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The Success and Survival of Repeat Corneal Grafts

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Summary

The results of 99 second grafts in individual eyes are reported. The five-year survival of these grafts was 49%. Allograft rejection was responsible for the majority of failures, but recurrence of host disease and endothelial decompensation were also important. Glaucoma was an important complication in 38% of eyes. Only 12 eyes in the series had no significant complication and 18 eyes achieved a corrected visual acuity of 6/12 or better.

Corneal grafts may fail for a number of reasons including endothelial rejection, gradual loss of endothelial function, infection, glaucoma, trauma and recurrence of the original disease. Patients in this situation often wish the graft to be repeated, particularly so, when the affected eye is the patient's only eye with useful vision. In any large unit, therefore, where corneal grafts are being performed regularly, regrafts will figure largely among the indications for keratoplasty. In a study from Moorfields Eye Hospital over a three-year period, just over 15% of all grafts performed were regrafts making this indication the second most common after keratoconus.[1] (Fig. 1).

Although they form a disparate group from the point of view of background diagnoses, regrafts may share certain similarities in that the host is more likely to be sensitised and allograft reactions leading to graft failure may be more common.[2] Patients embarking on this course of management need to know the probability of success and what to expect by way of complications from this further surgery.

In order to define the success of grafts and identify the commoner complications we reviewed a series of repeat keratoplasties performed under the care of the Corneal Clinic, Moorfields Eye Hospital.

Patients and Methods

Patients were identified retrospectively from the case notes of all patients attending the Corneal Clinic, Moorfields Eye Hospital. In order to avoid confusion only the second graft in any eye was included. Any third or further graft was excluded from the study. All surgery was performed by the surgeons of the Corneal Clinic. This ensured that each patient was managed in a broadly similar fashion thus minimising the so-called centre effect often found between different groups of surgeons. Patients not attending for follow-up for at least one full year after the repeat keratoplasty were excluded from study. Only those eyes undergoing a second graft before the end of 1986 were included. Recruitment then ceased to allow a minimum follow-up of at least one full year.

Wherever possible the originl diagnosis was confirmed by histopathology. Graft failure was diagnosed on the basis of sufficient obscu-

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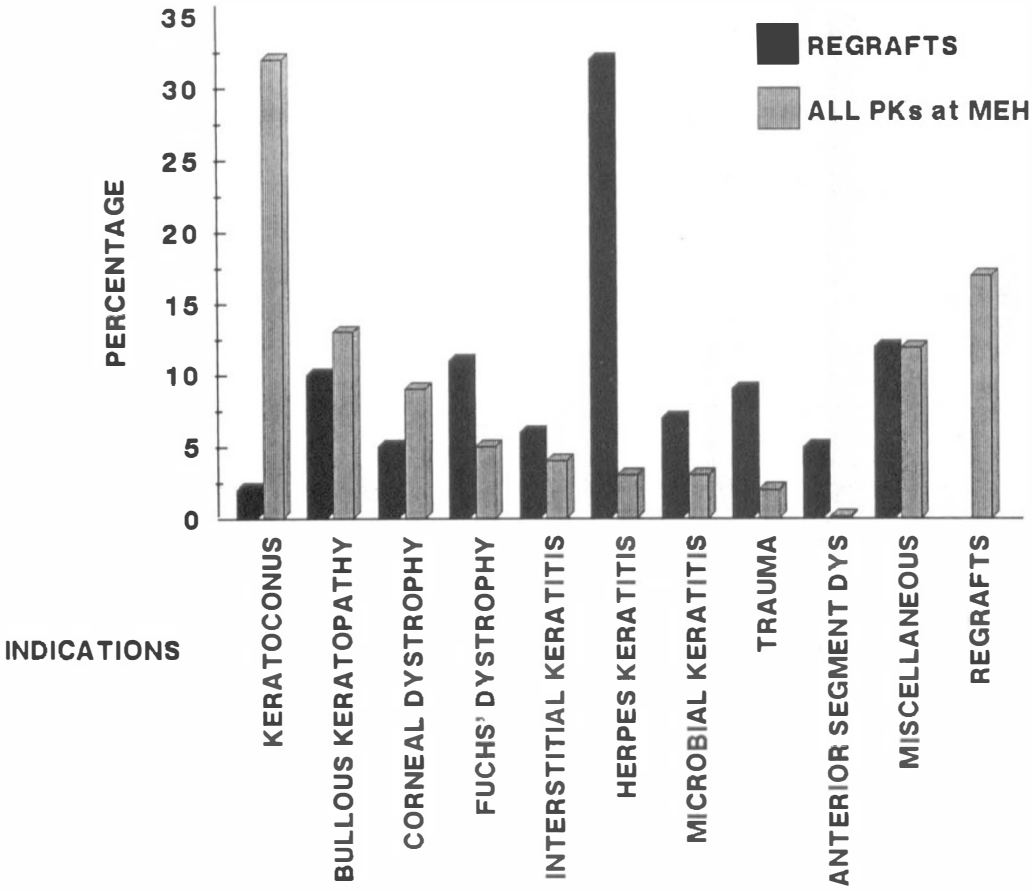

