Advances in Corneal Endothelial Transplant Surgery: DMEK

Introduction
Over 2500 corneal grafts are performed in the UK annually. In 2009 over 50% of these were endothelial transplants, primarily Descemet Stripping Endothelial Keratoplasty (DSEK). A little over a decade ago, endothelial transplants accounted for just 0.3% of all corneal grafts.

A large proportion of corneal diseases selectively affect one layer within its structure. This pattern of corneal disease allows selective transplantation of the affected layer. Endothelial transplants are the treatment of choice for loss of corneal clarity due to endothelial dysfunction, the two main indications being, Fuchs endothelial dystrophy and pseudophakic bullous keratopathy. The first selective approaches to corneal transplantations were described in the 1950’s. The endothelium with supporting posterior stromal tissue was transplanted after the creation of a corneal flap. The posterior lamellar keratoplasty (PLK) technique was refined in 1998, by Melles using a sutureless technique with an air bubble for fixation of the posterior lamella. Although effective, PLK ultimately proved too technically challenging for popular use. In 2004, the ‘descemetorhexis’, a simplified way of removing the dysfunctional endothelial layer was described by Melles and the technique named Descemet Stripping Endothelial Keratoplasty (DSEK). Preparation of the donor tissue was further improved in 2006 by Gorovoy with the use of a microkeratome; this technique was named “Descemet stripping automated endothelial keratoplasty” (DSAEK).

In the space of five years with these modifications in technique DSEK/DSAEK had revolutionized the treatment of corneal endothelial disorders worldwide. The advantages of DSEK/ DSAEK over penetrating keratoplasty were clear: avoidance of suture related complications such as infection, blood vessel growth, astigmatism; faster visual rehabilitation and greater tectonic strength of the globe. However after DSEK/DSAEK, a large proportion of patients did not achieve best corrected visual acuities (BCVA) exceeding 6/12. The dual stromal interface scar between the donor and host was postulated as being the primary cause of this diminished optical performance and a solution was sought.

In 2006 a successful transplant composed solely of Descemet membrane and its endothelium (Descemet Membrane Endothelial Keratoplasty or DMEK) was described by Melles. With no supporting stromal tissue, a smooth host to donor interface, and graft thickness reduced by 80% to below 20um, the improvement in visual acuity was remarkable. 80% percent of patients achieved ≥6/12 within six months of surgery. Endothelial corneal grafting had taken a significant step in its evolution.

Outcomes
DMEK offers a like for like replacement for dysfunctional endothelial tissue and near-perfect anatomical restoration of the recipient cornea. Although the improvement in outcome is not as pronounced compared to when DSEK/DSAEK superseded PK, DMEK has definite advantages over its predecessor. These include faster and more complete visual
rehabilitation with a greater proportion of eyes achieving 6/6; lower transplant rejection rates (approximately 1% versus 10% in DSEK/DSAEK); minimal refractive change; and due to a larger graft size, a greater number of transplanted endothelial cells. An additional benefit includes the possibility of increasing the efficiency of donor tissue use with a cornea 'split' into Descemet membrane (and endothelium) and stroma for use in two separate recipients.\(^2\)

A study published in 2012 compared the results of DMEK versus DSAEK.\(^3\) There was a significant difference in visual acuity at both 3 months (6/10 vs 6/18 respectively) and 6 months (6/9 vs 6/14 respectively) postoperatively. There was no statistically significant difference in endothelial cell density (ECD) at 6 months (1520 vs 1532 cells/mm\(^2\) respectively).

A prospective study of over 200 eyes at the NIiOS has demonstrated that at 6 months, 98% of eyes reached a BCVA of \(\geq 6/12\), 79% \(\geq 6/7.5\), 46% \(\geq 6/6\), and 14% \(\geq 6/5\). There was a small postoperative hyperopic shift of +0.33D and refractive stability was achieved at 3 months. These results are remarkably similar to those achieved by an earlier prospective study.\(^4\) ECD changes after DMEK are similar to DSEK/DSAEK in that there is an approximately 30% loss in the first three months stabilising thereafter to a rate of approximately 4% per annum. It has recently been suggested that this apparent 'loss' in ECD within the first 6 months after DMEK may be due to increased posterior corneal surface area associated with postoperative corneal deturgescence thereby overestimating the actual loss of endothelial cells by approximately 8%.

