope of this discussion, it is clear that our understanding of the process has increased dramatically in recent times, and, along with this, the management of the allograft reaction and related problems at a clinical level is very much improved.

The main strategy for decreasing the impact of the corneal allograft response is to avoid doing grafts in high-risk cases unless there are real improvements in lifestyle to be gained. When corneal transplantation must be carried out on such cases, one must be prepared to do all that is necessary to reduce the incidence of rejection.

Grafts done for inflammation or the sequelae of allograft rejection are prone to rejection. Quite often this inflammatory disease only affects one eye. In such cases, vision in the other eye is excellent. Corneal transplantation should be avoided in such cases whenever possible.

When it is necessary to offer corneal transplantation to patients with inflammatory disease, there are a number of things that can be done to reduce the chance of graft failure. The single most important step in preventing allograft rejection is to minimise post-operative inflammation. After surgery there is movement of cells from the limbus across the host cornea to the host-graft junction. This influx of cells is necessary for wound healing but also carries with it a cellular arsenal with the potential to initiate the allograft response.[10] What is required, is enough cell migration to achieve wound healing but not enough to initiate rejection. Pre-operative pathology and post-operative factors such as episodes of inflammation, from whatever cause, determine the tendency for cells to accumulate at the graft-host junction. Grafts done for keratoconus seldom become inflamed, are often very slow to heal, with instability at the graft-host junction for a year or more after surgery, and seldom reject. Grafts done for inflammatory conditions such as herpetic keratitis heal very quickly and the sutures can often be removed after only a few months; recurrent inflammation with subsequent allograft rejection is a common cause of graft failure. The tendency to accumulate cells can be modified to some extent by anti-inflammatory therapy. Topical corticosteroid preparations are most potent in this regard.

Inflammation must be avoided by carrying

out surgery in the most atraumatic manner, by optimal use of topical corticosteroids, and by promptly recognising and treating any post-operative inflammation as might occur with acute blepharitis, conjunctivitis, uveitis or any other inflammatory condition, or as may occur should a suture become loose and exteriorised.

In high-risk cases, those in which the blinding corneal disease has an inflammatory component, it is much more difficult to avoid post-graft inflammation and subsequent allograft rejection. In addition to the measures suggested above, histocompatibility matching[9] and systemic immunosuppression[11] can reduce the incidence of rejection. Neither of these options is simple or inexpensive.

Matching is difficult because of the extreme polymorphism of the major histocompatibility complex, and the expensive facilities required to pursue this strategy. Nevertheless, the benefits of matching for class I antigens, though incomplete, are quite definite.

Immunosuppression is not only expensive, it is potentially dangerous. It can only be considered for patients who are blind because they need a corneal graft and who have been well informed about the complications of systemic immunosuppression. The use of systemic cyclosporin has greatly improved the effectiveness of pharmacological immunosuppression for essential organ transplantation.[12] Topical preparations have yet to be shown to be effective in a clinical situation.

Measures to reduce the impact of refractive aberrations

A clear graft will not result in good vision if the optical properties of the cornea are inappropriate. Astigmatism is a common observation and may be regular (spherocylindrical) or irregular in form. Anisometropia due to the grafted cornea having significantly different optical properties to the cornea in the contralateral eye is also common.

Prevention of surgically-induced astigmatism

Post-operative optical correction can be very difficult, and prevention of post-corneal transplantation refractive errors is the preferred option. However, it is also difficult to achieve.

Prevention of post-transplantation astigmatism is a high priority for corneal transplantation surgeons. Refinements in cutting techniques and suturing strategies have been developed with this in mind. The expectation has been that if a perfectly circular graft is placed in a perfectly circular defect, the sides of the graft and recipient defect have complimentary configurations, and the suturing pattern is perfectly regular with regard to geometry and tension, astigmatism will be eliminated. Either this level of precision has not been achieved or the hypothesis is faulty.