Fig. 1. *The indications for the original keratoplasty for the 99 grafts in this series shown with the average percentage for the indications for grafts over three years from 1985 to 1987 (from Morris & Bates)*[1]

ration of the vision by corneal oedema due to endothelial dysfunction, or opacity or scarring, to render the patient visually handicapped or where there was such intolerable astigmatism that the vision could not be corrected adequately by spectacles, contact lenses or graft-refractive surgery.

Neither the donor material used for the initial nor for the repeat keratoplasties was tissue matched during the period of the study. At surgery, a graft, the same size as the original, was performed unless the first had been particularly large, as in the case of some emergency grafts done à chaud, when a graft size of more usual proportions (eg. 7.5 or 8 mm) was used. The usual surgical techniques for penetrating keratoplasty were employed.

Postoperatively, these eyes were managed in the usual way with topical steroids and antibiotics. Cycloplegia was used as necessary. However, most patients tended to be prescribed a higher than usual initial dose of topical steroids (eg. G. prednisolone 1% every two hours) and they stayed on the steroid longer—often more than a year but by that time the dose was down to once a day prednisolone 0.3%.

Survival of repeat grafts was plotted according to the methods of Kaplan and Meier[3] and modified by Machin and Gardner.[4]

Results

Over an eleven-year period up to 1986, 99 patients requiring regrafts were identified. There were 52 males and 47 females ranging in age from 12 years to 93 years with a mean age of 57.5 years. The median age was 74

