OPACIFICATION IN PERFORATING CORNEAL GRAFTS*†

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As the success of a grafting operation ultimately depends upon the transparency of the graft, the problem of opacification is of great interest and practical importance to the ophthalmic surgeon. This paper is the result of the study of some fifty personal cases in an attempt to elucidate certain aspects of the problem as it occurs in perforating corneal grafts.

A graft may become opaque for one of three reasons:

- (1) Incorrect choice of case.
- (2) Faulty operative technique or inadequate post-operative treatment.
- (3) Late complication in a graft which, during the immediate post-operative period, appeared to be progressing satisfactorily.

PRE-OPERATIVE CONDITION OF RECIPIENT CORNEA AND FATE OF GRAFT

Opacities

Isolated Central Opacity.—The ideal case for a perforating corneal graft is represented by a central, non-vascularized corneal nebula which can be removed completely by trephining. Fig. 1 shows the result in such a case. Here the whole nebula was included in the excised disc and the graft was laid in clear, normal cornea. Optical section shows that the only points of opacification at the junction of host and graft are at Bowman's and Descemet's membranes, the union through the substantia propria being clear and almost indiscernible.

Completely Opaque Cornea.—The worst type, of hopeless prognosis for the simple perforating graft, is the complete opacity involving the whole area and thickness of the cornea. This may be associated with gross changes in structure so that the cornea is replaced by abnormal tissue frequently the seat of degenerative changes. A penetrating graft placed in a cornea of this nature rapidly becomes opaque.

Intermediate Types.—If discrete islands of opacity occur in what

FIG. 1.—Perforating corneal graft for central nebula.

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appears to be otherwise structurally normal cornea the prognosis is good, even though the combined effects of multiple lesions of this type may result in considerable opacification. This type is seen in the more severe varieties of interstitial keratitis; Fig. 2 is an example of a diffuse opacity involving both corneae, the visual acuity in each eye being reduced to counting fingers at 2 ft. The grafts have remained clear for $2\frac{1}{2}$ years in the left eye and for one year in the right eye with visual acuity 6/6 and 6/9 respectively.

FIG. 2.—Perforating corneal graft of $2\frac{1}{2}$ years standing in case of old interstitial keratitis.

- A. Marginal opacification of graft adjacent to area of densest opacity in recipient cornea.
- B. Persistent deep vascularization not entering graft but forming loops at host/graft junction.
- C. Organized exudate in pupil.

Incomplete opacities associated with fibrosis, or hyaline or other degenerative process, are more likely to produce opacification within the graft particularly if these areas are in direct contact with it. Fig. 3 shows such an area of fibrosis within the recipient cornea and its effect upon the adjacent graft.

FIG. 3.—Perforating graft for diffuse opacification of stroma and associated vascularized superficial nebula.

- A. Opacity in margin of graft adjacent to dense corneal opacity.
- B. Vessel which supplied superficial opacity persists but does not involve graft, extending only to margin of graft.

In another case a leucoma adherens was trephined out, the iris abscissed, and a graft immediately placed in position. A very small portion of the opacity remains throughout the thickness of the cornea, but this appears to have been sufficient to stimulate the formation of a similar opacity in the adjoining graft, the remainder of which is clear.

Similarly (Fig. 4) a brush-like opacity developed in the stroma of a graft at the point of contact with the denser (presumably fibrotic) area of the residual opacity.

FIG. 4.—Brush-like opacity (a) extends into stroma of perforating graft, apparently originating from an area of similar opacity in recipient cornea.

The fate of a graft depends largely upon the condition of the cornea into which it is placed. A clear recipient cornea will maintain a clear graft, a completely opaque cornea will beget an opaque graft. We are faced therefore with the problem of deciding how much opacification will render a cornea unsuitable for a simple perforating graft. I suggest the following criteria:

Good results may be expected with:

- (a) A central localized corneal nebula.
- (b) A diffuse opacity occurring in a cornea in which the separate elements of the structure are still distinguishable.
- (c) Dense opacities of Descemet's membrane, provided that the remainder of the cornea is relatively clear.
- (d) The presence of one-third or more of clear cornea of normal structure.

Poor results may be expected with:

- (a) A completely opaque cornea.
- (b) The presence of fibrosis, hyaline or other forms of degeneration unless these occur only in scattered islets.
- (c) Gross superficial opacification especially if associated with degenerative changes.

Vascularization

Superficial Vascularization.—This presents a serious problem for it frequently occurs in association with gross changes in the corneal epithelium and the subjacent tissue. This type of vascularization is of two main varieties:

- (i) one or two large vessels passing to the site of some old superficial lesion;
- (ii) many fine vessels invading the cornea from all points of the circumference and frequently associated with generalized opacification and patches of degeneration.

