Pediatric Keratoprosthesis: A Promise Unfulfilled
Kathryn Colby, MD, PhD - Chicago, Illinois

My foray into pediatric keratoprosthesis began in 2003. I was managing a challenging patient, a young boy aged 4 years with severe herpes simplex keratitis. After 3 penetrating keratoplasties, each one plagued by nonhealing epithelial defects with subsequent corneal melting, I discussed the possibility of a Boston Keratoprosthesis (KPro) with Claes Dohlman. Cornea aficionados will need no introduction to Dr. Dohlman, who has spent decades developing and improving the Boston KPro. Claes was skeptical about placing a KPro in a child. He was getting ready to leave Boston for his annual summer sojourn to Sweden. I asked if he would at least think about my suggestion while enjoying his holiday. Claes, prescient as ever, replied in his characteristic Swedish accent, “I will think about it in my nightmares.” I did not end up placing a KPro in my patient; instead, we performed a near total permanent tarsorrhaphy, which stabilized his eye at the expense of his visual acuity.

The idea of pediatric KPro lay dormant until several years later when Esen Akpek reported the first experience of pediatric KPro in 2 children in 2006.1 The following year, the largest series of pediatric keratoprosthesis to date (21 eyes) was published, showing reasonable outcomes, albeit with a short follow-up period of less than 10 months.2 By this point, 2 of the most devastating complications with the Boston KPro in adults (endophthalmitis and device extrusion from melting of the carrier donor cornea) had been largely solved through modifications of the design of the device and changes to the postoperative regimen, so the stage was set for expansion of indications for the device, including its use in children.

The corneal community is well aware of the challenges of pediatric keratoplasty: increased risk of graft rejection and failure, prolonged visual recovery due to postoperative astigmatism or amblyopia, and the need for multiple examinations under anesthesia.3,4 Visit acuity results after pediatric keratoplasty are also suboptimal, with less than 50% of children with congenital opacities showing an improvement in vision after transplantation.5 Clearly, the field is in need of a better option for management of corneal opacification in children.

The potential advantages of KPro over penetrating keratoplasty—no chance of rejection, rapid visual recovery due to lack of postoperative astigmatism, potentially fewer examinations under anesthesia—were incredibly appealing to those of us who manage children with corneal opacification. Like a small handful of other KPro surgeons, I was an early adopter of the pediatric KPro.3 However, after some 20 cases in children aged younger than 6 years of age, a few facts became obvious. Although any corneal transplant surgery in children is technically challenging,5 it pales in comparison with the challenges involved in the postoperative management of the KPro in children. My results were dismal. Almost all devices extruded, most within 1 year, and all extrusions were associated with exuberant retroprosthetic membrane (RPM) formation. Those that did not extrude resulted in lost vision from intractable glaucoma (despite aggressive management, including tube placement and cyclodestructive procedures) or retinal detachment. Occasionally, ambulatory vision was able to be salvaged through device replacement or penetrating keratoplasty, but most of these eyes (~70%) had loss of vision to light perception only, and at least half of the eyes became phthisical. The last pediatric patient in whom I placed a KPro was a 15-month-old girl with severe corneal opacification from congenital glaucoma, who needed additional glaucoma surgery. She had a “Mass Eye and Ear triple”—glaucoma tube placement, pars plana vitrectomy with removal of the entire crystalline lens, including the capsular bag, and placement of a Boston KPro. She did surprisingly well for 5 years with vision as good as 20/100, but her device eventually extruded, requiring replacement, which was performed in 2015. She retains vision in the 20/200 range, but has continued to be troubled by borderline intraocular pressure.

Fast forward to 2017 when Dr. Fung and colleagues have confirmed Dr. Dohlman’s initial skepticism (see http://www.aaojournal.org/article/S0161-6420(17)30988-0/fulltext).6 These authors are to be congratulated for their summary of the Canadian results with the pediatric KPro. Unfortunately, it is not a happy story. Of the 11 children in their series, 5 lost light perception, only 2 retained vision of at least 20/400, and only 4 of the initial devices placed were retained at a mean follow-up of approximately 3.5 years. Complications were common, including endophthalmitis in 3 eyes and retinal detachment in 5 eyes. Retroprosthetic membranes occurred in more than 80% of children in this series, sterile keratolysis occurred in 45%, and glaucoma progression occurred in 27%. The authors conclude their article with the observation that on the basis of the available evidence, they do not recommend the pediatric KPro and, in fact, have stopped performing this surgery in children. It is hard to disagree with their conclusion.
Several points need to be addressed. First and foremost, why is there so little in the literature about the outcomes of pediatric keratoprosthesis? The last major article was 10 years ago. Since then, there have been a small number of case reports and reviews, nicely summarized by Fung et al. I suspect the answer lies in the hesitance of our field to publish bad outcomes. This certainly played a role in my case. But, data are critical to moving any field forward. We are grateful for the efforts of our Canadian colleagues in presenting this important series and to Ophthalmology for accepting it.