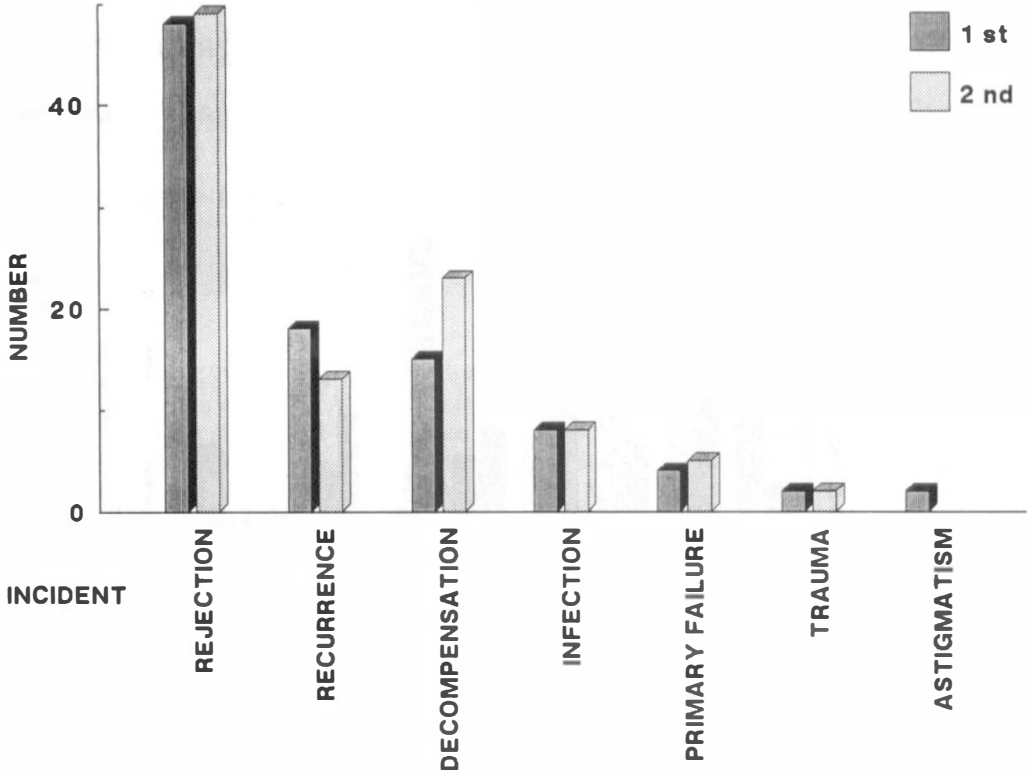

Fig. 2. *The reasons for failure of the original graft and by comparison the reasons for failure in those regrafts which did fail.*

years. The indications for the original keratoplasties were varied and are shown in Figure 1. The pattern is quite different from the figures for all grafts from Moorfields Eye Hospital, also shown in Figure 1. In two cases, the original graft was deemed unsuccessful owing to severe astigmatism; both of these regrafts have remained clear permitting good vision for over ten years. In all the rest failure was due to oedema, corneal scarring or opacity. Of these, the original grafts had failed from a documented rejection episode in 48 cases. In 19 grafts, the original disease process had recurred. This usually was herpes virus keratitis, both epithelial and stromal, but in seven cases a dystrophy such as macular corneal dystrophy had recurred in the graft.

Gradual endothelial decompensation was seen in 15 grafts. (Fig. 2) This could have been due to symptoms of rejection being missed or ignored by the patient, or when diagnostic signs of rejection were not seen because the patient had not attended as an out-patient clinic for some time. Most usually, it was due to observed and documented gradual endothelial failure. In three cases, it was possible to attribute the failure to subsequent intraocular surgery and in a futher two retention of an intraocular iris clip lens was probably a significant factor. Nine cases, mostly those with severe ocular surface disorders developed microbial keratitis and the graft failed. There were four cases of primary graft failure and two grafts were lost following trauma to the eye after the initial graft. In fact, graft rejection probably played a larger part than the figures indicate since many cases were multifactorial and the final event precipitating endothelial failure was a rejection episode.

The repeat grafts have been followed from a minimum of one-year up to 12 years, and, of those remaining clear, the mean follow-up has been six years. Overall, at the time of this review, only 42% of the grafts have survived.

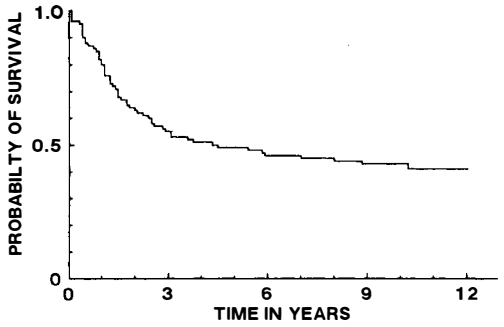

Fig. 3. *The overall survival of all the repeat keratoplasties in this series.*

Graft survival is dynamic, and, in order to see the true survival, it is necessary to study the life table (or the Kaplan-Meier survival curve) which shows a five-year survival from time of surgery of 49% or a 50% failure rate at 4.5 years. (Fig. 3)

Of those sub-groups within the series, only those where the original indication for keratoplasty was herpes simplex keratitis or bullous keratopathy (in one form or another) were large enough to justify plotting individual survival curves. (Figs. 4 and 5) These curves indicate that the regrafts in bullous keratopathy tend to survive better than those with herpes simplex keratitis, but the figures do not reach unequivocally clear statistical significance with a p value of only 0.1.