The presence of one or two large vessels does not constitute a contra-indication to a perforating graft, provided that the nature of the opacity (as discussed above) is otherwise favourable and that a considerable amount of the opacity supplied by the vessel can be included in the trephine disc. In most of these cases this vessel will not invade the graft (Fig. 3) but will extend to the line of union, where it will form a loop and then return to the limbus. Multiple fine superficial vessels are likely to cause trouble and invade the newly inserted graft. This complication is due to the presence of a type of opacity associated with fine superficial vascularization rather than to the invasive propensity of the fine vessels, the vascularization following, rather than causing, the opacification.

Deep Vascularization.—Although there is an intimate relationship between the presence of opacities and the vascularization of a graft, my experience suggests that the role of deep vascularization in the causation of opacification in grafts has been over-emphasized. On several occasions I have performed a perforating keratoplasty on an eye, the seat of old interstitial keratitis, where there has been considerable deep vascularization. Within a few days of the operation an acute reaction has occurred with the development of an extensive salmon-patch in the recipient cornea. With the exception of a few very fine deep vessels appearing within the graft on about the tenth day and disappearing some 3 to 4 weeks later, the grafts appear to be completely unaffected by the gross vascularization of the adjacent cornea, and in none of them has opacification occurred. In certain corneae some of the deep vessels of the salmon-patch persist (Fig. 2); these do not, however, enter the graft but form loops at the host/graft junction.

IMMEDIATE POST-OPERATIVE COMPLICATIONS

Dislocated Graft.—If, at the first dressing, a graft is found to be so grossly displaced as to require further suturing, then opacification is almost certain to occur. Such a graft is opaque when first seen, presumably as a result of the inhibition of fluid from the conjunctival sac. Even if the graft is successfully sutured into position clearing does not take place. Possibly this is due to the cut edges of both the trephine hole and the graft being sealed off with exudate so that the transference of tissue fluid between the host and the graft is prevented and the graft remains opaque. A graft which is slightly tilted, so that a small portion of the edge is elevated above the level of the recipient

cornea, does not become opaque, even in the vicinity of the ectasia. This is probably due to the rapid epithelialization of the exposed surface.

Loss of Vitreous.—The loss of vitreous, which may occur during an attempt to graft an aphakic eye, results in the development of an opaque graft. A possible explanation for this is that the interposition of vitreous between the graft and the recipient cornea prevents the exchange of fluid between them.

Infection.—Severe conjunctivitis, especially if seen at the first dressing, is a most serious complication, for it leads rapidly to opacification of the graft. It is interesting to observe that a small hypopyon, caused by the infection of a too deeply placed suture in the recipient cornea did not cause an opacity of the graft; but in this case there was no significant degree of conjunctivitis.

Anterior Synechiae.—These may be observed at the first dressing, and are frequently associated with slight clouding of the graft, which may in some cases progress to complete opacification. Anterior synechiae are a serious complication of corneal grafting, and, except in complicated cases such as leucoma adherens, occur as a result of faulty operative technique.

Oedema of the Graft.—This has occurred (a) in association with an infection; (b) concurrently with opacification due to the graft having been laid in a completely opaque cornea; (c) in two cases where the origin of the opacification was obscure.

In these last two cases a localized superficial oedema appeared in the graft during the immediate post-operative period. This condition persisted in one graft for 3 months and in the other for 6 months; after it had dispersed the grafts were quite clear.

I have not seen in my series the classical “*maladie de greffon*”.

LATE OPACIFICATION IN A CLEAR, OR RELATIVELY CLEAR, CORNEA

Apart from opacities which occur as the result of an unsuitable choice of recipient cornea or following a well-recognized complication, there remain those which develop suddenly in a graft which has seemed to be progressing favourably.

Case 1.—A female aged 58 had bilateral interstitial keratitis involving the central areas of the corneae, a most suitable type of eye on which to perform a keratoplasty. After a 5-mm. perforating graft the post-operative period was without incident, the graft being well-placed and clear except for a slight haze in the posterior layers; this haze was so fine as to cause no concern, being very similar to the post-operative haze which is sometimes seen and which clears leaving a transparent graft. This condition persisted for over 2 months with no apparent change when, quite suddenly, in the 14 days which elapsed between one visit and the next, the graft became completely opaque. It is necessary to emphasize that the opacity was not localized to the posterior portion of the graft but that the whole thickness of the graft was opaque. A further perforating graft of slightly larger diameter was performed and the opaque disc of the previous graft completely removed. Microscopical examination (Fig 5, opposite) showed a thick band of fibrous tissue spreading over the posterior surface of the cornea and obliterating the endothelium.

FIG. 5.—Section through graft/host junction of a completely opaque graft.

- A. Recipient cornea.
- B. Opaque graft.
- C. Descemet's membrane.
- D. Fibrous tissue extending over whole of posterior surface of graft.

Case 2.—This was due to an infection when a diffuse opacity appeared as a result of a severe post-operative conjunctivitis. This opacity was dense though not complete, but quite suddenly, again between visits, the graft (Fig. 6) became opaque throughout its whole thickness. This eye also was successfully regrafted (Fig. 7).

