This guest editorial is one of a series looking back at landmark articles published in the JCRS. This special series commemorates the 25th anniversary of the joint Journal of Cataract & Refractive Surgery. This issue: Descemet stripping with endothelial keratoplasty in 200 eyes: Early challenges and techniques to enhance donor adherence. J Cataract Refract Surg 2006;32:411–418.¹

Published 15 years ago, in March 2006, the landmark study by Francis and Marianne Price on Descemet-stripping endothelial keratoplasty (DSEK) represents a milestone for the transition from penetrating keratoplasty to endothelial keratoplasty (EK).¹ Shortly after Melles et al. had shown the concept of the implantation of an endothelial graft onto the posterior corneal surface after descemeto­rhexis at the 2003 American Academy of Ophthalmology Annual Meeting, the study by Price and Price was the first to describe a large EK case series of 200 eyes.²,³ Perfectly summarized in the first sentence of the article’s discussion, their work clearly paved the way of what was to follow in the field of corneal transplantation: “Descemet’s stripping with endothelial keratoplasty offers significant advantages over penetrating keratoplasty and earlier posterior keratoplasty techniques.” By meticulously describing the technical challenges they encountered and offering advice based on their surgical experience on how to promote graft adherence, this study certainly helped new DSEK surgeons to shorten their learning curve and accelerate the uptake of EK (Figure 1).

Looking back at the history of EK, it is astonishing to see how fast the landscape of corneal transplantation has changed since 2006. Although a first attempt to perform EK was made in the 1950s, it took almost half a century until the first clinically successful operation was performed in 1998.⁴ This first approach, introduced as posterior lamellar keratoplasty and later popularized as deep lamellar EK (Figure 1) in the United States by Terry et al., was technically challenging, which may have prevented widespread uptake even though the approach proved clinically successful with outcomes surpassing penetrating keratoplasty.⁵ Introduction of descemeto­rhexis made lamellar keratoplasty more accessible and cumulated in the DSEK landmark study by Price and Price.¹,² Especially, owing to the use of a microkeratome for the donor graft preparation technique, by which precut donor tissue became available to virtually all corneal surgeons, over a period of about 5 years, the number of DSEK and Descemet-stripping automated endothelial keratoplasty (DSAEK) surgeries performed worldwide increased exponentially (Figure 1).¹

Although the numbers of DSEK/DSAEK procedures were continuously rising worldwide, we introduced the next refinement of EK to optimize clinical outcomes: Descemet membrane endothelial keratoplasty (DMEK). By eliminating the posterior stroma from the donor graft entirely, a selective replacement of an autologous Descemet membrane and endothelium could be achieved (Figure 2).⁶ DMEK resulted in a near anatomic restoration of the corneal anatomy, provided unprecedented visual outcomes, and an even lower risk for endothelial immune reaction.⁷,⁸ Although, in some countries, DSEK/DSAEK may still be the standard technique for endothelial disease, DMEK seems to be gaining in popularity and has already become the preferred treatment option in some countries.⁸

This rapid development in the field of corneal transplantation is even more surprising when one considers that the introduction of EK was met with some antagonism. All the early articles on EK were rejected multiple times. The first article on DSEK had to be rewritten to only describe des­cemeto­rhexis, and with the introduction of DMEK, history repeated itself.²

In the meantime, new, exciting developments in kerato­plasty are on the horizon, and these may contribute to resolving the persistent worldwide shortage of suitable donor tissue because less tissue can be used with tissue­efficient surgical approaches such as Descemet-stripping only (DSO), also known as descemeto­rhexis without EK, and the quarter-DMEK technique.⁹ DSO may even allow for treatment of Fuchs endothelial corneal dystrophy without the use of donor tissue as only diseased tissue is removed (without replacement by a graft). Corneal clarity is restored by repopulation of the stripped region by the migration of peripheral endothelial cells, but results are not yet consistent.¹⁰ Topical use of ROCK-inhibitors may potentially help improve DSO outcomes, but further studies are still required. Quarter-DMEK, on the other hand, resembles conventional DMEK but may allow for multiple grafts from a single donor cornea as the graft is divided into 4 pie-shaped grafts to potentially treat 4 patients with 1 donor cornea.¹¹
Moreover, on the horizon is the use of cultured endothelial corneal cells that are injected into the anterior chamber. The first clinical trial, including 11 patients, showed promising initial results. The potential for widespread use of cultured corneal endothelial cells could be limited, however, by the strict regulation of advanced therapy medicinal products in many countries.

Next to other new treatment modalities such as bioengineered corneal grafts and gene therapy, the new emerging techniques, such as DSO, quarter-DMEK, and cell injection, will be further developed and tested in the near future to evaluate their full therapeutic potential. Moreover, only time will tell which place they will find in the treatment of corneal endothelial dysfunction. Until then, DSEK/DSAEK and DMEK may remain the standard of care for the management of corneal endothelial dysfunction and Francis and Marianne Price may look back on their pivotal role in how corneal transplantation developed over the past 15 years.

REFERENCES