The reasons for regrafts failing were substantially the same as those in the first graft except there was a slightly higher proportion with gradual decompensation, (Fig. 2) of which four cases were attributable to further intraocular surgery. A substantial number of eyes developed other serious complications which threatened either vision or the graft. (Fig. 6) The most common was the development of glaucoma or worsening of pre-existing glaucoma. This occurred in 20 patients, most of whom could be managed on medical therapy but some of whom required further surgery includng the use of silicone drainage tubes. Ten eyes had a single rejection episode which was successfully treated and the graft remained clear. In six, there was a recurrence of herpes simplex keratitis but the graft remained clear and three developed an episode of microbial keratitis which was successfully treated without losing the graft. Only 12 patients out of the 99 had no serious postoperative complication. (Fig. 6) A number of grafts failing did so purely as a result of rejection episodes but a number of other eyes developed other complications both before and after graft failure. (Fig. 6) Several eyes had more than one complication.

The visual acuity in those eyes clear at review is shown in Figure 7. Only 18 eyes achieved a refracted visual acuity of 6/12 or better and eleven had an acuity of 6/60 or worse despite a clear graft. This latter group had cystoid macular oedema in five cases, glaucoma in three cases, and diabetic maculopathy, cataract and amblyopia in one case each.

Discussion

It is clear from the median age of the patients at the time of repeat keratoplasty, that we are

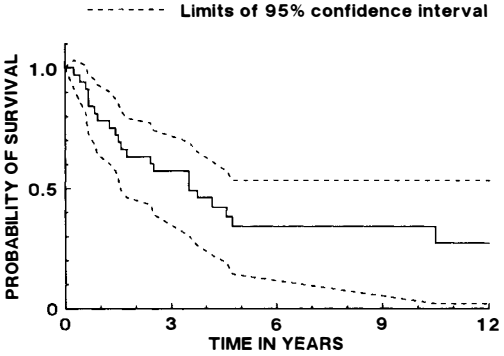

Fig. 4. *The survival of the second grafts for herpes simplex keratitis. The graphs are plotted with 95% confidence limits.*

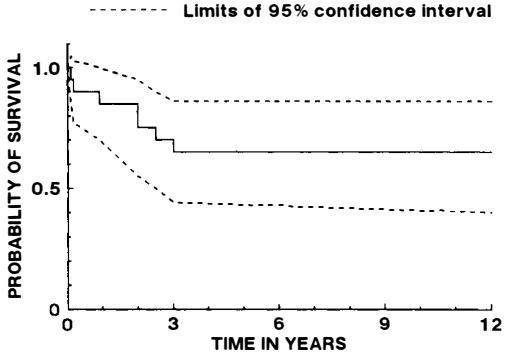

Fig. 5. *The survival of the second grafts for bullous keratoplasty (includes aphakic and pseudophakic bullous keratopathies). The graphs are plotted with 95% confidence limits.*