FIG. 6.—Post-operative opacification of perforating graft.

FIG. 7.—Case shown in Fig. 6 after re-grafting. This graft has remained quite clear since the operation 7 months ago.

Microscopical examination of the disc (Fig 8) showed a thick band of fibrous tissue growing over the posterior surface of Descemet's membrane, obliterating the endothelium, and presenting a picture remarkably similar to that seen in the first case.

FIG. 8.—Section of opaque graft shown in Fig. 6.

- A. Opaque graft.
- B. Descemet's membrane.
- C. Fibrous tissue extending over posterior surface of graft.

It is reasonable to suppose that the sudden complete opacification in these two cases resulted from the cutting off of the endothelium from the anterior chamber, thus disturbing the normal fluid interchange between the graft and the aqueous so that oedema developed. As this oedema was unrelieved, hyaline changes followed and a permanent opacity was formed in the corneal stroma.

METHODS OF DEALING WITH THESE PROBLEMS

Choice of Case.—The full cooperation of the patient is absolutely essential for the success of a grafting operation; for, however effective may be the fixation of the graft, it will be incapable of withstanding much disturbance during the first few days. It is essential, therefore, that the post-operative demeanour of the patient be correctly assessed. Young children should never be submitted to a perforating graft as they are quite un-cooperative, and I am inclined to the view that this operation should not be performed on any child under the age of 15 years. The psychological disturbance in certain patients is considerable and this may result in the patient losing all control of his actions and rubbing and squeezing his eye so that the graft is displaced, or, even in less severe cases, the lack of cooperation is such that the essential daily post-operative treatment cannot be carried out.

Operative Technique.—Whilst it is beyond the scope of this paper to describe my method of grafting, there are certain points of technique which I regard as extremely important in the prevention of post-operative opacities.

(1) The graft I cut by punching out. This method has two advantages:

(i) The graft is perfectly cut and there is no likelihood of rough, irregular edges,

especially at the level of Descemet's membrane, which can occur when the graft is trephined from the donor cornea.

(ii) The lamellae of the graft are kept compact by punching, whereas trephining tends to separate them. I consider that the compact lamellae play a most important part in the prevention of the invasion of vessels from the recipient cornea.

(2) The recipient cornea is cut by the same trephine with which the graft was cut. This enables a bung-like fit to be obtained between the graft and the host, so that, even before the patient has left the table, the anterior chamber has commenced to reform and the cornea is clearly seen to be separated from the iris. This prevents the development of anterior synechiae to the graft, and of peripheral anterior synechiae which may assist the development of post-operative glaucoma.

(3) I do not use direct sutures through the graft because this subjects it to considerable trauma by grasping and by the passage of the sutures, thereby opening up the lamellae and rendering oedema, vascularization, and opacification more likely. Again, however well the sutures are placed, some distortion of the fit of the graft in the recipient cornea must occur, so that there is more likelihood of a leakage of aqueous. For fixation I use two mattress sutures placed at right angles; the main technical point being that the sutures cross the graft and enter the recipient cornea as close to the margin of the graft as possible, so that there is very little lateral movement of the suture, which remains in correct position over the graft.

In my series I have experienced only two cases of post-operative anterior synechiae: one occurred on the occasion of a second attempt at a perforating graft, and the second where, after the removal of a leucoma adherens, a thin strand of iris remained attached to the cornea. No case of the series has developed post-operative glaucoma. The adhesion of the pupillary margin of the iris to the graft, or the formation of peripheral anterior synechiae (which may be the cause of post-operative glaucoma), are prevented by the rapid re-formation of the anterior chamber.

Post-Operative Treatment.—The first dressing of the graft should be done between 36 and 48 hours after the operation—never later. At this dressing a culture is taken of the conjunctival sac and 1 per cent. atropine drops together with gutt. penicillin are instilled; subsequently antibiotic drops are instilled twice daily and atropine once daily. Once every day the eye is cocainized and the cornea carefully cleaned of all mucus that may be adhering to it. Cortisone drops are begun on the 10th day and continued for several weeks. The sutures are removed between the 10th and 14th days; sutures left in for 14 days or more sometimes produce slight superficial opacities of the graft which usually disappear in a month or so. Such opacities do not interfere with vision as my sutures do not cross the centre of the graft.

Summary

Opacification in corneal grafts is usually due to incorrect choice of case, faulty operative technique, or inadequate post-operative care.

Two cases are described in which an opacity occurring after 6 to 8 weeks

was found to be due to the development of a plaque of fibrous tissue over the posterior surface of the cornea.

Certain points of operative technique are discussed; the importance of a compact graft, the value of indirect as opposed to direct sutures, and the necessity for the immediate re-formation of the anterior chamber are stressed.

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REFERENCE

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