CORNEAL TRANSPLANTATION AND REJECTION

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ABSTRACT

With technical problems largely solved and with improved quality of donor material, the immune allograft reaction is becoming the most frequent limitation to corneal transplantation. The overall frequency of the allograft reaction is 15% in the author's experience, varying from about 10% in the most favorable cases to about 35% in the less favorable. Preoperatively vascularized corneas showed a definitely higher incidence of allograft reaction even in the favorable prognostic group. The time of onset of the reaction tended to be earlier and the outcome less favorable in the preoperatively vascularized cases. Regrafted cases also showed a greater frequency of the allograft reaction, almost three times as frequent as in comparable primary grafts. Despite this, clear regrafts were obtainable in 64% of all regrafted cases and in 80% of the dystrophy cases.

Corneal transplants may fail from many causes most important of which are poor surgical technique, defective donor tissue, infection, glaucoma, and the immune allograft reaction. As the technical problems of keratoplasty have been progressively solved and as the availability and quality of donor material has improved the role of the allograft rejection as a cause of graft failure has increased in importance to the point that it may soon be considered the ultimate limitation to corneal transplantation. In the most favorable prognostic cases such as keratoconus the success rate is already approaching 100%. With technical improvements the reported incidence of the allograft reaction is decreasing but there is still a wide discrepancy in the incidence reported by various observers. This is true of the most favorable cases undergoing keratoplasty as well as of the least favorable. The allograft reaction in favorable cases such as keratoconus has been variously reported as 11% to 30%. This discrepancy might be explained either on the basis of technique, differences in period of observation, or differences in the criteria for the diagnosis of the allograft reaction. The diagnosis of an immune allograft reaction is not always simple. It was summed up during the Ciba Symposium on corneal graft failure held in 1972 as follows: 'An unequivocal clinical diagnosis of allograft reaction can be made, when, at least 10 days after a first transplantation a previously clear graft in a quiet eye rapidly develops edema with signs of inflammation in the anterior segment including ciliary flush, with cells and usually slight flare in the anterior chamber and when the area of edema in the graft moves across the cornea in the wake of an endothelial line (Khodadoust's rejection line) typically commencing at and moving away from a focus of vascularization in the
vicinity of the graft'. It should be added that while the rejection line is essential for a positive diagnosis it is frequently not visible because the cornea is not seen until a late stage of the reaction when it has become obscured by corneal edema or by the debris of the destroyed endothelial cells. The reaction has been held responsible for the majority of failures in the less favorable categories of corneal disease such as the chemical injuries. Maumenee (1973) and Khodadoust (1973) hold that the immune reaction is the most frequent cause of graft failure when gross technical failures have been eliminated. There are on the other hand others (Elliott, 1971; Moore and Aronson, 1971) who feel that there is insufficient evidence for specific donor antigen sensitization in human keratoplasty and that the phenomena observed clinically can be explained equally well by a large group of antigens, microbial, chemical, suture material, etc. Any of these may cause an inflammatory reaction in the recipient with proliferation of mononuclear cells and damage to the endothelium of the graft.

HISTOCOMPATIBILITY

The role of the HL-A histocompatibility antigens in the human allograft reaction has as yet not been clarified. Given the remote likelihood of obtaining a good match of histocompatibility antigens in random donor selection, it is difficult to explain why the great majority of patients receiving corneal allografts do not show a rejection reaction and why the success rate is as high as it is. It has been difficult to demonstrate a direct correlation between HL-A incompatibility and the fate of the graft (Allansmith et al., 1974). Those who have urged such a correlation have in general found their supportive observations limited to grafts transplanted into heavily vascularized corneas of poor prognosis in which greater HL-A incompatibility appeared to be associated with a higher risk of rejection. The suggestion has been made that it is in this latter group of poor prognosis cases that prospective HL-A matching, with all its difficulties and complexities, might be most rewarding (Gibbs et al., 1973; Ehlers and Kissmeyer, 0000; Stark et al., 1973).

CORNEAL VASCULARIZATION

The absence of blood vessels in the cornea has been accepted as an important factor in its relative privilege as a site for an allograft. It has been well documented, however, that the allograft reaction does occur in corneas that are completely avascular (Fine and Stein, 1973). It has been suggested that in such cases the reaction is mediated across the anterior chamber. On the other hand not all heavily vascularized corneas reject an HL-A incompatible donor. For example in a study of corneas scarred by herpes simplex keratitis with moderate to severe stromal vascularization pre-operatively, 20 to 25% showed signs of the allograft reaction (Fine and Cignetti, 1977).

Another type of vascularization worthy of attention but often misinterpreted is early post-operative vascularization following keratoplasty. Many surgeons fear the spread of vessels through the peripheral cornea towards the