## Commentary: Revisiting the methods of corneal preservation in the COVID-19 era

This issue of the Indian Journal of Ophthalmology features an interesting article which shows that glycerol preserved corneas provided therapeutic success similar to fresh corneal tissue in therapeutic penetrating keratoplasty.<sup>[1]</sup>

The current COVID-19 pandemic has brought into sharp focus the inadequacies in the corneal storage and preservation techniques. Traditionally, corneal preservation and storage have been classified as short term, intermediate, long term, and very long term.<sup>[2]</sup> The main limiting factor in donor corneal preservation is to maintain the viability of the corneal endothelium. Immediately after death, the production of aqueous humor stops, and the oxygen and nutrient supply to the endothelium ceases at room temperature.<sup>[2]</sup> It is important to limit this period of endothelial damage.

For a long time moist chamber whole globe preservation at 4°C was the only method available and even elective optical corneal transplantation was treated as an emergency procedure which had to be done any hour of the day or night. The recipients were admitted to the hospital for an indefinite time to be ready for fresh corneal tissue. Needless to say, it was an economic burden on the patient and the healthcare system.

Then came the McCarey Kaufman medium<sup>[2]</sup> which allowed the preservation of donor tissue and ensured good endothelial viability up to 3 days. This medium contains tissue culture medium 199 (TC 199) and dextran (5%, 40,000 molecular weight), HEPES (N hydroxyethyl piperazine-N-ethane-sulphonic acid) as buffer, penicillin, and a combination of gentamicin and polymyxin as antibiotics. This gave some time to the surgeon and to the patient who either came from long distances or suffered from comorbidities or needed anesthetic support as in pediatric cases. This also allowed inter eye bank transfer of tissue.

Further improvement in storage media came with the addition of chondroitin sulfate as in Optisol or Dexsol and tissues could be stored up to 2 weeks.<sup>[2]</sup> Cost-effective medium indigenously manufactured in India such as Cornisol have similar effectiveness. Cornisol is a sterile, 20 ml buffered corneal preservation medium supplemented with chondroitin sulfate (membrane stabilizer), recombinant human insulin (metabolism enhancer), dextran (osmotic agent), stabilized L-glutamine, ATP precursors, vitamins, trace elements, gentamicin, streptomycin, and pH indicator.<sup>[3]</sup>

The availability of such storage media allows more efficient utilization of corneal tissue and a lesser incidence of primary graft failure. Long-term and very long-term preservation techniques such as tissue culture and cryopreservation allow corneas to be preserved even up to 2 years. But the process is expensive and probably out of reach of most eye banks in the developing world. The demand–supply equation in case of corneal tissues being so skewed, the need for such long-term storage is seldom needed.

However, during the unprecedented coronavirus pandemic and the ensuing lockdown across the globe, eye banking was one of the sectors to be hit the hardest. All of a sudden, no eye donation calls were answered and donor corneal retrieval came to a standstill. All the sources of donor tissue: voluntary, hospital-based retrieval programs, and mortuaries suddenly dried up.

The demand persists for emergency therapeutic and tectonic grafts where it is important to provide integrity to the globe and remove the infected tissue as much as possible.

In all storage methods, the emphasis is on the corneal endothelial preservation. For tectonic and therapeutic purposes, the need is to provide a temporary but urgent replacement for the diseased tissue as a globe saving procedure. Here, the glycerol preserved tissue is like manna from heaven. This is a simple and inexpensive method to store tissues and provide for such eventualities.

Glycerol preserved corneal tissue can be kept at low temperature (cryopreserved) for up to 5 years.<sup>[4]</sup> However, corneal edema and loss of transparency (due to absence of viable endothelium) prevent them from use in optical penetrating keratoplasty, but their efficacy in therapeutic and lamellar keratoplasty is well proven.<sup>[4-8]</sup>

King used glycerol way back in the 1950s as a preservative medium for corneal tissues. Lamellar keratoplasties were done using these tissues in more than 50 patients and had results comparable to those obtained using fresh corneal tissues (FCT).<sup>[4]</sup>

Glycerol preserved tissue does not require refrigeration and can be transported without the need to maintain a cold chain. Acellular corneal tissue suitable for lamellar transplantation and tectonic or therapeutic keratoplasty can be stored in eye banks at a low cost and provided to corneal surgeons.

Transplantation using glycerol-preserved corneas may also be associated with a lower risk of transplant rejection.<sup>[4-8]</sup> The cellular components in FCT, including epithelium, keratocytes, and endothelium are sources of major histocompatibility complex antigens that can lead to activation of an immune transplant rejection pathway. Glycerol preserved tissue lacks antigen-presenting cells and cannot directly sensitize the recipient T-cells.<sup>[4]</sup>

As such, acellular corneal tissue, including glycerol-preserved or lyophilized corneal tissue, may significantly reduce the incidence of graft rejection.<sup>[4]</sup>

On the flip side, the tissue is thick, almost opaque causing difficulties in graft host apposition. There is almost a 100% incidence of graft failure and a high risk of glaucoma. However, secondary transplantation following a glycerol preserved tissue has lower incidences of graft rejection as compared to grafts following a failed FCT transplant.<sup>[1,4]</sup>

In conclusion, use of glycerol for long-term preservation increases the pool of donor corneas by almost 7,000-8,000 tissues annually as estimated by eye bank association of America in 2008<sup>[4]</sup> and in these tough times for eye banking, provides a source of much needed corneal tissue.

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