DSEK & DMEK: Present and Future of Endothelial Keratoplasty

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In this decade with the advent of DALK and DSEK, penetrating keratoplasty is being replaced more and more with Lamellar keratoplasty as only the diseased part of the cornea is replaced giving better results with low complication rates.

Why there is need for lamellar keratoplasty

- PKP induces astigmatism in range of 3 to 7 diopters
- Decline in endothelial cell count leading to graft failure
- Allograft rejection and endothelial decompensation were the major concerns
- Postoperative discomforts and wound healing time more
- Wound strength in lamellar graft superior
- Non penetrating surgery, it reduces the risk of intraocular complications like glaucoma, cataract, CME, RD, endophthalmitis

Endothelial keratoplasty (EK) represents the selective replacement of dysfunctional endothelium with healthy donor endothelium and is the preferred treatment for any cornea which has diseased endothelium and relatively normal overlying corneal tissue. EK has evolved over the past 10 years from very difficult, time consuming procedure of Deep Lamellar Endothelial Keratoplasty (DLEK) to its current form of DSEK and DMEK.

It includes:

- Descemet's stripping endothelial keratoplasty(DSEK)
- Descemet's stripping automated endothelial keratoplasty(DSAEK)
- Descemet's membrane endothelial keratoplasty(DMEK)

History:

- Dr. Gerrit Melles described a posterior lamellar keratoplasty (PLK) years later in 1998, where only a select portion of the cornea was transplanted.
- PLK was originally performed by creating a deep stromal pocket originating at the limbus with a 9 millimeter (mm) incision and then manually dissecting out posterior stroma, DM, and endothelium using a specialized trephine or scissors
- Dr. Melles later revised the technique by folding the graft, which enabled the incision size to decrease to 5 mm.
- Dr. Mark Terry subsequently adopted the technique in 2001, adding modifications including the use of viscoelastic to stabilize the anterior chamber, and renamed the procedure as deep lamellar endothelial keratoplasty (DLEK).
- Dr. Melles then described a procedure where the DM and endothelium were stripped from the host cornea (descemetorhexis) and replaced with a donor button consisting of posterior stroma, DM, and endothelium.

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- Dr. Francis Price was the first to publish clinical results of the technique, which he named Descemet's stripping endothelial keratoplasty (DSEK).
- Dr. Mark Gorovoy reported the use of a microkeratome for donor dissection in 2006 and coined the term Descemet stripping automated endothelial keratoplasty (DSAEK).
- In 2006, Dr. Melles developed another technique that he named Descemet's membrane endothelial keratoplasty (DMEK). DMEK involves only donor DM and endothelium being transplanted, in contrast to posterior stroma, DM, and endothelium used in DSAEK
- A modification of DMEK was described in 2009 where a rim of stroma was left at the periphery of the donor tissue.
- This was named Descemet's membrane automated endothelial keratoplasty (DMAEK)
- Another technique was described in 2010, called Descemet's membrane endothelial keratoplasty with a stromal rim (DMEK-S).
- The difference between DMEK-S and DMAEK is that DMEK-S donor tissue is prepared manually while DMAEK utilizes a microkeratome or femtosecond laser for the initial posterior lamellar dissection.
- In Descemet's stripping endothelial keratoplasty (DSEK), the patient's Descemet membrane is peeled off, using specially designed strippers and replaced with a partial thickness graft: a transplanted disc of Posterior Stroma, Descemet and Endothelium (20-30 % of the inner donor cornea)

Indications:

- Acquired Pseudophakic or Aphakic bullous keratopathy,
- Failed previous graft.
- Inherited Fuch's Endothelial Dystrophy and Iridocorneal Endothelial Syndrome.

Indian Scenario

Total no. of eyes being operated in India annually approximately 1 crore

Incidence of pseudophakic bullous keratopathy approximately 0.5%

This implies that 50,000 patients would require EK

Ideal time to perform DSEK :

- There is a significant relationship between Cataract Extraction to DSEK time and Best Spectacle Corrected Visual Acuity.
- Performing earlier (<6 M) DSEK for pseudophakic corneal edema appears to be associated with improved visual outcomes.

