Localization of Corneal Antigens

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The 'maladie du greffon' is assumed to depend upon an immunization process. In fact, this hypothesis is based on very few definite facts. We have no knowledge at all of how antibodies might be able to damage corneal transplants. It is only since early in 1960 that antibodies have been found in the serum of these transplantation patients [Nelken].

The findings in corneal transplantation cases are, as far as is known, as follows:

In 50% of cases, Boyden found humoral antibodies to corneal tissue in the serum. Their titre increases in the course of the transplantation. The titre, however, does not correlate with the clinical course. The antibodies are formed extra-ocularly and are specific for the species.

In one case, antibodies to the donor tissue were found; in this case, there was a correlation between the titre and the clinical picture. These antibodies were thus specific for the individual.

Using a precipitation reaction, humoral antibodies to the donor cornea are found in 50% of cases. These are specific for the individual. There is no obvious connection with the condition of the transplant. There is, however, a clear correlation with the presence or absence of signs of iridocyclitis; this is particularly true in the first three weeks after transplantation [Tsutsui]. In the cases where the 'maladie du greffon' is also present, this reacts well to corticoids.

In 1963, Remky demonstrated the local formation of antibodies in the cornea which are specific for the species. These are certainly different antibodies from those which occur in the serum; the time of their occurrence is different. Correlation with rejection is still uncertain.

It is probable that a series of antibodies is formed; their demonstration

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is often a question of the method chosen. To gain more insight into this subject, we must have sensitive methods of examination, specific antisera and antigens which are as pure as possible. A second reason why we wish to have pure antigens is that they can induce immunological tolerance [Medawar], probably on the basis of immunological paralysis. This principle was already put into practice by Löhlein in 1910 for corneal transplantations.

Broekhuysse isolated kerato-glycosaminoglycane (KGAG) from calves' corneae, using the method described by Robert, and made antisera to it. As appears from his paper, there are reasons to suppose that KGAG plays an important part in the rejection of corneal transplants. We have tried to determine, by means of indirect immuno-fluorescence, among other methods, whether these or similar antigens also occur elsewhere in the eye. It is an intriguing fact that a rejection reaction in a transplant is always accompanied by signs of iridocyclitis.

Indirect immuno-fluorescence was performed by the classical method of Coons and Kaplan, as described by Feltkamp and others. I have shown you a number of sections, from which the following conclusions can be drawn:

absorbed anti-epithelium sera only react to epithelium and the basal membrane;
anti-KGAG reacts to epithelium, basal membrane, stroma and the walls of the blood vessels in the iris, ciliary body and episclera;

anti-serum serum reacts to all vessel walls and also to epithelium, stroma and villi;

Anti-'soluble stroma protein' serum reacts to stroma and, to a much lesser extent, to the vessel walls.

The conclusion can be drawn from this that KGAG induces an anti-serum which attaches itself to antigens localized at those places associated with the clinical picture of the rejection reaction.