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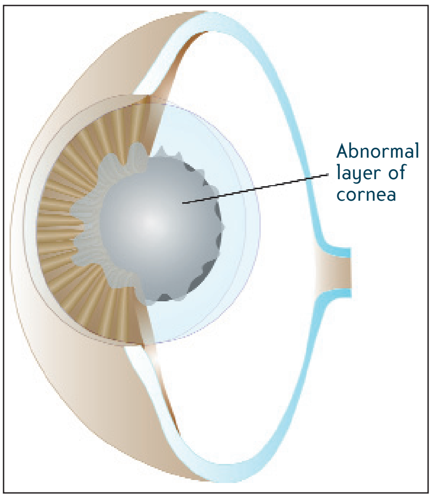
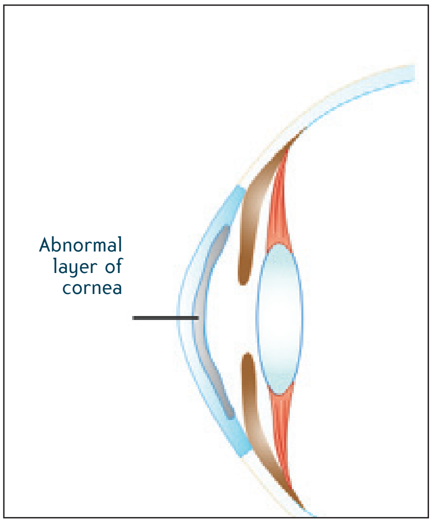
Selective cornea endothelial transplantation

A new frontier in surgical technique

For decades, cornea transplantation has been done by penetrating keratoplasty, in which the entire thickness of the cornea is removed, even when only a small portion is diseased. Recent, exciting developments in transplantation technique now permit selective replacement of the innermost, endothelial layer in diseases such as Fuchs' endothelial dystrophy. Moreover, the operation is done via a keyhole opening, only about 4mm wide. This remarkable development greatly improves the outcome of cornea transplantation.

The cornea is an exquisitely defined lens, designed to minimise optical aberrations. Its gross anatomy is layered, or lamellar. From anterior (surface) to posterior (in contact with the aqueous humour), it consists of the epithelium, stroma (the bulk of its structure) and the delicate innermost layer consisting of Descemet's membrane and adherent layers of endothelial cells. Many, perhaps most, cornea diseases 'respect' this lamellar structure. Epithelial diseases include map-dot-fingerprint dystrophy, recurrent erosions, herpes simplex and neurotrophic ulceration. The archetypal stromal disorder is keratoconus – others include dystrophies such as granular, macular, fleck and amyloid. Specifically, endothelial pathology includes Fuchs' endothelial dystrophy, pseudophakic/aphakic bullous keratopathy and herpetic disciform lesions. The first two of these account for a substantial proportion of cornea transplants performed in this country.





Figures 1a & 1b
The endothelial layer of the cornea is diseased and cloudy, for example in Fuchs' dystrophy

Drawbacks of PK

For decades, penetrating keratoplasty (PK) has been the standard treatment for disease so advanced that it has caused permanent cornea opacification. Despite many improvements over the years, this remains a somewhat crude and unpredictable operation. In essence, a circular blade is used to core out a full thickness disc of diseased cornea about 7.5mm in diameter. A slightly wider disc of tissue is excised from the normal cornea of a cadaveric donor. The transplant is sutured into place, typically with about 16 suture bites.

Most optometrists will have encountered PK and become aware of its strengths and weaknesses. It certainly has the capacity to restore vision, and many patients have cause to be grateful on this account. The drawbacks, however, can be severe.

Many practitioners will have experienced the disappointment of an apparently clear transplant with disabling irregular astigmatism in a patient who is not able to tolerate a gas permeable contact lens. The relatively enormous incision, and numerous sutures necessary to close it, entail a prolonged and frustrating healing process, which may last 18 months. Glaucoma may be induced or exacerbated, perhaps by trauma to the trabecular meshwork during suturing. Endothelial and keratocyte cell loss are high both during and after surgery, so that many transplants will not survive the lifetime of the patient and need to be replaced. There is always the risk that the patient's immune system will reject the alien tissue – some rejection episodes are reversible using intensive steroid, some are not.

Lastly, there is a fundamental fault with PK, which will be apparent from the earlier discussion of the lamellar anatomy of the cornea and the respect shown for this anatomy by many diseases. If a disease