Surgical Technique

- This procedure, which takes approximately 45 min, is done under local or general anesthesia.
- First the endothelium and Descemet's membrane of the cornea is stripped away through a corneal incision.
- Then a circular disc is removed from the inner lining of a donor cornea.
- This thin layer is then transplanted into the recipient eye and attached to the posterior cornea of the recipient.

Donor tissue preparation:

- Corneoscleral buttons are excised from donor globes and stored by organ culture.
- Each globe is mounted on a purpose-designed holder and the anterior chamber is filled with air to create an air-endothelium interface
- With dissection spatulas, a manual stromal dissection is made at approximately 95% stromal depth using air-to-endothelium reflex to monitor dissection depth.
- Stromal dissection is extended up to limbus over 360 degrees
- After dissection is completed, a 16.0 mm corneoscleral rim is excised from each globe and the endothelium is evaluated with an inverted light microscope and stored in organ culture until time of transplantation.

Surgical technique:

- With a reverse Sinskey hook, a circular portion of Descemet membrane is scored and stripped from the posterior stroma so a descemetorrhexis is created and the central portion of Descemet membrane is removed from the eye.
- A temporal self-scaling 5.0 mm sclerocorneal incision is created with a crescent knife. After trephinating an 8.5 or 9.0 mm diameter DSEK-graft from the predissected corneoslceral rim, the tissue is folded over 60/40, like a taco, and stained with trypan blue.
- A plastic glide is carefully inserted through the temporal incision.
- Then, the graft is inserted into the anterior chamber of the recipient by sliding over the plastic glide using a 30-gauge bent needle.
- The glide is removed, and the DSEK graft is unfolded in the recipient anterior chamber with balanced salt solution and an air bubble and positioned against the posterior stroma of the host.
- The graft is unfolded over the recipient peripheral iris, taking care of touch between stromal surface of the graft and the underlying structures to avoid endothelial damage intraoperatively.
- After the DSEK graft is unfolded, the anterior chamber is completely filled with air.
- Dilating drops are used to prevent any pupillary block from air bubble.
- Once the donor disc is in final position with no interface fluid the surgeon removes the air in the anterior chamber and replaces it with BSS to pressurize the eye.
- An air bubble of approximately 8 to 9 mm is usually left in place to help further stabilize the donor disc position over the first 24 hours postoperatively.
- The air bubble pushes the graft in place until it heals in an appropriate position, giving time for the pumping action of endothelium to help the donor tissue bind to its new host
- The structure of the cornea remains intact.

DSEK Procedure Advantages Over PK:

- Less Invasive, smaller surgical incisions
- No corneal-graft sutures
- Faster visual recovery

- Less risk of sight threatening complications and less induced astigmatism
- Post-surgery stronger eye (less prone to injury)
- Less risk of immune rejection of the transplanted corneal tissue
- Shorter post-operative care

DSEK itself:

- Increases overall donor tissue availability, using the posterior layer of the donor cornea in one patient and the anterior lamellar graft in another patient.
- Faster to learn. DMEK Surgical technique may require more training, technically more challenging.

DSEK Procedure Challenges Over DMEK:

- Suboptimal visual acuity.
- Optical irregularities due to stromal layers being transplanted in DSEK.
- Slow visual rehabilitation.
- Interface problems, folds in the donor disk from maladaptation to the recipient stroma, decentration of the donor disk, and excess donor corneal thickness.

Overcome Complications

- Primary graft failure: a primary graft failure rate of 5.7%. Endothelial pump function has an important role in graft adhesion. In many cases, graft fails to adhere because the surgeon was too aggressive in handling it and damaged endothelial cells.
- Graft Rejection: Rejection can develop months or years after the transplant. Patients can be asymptomatic. When patients develops redness, blurry vision and light sensitivity the rejection is severe. To prevent rejection patients should be under a close follow-up care and kept on a prophylactic tapering steroid eye drops regimen.
- Over expected cell-loss: Assessing endothelial cell density (ECD) after DSEK, it is expected a median cell loss of 32% in the perioperative period. After that the ECD declines at a linear rate of approximately 110 cells/mm2 per year between 6 months and 10 years. Gradual reduction in endothelial cell density over time can lead to loss of clarity and require repeating the procedure.