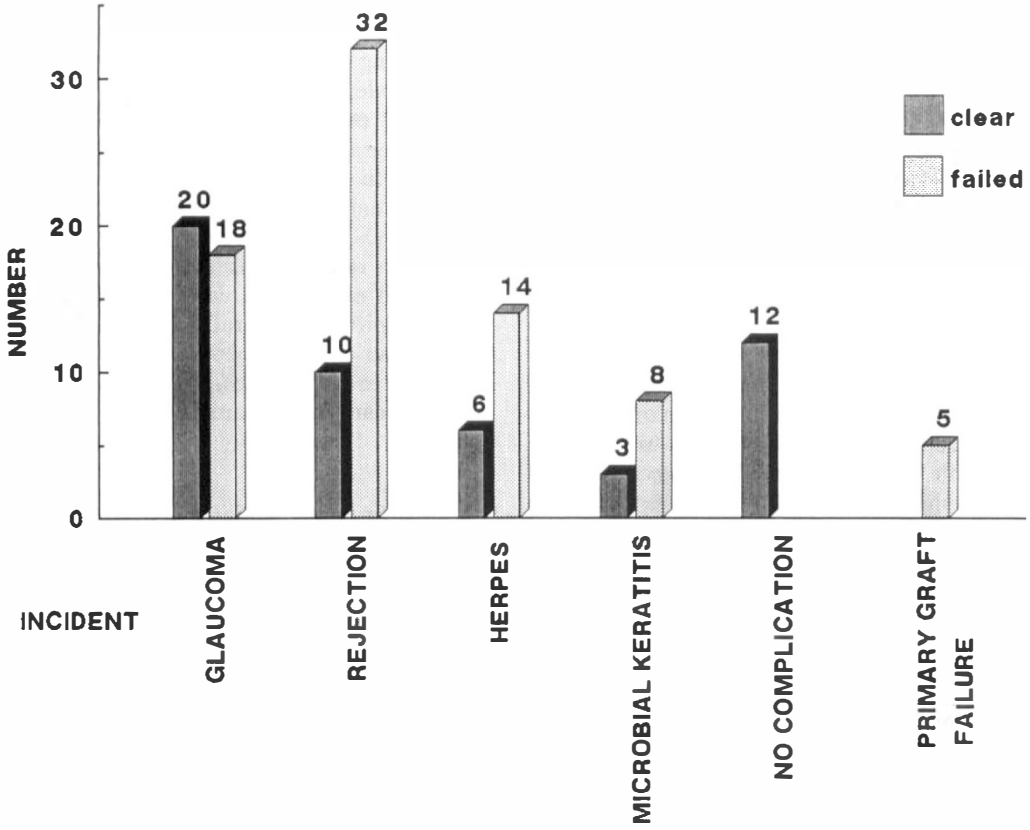

Fig. 6. *The complications occurring in both those grafts which did not fail, and in those which did. In many cases more than one complication occurred, particularly in those failing. Where rejection occurred secondary to another event it is* **not** shown.

dealing with a substantial number of elderly people in whom frequent visits to hospital may become very difficult. This, taken with the likely morbidity associated with a regraft, has two important implications. First, any problems developing in the graft may not be seen promptly enough owing to difficulty in the patient attending hospital immediately and consequently survival of the regraft may be prejudiced.[5] Secondly, repeated visits to hospital may be difficult for an elderly person and consideration should be given to this at the time of deciding whether a regraft is desirable.

This series deals with a group of patients undergoing repeat grafting. The reasons for the original grafts failing will reflect those reasons overall for graft failure but a substantial number of grafts do undergo regrafts and it is beyond the scope of this study to consider the reasons for all failures. The reasons for the repeated grafts failing were, however, remarkably similar to the reasons for the original failure.

The overall survival of repeat grafts at the time of review was 42% and the 50% survival time was 4.5 years. In individual sub-groups, the majority failed except for the bullous keratopathies and curiously those originally grafted following microbial keratitis. Those in which the original diagnoses were trauma and the anterior chamber cleavage syndromes did particularly badly. Of the sub-groups within the series, only those where the original indication for keratoplasty was herpes simplex keratitis or bullous keratopathy were large enough to justify plotting individual survival curves. These curves indicate that the regrafts for bullous keratopathy (with a five-year survival of 0.65) tend to survive longer