The surgical techniques proposed to reduce astigmatism are numerous. In particular, various patterns of suturing have been advocated. One approach that has received considerable attention recently, and which has been quite widely adopted, has been the use of a combination of continuous and interrupted sutures with selected removal of the interrupted elements in order to reduce early post-operative astigmatism and bring about early post-operative rehabilitation.[13] As Binder points out, the effect of selective removal of sutures is lost after all sutures are removed and the advantage is apparent only in the first year after surgery. This advantage in the first year after surgery must be balanced against the disadvantage of interrupted sutures. All suture materials, including monofilament nylon, are inflammatory to some degree and for some reason new vessels are encouraged by the presence of knots. Furthermore, interrupted sutures can be more difficult to remove than a continuous nylon suture and small fragments of nylon may be left behind in the cornea. The occasional tendency for vascularisation towards the graft margin may be a high price to pay for the temporary reduction of astigmatism in the early post-operative period.

Since all surgeons continue to get some astigmatism in their grafts, although perhaps less today than in the past, it remains important to lessen the impact of astigmatism on the visual outcome of transplantation. Careful selection of appropriate optical aids is a very important element in the management of all patients receiving corneal grafts. Most cases of post-transplantation astigmatism can be managed with spectacles or contact lenses. However, deciding on the appropriate correction demands considerable skill.

Refraction after corneal transplantation

Achieving the full visual potential of a corneal graft may be as large a problem as achieving and maintaining a clear graft. Of course the preferred outcome is that a graft is so physiological that no optical correction is required to achieve a high level of binocular vision. When this has not been achieved, spectacles are the next most acceptable solution, but sometimes it is necessary to use contact lenses to achieve the full visual potential of the operated eye.

It is important for the patient to understand the complex nature of the process of refraction and rehabilitation, and in particular that the process must be repeated a number of times in the post-operative period and that a stable result will usually not be achieved within 18 months of surgery. The prolonged nature of the process and the unphysiological shape of the corneal graft contribute to the overall difficulty of achieving a satisfactory optical correction for patients who have had corneal grafts.

Although the principles of refraction apply as much to patients with corneal transplants as anyone else, some additional information is often helpful. It is important to utilise information from the distance and near acuity, pinhole acuity, retinoscopy, keratometry, and photokeratoscopy. Irregular astigmatism is common after corneal transplantation and is often the reason why it can be so difficult to correct a patient's acuity up to the level achieved with a pinhole. The nature of irregular astigmatism can be appreciated with retinoscopy and keratometry, but can only be fully appreciated with photokeratoscopy or with the use of other more complex systems for demonstrating the three dimensional characteristics of the cornea. A number of highly sophisticated systems have been developed to evaluate the complex relationship between variations in corneal shapes and optical performance. These systems are among the tangible fruits of the development of corneo-refractive surgery. They work on a number of different principles, provide information in various forms, and are invariably expensive. It is not clear that they provide information about the topography of corneal grafts that cannot be achieved by obscuring the pattern of fluorescein under a rigid contact lens. A flow chart for refracting patients with corneal grafts is set out in Figure 4.

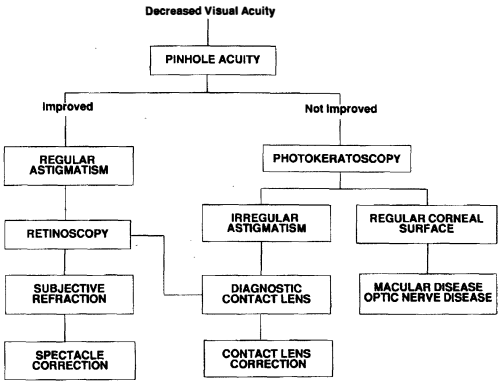

Fig. 4. *An algorithm for refraction of patients with corneal grafts.*

Contact lens fitting

When the topography of the grafted cornea is irregular, it is necessary to use a contact lens to achieve the full visual potential. In selecting the appropriate lens design, the central corneal curvature as determined by keratometry, the topography of the optical zone of the central cornea, the wound edge configuration, and the relationship of the graft curvature to the host curvature are the critical factors. Irregular astigmatism can only be corrected with a relatively rigid contact lens. However, a more flexible, more forgiving material may be required to overcome irregularities in topography at the graft-host junction. In such circumstances, a soft lens may be employed but if there is also central corneal irregularity a soft lens will not deliver good vision. Under these circumstances it may be necessary to employ a system of soft lens and