Follow up care

- Use the slit lamp: to ensure that the graft is fully attached and to look for signs of rejection (scattered keratic precipitates, edema or conjunctival hyperemia).
- Check IOP: monitor for steroid-induced pressure spikes.
- Check the refraction after first month.
- Check the central corneal thickness: a graft that is getting thicker over time may be failing and a graft that gets thicker suddenly signals rejection.
- Watch for detachments: Anterior segment OCT can assess for graft detachments. If the graft is detached, it has to be reattached by rebubbling the anterior chamber. Since the graft has been in aqueous fluid, it often works well after reattachment.

Descemet's membrane endothelial keratoplasty (DMEK)

- Descemet's membrane endothelial keratoplasty (DMEK) is a partial thickness cornea transplant where the host Descemet membrane (DM) and endothelium are replaced by donor DM and endothelium. The Indications are same as those for DSEK.

ADVANTAGES:

- Reduction of interface haze
- Less incidence of graft dislocation
- Shorter visual recovery as total corneal thickness remains same
- Larger donor surface provides more viable endothelial cells
- Less strong graft-host apposition at interface allows easier removal of failed/rejected donor lenticule
- No costly instruments for donor lenticule preparation

DISADVANTAGES:

- Difficult and more traumatic manipulation of DM
- Higher endothelial cell loss rates with current techniques

SURGICAL STEPS:

A. Preparing recipient eye:

- Perform retrobulbar injection. DMEK can also be done under general or topical anesthesia.
- A Honan balloon is placed to add ocular pressure for 10- 15 minutes to reduce posterior pressure.
- Adjust calipers to 3.5 mm and mark clear corneal limbus at 12-o' clock position for main wound. Mark with marking pen
- Create 2-3 additional markings for paracentesis sites (1-o' clock, 6-o' clock, 11-o' clock adjust to surgeon preference)
- Using 1 mm diamond keratome, create the paracentesis sites indicated by the markings
- Fill the chamber with Healon
- Use 8.0 mm trephine to mark the central surface of the cornea
- Use the marking pen to create multiple spots along trephination mark
- Insert reverse Sinskey hook via paracentesis and score Descemet's membrane along 8.0 mm marking
- Refill the anterior chamber with Healon to pressurize the eye
- A keratome is used to make a 3.5 mm incision at the corneal limbus along the marking
- Insert reverse Sinskey hook through paracentesis or main wound to continue stripping of Descemet's membrane
- Remove host Descemet's membrane through main wound
- Utilize the phacoemulsification irrigation/aspiration device to remove all the Healon from the anterior chamber
- Observe the size of the pupil. Ensure the pupil in as small as possible

- Stroke the iris surface or use miochol or miostat in order to constrict larger pupils
- The IOP is left normal or slightly soft by using BSS injections

