

## CORNEAL REPAIR: A CLEAR VISION

*Damage to the surface of the cornea causes pain and loss of vision, but regenerative therapies are providing a clearer, brighter future.*

BY DAVID HOLMES

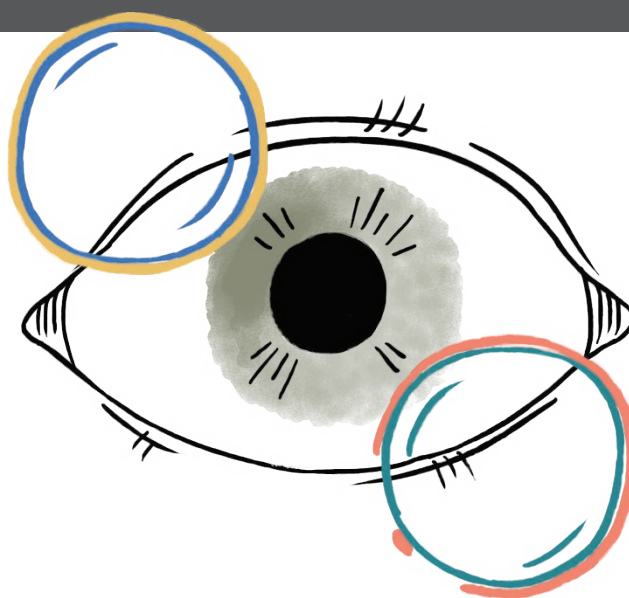
If the eyes are the window to the soul, then it is the cornea that lets the light enter.

For more than 200 years, physicians have been preoccupied with keeping this dome-shaped, transparent surface in front of the iris and pupil clear. German surgeon Franz Reisinger was the first to attempt a corneal transplant in animals in 1818. And in 1838, US ophthalmologist Richard Kissam tried to replace the opaque cornea of a young patient with the healthy cornea of a pig, but the procedure failed when the transplant was rejected. The first successful transplant in humans was in 1905, but outcomes remained poor until the mid-twentieth century, when developments in infection control, anaesthesiology, surgical techniques and immunology vastly improved the success rate of corneal transplantation. In the twenty-first century, advances in cell-culture techniques and bioengineering have opened the door to regenerative treatments for people with damage to one or both corneas.

Unclouded vision requires a clear cornea. Its epithelial surface constantly renews itself to maintain an unblemished, uniformly refractive surface. Cells that are shed from the surface are replaced by new ones that emanate from a small population of stem cells located at the edge, or limbus, of the cornea.

If the stem cells at the limbus are damaged, the renewal process is interrupted. The complete or partial loss of these stem cells — limbal stem-cell deficiency (LSCD) — allows the opaque conjunctiva to grow over the cornea. This can lead to intense pain and, in the most-severe cases, blindness.

Data on the incidence of LSCD are limited. Best estimates suggest that there are at least 240 cases each year in the



United Kingdom alone (A. J. Shortt *et al. Br. Med. Bull.* **100**, 209–225; 2011). The leading causes of LSCD in the United Kingdom are chemical and thermal injury, Stevens–Johnson syndrome (a rare hypersensitivity reaction often triggered by infection or medicine), aniridia (absence of the iris) and ocular cicatricial pemphigoid (an autoimmune disease that affects the conjunctiva).

In severe cases of LSCD, often the only option is to replace the entire cornea. But, increasingly, surgeons can intervene at an earlier stage of disease to regenerate the lost cells. This means that people with LSCD have a range of treatment options depending on the severity of their disease, although each comes with drawbacks. Advances in induced pluripotent stem-cell technology might further expand these options.

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