Second, and more important, why do the results of pediatric KPro lag behind those seen in adults? The history of the Boston KPro in adults may shed light here. Anyone who spent time in the Cornea Service at Mass Eye and Ear before 2000 will recall the challenges of adult KPro in that era. As Claes’s fellow in the late 1990s, I recall quite vividly the amount of time he spent in the minor operating room wrapping strips of donor cornea around the stems of KPros to reinforce melting carrier corneas. The entire team was devastated when a patient whose vision had been restored by a KPro presented with endophthalmitis, a not uncommon event during that time. It would have been easy to give up on the device given the immense challenges that existed.

Why did the situation change? The first step was development of prognostic categories. A review of early KPro data showed that vision-threatening complications were more common in autoimmune diseases such as Stevens–Johnson syndrome (SJS) and ocular mucous membrane pemphigoid, whereas KPros for graft failure did better. Chemical burns had an intermediate prognosis. In hindsight, this seems obvious, but it was only on careful analysis of outcomes that this finding was demonstrated. Our assessment of outcomes of pediatric corneal transplants is hampered by our lack of standard nomenclature. Ken Nischal has advocated for a new nomenclature for congenital corneal opacification, based on underlying pathophysiology and anatomic changes as determined by ultrasonic biomicroscopy, rather than nonspecific terms such as “sclerocornea” or “Peter’s anomaly.” Better classification will help us determine whether there are subpopulations within pediatric corneal opacification with a better prognosis for any form of transplantation. Interested readers are encouraged to review (and implement) Dr. Nischal’s schema.

Another major advance was the realization that the solid KPro back plate hampered nutrition to the donor carrier cornea, promoting necrosis of the carrier cornea with eventual device extrusion. Holes in the back plate to allow access of aqueous to the donor cornea coupled with a bandage lens to prevent desiccation of the carrier graft helped to solve the issue of device extrusion in “good” prognosis cases. The problem of endophthalmitis stems from lack of bio-integration of the KPro device with the donor cornea, allowing a potential route of ingress of microbial pathogens on the ocular surface into the eye. Addition of prophylactic topical antibiotics dramatically reduced the occurrence of endophthalmitis, although this requires patient compliance. Adoption of these changes improved outcomes to the point that some 900 to 1000 Boston KPros are now placed worldwide yearly. Autoimmune diseases still struggle with device extrusion and endophthalmitis, however, and use in these conditions remains low and fraught with complications.

Challenges still exist even in “good” prognosis adult KPro, most notably glaucoma, which is currently the major threat to long-term preservation of vision. To address this issue, an animal model has been created and is yielding important insights regarding optic neuropathy after KPro. Retoprosthetic membrane formation is the most common complication, occurring in up to 75% of patients, and although mostly a time-consuming nuisance, RPM formation occasionally can lead to corneal necrosis and device extrusion, similar to when solid back plates were used. Better apposition of the posterior graft—host junction may provide a physical barrier to reduce RPM formation. Modulation of intraocular inflammation also may be a fruitful strategy to reduce this complication. The point is although we have learned a lot regarding adults KPros, there is still more work to be done.

What can we learn from this that we can apply to our care of children with corneal opacification? Certainly, pediatric corneal opacification is a “poor” prognosis diagnosis, in many ways similar to the prognosis of SJS or ocular mucous membrane pemphigoid. Would systemic immunosuppression improve outcomes of the KPro in children, as has been suggested in SJS? Would another antibiotic delivery system reduce endophthalmitis? Would oversized back plates reduce RPM formation? There are more questions than answers at present.

Where does this leave us in 2017? Until we have a better understanding of how to improve KPro outcomes in children, corneal surgeons should “just say no.” Although this can be very difficult with an insistent parent with access to the internet and a desire to do the best for their child, at this point the pediatric KPro is not a long-term solution for pediatric corneal opacification. Better a failed graft with 20/400 (but ambulatory) vision than a no light perception eye.

References

Footnotes and Financial Disclosures

Financial Disclosure(s): The author(s) have no proprietary or commercial interest in any materials discussed in this article.

Correspondence:
Kathryn Colby, MD, PhD, 5841 S. Maryland Avenue, MC2114, Chicago, IL 60637. E-mail: kcolby@bsd.uchicago.edu.