Preparing, injecting and positioning donor endothelium-Descemet's membrane

- Using tying forceps, remove prepared DMEK tissue from viewing chamber and use swab spears to remove excess fluid from scleral rim. Use caution to ensure graft does not displace from stroma. If graft displaces, use BSS and swab spears to encourage replacement.
- Place corneoscleral rim in empty shallow container
- Stain with VisionBlue by applying enough dye to cover the surface of the endothelium for 60 seconds
- Remove stain and gently rinse with BSS
- Ensure that the endothelium-Descemet's membrane is lying flat on the posterior stroma • If tissue is not laying flat, refloat with BSS and use spear sponges to draw the tissue toward the edges.Be careful to avoid touching the endothelium
- Mount and center tissue on vacuum block endothelial side up
- Apply suction by depressing syringe attached to vacuum block to secure tissue in place
- Obtain and slowly lower trephine punch onto vacuum block until trephine is resting on endothelium
- Gently apply pressure and tapping to cut donor Descemet's membrane and minimal stroma 360° around the edge of the graft. Do not perform complete trephination
- Optional: If S stamp is not used, obtain 1.0mm trephine and punch three holes along peripheral edge of graft in a manner that will allow distinguishing between the endothelial and epithelial views. If possible, position these marks at locations of larger tags or tears
- Use tying forceps to remove peripheral Descemet membrane and place in shallow container filled with BSS (For practice loading and unloading modified Jones tube).
- Be careful not to remove peripheral tissue too quickly as some of the graft may not have been cut. If areas are still attached, use diamond knife to hand cut or repeat trephine
- Apply BSS on top of graft to submerge endothelium
- Use tying forceps to gently lift the edge of the graft 180° from the marked hinge
- Slowly peel graft back toward hinge and lift out of BSS
- While holding tissue with forceps, fill corneoscleral button with VisionBlue
- Lower graft into stain and apply further stain on top to completely submerge tissue
- Allow staining for 3 minutes
- During this time, construct the insertion device
- Obtain 14 French gastric tubing and cut 1.5-2.0cm section with drape scissors
- Soak the inside with BSS
- Connect one end of tubing into Luer lock of 3cc syringe
- Attach the other end of tubing to the proximal tip of modified Jones tube

- Draw BSS into syringe via Jones tube and withdraw to ensure tight junctions
- Retain enough BSS to fill Jones tube
- Test the injection device by drawing peripheral segments of the graft set aside earlier. Practice loading and unloading into BSS to appreciate the amount of pressure required in doing so. Avoid aspirating air during this process
- Return attention to donor tissue submerged in VisionBlue
- Use spear sponges to remove VisionBlue. Use caution to prevent touching tissue
- Gently apply BSS onto corneoscleral rim to dilute VisionBlue and remove with spear sponges
- Repeat until blue graft is floating in almost clear solution
- Use tying forceps to carefully transfer corneoscleral rim to shallow chamber filled with BSS and float graft off of corneoscleral button and into the shallow dish
- Use forceps to remove corneoscleral rim
- Obtain assembled injecting device
- Submerge tip of Jones tube into BSS containing donor graft and situate bevel next to the end of the EDM
- Gently aspirate tissue into Jones tube keeping in mind the amount of pressure needed as tested prior
- Check orientation of EDM by observing the direction of curling edges. Edges should be curling upward
- Insert tip of modified Jones tube into main wound of recipient while maintaining correct orientation of graft. Tip of Jones tube should end on top of pupil
- Again, check orientation of graft ensuring that scrolls are facing upward. Rotate injector as necessary
- Slowly depress syringe plunger to inject graft into anterior chamber while removing injector even more slowly. Inject extra bursts of BSS to help orient the graft perpendicular to main wound and prevent efflux.
- Be careful that the graft does not eject from wound. Prevent this by allowing fluid to drain from main wound or paracentesis or use a cannula to close the main wound while withdrawing injector.
- Use 10-0 nylon to place one interrupted suture closing the main wound
- Again, check orientation of graft ensuring that the scrolls are facing upward while the graft is floating in the anterior chamber
- To manipulate the graft in the anterior chamber, utilize bursts of BSS if necessary to flip graft into correct orientation, center the EDM, or open a tightly scrolled Descemet roll
- Use the cannula to perform short swift taps to the external cornea to help center the graft and open the scroll
- Manipulating the graft is facilitated by obtaining a shallow anterior chamber. This can be done by using the index finger on the non-dominant hand and applying pressure about 5mm from the limbus
- After centering and fully unrolling the graft, introduce tip of cannula attached to 20% SF6 into the anterior chamber, posterior to the graft taking care never to touch the endothelium
- Once the tip is above the pupil, slowly inject gas to allow apposition of the graft to the posterior stroma allowing the edges to unfold and the center to touch stroma

- Fill the anterior chamber with gas
- Observe the entire margin of the graft evaluating for any folds and detachments
- Manipulation of the bubble, or bubble bumping, can help reduce folds and detachments
- Once all the edges are checked, perform sweep of entire surface of cornea with a barraquer spatula

Postoperative Management

- One sample medication regimen: Prednisolone acetate 1% should be used every two hours while awake for the first week, 4 times daily over the next 3 months, then slowly tapered and stopped at year
- Antibiotic drops should be used for 1 week after surgery.