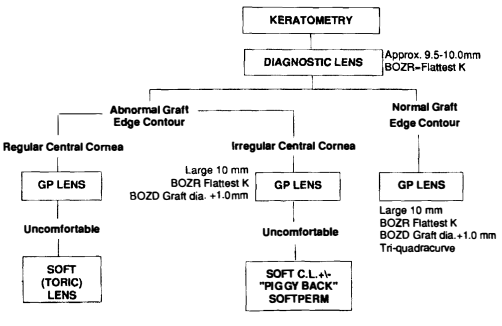

Fig. 5. *An algorithm for the fitting of contact lenses to patients with corneal grafts.*

an over-riding hard lens centrally. Recently, hybrid lenses have been introduced which have a progression of rigidity from the periphery to the centre. Softperm is one such lens which has a definite but limited place in the rehabilitation of patients who have had corneal grafts. Unfortunately, the current lenses of this type are not high performance lenses in the physiological sense and this limits their usefulness in the context of corneal transplantation. A flow chart setting out the principles of lens fitting and the usual lens parameters for patients with corneal grafts is set out in Figure 5.

Surgical correction of astigmatism

Corneal astigmatism is the usual but not the only indication for contact lens fitting after corneal transplantation. Anisometropia can also be a significant post-operative problem, particularly when the surgery is done to improve binocular function.

Correction with spectacles and contact lenses is not always possible despite the best efforts of the most experienced practitioners. Not only does the post-operative optical correction need to deliver excellent vision, it must be acceptable to the patient. Whether the form of correction is acceptable is determined to some extent by the patient's physiology but more by the patient's lifestyle and attitudes. When it is necessary to improve visual performance beyond what can be achieved with optical devices acceptable to the patient, and there is residual regular corneal astigmatism, surgical options are available. Various approaches have been advocated over the years including relaxing incisions, wedge resections, non-radial keratotomy and regrafting.[14]

Relaxing incisions placed in the axis of the greatest curvature have proved to be the most effective. This simple procedure is safe and predictable. Of the corneal grafts done at Flinders Medical Centre, 8% go on to have relaxing incisions. A standard procedure is used with two deep incisions, as deep as one can safely go, bearing in mind the unpredictable thickness of the graft host margin, each incision being three clock hours in length. The average correction with this procedure is slightly less than five diopters.

For higher levels of astigmatism, wedge resections have been employed. These produce a greater degree of correction but the results are less predictable. Again, using a standard procedure of two wedges in the flattest meridian, each with a width of 1 mm and a length of three clock hours, we achieve an average correction of nine diopters when all sutures are removed. It is necessary to achieve over-correct initially because invariably some correction is lost when the sutures are removed.

Anisometropia after corneal transplantation

Astigmatism is not the only troublesome refractive problem for patients having corneal grafts. Anisometropia can be particularly troublesome if the principal aim of the corneal transplantation is visual and the patient is aphakic, pseudophakic or needs cataract surgery along with the corneal graft. In many communities, pseudophakic bullous keratopathy is the commonest indication for corneal transplantation. Under these circumstances, avoiding anisometropia becomes an important consideration. When the crystalline lens has been removed or needs to be removed in a patient with a corneal graft, the options for avoiding anisometropia are restricted to selecting an appropriate power for the intraocular lens. Very little can be done to control selectively the spherical refractive power of the corneal transplant. Since aphakic contact lenses, even of the most sophisticated kind, impose a considerable physiological stress on the corneal graft, an intraocular lens is the preferred option. A posterior chamber lens is desirable since the survival of corneal grafts is much better with a posterior chamber lens than with an iris fixated or anterior chamber lens (Fig. 6).

