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Corneal Transplantation and Immune Tolerance

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Revised May 2026

Corneal transplants are generally well tolerated (not rejected), with relatively low rejection rates compared with solid organ transplants such as heart, lung, kidney, and skin grafts. For many years, it was believed that this phenomenon occurred because of the absence of blood vessels and lymphatics in the cornea, resulting in antigen "invisibility" of non-self tissue (i.e., a donor cornea) from the recipient's immune system, and therefore a reduced immune response against the transplanted cornea. Indeed, a British immunologist was awarded the Nobel Prize in Medicine in the early 1950's for his experiments on this topic, and his description of the phenomenon of immune tolerance. However, it was later discovered that the process was more complex than initially supposed 40 years ago.

We now know that non-self corneal antigens on the transplanted cornea are not invisible to the recipient's immune system but are, in fact, recognized by it. However, rather than an "attack-and-destroy" response, a form of "immune deviation" response develops, in which regulatory cells actively suppress the generation of destructive effector cells; the continued activity of these regulatory cells accounts for the relative tolerance observed in most corneal transplants. This is called anterior chamber–associated immune deviation (ACAID) and it means that antigens introduced into the eye's anterior chamber trigger a systemic, antigen-specific suppression of delayed-type hypersensitivity. This mechanism helps protect the eye from inflammatory damage by promoting the generation of regulatory T lymphocytes.

This tolerance can be disrupted if the immune system is perturbed—particularly when it is "revved up" by an upper respiratory infection or immunization—resulting in the activation of "attack-and-destroy" immune cells that may target the corneal transplant. Fortunately, in most instances, the patient and/or the ophthalmologist will recognize this quickly, treat the eye with frequent application of steroid eye drops, and eventually discontinue steroid drops. This phenomenon clearly confirms that the recipient's immune system can recognize the non-self cornea tissue and mount a stimulatory immune response against it.

The temporary use of steroid drops has allowed the brief perturbation in the immune system to subside and has enabled the patient's regulatory cells to once again gain the upper hand, mediating the continued freedom from transplant rejection.

The key take-home messages for patients are as follows:

1. Corneal transplantation has a success rate of over 90%.
2. Although episodes of corneal graft rejection may occur, early recognition of symptoms (discomfort, photophobia, redness, and decreased vision), coupled with prompt ophthalmologic evaluation and initiation of corticosteroid therapy, can result in successful graft salvage in approximately 90% of cases.