Complications

- Graft detachment
- Damage to tissue during preparation or surgery
- Upside down grafts
- Epithelial defect or erosion (3.0%)
- Raised intraocular pressure (IOP) in as high as 12% of patients, with ~ 2.8% developing secondary glaucoma
- Descemet graft folds (1.9%)
- <1% risk of anterior synechiae, hypotony, pupillary block, subepithelial haze, and interface pigment deposits.
- Cystoid macular edema (CME): one study reported a high rate of CME of 12.5% in eyes with DMEK alone and 13.3% of eyes with DMEK and cataract extraction.

Surgical Outcomes:

- Visual acuity at 3 months: 63% with vision ≥ 20/25 and 26% ≥ 20/20.
- Visual acuity at 6 months: 79–94% with BCVA ≥ 20/40 and 22–47% ≥ 20/20.
- Multiple studies have reported that DMEK causes a mild hyperopic shift of < +0.50 D after 6–12 months follow-up. DSEK has been reported to have a hyperopic shift of around +1.00, due to the shape of the donor tissue.
- Postoperative refraction stabilizes at 3 months with no significant spherical equivalent change between 3 and 6 months postoperatively.
- Endothelial cell loss estimates following DMEK vary widely, from 32-40% at 3 months to 36-40% at 6 months.

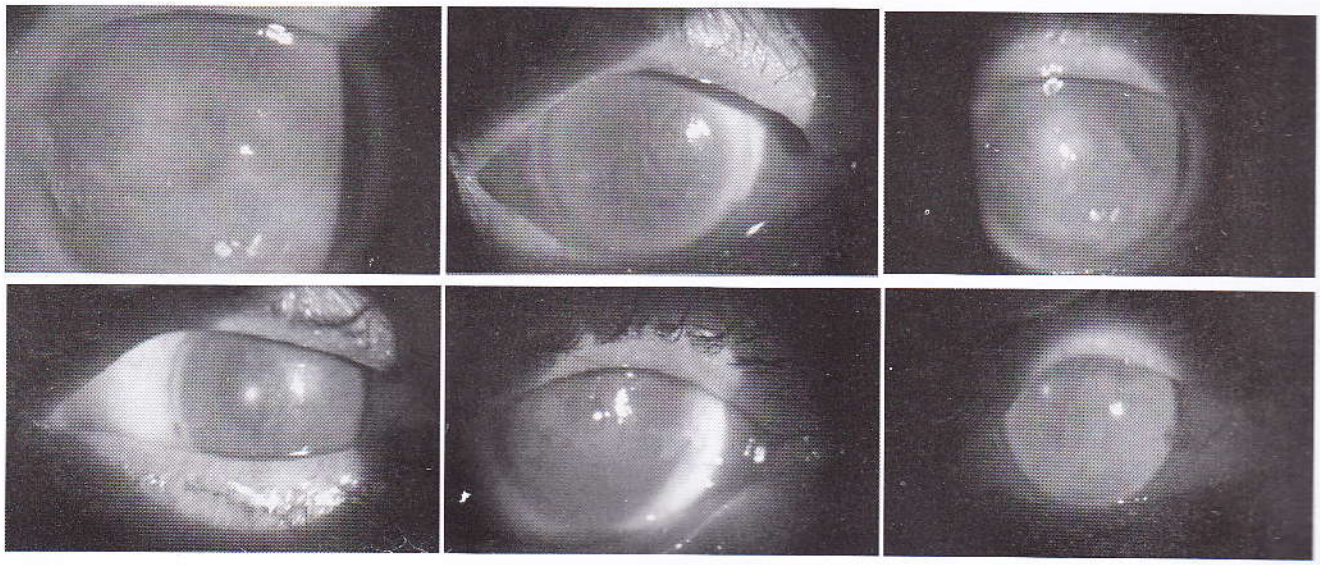
Our Experience with DSEK/DMEK

We have been doing DSEK regularly since 2008 in the Dept. of Ophthalmology, IMS, BHU and DMEK since 2016 at Chandra Eye Care, Lanka, Varanasi. The results of the Surgery are extremely gratifying with more than 90% success rate and more than 50% patients achieving BCVA of more than 20/30.

