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Lessons From the Pathology Laboratory: Hints to Improve Outcomes

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Although successful full-thickness corneal transplantation has been performed for over a century¹, popularization of posterior lamellar transplantation is a recent phenomenon. In fact, we are currently in the midst of a corneal surgery revolution. Many of the corneal transplants done for endothelial-related disease may potentially be replaced by endothelial keratoplasty (EKP). Work on EKP began in the late 1990s, with the introduction of endokeratoplasty² and microkeratome-assisted posterior keratoplasty.³ In these surgeries, an anterior flap is created, a posterior lamellar dissection is performed, and a posterior lamellar donor including posterior stroma, Descemet's membrane and endothelium is sutured into place.

A review of the history of the development of Descemet's stripping endothelial keratoplasty has been published.⁴ The paradigm shift occurred when Melles of the Netherlands used a limbal incision approach for endothelial keratoplasty and performed the first posterior lamellar keratoplasty (PLK) in a human.⁵ Subsequently, Terry of the United States began modifying this technique.⁶ This procedure was initially termed "deep lamellar endothelial keratoplasty" (DLEK). A succession of refinements in technique ensued, with development of "Descemet's stripping with endothelial keratoplasty (DSEK)", "Descemet's stripping automated endothelial keratoplasty (DSAEK)", and "Descemet's membrane endothelial keratoplasty" (DMEK). These procedures all include limbus-based surgical stripping of Descemet's membrane and the endothelium, either alone (DSEK) or with posterior stroma lamellae (DLEK) and insertion of a prepared lenticule of either Descemet's membrane and endothelium (DMEK), with attached stroma prepared by a microkeratome (DSAEK) or prepared freehand (DLEK, DSEK). These procedures obviate the need for sutures in the graft and hence reduce post-operative astigmatism. Problems with these new techniques center around detachment of the donor lenticule from the posterior stroma of the host. Additionally, although post-operative best corrected visual acuities are often better than 20/40, it is difficult to obtain 20/20 vision after these procedures.

Two papers in this issue of *Ophthalmology* discuss the pathologic findings in failed DSAEK specimens and penetrating keratoplasty specimens after failed DSAEK.^{7,8} The main reason for graft failure appears to be endothelial cell loss.^{7,8} This is likely due in part to surgical technique. During surgery, the donor lenticule is folded, grasped with forceps, inserted, and unfolded. As in any new surgical procedure, there is a learning curve. A surgeon first learning this technique may experience a higher rate of primary graft failure than an experienced surgeon, which is likely due to endothelial cell loss during the insertion of the lenticule. An additional problem that a surgeon new to this procedure may encounter is incomplete removal of the recipient Descemet's membrane. Evidence for this is provided in the two current

pathology studies as both reported examples of host Descemet's membrane at the interface between the donor lenticule and host stroma.^{7,8} It is likely that there is a steep learning curve, and after a certain number of procedures, the surgeon will overcome these technical issues. Non-compression forceps that grasp the edge of the folded lenticule rather than the entire length of the folded lenticule or various inserters or shovels may help reduce endothelial cell loss during implantation. It should be remembered that patience is required during this surgery, and high surgical volumes in a busy practice may be counterproductive to the time required to ensure insertion of the donor with minimal endothelial damage. Advances in surgical techniques and instrumentation I hope will diminish endothelial cell loss in the future.

A second reason for failure encountered in several specimens is epithelial implantation.⁸ This is likely due to the preparation of the lenticule rather than introducing surface epithelium at the time of surgery. During trephination of the donor, care must be taken in order to mark the edges of the microkeratome cut so that the trephination is centered where the anterior flap was cut. Practice with meticulous trephination is required to prevent decentration of the cut, which may include epithelium and full thickness cornea with the lenticule. Epithelial implantation is also possible from lenticules prepared at eye banks. The anterior lamellar flap is placed back on the posterior lamellar portion of the donor cornea and transported in Optisol™. As lenticule preparation techniques become more developed, epithelial implantation I expect will be a rare complication.

A third reason for graft failure is non-adherence to the recipient. This presents a paradox, as a lack of lamellar, horizontal healing is desirable in order to maintain optical clarity. We learned this by studying the central, horizontal, hypocellular wound after successful LASIK surgery.⁹ A certain lack of healing is why LASIK is successful-there is only a primitive scar in the central portion of the wound. The healing and scar formation, which holds the LASIK flap in place, occurs at the periphery. Without any significant central wound healing, the DSAEK lenticule will also remain relatively optically clear, although some wound healing in the periphery near Descemet's membrane breaks may be required for adherence of the lenticule to the posterior stroma of the recipient. Some have recommended roughening of the peripheral recipient bed to promote donor edge adhesion.¹⁰ There will be proteoglycans in the interface, and it will never be possible to perfectly align the stripped posterior stromal collagen lamellae with the microkeratome cut collagen lamellae in the lenticule. The wound interface will chronically serve as a potential space for fluid accumulation in conditions that lead to corneal edema, similar to the central, hypocellular LASIK wound.¹¹ After successful endothelial keratoplasty, it may be difficult to obtain 20/20 vision due to forward-scatter of light at the donor/host interface.¹² Additionally, after chronic corneal edema, there are anatomic changes in the anterior stroma causing back-scattering of light that will likely persist after restoration of the endothelial pump function, thus precluding 20/20 vision.¹³

There is great hope during the introduction of a new surgical procedure that outcomes will improve from those achieved with prior techniques. In order for the new procedure to be widely accepted, the technique must be transferable so that the majority of surgeons are able readily to perform the surgery. At the initial stages, there are often technical issues that need to be resolved and a surgical learning curve. This is the case in endothelial keratoplasty procedures, such as DSAEK. Additionally, there is utility in examination of tissue from failed procedures in order to gain insight into why there are failures and how the procedure may be improved. This is also the case with DSAEK.^{11,12} Learning from the pathologic findings in failed DSAEK specimens will help guide refinement to the instrumentation, surgical techniques, and ultimately, patient outcomes.

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