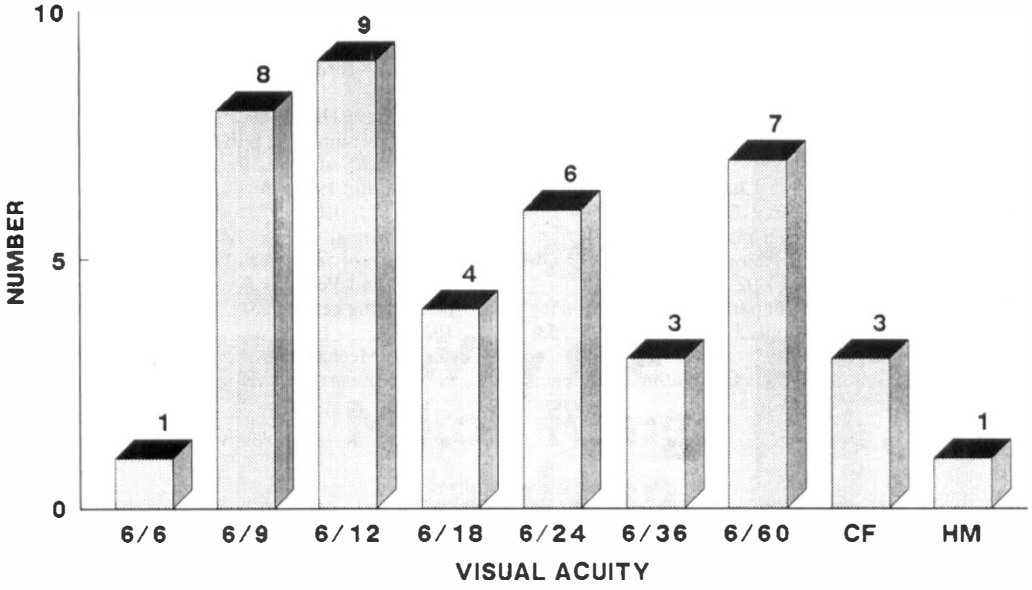

Fig. 7. *The visual acuity in those eyes with clear grafts at the time of review.*

than those for herpes. This may reflect the fact that the inflammatory status of these eyes is important and quiet eyes had fewer initial rejection episodes than others though this is not statistically highly significant with a p value of only 0.1.

Comparison with other published series is difficult. Völker-Dieben *et al.*[6] report survival curves, presenting a three-year survival figure of 53% for 112 second grafts. (Their maximum quoted survival time is three years). This percentage is very similar to our figure of 56%. MacEwan *et al.*[7] presented a series of 61 regrafts of which 31 were the second graft in an eye. They also used survival curves indicating a five-year and beyond survival rate of 66%. Their patient population was somewhat different from the present series with fewer herpetic eyes and slightly more bullous keratopathies. The follow-up was similar, however, but unlike the present series there were no failures after just under two years. The present series shows failures occurring as late as nine years and even in the group showing the best survival (the bullous keratopathies) there are failures at around three years.

Insler[8] in a small series of 29 grafts found clear grafts in 18, but survival curves are not used and the follow-up was only 15 months. Coster[9] reporting the results of a single centre study in a wide-ranging review found a five-year survival of 43%, for second grafts (n=36) compared to 80% for first grafts (n=163) but the indications for keratoplasty and the complications were not discussed.

Völker-Dieben[6] similarly noted a decreased prognosis for second grafts compared to first grafts, and that this trend tended to follow the original diagnosis ie. that bullus keratopathy had a better prognosis than herpes. This series, though with shorter follow-up, was begun about the same time as our series and so the two can be considered as parallel series with similar results.

The authors have not been able to identify a series where the influence of HLA tissue matching has been demonstrated on the survival of repeat grafts. None of the tissue in this series was tissue matched but the possibility exists that this is an area where tissue matching may have a significant role.

These figures showing a high failure rate for repeat grafts emphasise the need for added vigilance over graft patients and continued patient education so that original grafts developing rejection episodes and other graft-threatening complications may be treated early and be less likely to fail. Once a graft has failed careful consideration must be given to the prognosis of a second graft and the patient

should clearly understand the very much greater risk that further surgery involves. Only if the patient and surgeon can co-operate closely is the outcome in this difficult group of patients likely to improve.

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