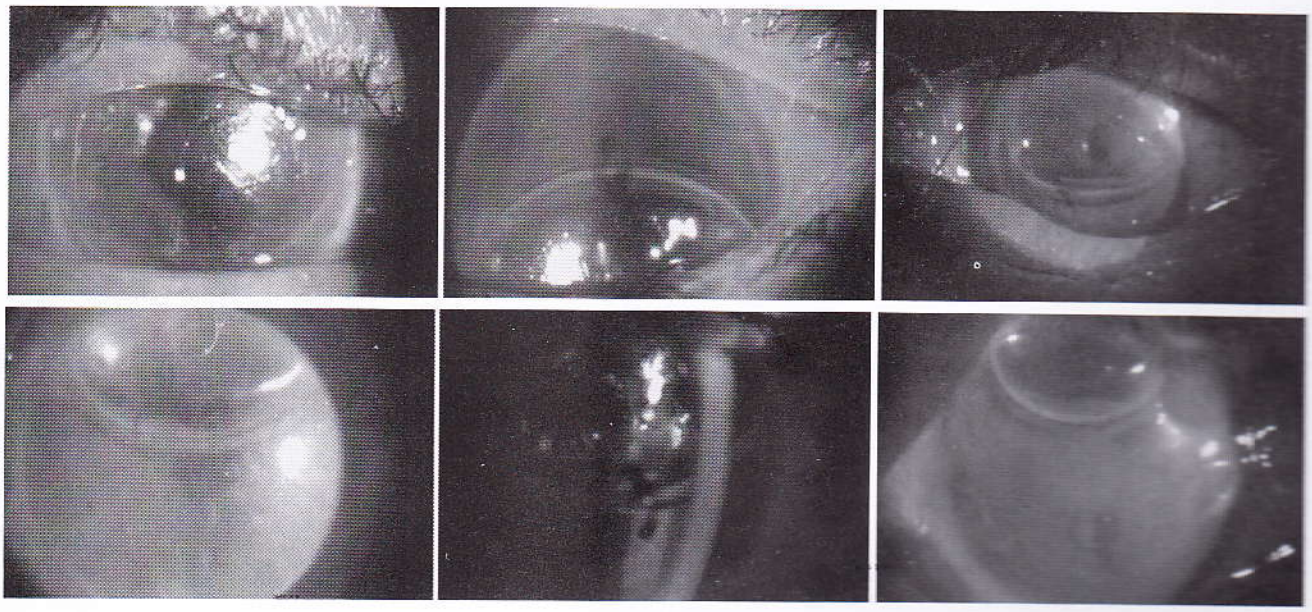
With DMEK the results are even better with 80% patients achieving BCVA of more than 20/30. Presently we are doing 6-8 cases of DMEK every month. Now we have almost completely shifted to DMEK from DSEK. However there are few indications where we still do DSEK. These are Aphakia, Vitreous in Anterior Chamber, Vitrectomised Eye, Large Peripheral Iridectomy in an operated eye.

The Donor criteria with DMEK is very stringent. The Donor age typically should be between 50 to 70 with endothelial cell count of more than 2700 per mm2. Now with the help of Sight Life and other Community Eye Bank it is relatively easier to get such tissues.