This has some implications when grafts are done for pseudophakic bullous keratopathy. Whenever possible, posterior chamber lenses should be left *in situ,* and iris clip lenses or anterior chamber lenses are best removed if this can be achieved without significant trauma. Whether posterior chamber lenses sutured into the ciliary sulcus have a comparable prognosis with regard to graft survival as those supported by an intact lens capsule, remains to be determined. Selection of the

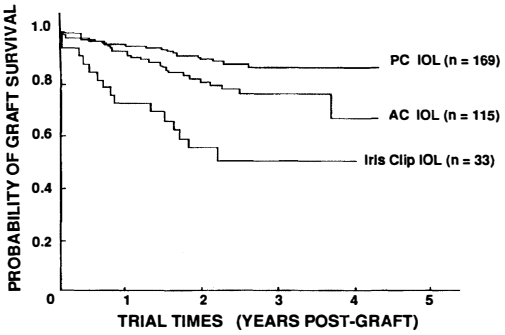

Fig. 6. *Australian Corneal Graft Register Report 1987. Survival of corneal grafts in pseudophakic patients with posterior chamber, iris-clip, or anterior chamber lenses.*

dioptric power of the intraocular lens to be used in conjunction with corneal transplantation is not always straight forward. Keratometry may be difficult or impossible in patients with corneal disease, forcing the less predictable option of measuring the corneal curvature of the contralateral eye. Another difficulty is predicting the spherical equivalent of the post-operative cornea, particularly in aphakic patients. Avoiding anisometropia can therefore be quite difficult in patients having triple procedures or corneal transplants for aphakic or pseudophakic bullous keratopathy.[15] In patients having grafts for pseudophakia or aphakic bullous keratopathy, it is clearly preferable to place the intraocular lens at the time of corneal transplantation. Lens placement is easier under these circumstances. However, when considering a patient who needs a corneal graft and insertion of an intraocular lens, an argument can be made for staging the procedure so that the curvature of the corneal graft can be used to predict accurately the lens power required to avoid anisometropia. The risk of this approach is in jeopardising the graft's survival with the subsequent surgical procedure. However, it appears that a subsequent cataract extraction and lens implantation does not significantly alter graft survival (Fig. 7). Whether this approach provides a better visual outcome with regard to binocularity has not been determined.

Measures to reduce the impact of co-morbidities and complications on the outcome of corneal transplantation

Co-existing disease, such as cataract, glaucoma and retinal conditions, can also account for a poor visual result despite a functioning graft. The conditions which have contributed to poor visual results in the group of patients followed in the Australian Corneal Graft Register are set out in Table III. Pathology prejudicing a good visual result may have been present prior to corneal transplantation (co-morbidity) and can be very difficult to detect in patients who have severe corneal disease. Techniques for assessing visual potential are not particularly reliable under these circumstances, even if a contact lens is used at the time of testing to overcome surface irregularities.

The importance of other potentially sight-limiting disease in patients being considered for corneal transplantation can only be assessed in relation to the patients' expectations. Although an eye may harbour a disease which might severely limit the outcome after transplantation, the patient may stand to gain significantly without achieving what we might otherwise consider good vision. For a patient with severe bullous keratopathy and extensive maculopathy, a visual outcome which is barely sufficient to provide some independent movement may be an outstanding result if vision was reduced to perception of light or hand movements prior to surgery.

Improving the attitude of patients to surgery and disability

A person's attitude to surgery and disability can profoundly alter their perception of the

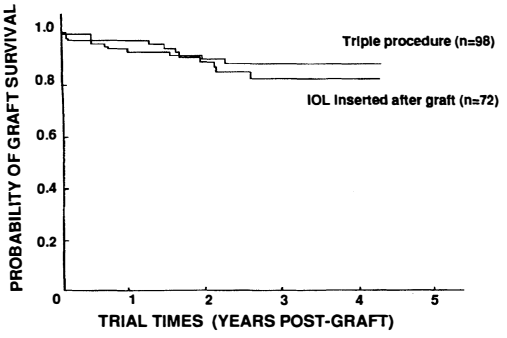

Fig. 7. *Australian Corneal Graft Register Report 1989. Survival of corneal grafts in patients who have had triple procedures or lens insertion as a secondary procedure. There is no statistical difference between the two groups.*

value of the procedure. Patients for whom the post-operative result did not meet their pre-operative expectations, tend to be unhappy. So too are patients who have negative attitudes to contact lenses and end up requiring the devices to achieve their best vision.