**Technique: Challenges and Solutions**

Although graft preparation is challenging, with experience, the rate of loss of donor tissue during preparation can drop to 5% or even lower. Standardized graft preparation techniques have been published by a number of groups including Melles and Kruse. Furthermore, preparation of the donor tissue may be carried out in an eyebank by trained technicians thereby maximising the use of operating theatre time. Modifications in surgical technique have seen reported rates of re-bubbling due to graft detachment fall from over 50% to below 10%. Standardisations of the intra-operative techniques, and in particular, judging the orientation of the Descemet roll and positioning of the graft have made DMEK successful even in relatively inexperienced hands.

DMEK is routinely performed under local anaesthetic; however sufficient time must be allowed to obtain a 'soft eye' otherwise there is an increased risk of graft expulsion from the anterior chamber. Descemetorhexis should be performed using air to allow complete removal of the host membrane. Trypan blue staining of the graft after thorough rinsing of the culture medium facilitates better visualisation of the roll. The graft is then loaded into a glass pipette after obtaining a 'double roll'. The surfaces of the glass pipette are smoother than plastic injectors and minimise trauma to the endothelial cells that are located on the outer surface of the roll. Once inserted into the anterior chamber, the graft needs to be orientated with the endothelium facing the iris prior to unfolding. Unfolding is achieved by external pressure on the cornea and/or sclera, sometimes with the use of a small air bubble in the anterior chamber. Graft centration is then rechecked, although clinical observations suggests that as long as the central cornea is covered decentration makes little difference to the visual outcome as the denuded area is usually small with a standard 9.5mm graft and is repopulated with endothelial cells. The graft is then apposed to the host posterior stroma by first gently fully flattening the graft against the iris with an air bubble and then removing the air bubble from above the graft and in a single manoeuvre placing the air cannula under the graft to lift it against the stroma. Inward curls of the peripheral graft at this stage can precipitate detachments later can be removed by a process of peripheral corneal taps termed 'bubble bumping'. The air bubble under the graft is then enlarged, pressurising the eye to approximately 20mmHg for 60 minutes after which the air bubble is reduced to approximately 50% of the volume of the anterior chamber. The patient is then positioned for 24 hours. This "no-touch" technique for descemet membrane endothelial keratoplasty had been described in the literature.\(^5\)

**Clinical Scenarios**

As the ophthalmic community's experience with DMEK grows, it has been demonstrated that DMEK can be performed successfully in clinical scenarios which would previously have been considered to be contraindications. This includes in phakic eyes, eyes with anterior chamber intra-ocular lenses, eyes with glaucoma drainage devices, and eyes which have had previous corneal grafting including penetrating keratoplasty, DSEK/DSAEK and DMEK.

DSEK/DSAEK remains the preferred option when anterior chamber visibility is diminished enough to prevent visualisation of the stained DMEK roll. Eyes that do not have a stable lens-iris diaphragm or eyes that have had a vitrectomy pose difficulties in manipulating the graft due to a deeper anterior chamber and also in obtaining a sufficient anterior chamber air tamponade predisposing to graft detachment.

**Summary**

In 2006, a century after the first successful full thickness corneal transplant was performed the isolated transplantation of corneal endothelium on its supporting membrane was described. Continued scientific endeavour in the search for improved surgical techniques and treatments, such as the development of Rho-associated kinase (ROCK) inhibitor eye drops, has led to an altogether novel avenue of non-transplant treatments for corneal diseases. Spontaneous corneal clearance after descemetoirhexis alone and after total DMEK graft detachments has also been reported in the scientific literature raising interesting questions about endothelial regeneration and endothelial cell transfer.

However, at the present time, DMEK sets the benchmark for the treatment of corneal endothelial dysfunction with a technique that is inexpensive, standardised, minimises transplant rejection and restores vision rapidly and more completely, than any of its predecessors.