Present Status Of Optical Corneal Grafts

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The prime consideration of optical keratoplasty is maintenance of corneal transparency. All too frequently, corneal transplants become clouded even when the surgical technique has seemed to leave nothing to be desired. Some of the donor and host factors influencing final graft clarity are yet to be fully understood, but certain principles have become apparent. It is the primary purpose of this paper to review what is "known" along this line, together with some of the less well established or frankly speculative aspects.

Reports on results with optical keratoplasty are numerous, and rather variable, there being general lack of uniformity of material, criteria of success, and standards of procedure. A reasonably typical report in 1950 stated that of 241 keratoplasties 16.4% resulted in worse vision, 30.3% remained unchanged, and 53% resulted in improved vision. Reports on results with optical keratoplasty are numerous, and rather variable, there being general lack of uniformity of material, criteria of success, and standards of procedure. A reasonably typical report in 1950 stated that of 241 keratoplasties 16.4% resulted in worse vision, 30.3% remained unchanged, and 53% resulted in improved vision.3,4

Gross comparison of various selected series suggests the following corneal conditions to be favorable for keratoplasty (in order): 1) Non-edematous "degenerations"; 2) residue of chronic infections or non-specific inflammations; 3) traumatic lesions. Edematous degenerations appear strongly to have the least favorable prognosis, while grafts for keratoconus, a "dry" avascular "degeneration" usually confined to the central portion of the cornea, yield the most satisfactory visual results.

For best results, both the donor cornea and the recipient bed need be transparent. The importance of corneal transparency lies in the biophysical implications of the state: Viability, critical hydration, normal intraocular pressure, intact endothelium, and precise structural arrangement of stromal fibers and cementing substances. The significance of the factors mentioned which determine corneal transparency lies in the role they play upon the ultimate fate of the graft.

The weight of evidence supports the view that the cells of the graft are replaced by the host (epithelial cells almost immediately, stromal cells and endothelial cells very gradually) but that Bowman's membrane, collagen framework of the stroma, and Descemet's membrane persist morphologically. Cell death occurs at a considerably increased rate after keratoplasty, but even so, goodly proportions of the donor cells remain viable usually for months, possibly for years. Simultaneous death of all stromal cells in the graft does not occur. It is felt that the speed of replacement of donor stromal cells by host cells is inversely correlated with the "success" of the graft.4

The orderly regeneration of normal transparent cornea can be impeded or prevented by structural and metabolic disturbances of both the recipient bed and donor cornea. This may occur in at least three ways:

1. Immunological response of host to donor tissue

The necessity of utilizing homografts carries with it the possibility of an undesirable immunobiological response of the host to the donor cornea. Fortunately, there is low antigenicity of corneal tissue, attributable to its avascularity and cellular paucity. However, hypersensitivity reactions do occur and may lead to vascularization,
Balian

infiltration and permanent clouding of the graft. Vascularization of the graft must take place before such a reaction exhibits the leukocytic, lymphocytic and fibroblastic infiltration which is found in other unacceptable homograft tissue.

It has been demonstrated in rabbits that sensitization can result in corneal clouding up to a period of eight weeks after keratoplasty. Experiments have shown that graft clouding is almost inevitable if a piece of skin from a donor rabbit is implanted under the abdomen of the recipient animal two weeks prior, concomitant with or even shortly following the actual keratoplasty.

Corneal vascularization seems (usually) necessary for opacification of a human homograft on the basis of a hypersensitivity reaction. The presence of adventitious corneal vessels certainly appears to increase the likelihood of such reaction. Corneal stromal cells will not die following intracorneal injection of an antigen (e.g., horse serum) to which the animal (e.g., rabbit) has been highly sensitized until blood vessels grow into immediate proximity to the particular corneal stromal cells under consideration. This may well be due to the low antibody titre of non-vascularized cornea. Preoperative treatment of vascularization by surgical means has its place, although revascularization occurs only too often. Irradiation methods, once widely used, now appear on the whole to have been worse than useless.

The role of the donor cells in eliciting the hypersensitivity reaction seems dependent upon their number and their survival. The corneal epithelium which consists of five or six layers of cells, added to the stromal tissue, does appear to increase the tissue reaction to the graft in laboratory animals. A potential immunological hazard is evident when the corneal tissue of the very young is utilized, since keratocytes are more numerous in the young cornea. In addition, the direct relationship of graft size to the number of cells must be remembered in light of this problem.

While considerable experimental evidence supports the view that a hypersensitivity reaction can underly delayed clouding of corneal grafts, the exact nature and cause(s) of the reaction in human corneal homografts remain to be elucidated. Race and sex are considered insignificant in the selection of donor material, while blood type incompatibility (ABO, Rh) does not alter the incidence of success.

II. Physical chemical aspects of donor and host cornea

Consideration of the donor cornea as a precise architectural framework upon which the regenerating host tissue is dependent would suggest that any divergence from structural normality by the donor cornea would unfavorably influence the final clarity of the graft. The orderly and gradual replacement of donor elements can be prevented by dissimilarity in the thickness of donor and recipient corneas. Further, the precise apposition of the host and donor corneas is important in keeping the graft-host interval relatively impervious to water and vascular ingrowth, while the integrity of the endothelial surface plays an important role in the critical hydration of the graft. Cogan attributes vascularization of the cornea to a reduction in the compactness of the tissue in the vicinity of pre-existing vessels. The presence of even one large vascular trunk in the cornea is considered a hazard to optical keratoplasty and emphasizes the need for a normal corneal bed.
Optical Corneal Graft

In summary, presence of scar tissue can impede the regenerative process by constituting a "stumbling block" to the migrating host cells, while the presence of adventitious blood vessels in the normally avascular cornea signifies a derangement of physical chemical factors underlying corneal transparency.

III. Metabolic deficiencies of host cornea

In the broadest sense, at least two factors would appear to be involved in the resumption of normal metabolic activity following keratoplasty: 1) Supply of metabolites via limbal blood vessels, 2) normal host cells. Tracer studies reveal that there is a negative balance of sulfur-containing amino acids in the donor cornea following transplantation. An intact vascular plexus of the limbus is necessary if amino acids and other metabolites are to reach the regenerating cornea. In addition, intracellular enzymes, on which the synthesis of protein and ground substance depends, are deficient if the corneal cells of the host are quantitatively or qualitatively abnormal.

The importance of structural integrity and normal viability is appreciated and has resulted in much experimental effort toward the long-term storage of corneal graft tissue. Factors which influence the viability of stored cornea are temperature, duration of storage, pH of the storage solution, nature of storage medium and the state of the cornea upon enucleation. At present, refrigeration at 4°C in a moist chamber yields fairly clear corneal material if used within about 48 hours. A more important factor is how soon corneal material is refrigerated after the death of the donor. Newer methods of preservation include pretreatment in varying concentrations of glycerine and saline and deepfreezing at -79°C. In the end, the most important criterion of suitability of donor material is felt to be its transparency at the time of keratoplasty.

SUMMARY

The many problems involved in successful optical keratoplasty are being more thoroughly appreciated and, especially from the technical standpoint, are being resolved. Further elucidation of the various biologic and physicochemical factors, relative to the graft and the recipient bed, which cause opacification in corneal grafts can be expected to increase the applicability of the procedure. Careful case selection at the present time, as evidenced by the success in keratoconus, permits reasonably good prognostication.

REFERENCES

1. Lohlein, cited by Fine.
   (b) On the metabolism of the corneal graft, Ibid. p. 303.