That a person's attitude affects the way he copes with illness, and that depression may have a devastating effect on the way a person is affected by illness, is well known to all clinicians. It is also generally well appreciated that improving a patient's attitude to illness, and therefore his ability to cope, can be very difficult. For patients having corneal transplantation, the problem is a little easier to address because the attitudes which require attention are more readily identified.

Considerable effort must be made to ensure that the patient's expectations and the surgeon's expectations match. To achieve this takes a long time and is usually beyond the personal resources of most surgeons. The task can be simplified by using trained counsellors, distributing reading materials, using audio tapes and video material. Whatever approach is employed, it is important for the surgeon and patient to come together prior to surgery to ensure that the surgeon's expectations and the patient's expectations are the same. Failure to achieve matched expectations can often result in a patient being dissatisfied and unhappy. Even when surgery is perfect and the case selection, based on medical grounds, is appropriate and when the outcome has matched the expectations of surgery, there are still disappointed patients for whom the results have not fulfilled their own expectations. Disparities between the expectations of surgeons and patients are a major cause of unacceptable results for patients. Every effort must be made to inform the patient of the process of surgery and after-care and to describe to them the likely outcome. With all the will in the world, this cannot always be achieved as it is the inherent attitude of patients which influences the results. The assessment of patients' attitudes and of ways to direct them beneficially is the corner stone of the art of medicine and is not readily amenable to quantification and experiment.

Attention must also be directed to the patient's attitude to contact lenses. Similarly, patients who need contact lenses to achieve the desired level of vision after a graft but who, for one reason or another, are unable to tolerate lenses are also unhappy graft recipients. Since as many as 15% of graft patients will need contact lenses after surgery to achieve optimal vision, patients with an aversion to contact lenses should be avoided wherever possible.

Some patients present for corneal transplantation because they are averse to wearing contact lenses. These patients are likely to be unhappy if they need to wear lenses post-operatively to correct astigmatism or anisometropia. Often a re-education programme prior to surgery, so that lens wear is tolerated, can be a worthwhile investment and avoid much unhappiness after surgery.

The importance of case selection

Corneal transplantation is a remarkably successful procedure, but, as with most other surgical procedures, there is room for improvement. Patients expect that their surgeons will deliver meticulous surgery which will minimise the risk of complications and maximise the visual results of surgery. These are understandable and reasonable expectations, but outcomes are not invariably successful. There are some unhappy patients. Over the years, a powerful approach to improving the effectiveness of medicine and surgery has been a close examination of our mistakes and unsuccessful undertakings. If we are prepared to assess surgical procedures done for disability, including visual disability, in terms of the impact on our patients' lives, and then to allow our patients to make this judgement, we are shown the way forward.

The most powerful approach to improving the outcome for our patients is to be even more stringent in our selection criteria. Patients who achieve better vision in the operated eye than the contralateral eye are almost invariably pleased with the results of surgery. Surgeons who wish to work exclusively with satisfied patients and who wish to ensure that precious resources, including their own time, are used to maximum advantage should avoid operating on patients in whom a corneal graft is unlikely to improve vision beyond what is present in the other eye.

If there is one lesson that has to be learned and relearned, it is the need to select patients carefully. This was well recognised at the dawn of corneal transplantation, before the procedure had been introduced into clinical practice. In his paper of 1837, Bigger wrote "... the operation should not be sanctioned under any circumstances, when the patient enjoys even a tolerable degree of vision with the other eye, at least until our knowledge has been increased by further experiments and observations." These words remain true to this day.

Key words: corneal transplantation, visual outcome, refraction, contact lenses, rehabilitation.

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