Figure 2
The diseased endothelium of the patient is removed

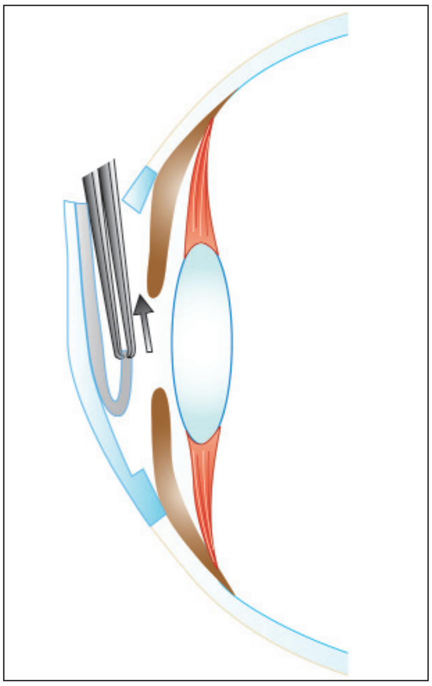
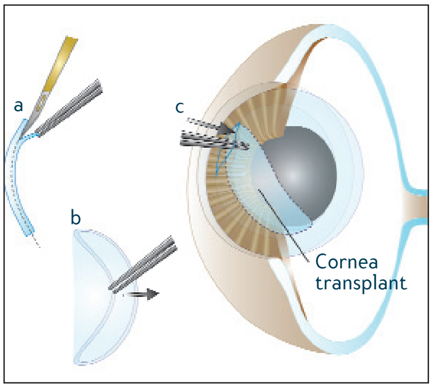


Figure 3
The healthy donor cornea endothelium is removed from the transplant (a), folded in half (b) and inverted as a 'taco' into the recipient patient's eye (c)



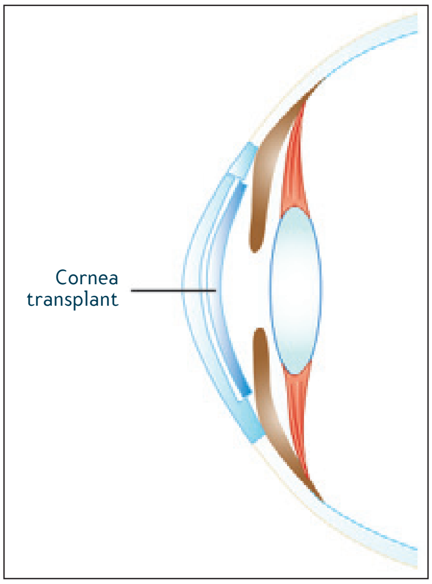


Figure 4
Once inside the eye, the transplanted endothelium unfolds and lies next to the recipient patient's cornea stroma

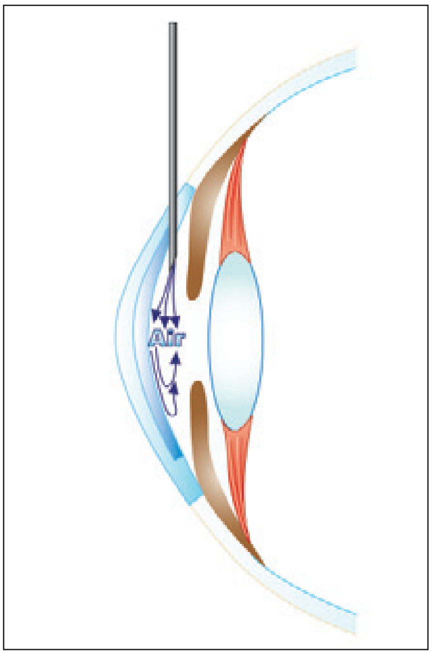


Figure 5
Air is injected into the eye to force the transplant against the recipient patient's stroma, to which it will subsequently adhere tightly

such as Fuchs' endothelial dystrophy only affects the endothelium (stromal oedema being merely a response to loss of endothelial function, not a primary event) why should one wish to replace any more tissue than the endothelium itself? The stroma and epithelium are normal – so why remove them? If it ain't broke, why fix it? Basically, PK often requires the removal of more normal than diseased tissue. It would plainly be greatly advantageous if it were possible to remove and replace only the layer of the cornea that had failed.

Promising new alternative

The era of selective corneal endothelial transplantation has arrived, thanks to the pioneering work of two ophthalmologists – Gerrit Melles in Holland and Mark Terry, an American.

Selective endothelial transplantation is indicated for diseases of the endothelium such as Fuchs' endothelial dystrophy (**Figures 1a and b**) and pseudophakic/aphakic bullous keratopathy. The demise of the endothelial cells and loss of their pumping function causes secondary oedema of the stroma. Initially, the patient notices blurred vision in the morning when overnight eyelid closure increases incipient corneal oedema through hypoxia. Later, oedema is permanent and progressive, leading to blindness and sometimes painful epithelial blisters.

The new operation can also be performed to replace the endothelium of a PK, which had been irreversibly damaged by rejection; 're-do' penetrating keratoplasties are notoriously unsuccessful and the much gentler procedure of selective endothelial transplantation seems very promising in this context.

Surgical technique

The technique requires a quantum improvement in surgical performance. The eye is entered via a phacoemulsification-style incision about 4mm wide. The diseased innermost layer (Descemet's membrane and the adherent endothelial cells) is then gently peeled away from the remainder of the cornea, leaving a denuded stromal bed (**Figure 2**). The donor tissue, obtained in this country from the United Kingdom Transplant Authority, consists of cornea and a rim of sclera. This is clamped in to an 'artificial chamber' – a device which creates an artificial eye, enabling the donor tissue to be manipulated.