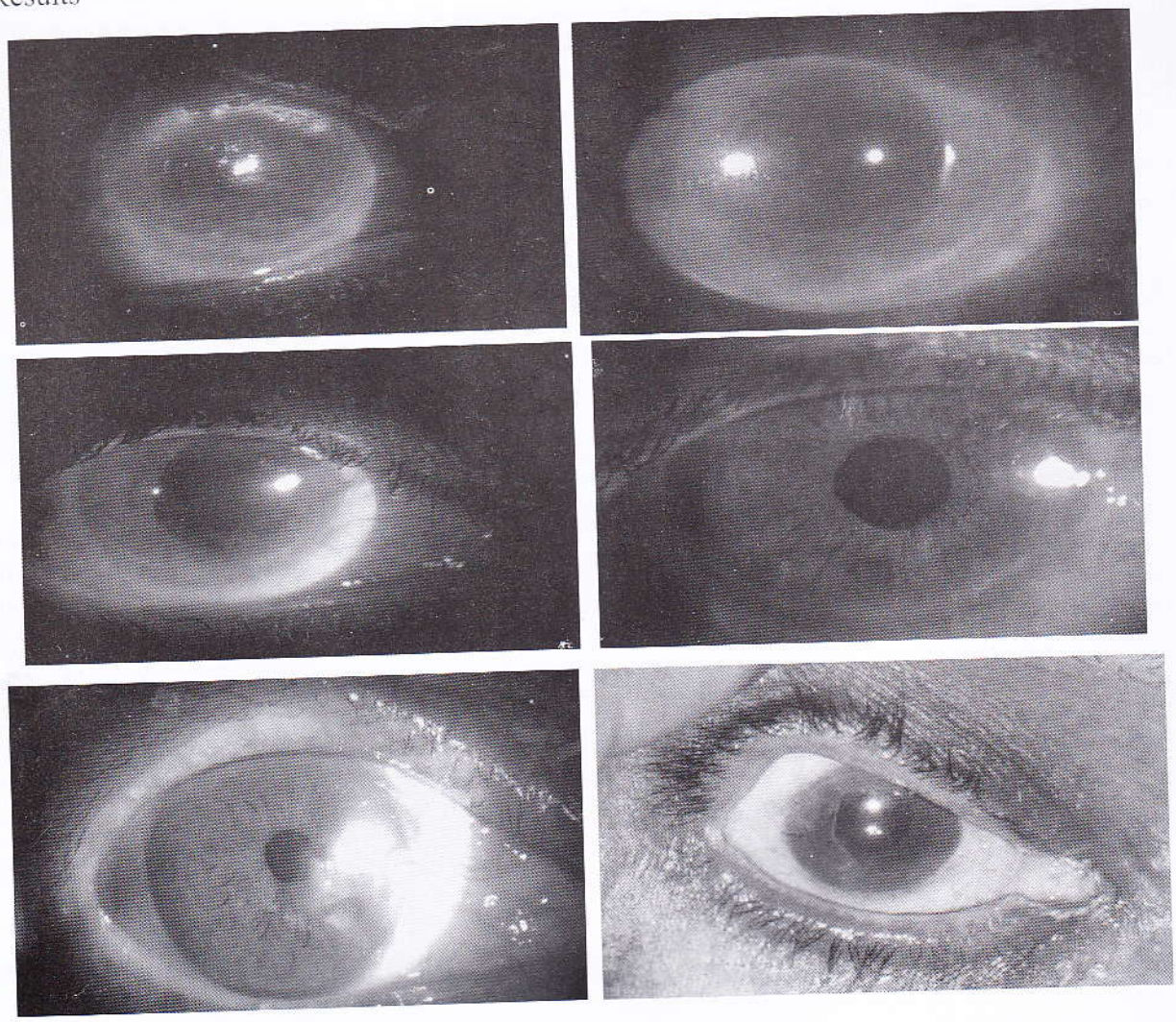
Pre-operative Phtographs



Stamped Corneas as seen post-operativel



Final Results



Conclusion:

DMEK is now a preferred technique in corneal endothelial dysfunction. The advantages of DMEK outweighs penetrating keratoplasty by early visual rehabitilation, low astigmatism, better ocular surface, absence of suture related complications, low incidence of graft rejections and minimal risk of wound rupture. The visual recovery time has now come down to 1 month in DMEK which was almost one year in Penetrating Keratoplasty.