Instruments are then used to split the donor cornea into two layers, an outer layer of about 0.35mm consisting mostly of stroma, and an inner layer of about 0.15mm containing the all important donor endothelium. The latter is next trephined in to a disc about 8mm wide, gently folded in half and then inserted in to the patient's eye (**Figure 3**). At this stage, it will look like a 'taco', an oyster shell or a split pitta bread, depending on one's gastronomic preference, i.e. the disc is folded with the important part, the donor endothelial cell layer, on the inside.

The tissue is unfolded and expanded into a disc by inserting an air bubble between the leaves, so blowing them open (**Figure 4**). The surgeon may experience a certain trepidation at this moment, for it is imperative that cornea anatomy is correctly re-established – the endothelial cell layer must face the inside surface of the eye and not be adherent to the stroma or the transplant will fail. At this point of the operation, the miracle of selective corneal transplantation occurs.

Having unfolded the transplant and established that it is facing the correct direction, a further air bubble is applied forcing the ultra thin donor disc against the bare stromal surface (**Figure 5**). Unbelievably, it adheres firmly without any further surgical manipulation. It is quite unnecessary to stitch or glue the transplant in place. In fact, it adheres so strongly that within a few seconds, it is quite difficult to shift the transplant even with surgical instruments.

Endothelial transplant adherence seems even more remarkable than the similar behaviour of a Lasik flap, in that the transplant does not have a hinge and is 'submerged' in aqueous humour (**Figure 6**).

Advantages and disadvantages

Selective corneal endothelial transplantation via a phacoemulsification incision (which requires no or at the most one suture) is self-evidently much gentler on the eye than PK, which seems positively brutal by comparison. Only the diseased tissue is replaced, leaving normal tissue undisturbed. There is no post-operative astigmatism and gas permeable contact lenses are a thing of the past. Likewise, suture-related complications, such as vascularisation and subsequent transplant rejection, should not occur. The operation may be done in circumstances when PK would be too risky, such as a poor quality ocular surface, since the transplant is not exposed to the exterior of the eye. Recovery, whilst not an overnight phenomenon, is certainly quicker than after PK, and may be complete within three or four months.

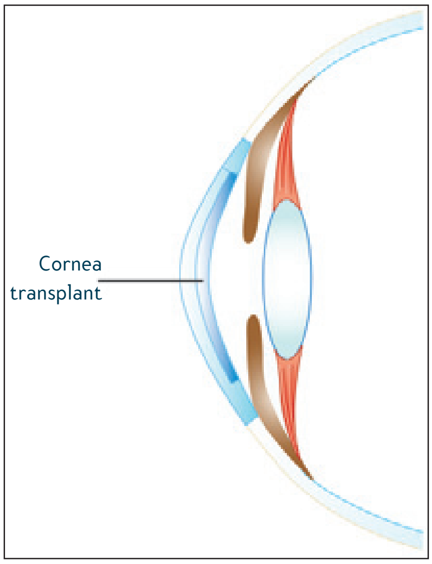


Figure 6
At the end of the operation, the transplanted endothelium has adhered to the recipient patient's stroma and will proceed to clear the patient's cornea of oedema

Innovative surgery is never without its downside, however, especially when at a relatively early stage of its development. The disadvantages of selective endothelial transplantation include the fact that it is not an easy operation to do. The endothelial cell layer is handled in a more direct manner than in PK, with the potential for greater damage. Time will tell how the lifespan of this form of transplant will compare with traditional PK.

Another issue is that one might expect reduced contrast sensitivity from a cornea that is thicker than normal and has an interface between the patient's tissue and the transplant, something that is not present in PK. Again, studies will determine to what extent this is a problem. In the author's opinion, an uncorrected acuity of 6/9 is preferable to a potential acuity of 6/6 obtained by PK – but only when a gas permeable contact lens is worn.

Conclusion

The future looks bright for selective corneal endothelial transplantation. There will be improvements in surgical instrumentation and technique. Cadaveric transplants will very likely be replaced by sheets of human corneal endothelial cells cultured in the laboratory, their structure perhaps manipulated so that they are more resistant to ageing, infection and auto-immune assault. The beneficiary of this leap in surgical technique will of course be our patients.

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About the author

Simon Levy is a Consultant Ophthalmologist at North West London Hospital's NHS Trust. He specialises in disorders of the front of the eye, namely cataract, cornea, comprehensive refractive surgery and external eye disease.

His website – www.eyesite.org – has detailed information and video on selective endothelial cornea transplantation and other surgical procedures.

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Case study

A 78-year old patient suffers from Fuchs' corneal endothelial dystrophy. Her right eye received a full thickness cornea transplant several years previously. Sixteen sutures were required to secure the transplant in place. It was 18 months before healing was complete. She can only see from her right eye whilst wearing a gas permeable contact lens. By contrast, her left eye received a selective corneal endothelial transplant a few months ago. Recovery was complete after three months, no sutures were needed and she sees well from her left eye without needing to wear a contact lens (**Figure 7**).

Figure 7

Post-operative appearance of a selective cornea endothelial transplant. The circular outline of the transplant can just be seen on the inner surface of the (now transparent) cornea